

## **Physiological chemistry (Volume 2).**

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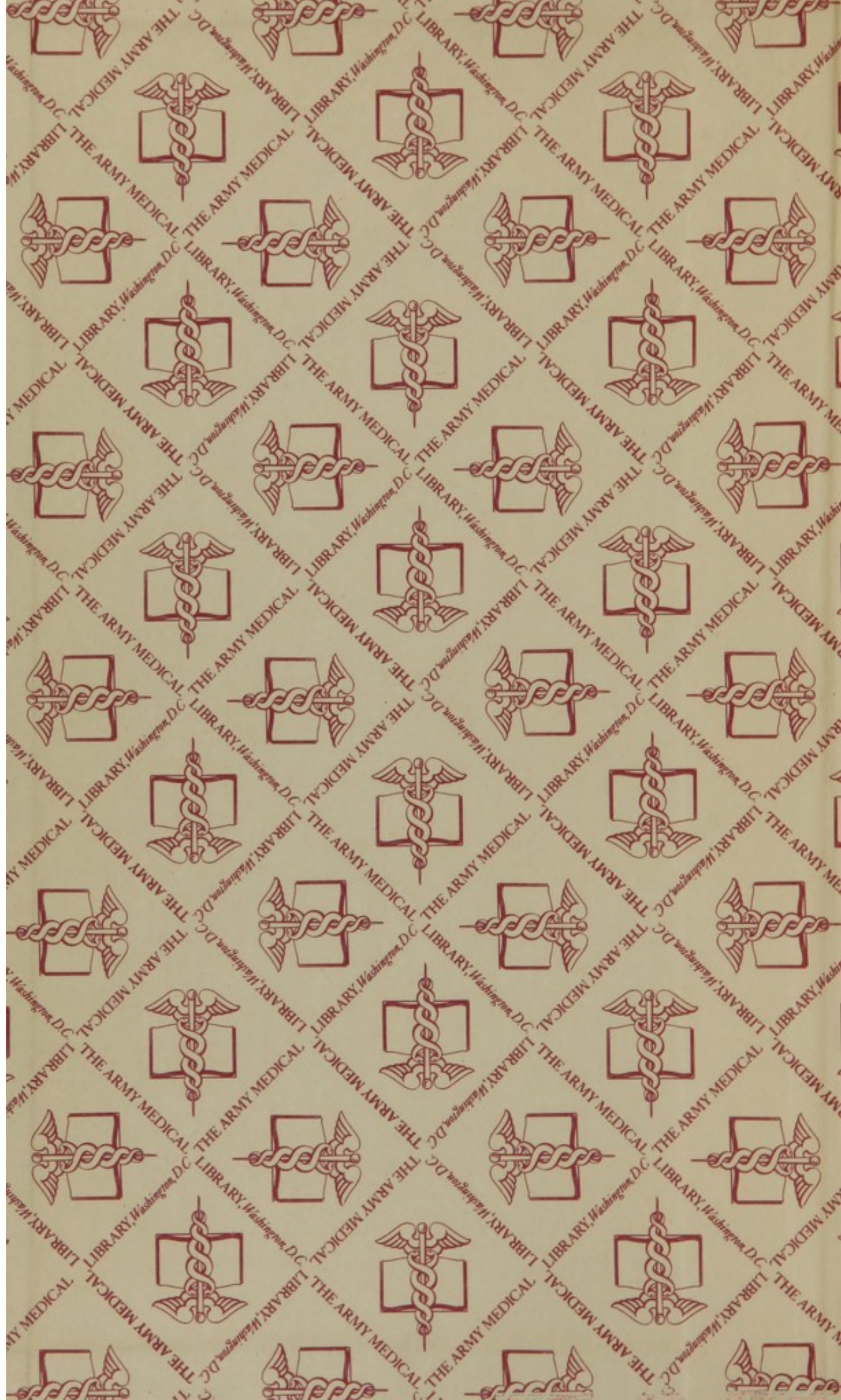
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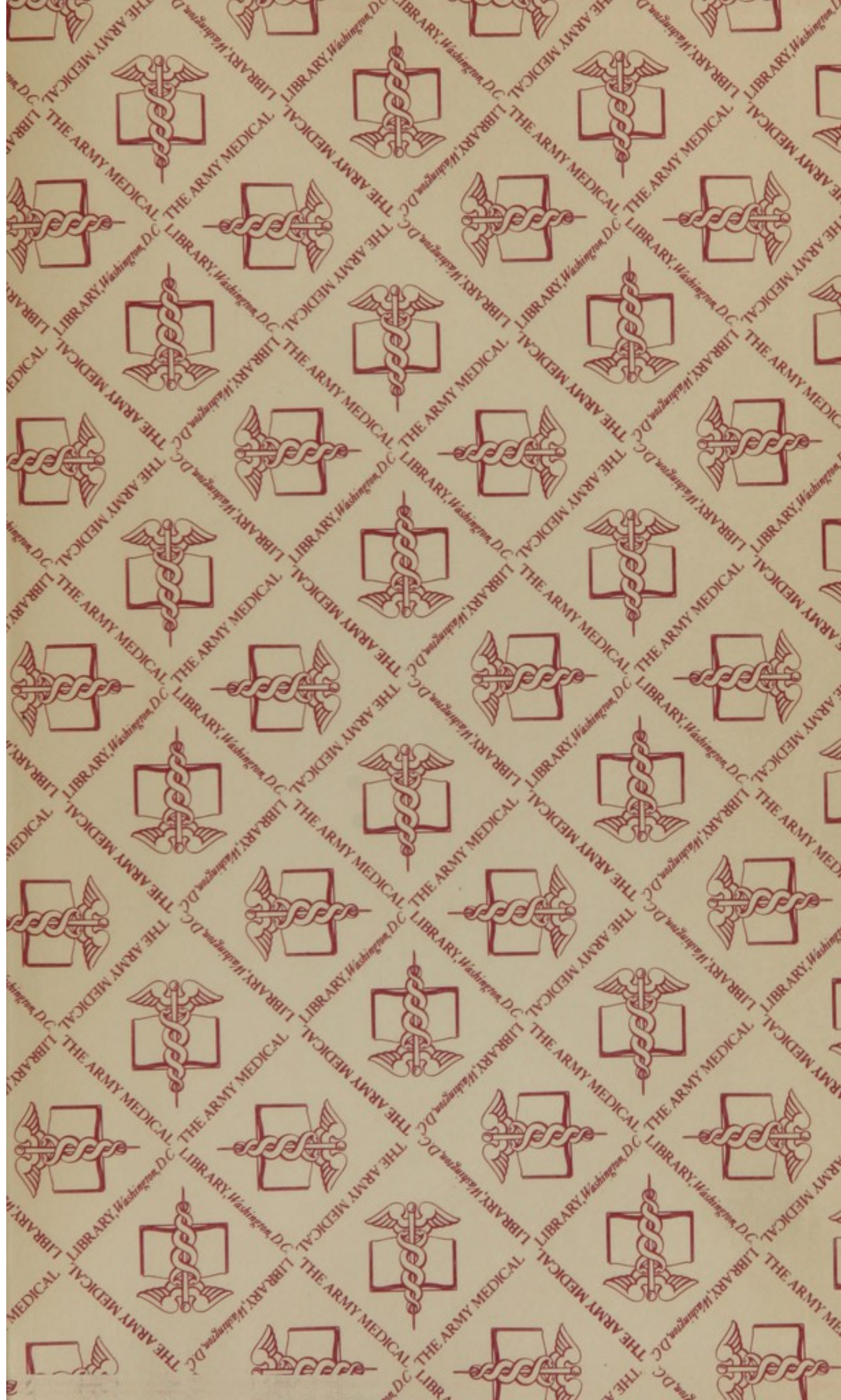
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PHYSIOLOGICAL CHEMISTRY.



PHYSIOLOGICAL

CHEMISTRY

PROFESSOR OF PHYSIOLOGY

GEORGE E. DAY, M.D., F.R.S.

PHYSIOLOGICAL CHEMISTRY

WITH ILLUSTRATIONS

AN APPENDIX ON PLATES

VOL. II



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1882

# PHYSIOLOGICAL CHEMISTRY.

BY  
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TRANSLATED FROM THE SECOND EDITION

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WITH ILLUSTRATIONS,  
SELECTED FROM FUNKE'S ATLAS OF PHYSIOLOGICAL CHEMISTRY,  
AND  
AN APPENDIX OF PLATES.

COMPLETE IN TWO VOLUMES.

VOL. II.



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# PHYSIOLOGICAL CHEMISTRY.

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## CHYLE.

THE chyle presents various physical properties which differ with the condition of the animal (as for instance, whether it is fasting or has been lately fed), the part of the chyloferous system from whence it has been procured, and the nature of the food that has been taken. It commonly forms a milky, opalescent, yellowish-white or pale reddish fluid with a faint animal odor, a somewhat saline and mawkish taste, and a very faint alkaline reaction. Like the blood, it coagulates in nine or ten minutes after its removal from the chyloferous system; the coagulum, which contracts in from two to four hours, is much smaller than that of the blood, and is very soft, friable, and sometimes merely gelatinous. When exposed to the air, it generally assumes a somewhat light-red color, if it had previously been yellow. This is especially observable in the chyle of horses. The serum of the chyle, although clearer than fresh chyle, still in general retains some degree of turbidity; when merely diluted with water, it seldom becomes more turbid, but when boiled, it becomes of a milky-white color, and commonly deposits a few minute clots. Acetic acid often induces turbidity (Nasse);<sup>1</sup> on evaporating the fluid filtered from the albuminous coagulum, the surface appears covered with a colorless transparent membrane (albuminate of soda). The chyle-serum does not coagulate when treated with ether, but is rendered clearer. A dirty yellowish-white, cream-like stratum is formed between the ether and the chyle-serum.

According to Tiedemann and Gmelin, as well as according to Nasse, the chyle is almost colorless and transparent in birds, amphibia, and fishes; while, according to J. Müller, Gurlt, Simon, Nasse, and my own observations, it is of a deeper red color in horses than in any other animals which have hitherto been examined with reference to this subject. Nasse found the chyle of cats of a perfectly milky-whiteness. During digestion the chyle is in general extremely turbid; at other seasons it forms a faintly opalescent fluid, which only exhibits a reddish color in the thoracic duct.

The chyle that has been collected during digestion is very rich in morphological elements, since it exhibits, as a highly plastic fluid, the

<sup>1</sup> Handwörterbuch der Physiologie. Bd. 1, S. 235.



most varied stages of cell-formation. Hence a great variety of molecules have been distinguished in it, and the products of different stages of development have received the name of chyle-corpuscles (J. Müller,<sup>1</sup> Schultz,<sup>2</sup> R. Wagner,<sup>3</sup> Henle,<sup>4</sup> Nasse,<sup>5</sup> Arnold,<sup>6</sup> Kölliker,<sup>7</sup> Herbst,<sup>8</sup> H. Müller).<sup>9</sup>

As a more detailed description of these molecules falls rather within the province of histology than of chemistry, we refer our readers to the works of the above-mentioned observers, limiting ourselves here to a notice of the most important points in reference to the microscopical investigation of the molecules of the chyle. In the first place, chyle which has been taken from the minutest lacteals during digestion, exhibits *extremely minute granules*, which cover the field of view like a thin veil. These granules, which have been especially examined by H. Müller, and recognized to be fat-granules surrounded by a protein-like capsule, remain unaltered on the addition of water, but flow together and form the ordinary fat-globules when the chyle is treated with acetic acid or dilute caustic potash. A similar result is observed when the chyle is suffered to dry and the residue is again dissolved in water. Most observers agree in the opinion that *no true fat-globules* are generally contained in the fresh chyle of animals, although they have frequently been found in human chyle; this may, however, be owing to the circumstance that the chyle which is usually taken from the body some time after death, may already be partially decomposed, and may therefore be acted upon by putrefaction, somewhat in the same manner as by the potash.

In addition to these fine molecular granules, the chyle, more especially at the origins of the vessels, contains also *coarser granules* which are grouped into masses and appear to be held together by means of a hyaline substance (H. Müller), and distinct, sharply-defined *nuclei* with nucleoli, which are in some cases covered with individual granules (Kölliker).

It has generally been assumed that there are special *chyle-corpuscles* which are the distinguishing constituents of the chyle; but these bodies do not actually differ from the lymph-corpuscles or the colorless blood-corpuscles, being distinguished from the latter only in this, that they represent different stages of the development of these cells. They present considerable variety of size and form, exhibiting in some cases a distinct, and in others an indistinct nucleus, and sometimes even a cleft nucleus which frequently remains indistinct until it is treated with water, and hence these corpuscles appear in the chyle itself like mere faintly translucent vesicles. It is worthy of notice that many of these bodies have frequently a magnitude of 1-200th of a line in the lacteals of moderate calibre, whilst the size of those in the chyle of the thoracic duct seldom exceeds 1-250th or 1-350th of a line.

<sup>1</sup> Handb. d. Phys. Bd. 1, S. 235 [or English Translation, 2d Ed., vol. i. p. 281].

<sup>2</sup> System der Circulation. Stuttg. 1836, S. 45.

<sup>3</sup> Beitr. z. vergl. Physiol. Bd. 2, S. 56.

<sup>4</sup> Allg. Anat. S. 421-471.

<sup>5</sup> Handwörterb. der Physiol. Bd. 1, S. 226.

<sup>6</sup> Anatomie, S. 260.

<sup>7</sup> Entwicklungsgeschichte der Cephalopoden. Zürich, 1844, S. 50, and Zeitschr. f. rat. Med. Bd. 4, S. 142-147.

<sup>8</sup> Lymphgefässyst. u. seine Verrichtungen. Gotting. 1844, S. 603.

<sup>9</sup> Zeitschr. f. rat. Med. Bd. 3, S. 239.



We have already noticed their chemical relations in speaking of the colorless blood-corpuscles, and we purpose again reverting to the subject under the head of pus-corpuscles.

If the search be conducted with care, *colored blood-corpuscles* may always be found in the chyle of the thoracic duct, although they are not present in large quantities.

In order to obtain the largest possible quantity of fresh chyle, the animal should be killed from two to five hours after feeding, either by strangulation or pithing, the thoracic cavity opened, and the thoracic duct tied immediately before its entrance into the subclavian vein. After a short time the duct will be filled with chyle, and will appear distended or as if it were injected. It must then be carefully dissected into the abdominal cavity as far as the receptaculum, and the contents discharged with care (in order to avoid all admixture of blood), either by means of a fine trochar or by simple incision. A greater quantity of chyle may be obtained by laying open the thoracic portion of the duct and suffering the chyle to flow from the incision; but the precipitous flow of chyle in the freshly-killed animal may possibly give rise to a more abundant flow of lymph and aqueous fluid, so that the chyle may not possess a perfectly normal character.

In reference to the *chemical constituents* of the chyle, we may observe that they entirely correspond with those of the blood; and hitherto only very slight, or even wholly unimportant differences have been observed to exist between the plasma of the blood and the chyle. This admits of a ready explanation, for an accurate chemical analysis is only practicable in the case of the chyle of the thoracic duct, which not only resembles the blood far more closely than does the chyle of the smaller vessels, but which has even taken up blood that is already colored, together with blood-corpuscles, from the lymphatics of the spleen.

Next to the undissolved molecules of the chyle, whose chemical constitution lies even further beyond the range of our inquiries than that of perfect blood-cells, the *fibrin* has the principal claim on our attention. It differs from that of the blood in generally exhibiting a less considerable contractility, and the somewhat gelatinous consistence to which pathological anatomists have applied the term "fibrin infiltrated with serum." Like the fibrin in many morbid exudations, it is occasionally redissolved some hours after its coagulation, especially when the surrounding temperature exceeds the usual mean. It does not often exhibit the fibrous texture of solidly coagulated blood-fibrin under the microscope, but dissolves very readily in diluted alkalies and organic acids, and, after being digested for a short time, in a solution of nitre or even of hydrochlorate of ammonia. It may be completely precipitated from the acetic-acid solution by hydrochlorate of ammonia, and again almost perfectly separated from this solution by acetic acid. I found only 1.77% of strongly alkaline ash in chyle-fibrin which had been duly deprived of its fat, well washed, and dried. Like the fibrin of the blood, the chyle-fibrin always contains some of the above-named morphological constituents of the chyle, and is therefore even richer in fat than the blood-fibrin, but it very seldom happens that the fibrin of the chyle encloses in its coagulation all the elements which were suspended in the



intercellular fluid; and on this account the serum of the chyle is in general clearer than the original chyle, although it always retains some degree of turbidity, or at all events of opalescence.

In the serum of the chyle *albumen* is also the preponderating solid constituent. This albumen has been regarded as imperfectly developed (Prout), owing to the circumstance that it coagulates on being heated, and is at the same time precipitated to a certain degree by acetic acid. Independently of the illogical character of the argument which can assume the existence of a chemically imperfect substance,—and we might just as rationally assume that malaria is a more perfect carburetted hydrogen than olefiant gas, or the reverse,—every one who has read the observations in page 296 of vol. i. must at once conclude that the only difference presented by the albumen arises from its being combined with more alkali in the chyle than in normal blood; and this, moreover, is confirmed by direct investigation, at least in the chyle of the thoracic duct of horses. The chyle-serum is not rendered turbid by strong dilution with water; when boiled, it does not so much form coherent flakes as a milk-white, opaque fluid; and it becomes covered on evaporation by a colorless membrane. The aqueous extract of the residue of the chyle exhibits a strongly alkaline reaction, and the solution may be rendered turbid by neutralizing it with acetic acid. After this turbidity has been removed by a more copious addition of acetic acid, ferrocyanide of potassium gives rise to a considerable precipitate. The aqueous extract of the residue of the chyle presents great turbidity on being boiled with hydrochlorate of ammonia, as well as on the addition of nitric acid. The albumen, after being thoroughly washed with water, alcohol, and ether, was found to yield on incineration 2.068% of mineral constituents, including a considerable amount of alkaline salts, which effervesced on the addition of acids. The supposed presence of casein in the chyle, instead of being proved, seems therefore to be rendered very improbable.

It would be an important point if we could show that the *peptones* of the albuminous substances in the food are present in the chyle, but from our ignorance of the necessary reagents, this question cannot at present be decided by direct investigation. As the chyle contains from 2.5 to 3.0% of non-coagulable substances which are only soluble in water, and consists of a large proportion of albuminate of soda and mineral salts, it is at all events improbable, to say the least, that peptones should be present in the chyle discharged from the thoracic duct of the horse; and hence the question, whether the peptones are elaborated in the mesenteric glands into albumen and fibrin, still continues wholly undecided.

Our microscopical and microscopico-chemical investigations prove that *fat* is contained in large quantity in the chyle, and even show with some degree of probability that the chyle contains a considerable quantity of non-saponified fat in the smaller lacteals, whilst in the thoracic duct the proportion of saponified fat preponderates. I was unable by any method to obtain a crystallizable fat from the saponified or non-saponified fats of the chyle of the horse; and other observers have stated that they could only discover a greasy and tallow-like fat, although they may not always have attempted to detect the fat-crystals by the aid of the microscope.



Some authors profess to have found *sugar* in the chyle; others could not discover this substance. Trommer<sup>1</sup> believes he has detected its presence in the chyle of horses by means of his own sugar-test, but it is well known that many causes concur in destroying the practical value of this test. Thus, for instance, the chyle contains albuminate of soda, which passes into the alcoholic extract, and exerts a disturbing influence on the reaction; this substance may yield the most beautiful blue solution with sulphate of copper and potash, and at all events, after prolonged boiling, may give a yellowish red precipitate without the chyle containing a trace of sugar. The substance which is formed is the albuminate of the oxide of copper, investigated by Lassaigne, which on prolonged boiling with potash likewise precipitates suboxide of copper. I have never been able to detect any sugar in the chyle of horses fed on bran, but the presence of this substance could be determined with certainty in the case of horses which I had fed for a considerable period on starch or highly amylaceous food, by applying the method indicated in p. 251, vol. i., and with due attention to all the precautions specified, and also by the fermentation-test. It would appear, therefore, as if sugar only passed into the chyle in appreciable quantities where there was an excess of it in the intestine.

*Biliary constituents* cannot be detected in the chyle by any method hitherto attempted. (See pp. 467 and 483 of the first volume.)

I have determined with certainty the presence of *alkaline lactates* in the chyle, at least after feeding animals with amylaceous food. (See p. 95 of the first volume.)

The chyle is very rich in *alkalies*, which are combined partly with albumen, partly with lactic acid, and partly with fatty acids; hence the aqueous solution of the ash exerts a strongly alkaline reaction, and effervesces with acids.

*Alkaline sulphates* do not exist preformed in the chyle, but occur in its ash. Thus, for instance, if the aqueous extract of the solid residue of the chyle, after being treated with alcohol and ether, be carefully neutralized with acetic acid, evaporated, and again dissolved in water, filtered, and finally treated with a salt of baryta after being previously acidified by nitric acid, there will not be the faintest trace of turbidity nor any subsequent deposition of the slightest sediment.

We find no trace of *sulphocyanides*, which might possibly have passed into the chyle with the saliva conveyed to the intestine; at all events the salts of peroxide of iron do not impart any perceptible redness to the alcoholic extract of the chyle.

The *alkaline phosphates* occur only in very small quantities even in the ash of the chyle produced from vegetable food.

The *chlorides of sodium and potassium* are present in the chyle in large quantities. Salts of ammonia, and especially the hydrochlorate, have also been supposed to occur in the chyle; we would here simply refer to p. 494, vol. i., where the reasons are given which have led to the adoption of this erroneous view. The efflorescent appearance of the chlorides of sodium and potassium, as seen under the microscope on examining the evaporated spirituous extract, has led to their being

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 39, S. 360.



mistaken for hydrochlorate of ammonia; but if such appearances were due to the latter substance, there would be no crystals of phosphate of soda, but simply the very easily recognizable crystals of phosphate of ammonia and soda. Moreover, bichloride of platinum precipitates the potassium-compound, but not the ammonium-compound, from the spirituous solution. We have, further, explained in p. 148, that the occurrence of the octohedral and tetrahedral forms in which the chloride of sodium is so frequently observed under the microscope in evaporated animal fluids, and frequently also in the chyle, is no evidence of the presence of urea.

It is very difficult to determine whether or not the serum of the chyle is free from *iron*, like that of the blood; Reuss and Emmert,<sup>1</sup> Vauquelin,<sup>2</sup> Rees,<sup>3</sup> and Simon, believe that they have ascertained the presence of iron in the serum of the chyle, and they regard it as more loosely combined than in the blood, that is to say, they suppose that it is united with phosphoric acid or other substances which do not impede the ordinary reactions of the salts of iron. We do not, however, consider ourselves justified in concluding from our own observations, or from those of the above-named chemists, that the serum of the chyle contains iron, because, as it can never be obtained perfectly free from colored, or at all events, colorless cells, the iron that is found may very probably belong to these cells. No one, indeed, would maintain that there is an entire absence of iron in the serum of the chyle, any more than in that of the blood; for the iron must necessarily pass from the plasma of the chyle into the cells, returning in the blood to the intercellular fluid from the cells which are undergoing the process of destruction; but the iron does not appear to constitute an integral constituent of either fluid.

Little remains to be noticed in reference to the *method of analysis* to be pursued in the quantitative investigation of the chyle, after the remarks we have already made in treating of the analysis of the blood and of the animal juices generally. It will be obvious from the properties of its constituents which have been already noticed, that the quantitative determination of the cells, of the fibrin, and of the albumen in the chyle, must be very uncertain, for we do not possess any means by which we can retain the chyle-corpuscles and other molecules on the filter, or which will enable us to compute their weight. These bodies are distributed, together with the other molecules suspended in the chyle, through the fibrin and albumen: and as the fibrin of the chyle in general coagulates very imperfectly, the lymph-corpuscles are less completely enclosed than in the fibrin of the blood, and the molecules which remain suspended in the chyle are therefore enclosed by the coagulated albumen. The sinking capacity of the chyle-corpuscles is so inconsiderable, that the coagulated albumen often reddens when exposed to the air, in consequence of the inclosed pigment-containing cells, in the same manner as the fibrin of the chyle. We can, therefore, only arrive at a moderately approximate determination when, as in the case of the blood, we abstract from the solid residue of the chyle-clot the fibrin determined by whipping. Hence, that which is supposed in ordinary analyses to be

<sup>1</sup> Reil's Arch. Bd. 8, S. 147-218.

<sup>2</sup> Ann. du Muséum nation. d'hist. nat. T. 18, p. 240.

<sup>3</sup> London Medical Gazette, Jan. 1841.



fibrin, is very often scarcely half composed of this substance, in reality consisting, in addition to these molecules, of a very large quantity of fat which has been inadvertently suffered to remain, as is frequently the case in analyses of the blood. The precautionary rules which we have already laid down for the determination of albumen, apply to the investigation of chyle, more, perhaps, than to that of any other animal fluid. All the directions indicated for the determination of the fat in the blood, refer with equal force to the chyle. The ordinary rules hold good for the determination of the individual extracts and the various mineral constituents. The older analyses, however, to which we might look for assistance, are scarcely able to yield us any purely physiological results, in consequence of their having been prosecuted without the benefit of those aids to analysis which we possess in the present day. The following observations give the results of the *quantitative investigations* of other observers, in addition to my own.

The *quantity of water* in the chyle of horses fluctuates, according to the investigations of different inquirers, between 91 and 96%; this chyle contains, therefore, as a minimum 4, and as a maximum 9% of *solid constituents*. Nasse found 90.57% of water in the chyle of a cat.

The number of *cells, cell-nuclei*, and other *molecules* contained in the chyle must vary with the nature of the food that has been taken, but these relations, as we have already observed, do not at present admit of being determined. Except during the period of digestion, the chyle contains few cells and in almost all respects resembles the lymph.

The quantity of *fibrin* in human chyle has not been determined; but attempts have frequently been made to ascertain the amount of this substance in different animals, and especially in horses, although this has seldom been accomplished without an admixture of corpuscles and fat. In the chyle of the horse Tiedemann and Gmelin<sup>1</sup> found from 0.19 to 0.7%, and Simon,<sup>2</sup> from 0.09 to 0.44%; I found a coagulum which was very rich in cells amount to 0.495%, while the fibrin, as free from cells as possible, determined from the same chyle, amounted to 0.301%. Tiedemann and Gmelin found from 0.17 to 0.27% in the dog, and from 0.24 to 0.82% in the sheep; Rees found 0.37% in the ass, and Nasse, 0.13% in the cat.

Tiedemann and Gmelin found from 1.93 to 4.34% of *albumen* in the chyle of horses, and I found 3.464% as the mean of several analyses in the chyle of horses fed upon bran, and 3.064% in that of horses fed on starch.

Tiedemann and Gmelin found 1.64% of *fat* in the chyle of horses, Simon from 1.001 to 3.480%, while I found from 0.563 to 1.891%; Rees found 3.601% in the chyle of the ass, and Nasse 3.27% in that of the cat.

Simon found from 8.874 to 9.892% of *extractive matters free from salts* in the solid residue of the chyle of horses, while I found 7.273% in that of horses, when fed upon bran, and 8.345% when fed upon starch.

The chyle of horses contained, according to Simon, from 6.7 to 7.3% of *soluble salts* (determined from the ash), while according to my own researches, it yielded 7.45% when the animals were fed upon bran, and

<sup>1</sup> Verdauung nach Versuchen. Bd. 2, S. 75.

<sup>2</sup> Med. Chem. Bd. 2, S. 241-244 [or English translation, vol. i. pp. 354-359].



6.784% when they were fed upon starch. The chyle of the cat contained, according to Nasse, 9.4% of soluble salts, of which 7.1 was chloride of sodium.

The chyle contains about 2% of *insoluble salts*. The mineral constituents of the solid residue of the chyle amount, therefore, on an average to 12%, of which from 9 to 10% are soluble salts.

Numerous observations have been made on the influence which the *nature of the food* exercises on the constitution of the chyle, but these results, or rather the conclusions deducible from them differ considerably. This much, however, seems certain, that the chyle is somewhat poorer in solid constituents after prolonged fasting or where the food has been scanty, and that it then contains a much smaller quantity of fat, so as to appear only slightly turbid, but not milky. It has been generally maintained, that the chyle becomes richer in fat after animal food, but this is only the case where the nutriment has consisted of flesh, bones, milk, or other fatty kinds of animal substances; for Tiedemann and Gmelin found that the chyle of dogs was rendered only faintly turbid, when these animals were fed on albumen, fibrin, casein, and gelatin. All observers agree in the opinion that the chyle becomes milky and very rich in fat when the food has been of a fatty kind. According to my observations, non-nitrogenous substances do not produce any decided augmentation of fat in the chyle. No definite conclusions can be drawn from the inquiries and opinions of observers in reference to the influence exerted by the nature of the food on the quantity of albumen and fibrin in the chyle, for these substances owe their origin partly to transudation from the blood in the mesenteric glands, and partly to the lymphatics of the spleen, while moreover the chyle of the thoracic duct is the only kind which has been accurately examined with a view of ascertaining its quantitative relations.

Nor can we attach any great weight to Millon's<sup>1</sup> elementary analyses of the chyle and blood of dogs which had been fed on different kinds of food; at all events we cannot concur with that observer, when he believes himself justified in concluding that the special purpose of the lacteals is not the absorption of fats only, but also of other nutrient substances in an equal degree.

The chyle undergoes many alterations during its passage from the lacteals of the intestines through the mesenteric glands to the thoracic duct. We have already spoken of the diversity existing in the morphological elements in the different parts of the chyliferous system, in reference to the fibrin which, according to Tiedemann and Gmelin, occurs in the smaller lacteals either in very small quantities, or is entirely absent; we only know that its quantity appears gradually to augment during the passage of the chyle through the glands. A similar observation applies to the albumen, which, according to the same observers, is conveyed in large quantities to the chyle in the glands, so that this fluid appears to increase in density in proportion as it approximates to the receptaculum chyli. Fat is the only substance which seems to be gradually diminished during the passage of the chyle to the blood, and this may be owing to its participation in the formation of cells, that is

<sup>1</sup> Compt. rend. T. 29, p. 817-819.



to say, of the chyle-corpuscles, which are very rich in fat, and partly to its transition into a state of saponification, as we may judge from the quantity of the alkaline salts of the fatty acids present in the chyle of the thoracic duct.

No direct observations have as yet been made concerning the *pathological relations* of the chyle.

We cannot regard the question of the *quantity of chyle* which enters the blood in a given time, as satisfactorily settled. Cruikshank<sup>1</sup> assumes the quantity of chyle which is hourly mixed with the blood to be 4 pounds. His calculation rests upon an observation of the rapidity of the motion of the chyle in the mesentery of a dog, which he found to be four inches in a second, and hence he assumed a similar rate of velocity in the thoracic duct. But independently of the untenability of the latter position, the rapidity of the motion of the chyle in the lymphatics of the mesentery depends upon many different relations, which, from their variable character, can scarcely be adequately appreciated in observations made during vivisection. Magendie, who endeavored to determine the quantity of the chyle by opening the cervical portion of the thoracic duct of well-fed dogs, and observing the quantity which flowed in a given time, found that half an ounce escaped in five minutes, which was at the rate of six ounces in the hour. Bidder, who has made similar experiments on dogs that had been previously strangled, arrived at nearly similar results; but unfortunately, as this observer remarks, such experiments scarcely warrant us in drawing any definite conclusion. If, for instance, as Vierordt<sup>2</sup> observes, the ascent of the chyle be arrested by cutting the thoracic duct, which is one of the most efficient causes of its motion, it must not be forgotten, that this operation may be followed by too abundant a discharge; for here, as in the analogous but more strongly-marked case of the blood, there will necessarily be an afflux of juices from all sides, which must increase in an extraordinary degree the *vis a tergo*, however small it may be, by which the chyle is propelled. The lymph will at all events flow more abundantly, rendering the result of the inquiry so uncertain as to prevent any proper solution of the physiological question concerning the quantity of the newly-formed and elaborated nutrient matter which passes through the chyle-vessels.

Vierordt proposes the following method for computing the quantity of the chyle which passes into the blood of an adult in 24 hours:—As 100 grammes of dry nitrogenous matters are daily consumed by an adult man, and as the chyle contains about 4% of such matters, the quantity of chyle daily formed will amount to  $2\frac{1}{2}$  kilogrammes, or about 5 pounds.<sup>3</sup> Vierordt himself observes that this calculation does not admit of a comparison with those of the earlier inquirers, because the lymph mixed

<sup>1</sup> [Lehmann refers in a foot-note to p. 78 of Ludwig's translation of Cruikshank's "Anatomy of the Absorbing Vessels" as his authority for this assertion. All that Cruikshank says is: "The chyle in the lacteals of the mesentery of dogs, in some of my experiments, evidently run through a space of four inches in a second, which is twenty feet in a minute." 1st Ed., Lond., 1786, p. 29. In neither his first nor his second edition (published in 1790) does he attempt to determine the quantity of the chyle.—G. E. D.]

<sup>2</sup> Arch. f. phys. Heilk. Bd. 7, S. 281–285.

<sup>3</sup> [The kilogramme = 2.2 pounds avoirdupois; hence  $2\frac{1}{2}$  kilogrammes = 5½ pounds.—G. E. D.]



with the chyle and flowing from the lymphatics, is not included in the computation, and because the quantity cannot be even approximately computed, owing to our uncertainty regarding the quantity of the lymph. The quantity of albumen which the chyle receives in the mesenteric glands, is excluded by Vierordt in his calculation, because he regards it as too small to require notice. To those who believe with Vierordt, that nitrogenous nutrient matters can only reach the blood through the lacteals, his mode of calculation may serve as an index of the quantity of the chyle; but all who concur with Frerichs and other observers, in assuming that the peptones are resorbed by the stomach and intestinal canal through the veins—an opinion which appears to be borne out by many circumstances—will necessarily attach more weight to the direct observations of Magendie and Bidder, than to Vierordt's calculation.

On the other hand, Vierordt would have approximated more nearly to the truth, if, instead of selecting the nitrogenous constituents, he had based his calculation on the quantity of fat in the chyle and the amount of fat which was daily resorbed in the intestinal canal. We know from Boussingault's<sup>1</sup> admirable experiments on ducks, that these animals are not able to take up more than 19.2 grammes in 24 hours, however rich in fat their food may be. We are, therefore, led to presume that there may be a similar limit to the resorption of fat in other animals. From numerous experiments on cats, Schmidt, Bidder, and Lenz<sup>2</sup> have indeed convinced themselves of the correctness and general applicability of Boussingault's observation; for they found that cats weighing 1000 grammes were able to take up from 0.6 to 0.9 of a gramme of fat in one hour, the surplus being carried off with the excrements. It is far more probable that all the resorbed fat should reach the blood through the lacteals, than that all the protein-bodies should pass into the chyle; and hence we shall probably obtain a nearer approximate number for the chyle which passes hourly into the blood, by adopting the amount of fat in the chyle of cats as the other basis of our calculation. Nasse, as has been already observed, found 3.27% of fat in the chyle of a cat; now, if no lymph flowed into the chyle, and if we assume that lymph contains some, although not much, fat (for Tiedemann and Gmelin found only traces of fat in the contents of the thoracic duct of fasting horses), and if it were shown that the chyle does not actually lose any fat in the mesenteric glands (this substance only becoming saponified), and that all the fat of the chyle of the thoracic duct has originated directly from the intestinal contents, cats weighing 1000 grammes would pour 22.9 grammes of chyle into the blood in one hour (supposing that they absorbed 0.75 of a gramme of fat in the same time), or 549.6 grammes of chyle in 24 hours. But as this would be more than half their weight, it is very improbable that this is the correct quantity. If we assumed six hours as the period during which true chyle passes into the blood, a cat weighing 1 kilogramme would daily elaborate 137.4 grammes of chyle. These calculations, more especially when they are extended to the human organism, are, however, far too uncertain to afford any stable

<sup>1</sup> Ann. de Chim. et de Phys. 3 Sér. T. 19, p. 117-125.

<sup>2</sup> De adipis concoctione et absorptione. Dorp. Liv. 1850, p. 62-79.



support to our future inquiries into the mechanical metamorphosis of matter, for there exist innumerable relations by which the result of such calculations may be completely modified. It would carry us too far from our subject were we to enumerate all these relations; we will, therefore, simply remark that probably a large quantity of fat is not conveyed from the chyme to the lacteals, but is resorbed by the veins, for how otherwise could the portal blood of animals be almost twice as rich in fat during the process of digestion as in the fasting condition? (See p. 619 of the first volume.)

We cannot entertain any doubt as to the *origin* of the chyle, since nature itself has clearly manifested its source to us. Certain questions here present themselves as to the mode in which the individual constituents pass into the lacteals, and the alterations which they undergo within these vessels. The lacteals originate in the axis of the villi which are spread over the whole of the small intestine, and present small club-like dilatations. The lacteals are surrounded at their origins by vesicles or cells which appear as if imbedded in an indistinct fibrous mass; while nearer to the exterior and to the peripheral investment of cylindrical epithelium covering the intestinal villi, there lie the trunks of the minute bloodvessels, which communicate together by means of a very fine network of capillaries. According to E. H. Weber,<sup>1</sup> there is a layer of round cells situated immediately below the epithelium, which are collapsed during fasting, and inflated like well-filled vesicles during the process of digestion. All observers concur in the opinion that each individual particle of cylindrical epithelium participates in the process of resorption, and is filled with a granular substance which causes its distension, and in some cases even a slight distortion. It is, however, more especially and almost exclusively during digestion that this layer of round cells appears under the epithelial investment; some of these cells being then filled with a clear, transparent, faintly yellow fluid, others with a granular substance. Thus we often find a cell of this kind filled with limpid fluid situated on the apex of an intestinal villus, and close by it another cell of equal size, filled with granular emulsive matter.

Besides numerous observations on animals in relation to this point, I remember noticing this appearance most strikingly and distinctly in the intestinal villi of a decapitated criminal, in whose examination E. H. Weber had permitted me to take part. The microscopical preparations made by Weber at the time have kept so well, that they still fully testify to the accuracy of his observations, and show that the structures in question are neither epithelial cells filled with fat (as was conjectured by Frerichs) nor fat-globules merely adhering to the surface of the villi. The distortion of the cells which Frerichs was also unable to detect, may likewise be easily recognized in these preparations.

The limpid contents of these clear globules, which are probably the oscula of the intestinal villi, according to the views of the older physiologists, can from their refractive power scarcely be anything but *fat*,

<sup>1</sup> Müller's Arch. 1847, S. 399. [We may also refer the reader to Professor Goodsir's remarks on this subject in his "Anatomical and Pathological Observations," pp. 5-10.—G. E. D.]



and this leads us at once to the hypotheses regarding the resorption of fat by the intestinal villi. R. Wagner<sup>1</sup> assumes that the solid neutral fats must be fused by animal heat previously to their resorption, whilst the fluid fats are resorbed unchanged. In order to explain the passage of the fats into the intestinal villi, Wagner has assumed that some portions of the intestinal canal are intended solely for the absorption of the fats, and others only for taking up the aqueous fluid. We should, however, rather be disposed to assume with Lenz<sup>2</sup> that certain cells in each intestinal villus are solely destined for the absorption of fat,—a mode of explanation which would be especially convincing to the chemist, who is accustomed to separate fatty from aqueous fluids by means of a filter saturated in one case with water, and in the other with oil. If we constantly observed (as we might often do) that the apex of each intestinal villus exhibits one vesicle more conspicuous than others for its size, and filled with a clear, strongly refractive fluid, together with another equally prominent vesicle, filled with granular matter, we should the more readily be led to the adoption of this hypothesis, since it affords an explanation of the view advanced by Boussingault, and confirmed by Bidder and Schmidt, that the absorption of fat from the intestine is confined within definite limits. Lenz adopted a very ingenious method for the further support of this hypothesis, which, however, did not prove so satisfactory as might have been desired. He injected butter, that had been colored with alcanna pigment, into the stomachs of cats, and killed the animals some hours afterwards. Most of the cells were found to be filled with yellowish fat, but this appearance could not afford any decisive explanation of the subject under consideration. However ingeniously this experiment was conceived, its frequent repetition was scarcely calculated to yield perfectly reliable results, for the fat would certainly become mixed in some places with the aqueous fluid, and as it would have to penetrate through several cells before it reached the smaller lacteals, it would enter those vessels mixed with the watery fluid; and this admixture would likewise go on in the villi of the cells surrounding the origins of the lacteals. If the cells filled with fat, and situated on the periphery of the villi and at their outer extremities, did not differ so strongly from the others, it would be illogical to attempt to explain the occurrence of a process in the interior which has been regarded as improbable at the surface, the relations existing in both being very nearly identical. Here, however, these relations are somewhat different, for we find some cells containing fat, and others filled with an albuminous fluid, appearing to be closely compressed together. This pressure may easily exert a modifying action on the permeability of the delicate cell-membranes, in the same manner as we find that on pouring an oily, emulsive, watery fluid on a filter, which has been completely saturated with water, oil will penetrate at some spots. The extreme comminution of the fat in the intestinal canal, which is occasionally observed to take place under ordinary relations, through the agency of the bile and the pancreatic juice, is by no means necessary; at all events, Schmidt and Bidder found that in animals into whose intestine pure fat had been conveyed after the

<sup>1</sup> *Lehrb. d. spec. Physiol.* 3. Aufl. 1845, S. 263. Anm. 3.

<sup>2</sup> *Op. cit.* p. 86-89.



exclusion of the bile and pancreatic juice, the lymphatics of the mesentery were as completely filled with milky chyle, as they usually appear to be after the use of fatty nutriment, when there is a free access of these glandular secretions. We cannot, therefore, assume the occurrence of an extreme comminution of fat in the aqueous fluid at the surface of the villi; but as the separate cells of the villi rapidly fill, and soon begin to exchange and blend their contents, the repetition of the experiment made by Lenz can scarcely afford any decisive results; for although the coloring by alcanna may cause the cells to be more conspicuous under the microscope than they would otherwise appear, the cells which were originally filled only with an aqueous fluid would speedily acquire the same hue, in consequence of their being partially permeated by colored fat. We must, moreover, confess that we are as yet unable to explain, from any known physical facts, the relations of transudation occurring in the cells. We will here merely refer to the rapidity with which the cells are frequently filled with granules of fat in certain pathological conditions, and to the still greater rapidity with which they are emptied—processes which have been most carefully studied by Virchow. A dehiscence of the cells may very probably occur only at individual points, and in such a manner, that the cell recovers its original integrity after the discharge of the superfluous substance. But these are all questions for whose further elucidation we must look to future physico-physiological inquiries.

We find more free and much less saponified fat in the small and intermediate lacteals than in the thoracic duct; and hence we are led to assume that a gradual saponification of the fat takes place in the mesenteric glands, where the chyle is undoubtedly brought in closer contact with the blood; this process being effected by means of the alkali of the latter fluid. A portion of the free fat is undoubtedly employed in the cell-formation which then ensues, but we can scarcely hazard a conjecture as to the chemical mode in which those metamorphoses are effected, which the fats themselves undergo in this process. But as it is certain that more alkaline salts of the fatty acids exist in the chyle of the thoracic duct than in that of the smaller lacteals or even than in the blood, these saponified fats cannot originate from the lymph that is mixed with the chyle, or from the plasma of the blood, but must rather be owing to saponification within the lacteals themselves.

The two following questions especially force themselves upon our notice, in considering the origin of the *albuminous substances* contained in the chyle:—1. Is the fibrin found in the chyle formed within that fluid, or does it originate in the intercellular fluid transuded from the blood? and 2. Does the *albumen* reach the intestinal villi in its perfect state, or are the absorbed peptones elaborated into albumen within the cells of the villi and in the lacteals? In respect to the latter of these questions, we have already (at pp. 494 and 514, vol. i.) indicated the grounds which have led us to the view that the peptones are not converted into albumen in the intestinal canal itself, notwithstanding the incontrovertible facts which have been advanced by Frerichs in favor of the opposite opinion. The system of cells through which the absorbed albuminous substances (and consequently the peptones, according to our view) have



to pass before they can enter their proper vessels (the lacteals) and the abundant network of capillaries enclosing these cells, appear to us clearly to indicate that these substances have here still to undergo important changes, whose final product can scarcely be anything else than true coagulable albumen containing alkali. It has further been found that the chyle after its passage through the mesenteric glands, is richer in albumen than it previously was; and this augmentation is solely referable to the absorption of blood-albumen in the glands. In proportion to our certainty on these points, so much the more probable it becomes that the augmentation of the albumen, at all events in part, depends upon the complete metamorphosis of the peptones into coagulable albumen.

In regard to the second question, we must remain undecided between the opposite results of Prout<sup>1</sup> and of Tiedemann and Gmelin,<sup>2</sup> as to whether the chyle contains true *fibrin* before its passage through the glands, or whether the coagulum observed by the former chemist, did not consist of fat-cells, and other albuminous matters. If the plasma actually passes from the blood into the lacteals, which, indeed, cannot be doubted, it would seem most probable that the whole of the small quantity of fibrin which is contained in the chyle originates from the blood or from the lymph. This view is further supported by our observations (in pp. 322-325, vol. i.) regarding the origin and the physiological importance of the fibrin. The soft, friable character of the chyle-fibrin has usually been regarded as affording a proof that it is first produced from albumen in the chyle, and that hence it appears there in such an imperfectly formed state. But we have already remarked in reference to the albumen, that the idea of greater or less perfection in regard to chemical substances is altogether inadmissible; we can only speak of an imperfect development when we treat of morphological objects. The reason why the fibrin in the chyle often (although not always) separates in this peculiar form is in no way connected with its being imperfectly elaborated from albumen; it solely depends on the character and chemical composition of the fluid from which the separation takes place. In diseased blood and in pathological exudations, we likewise observe that the fibrin separates in the same loose, friable, and sometimes even diffuent form as from the chyle; indeed, we are able to induce this loose, friable coagulation of the fibrin by artificial means, as, for instance, by diluting the plasma with water, by the addition of alkalies, &c. On these grounds, it seems far more probable that the fibrin of the chyle is due to the blood-plasma and lymph which have been absorbed into the lacteals, than that perfectly formed albumen should be here oxidized into fibrin.

With regard to the other constituents of the chyle, they are already formed in the chyme, and pass unchanged into the lacteals; it is singular that sugar, which I only found in such very small quantity in portal blood, is also only present in extremely small quantity, or is altogether absent, in chyle. This circumstance may be, in some degree, explained by the consideration that the conversion of starch into sugar in the intestine usually proceeds only very slowly, and that hence only very small quantities enter the lacteals and bloodvessels.

<sup>1</sup> Annals of Philos. Vol. 13, pp. 12 and 265.

<sup>2</sup> Op. cit., p. 157.



We have already noticed the development of the *morphological elements of the chyle* within the lacteals, in our remarks on the origin of the colorless corpuscles (see p. 642 of first volume).

It has been maintained by several of our leading authorities, that *hæmatin* occurs in solution in the chyle-serum, and that hence it must be formed in the chyle; but independently of the circumstance that a similar relation to that in the case of the fibrin may also hold good here, that is to say, that it may owe its origin to the blood-cells of the splenic lymphatics, it cannot have been possible for these chemists, with the aids at their command, to decide with certainty whether the hæmatin that was found, did not belong to the red corpuscles of the chyle. At all events, I have been unable to detect any dissolved hæmatin in the chyle-serum from the thoracic duct in horses, which is most commonly of a red or cinnamon color, and holds in suspension true hæmatin, containing blood-corpuscles; if, however, decomposition has commenced in the chyle, hæmatin will then be found in the plasma in consequence of the disintegration of the blood-corpuscles.

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## LYMPH.

The lymph forms a colorless or yellowish fluid, which is only red if blood-corpuscles happen to be mixed with it; it is sometimes transparent, sometimes slightly turbid or opalescent, of a faintly saline taste and mawkish animal odor; its reaction is usually alkaline; it coagulates in from four to twenty minutes after its discharge from the lymphatics; it then forms a gelatinous, trembling, colorless coagulum, which gradually contracts more firmly, and encloses a large number of the so-called lymph-corpuscles; in relation to the serum this coagulum usually occupies only a very small space.

Besides fat-globules and nucleus-like formations, we especially notice amongst the *morphological elements* the true lymph-corpuscles which, however, do not essentially differ from mucus- and pus-corpuscles. In lymph that has been carefully collected, we only find blood-corpuscles when the fluid has been obtained from the lymphatics of the spleen or from animals that have been starved to death (H. Nasse).<sup>1</sup>

There are many difficulties in the way of our *obtaining* pure lymph; it is sufficient to mention that, except in the very largest animals, it is often extremely difficult to find and dissect the lymphatics, and that even in the most favorable cases we cannot avoid an admixture of blood and fat, on cutting into the vessel and allowing its contents to discharge themselves. Hence recourse has generally been had to accidental cases, and lymph has been analyzed which escaped spontaneously in consequence of a wound or from a true lymphatic tumor. By the method described by J. Müller,<sup>2</sup> we can in a short time obtain from frogs a very considerable quantity of lymph, which, however, usually contains a slight

<sup>1</sup> Handwörterb. der Physiol. Bd. 2, S. 363-410.

<sup>2</sup> Handb. der Physiol. des Menschen. 4 Aufl. Bd. 1, S. 203 [or English translation, 2d Ed., vol. 1, p. 278].



admixture of blood; we make a crucial incision through the skin of a frog's thigh, and dissect a portion of skin, above and below, from the subjacent muscles; from this wound there flows such a quantity of lymph, that if we amputate the thigh, we often obtain more lymph than blood. Fishes usually have tolerably large lymphatics in the lower part of the orbit, and we may readily collect their lymph by opening the orbit from below and then cutting the absorbents.

The simplest method of obtaining a large quantity of lymph would be by cutting the thoracic duct of animals which had been for a long time deprived of food; but I agree with Nasse in considering this method as unfit for yielding a lymph sufficiently genuine and pure for chemical analysis.

The *chemical constituents* are, in general, very similar to those of the blood without red corpuscles. The spontaneously coagulating substance of the lymph is perfectly identical with the *fibrin* of the blood; like ordinary fibrin, it is converted, by digestion in a solution of nitre, into an albuminous substance coagulable by heat and precipitable by acetic acid. As in the case of the chyle, it is impossible here also to determine its quantity very accurately, since we are unable to separate it completely from cell-formations. In human lymph (obtained in cases of disease or injury), Marchand and Colberg<sup>1</sup> found 0.52% and L'Heritier 0.32% of fibrin, while in the lymph of the horse from 0.04 to 0.33% has been found (Reuss and Emmert,<sup>2</sup> Gmelin,<sup>3</sup> Lassaigne,<sup>4</sup> Rees,<sup>5</sup> Geiger and Schlossberger<sup>6</sup>). J. Müller found that frogs which had been starved during the winter, yielded a lymph perfectly free from fibrin, while on the other hand, Nasse found that the lymph of frogs which had been kept in a heated room, still coagulated.

The *albumen* of the lymph has the same general properties as that of the blood; Geiger and Schlossberger have, however, recorded the singular result that the albumen from the lymph of a horse, although it exhibited no reaction with vegetable colors, did not coagulate on boiling, but that on evaporation there was a membrane formed on the surface of the fluid as if a strongly alkaline albuminate of soda had been present; this lymph-serum was not rendered turbid by acetic acid, unless after being thus acidified it was boiled; as no coagulum was induced by rennet, it was obvious that no casein was present; moreover this serum was not coagulated by ether. In human lymph the albumen has been found to vary from 0.434 (Marchand<sup>7</sup>) to 6.002% (L'Heritier), and in that of the horse from 1.2 to 2.75%.

In the ash of the albumen of the lymph, even after repeated extractions with water and spirit, Nasse found an extraordinarily large quantity of alkaline carbonates: according both to his experiments and those of Geiger, the lymph contains that strongly basic albuminate of soda which, in the absence of other alkaline salts, communicates no alkaline reaction to the solution, and even when coagulated retains much alkali.

<sup>1</sup> Pogg. Ann. Bd. 43, S. 625.

<sup>2</sup> Allg. Journ. d. Ch. Bd. 3, S. 691.

<sup>3</sup> A. Müller, Diss. inaug. Heidelb. 1819, p. 59.

<sup>4</sup> Recherches physiol. et chimiques etc. Paris, 1825, p. 61.

<sup>5</sup> Phil. Mag. Feb. 1841, p. 156.

<sup>6</sup> Arch. f. phys. Heilk. Bd. 5, S. 392-396.

<sup>7</sup> Simon's Beitr. z. phys. u. pathol. Chem. Bd. 1, S. 449.



*Fat* occurs in the lymph only in small quantities, and is for the most part in a saponified form: in the lymph of the horse Nasse found 0.0088% of free fat and 0.0575% of alkaline salts of fatty acids, while in human lymph Marchand and Colberg found 0.264% of a pale reddish-colored fat.

The *extractive matters* of the lymph have not been closely examined, although their quantity in relation to the albumen is by no means small. In horses' lymph Nasse found 0.0755% of extractive matters soluble in alcohol, and 0.9877% soluble in water only, while according to Geiger and Schlossberger, the whole of the extractive matters amount to 0.27%.

Nasse was unable to detect *urea* in the lymph of the horse.

We have already noticed the existence of *lactates* in the lymph. (See vol. i. p. 96.)

As in all the animal fluids *chloride of sodium* is the preponderating mineral constituent; in horses' lymph it amounted, according to Nasse, to 0.4123%.

Moreover, *alkaline carbonates* were found by Nasse in horses' lymph, but Geiger failed in detecting them; Nasse calculates their quantity at 0.056%, and he assured himself of their presence by observing, with the microscope, the development of bubbles of gas on the addition of acetic acid. In the ash of the solid constituents of the lymph, Geiger also found an abundance of alkaline carbonates.

The presence of *ammoniacal salts*, which was suspected by Nasse, has been definitely established in horses' lymph by Geiger and Schlossberger.

Nasse found that horses' lymph was comparatively rich in *sulphuric acid*, which existed there preformed: he calculated the quantity of sulphate of potash at 0.0233%.

*Alkaline phosphates* occur only in very small quantities in the lymph.

The *earthy salts*, with a little peroxide of iron (arising probably from the presence of a few blood-corpuscles), were found by Nasse to amount to only 0.031% in horses' lymph.

The *quantity of water* in the lymph appears to be very variable, but never to be nearly so great as in the blood-plasma; in human lymph Marchand found 96.926%, and L'Heritier 92.436% of water; in the lymph of horses the quantity has been found to vary from 92.5% (Lassaigne) to 98.37% (Geiger).

Nasse has instituted an interesting comparison (based on direct analyses) between the composition of the lymph and of the blood-serum of the horse, from which it follows that the individual salts stand to one another in precisely the same ratio in both fluids, although their absolute quantity is very different in consequence of the larger amount of water in the lymph. Besides the differences in the amount of water in the two fluids (the water of the blood-serum being 7.8%, and that of the lymph being 5.0%), there are also considerable differences in the proportions in which the mineral constituents stand to the organic matters in the two fluids; while 100 parts of salts correspond to 1036 parts of organic matters in the blood-serum, the ratio in the lymph is as 100 to



only 785; according to Marchand and Colberg, human lymph contains inorganic and organic matters in almost equal parts.

It is hopeless at present to attempt to calculate the *quantity* of lymph contained in the whole animal body, since we have no fixed points of support to assist us in such a calculation. Even if the lymph of different parts were not so variously constituted as from certain facts and on theoretical grounds appears to be probably the case,—and if the rapidity of the lymph-current in the different vessels (before and after the passage of the lymph through the glands) were not so various, and, moreover, so dependent on internal and external (that is to say, physical and chemico-physiological) conditions, as has been shown by Noll,<sup>1</sup>—we should still be far less able to calculate the capacity of the lymphatics than of the bloodvessels, since we are much less acquainted with the anatomy of the former than of the latter. We referred, in our remarks on the quantity of chyle formed in a definite time, to the reasons which render the amount of fluid escaping from the main branch of a lymphatic system, an inefficient criterion of the quantity of this juice formed within any given period. The following facts may, however, aid us in arriving at an approximate idea of the quantity of lymph formed or flowing into the vessels; Collard de Martigny<sup>2</sup> found that 9 grains of this fluid flowed in 10 minutes from the thoracic duct of a rabbit which had fasted for 24 hours. J. Müller assumes the capacity of the four lymphatic hearts which he discovered in the frog, at about 4 cubic lines, and as these would make about 60 pulsations in a minute, these four lymphatic hearts would drive about 240 cubic lines of lymph into the veins in this period, provided that they are completely emptied at every contraction, which, however, is not the case. Moreover, the lymphatic system is of far more relative importance in frogs and cold-blooded animals than in those in which there is warm blood.

Bidder<sup>3</sup> believes, from his experiments on animals, that in an adult man about 13 kilogrammes [about 28·6lbs.] pass in the course of 24 hours from the thoracic duct into the subclavian vein. He is of opinion that only 3 kilogrammes [6·6lbs.] are true chyle (or digested nutrient matter), and that 10 kilogrammes [22 lbs.] are true lymph. Hence in the course of 24 hours a quantity of lymph, averaging from 1·8th to 1·7th of the weight of the body is formed and poured into the blood.

The *origin* of the lymph has been referred by all physiologists to the juice which flows from the capillaries into the parenchyma of the organs, either for their nutrition or for the formation of the secretions. Although physiologists had previously shown that the character and quantity of the lymph depend upon the fluid conveyed through the capillaries, and transuded from them, these views have recently been fully confirmed by Noll. It therefore now only remains for the chemist to institute an accurate comparison of the blood-plasma, the parenchymatous fluid, the secretions and the lymph, in order to deduce the chemical equations giving the scientific expression for the processes which give rise to the formation of the lymph. We are, however, still very far distant from the attainment of this aim, towards which our chemical investigations

<sup>1</sup> Zeitschr. f. rat. Med. Bd. 9, S. 52–93.

<sup>2</sup> Journ. de Physiol. T. 8, p. 266.

<sup>3</sup> Verdauungssäfte und Stoffwechsel. S. 285.



ought to be directed; for even if we assume that the differences in the transuding blood-plasma and the resorbed lymph can be investigated with chemical accuracy in the same individuals, we are yet unable to draw any certain conclusions in reference to the metamorphoses which the blood-plasma undergoes in each individual organ, or even generally, or to trace the origin of the separate constituents of the lymph. Moreover the lymph which is accessible to chemical inquiry by means of the physiological aids at present at our command, cannot be regarded as the product of the nutrition of these organs. For there is not only a larger quantity of plasma exuded through the capillaries than is necessary for the nutrition of the organs and the formation of the secretions (so that a large proportion of unchanged plasma is blended with the substances which are either metamorphosed by nutrition, or have not passed into the secretions), but it is further proved by innumerable physiological facts, that the fluid which is resorbed by the lymphatics undergoes further metamorphoses in its passage through the lymphatic glands. It may be inferred from the appearance of cells, which, however, are probably not formed until after the passage of the absorbed fluid through the glands (at least in the animals provided with lymphatic glands), that the lymph contains not only the products of regressive metamorphoses, but even true plastic substances. The lymph of certain organs appears to possess so high a degree of plastic force, that blood-corpuscles are even formed in it; the lymph of the spleen frequently, and indeed generally, contains blood-corpuscles, as has been already noticed. According to Huschke,<sup>1</sup> the Malpighian corpuscles of the spleen are nothing more than dilatations of the lymphatics, but from the coincident observations of Gerlach<sup>2</sup> and Schaffner,<sup>3</sup> it seems much more probable that this organ is one of the main factories for the blood-corpuscles. If, however, the lymph must vary according to the quantity of unchanged blood-plasma which it may contain, we find a new ground established for the great differences which it presents in different parts, when we consider that the chemical constitution of the transuded plasma depends upon the character of the capillaries of each organ, that is to say, upon their width, upon the density of their walls, the velocity with which the blood streams through them, &c. Gerlach draws especial attention to the fact that the spleen has very wide bloodvessels, which may be classed amongst the capillaries from the absence of a circular fibrous coat, and which would appear from the thinness of their walls to be better adapted than the capillaries of other organs to admit of the transudation of a perfectly unchanged blood-plasma, that is to say, of an intercellular fluid, and would therefore afford the most abundant materials for the formation of cells. If we may regard certain normal or even dropsical exudations in the animal body, as for instance, the transudations of the choroid plexus of the brain (which are very remote from the lymphatics that lie only on the periphery), as the direct secretions or transudations of the capillaries, the view which is based on the difference in the capillaries will derive additional support from the chemical investigation of the transudations of the different capillary systems. Thus, for instance,

<sup>1</sup> *Lehre von den Eingeweiden*. S. 175, ff.    <sup>2</sup> *Zeitschr. f. rat. Med.* Bd. 7, S. 75-82.

<sup>3</sup> *Ibid.* p. 345-354.



C. Schmidt<sup>1</sup> has drawn the following conclusions from the comparison between the composition of the transudation of the capillaries of the peripheral membranes of the brain, and that of the transudation which issues from the central capillaries of the same organ; namely, that the fluid of the brain and spinal cord is by no means mere blood-plasma separated, as it were, by mechanical filtration from the more widely circulating blood-cells, and robbed of some portion of the nitrogenous and fatty matters, which are taken up by the cerebral substance. When we proceed to consider the exudations, we shall have to revert to those investigations of Schmidt, which tend to show that the fluids permeating through the different capillary systems of the body possess a constitution, which, although constant for the same system, differs in the different systems, exhibiting its principal differences in respect to the amount of albumen, while the inorganic constituents remain nearly the same as in the blood. According to Schmidt's investigations, protein-bodies transude through the capillaries of the pleura in the largest quantity; scarcely half so large a quantity passing through the capillary vessels of the peritoneum, still less through those of the brain, and least of all through those of the subcutaneous areolar tissue.

These, and similar points of consideration, appear to us to be necessary for the establishment of a physiologico-chemical investigation of the origin and physiological import of the lymph; for any chemical equation would afford a false representation of the sources of the lymph, and of its importance in respect to animal life, if it were derived from the simple chemical analysis of the lymph of the larger vessels, without reference to these points. Unfortunately, however, we are here merely on the borders of a department in which we scarcely know the course or the direction which may lead us to the object of our inquiries. Nasse was the first who endeavored to throw light on this subject, by comparing, as we have already mentioned, the serum of the blood of the horse with the lymph taken from the cervical region of the same animal. The following are the results of this inquiry.

The lymph always contains more *water* than the liquor sanguinis; hence it is not perfect plasma which is exuded from the blood; but proportionally more water and less solid constituents are transuded, than correspond with the liquor sanguinis. The circulating blood must therefore be more concentrated.

On comparing the solid constituents of the lymph and of the serum, we find that the former contains far less *albumen* than the latter; with every 100 parts of soluble salts there occur in the blood-serum 838, and in the lymph only 697 parts of albumen. This relative deficiency of albumen in the lymph cannot merely depend upon the circumstance that less albumen has originally escaped from the capillaries, but principally on the fact that a portion of it has been applied to the restitution of the textural elements which have become effete, as well as to the formation of the lymph-corpuscles.

Moreover, we find far less *fat* in the solid residue of the lymph than in that of the blood-serum; Nasse found the ratio of the soluble salts to the ether-extract to be 100:1.57 in the lymph, and 100:4.8 in the

<sup>1</sup> Charakteristik der Cholera, u. s. w. S. 124-148.



serum. Since it follows from the examination of morbid transudations that they contain very little fat, we might assume that the excess of fat remains in the serum, especially since the venous blood has been found to be richer in fat than the arterial; a part, however, of the transuded fat may be applied to the formation of cells within the lymph, although in Nasse's comparative analyses, the fibrin and lymph-corpuscles are calculated with the albumen, and hence their fat is included in the analysis of the residue of the lymph; on the other hand, the neutral fats extractable by ether have become in part saponified, and must be sought for in Nasse's alcohol-extract.

The solid residue of the lymph contains relatively more *extractive matters* than that of the serum; if we here also take 100 parts of soluble salts as the standard of comparison, the ratio (according to Nasse's analyses) is as 100:50.4 in the serum, and as 100:87.0 in the lymph. This augmentation of the extractive matters in the lymph seems obviously due to the *detritus* of the more or less active metamorphosis of the tissues, although a portion of this *detritus* probably transudes from the capillaries even more readily than the soluble salts; at all events we generally find far more extractive matters in the morbid transudations of the capillaries than in the blood. Hence these matters cannot be regarded merely as the remains of textural metamorphosis, but also of the cell-formation already existing in the blood. There are, however, undoubtedly concealed in the extractive matters a number of substances, whose accurate chemical examination promises to throw much light on the metamorphosis of the animal tissues. According to Nasse's analyses, there is an augmentation of the alcohol-extract in the lymph; this is due to the soaps that are formed, and to the lactic acid and the urea. It is true that no urea can be directly detected in the lymph, but we can hardly do otherwise than suppose that the urea—a product of the metamorphosis of tissue—passes rapidly through the lymphatics before it reaches the blood and is finally separated by the kidneys. The fact that Schmidt<sup>1</sup> found urea in the fluid in chronic hydrocephalus, might probably be taken as a proof that urea is necessarily present in the lymph, if the non-existence of a simultaneous renal disease had been demonstrated in this case; and Scherer's admirable discoveries regarding the secreted matters found in the parenchyma of the spleen speak still more strongly in favor of this view. Nasse certainly assumes a regressive movement of the transudation, or of some of its constituents, into the capillaries, and according to this view the secreted matters might also be taken up directly from the parenchymatous fluid by the capillaries, but not by the absorbents; but although, according to the experience of several observers, the lymphatics certainly appear to make a selection in the substances which they absorb, yet the latest investigations of physiologists (and especially those of Noll) regarding the force which propels the lymph, indicate that it is the pressure proceeding from the capillaries which chiefly occasions the movement in the lymphatics. It is not to be expected that, under the pressure which the lymphatics tend to lessen, any considerable part of the transudation could be re-conveyed into the capillaries by an opposite current.

<sup>1</sup> Op. cit., p. 123.



According to Nasse's analyses, the ratio of the water to the *soluble salts* is as 100 : 0.871 in the blood, and as 100 : 0.561 in the lymph of the horse. Hence, even in the normal state, the quantity of water which transudes from the capillaries is even proportionally greater than that of the soluble salts which escape. No one will, however, believe that the water which is formed by the metamorphosis of the tissues contributes in any essential degree to the augmentation of the water in the lymph. The venous blood is consequently found to be poorer in water than the arterial blood. Unfortunately the ash-analyses of the residues of the lymph and serum which were instituted by Nasse, are not of a nature to warrant our drawing any exact conclusions from them. Future and more accurate analyses must show whether the same relations hold in the lymph that Schmidt found to occur in dropsical transudations; that is to say, whether on the whole the salts remain the same as in the blood, excepting that the chlorides are rather more abundant than the phosphates, and that the salts of soda preponderate over those of potash. We may conclude from the analyses of the lymph made by Nasse and others, that the alkaline sulphates are contained in this fluid in much larger quantity than in the serum of the blood. The only process by which these salts can be produced is the disintegration of the sulphurous tissues with the co-operation of the oxygen escaping with the plasma from the blood.

Lastly, Nasse has found that there are far more earthy phosphates in the serum of the blood than in the lymph; this is, however, only dependent on the circumstance that the albuminates in which the earthy salts are contained, occur in a less proportion in the latter fluid.

From a comparison of these analyses of the blood and of the lymph, it follows that the function of the lymphatics consists not merely in conveying those parts of the tissues which have become effete into the blood, from which, after undergoing further changes, they are separated by the organs of excretion, but also in elaborating the still plastic portions of the blood into cells—namely, the blood-corpuscles; for how, if this were not the case, could cells occur directly in the lymph, if it merely carried off the disintegrated remains of the tissues? for what purpose would its motion through the lymphatic glands be suspended, or at all events considerably impeded, if the absorbents were not, like the lacteals, organs for the elaboration and formation of the blood?

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## TRANSUDATIONS.

While pathologists include under the term *exudations* all kinds of fluid, semi-solid, or solid substances which, in consequence of morbid action have been deposited in serous cavities, or in the parenchyma of organs, and have there undergone many metamorphoses, chiefly in a morphological point of view, we regard it as most expedient, in so far as the interests of physiology are concerned, to draw a distinction be-



tween the *transudations* which consist of fluid constituents of the intercellular portion of the blood escaping from the capillaries, and exudations in which a change has already commenced. These transudations include all those fluids which are normally or abnormally effused from the blood-vessels (without laceration) into the parenchyma of organs, or into enclosed or open cavities, or even on the surface of the animal body. Hence we include amongst the transudations the normal secretions of the serous membranes, and not merely those of the lining membrane of the cerebral ventricles, of the pericardium, the pleura, and the peritoneum, but also the tears, the aqueous humor of the eye, and the liquor amnii, and especially the parenchymatous fluid or juice which moistens and nourishes the tissues; if these transudations are excessive, they form the albuminous and fibrinous exudations of pathologists. Although pathological transudations are now frequently submitted to chemical investigation, and have been more accurately analyzed than the normal transudations, in consequence of the greater quantity in which they accumulate, we regard it as most expedient to follow the purely physiological view regarding the escape of these fluids from the capillaries, lest we should lose ourselves in the labyrinths of pathological systems and pathological fictions; for the assumption of watery and serous transudations, of croupous and fibrinous, and again, of serous and albuminous, can find no support either in physical or chemical physiology. We have already seen, when treating of the lymph (a subject closely allied, in more points than one, to that we are now discussing), that in accordance with the views of the most eminent physiologists of the present day, we must consider the escape of water and certain constituents of the liquor sanguinis through the walls of the capillaries as the result of a physical necessity consequent on the penetrability of the walls of the capillaries, the rapidity of the motion of the blood in them, and the physical and chemical characters of the circulating fluid itself. This variety in the conditions affords at the same time an explanation of the differences in the physical and chemical properties of normal as well as of excessive transudations, and of the uncertainty of those attempts at classifying them, which are based either on their incidental properties, or on the form of the metamorphoses which they are more or less inclined to undergo. Hence, without attempting any system of classification, we will proceed to notice their ordinary physical characters, and their essential and incidental constituents.

The normal as well as the excessive transudations have in general the same *properties* as the intercellular fluid or the serum of the blood; they are colorless, transparent, of a sickly and faintly saline taste, of an alkaline reaction, and generally of lower specific gravity than the serum of the corresponding blood. Their *morphological elements* vary with the surfaces on which they are effused; and hence we may meet with epithelial structures, molecular granules, bodies resembling nuclei and cell formations, which, however, are not peculiar to transudations; blood-corpuscles only occur in them when the capillaries have become lacerated in consequence of some disturbing influence, and blood has thus been actually mixed with the transudation.

Moreover, the chemical constituents of the transudations are precisely



similar to those of the blood-plasma; except that, as has been already noticed in regard to the lymph, all the constituents occur in a less ratio than in the plasma, and hence their water is increased; and further, that some even of the organic constituents are so subordinate, that they appear to be altogether wanting, and under the specially existing conditions, to be incapable of transudation. Hence we might classify the transudations according to the absence of one or other constituent of the plasma, if only we could draw any definite limit, and could exhibit the perfect absence of the substance in question even in special cases.

The absence or presence of *fibrin* in the transudations has in this way occasioned the division of those effusions in the animal body which do not contain blood-cells into two principal classes, namely, into albuminous and fibrinous; or, if they are very excessive, into serous and fibrinous dropsy (Jul. Vogel).<sup>1</sup> No fibrin is to be found in the normal transudations of serous membranes, and in those excessive effusions which are not accompanied by that affection of the capillaries which we assume to exist in inflammations; it is, therefore, absent in the cases of excessive accumulation of serum which arises either from a disturbed state of the functions of the lymphatics, or from an excess of water in the blood. If, however, the blood-current be much impeded, or if it be perfectly stopped in the capillaries, fibrin always escapes through the attenuated walls of the vessels, and gives rise to more or less plastic exudations. Whether, as Vogel assumes, the transudation in non-fibrinous dropsy proceeds chiefly from the smaller veins, and in fibrinous dropsy from the true capillaries, is a point which must be established by further histological investigations. Some capillaries may, in their perfectly normal state, possess the property of allowing the passage of fibrinous transudation. If the parenchymatous juice which has become effused for the nutrition of the organs cannot be readily isolated, and if we, consequently, are unable to prove, by a direct method, that it contains fibrin, yet, independently of the general belief, it is in the highest degree probable that this nutrient fluid actually contains fibrin; for this view is supported by the amount of fibrin occurring in lymph, by the constitution of the nutrient fluid in the lower animals which do not possess distinct blood-canals, and by the constant presence of fibrin in the ordinary plastic exudations, as is very well seen in the non-sanguinous secretion of fresh-incised wounds—a secretion which has been accurately analyzed by Schmidt.<sup>2</sup>

Fibrin may very often be contained in the transudations, when, from its small quantity, or from the metamorphoses which it has already undergone, it may evade chemical detection. If we consider that in the plasma of normal blood the quantity of fibrin is only one-fortieth of that of the albumen, and if we suppose that the diminution of the fibrin in the transudation only corresponds with that of the albumen, there could never be more than a very small, often almost inappreciable, quantity of fibrin in the effused fluid; if we further consider that the fibrin in the parenchymatous juices is very often applied to the renovation or reparation of tissues, and that in morbid transudations it soon commences to

<sup>1</sup> Path. Anat. Th. 1. S. 12-35 [or English translation, pp. 33-57.]

<sup>2</sup> Charakteristik d. Cholera, S. 134.



form the groundwork of morphological structures, we need not wonder that the fibrin is so often found to be absent. Most, however, of the dropsical transudations which depend on too aqueous a condition of the blood, or on a disturbance in the function of the lymphatics, appear to be formed without any simultaneous separation of fibrin; at all events, the fact that too aqueous blood is usually found to be a little richer in fibrin than normal blood, seems to favor the view that in this case the fibrin is retained in the circulating fluid. But however this may be, the fact elicited by Vogel remains established, that fibrinous transudations are far more frequent than is usually supposed to be the case, trusting to ocular examination alone.

The physical and chemical properties of the fibrin occurring in transudations perfectly coincide in all essential points with those of the blood-fibrin; the peculiarities which the transudation-fibrin presents, are solely based on the physical and chemical relations under which it is separated, as in the case of the fibrin of the lymph and chyle, to which reference has already been made: the chemist can lay down no such differences as "a fibrin infiltrated with serum," a croupous or aphthous fibrin, or a pseudofibrin. The fibrin occurring in transudations most frequently coagulates in the form of those soft gelatinous masses which appear infiltrated with serum, or to which we apply the name of pseudofibrin. We know (see vol. i. p. 580) that this form of coagulation is entirely dependent on an excess of water in the fluid in which the fibrin was previously suspended; and hence we should wonder why this form of coagulation is not far more frequently found in the dead body than is actually the case, if we did not know that the fibrin is usually extremely slow in coagulating in the fluid which transudes in the living body, and that in consequence of the continuous motion in the cavities of the pleura, the pericardium, and the peritoneum, a flocculent coagulum somewhat resembling whipped fibrin must be formed. Moreover, if we take a chemical view of the subject, we cannot accept the idea of a peculiar morbid fibrin; the peculiar forms in which fibrin coagulates in certain morbid processes, and which have led to this assumption, are entirely dependent on the conditions under which the coagulation of the fibrin takes place. However accurately we observe the different forms of fibrin in the varieties of morbid exudations, and however important may be the observations regarding the capacity for organization or the disintegration of one or other form of coagulation, that part of the exudation which is actual fibrin is not to be distinguished in a chemical point of view from the fibrin of the blood. Neither in croupous nor aphthous, nor in any other fibrinous exudation, have I even once found a fibrin which in its microscopico-chemical or purely chemical examination has proved to be essentially different from the ordinary fibrin of the chemists; amongst other things it may be mentioned, that the one fibrin, like the other, was dissolved after a longer or shorter digestion in a solution of nitre, into an albuminous coagulable substance; there was merely a difference of the time in which the change was completely accomplished; and the time was generally almost in a direct proportion to the coherence of the coagulated fibrin. (The exudation-fibrin was, of course, not digested in a solution of nitre until the mechanically comminuted and washed exuda-



tion-coagulum no longer contained a trace of any substance coagulable by boiling or by acetic acid.) In many transudations, especially those in serous membranes (in the fibrinous dropsies of Vogel), the fibrin is held in solution, and does not coagulate till the fluid discharged by paracentesis has been for some time exposed to the action of the air; more than an hour often passes before coagulation takes place; and sometimes we may observe the formation of a coagulum in these fluids after they have stood from 10 to 24 hours (Schwann and Magnus,<sup>1</sup> Delaharpe,<sup>2</sup> Scherer,<sup>3</sup> Quevenne).<sup>4</sup> Moreover, this fibrin does not differ chemically from blood-fibrin; we know also that a "fibrin of slow coagulation" may occur in the blood, of which Polli<sup>5</sup> has given numerous examples. We certainly cannot always state with accuracy in individual cases what it is that impedes the coagulation, but the causes are generally much the same, namely, moderate attenuation with water, an excess of alkaline salts, abundance of carbonic acid, &c., which, as we have already seen in vol. i. p. 577), more or less impede the separation of the fibrin. Moreover, the chemical reactions presented by this fibrin are precisely the same as those of ordinary fibrin.

If we should suppose that the question, whether or not the fibrin in these pathological effusions is of a different kind, could be decided by elementary analyses, we should be very far from the truth; for, as in all experiments of this nature, we should find differences enough, but they would depend upon the impossibility of our obtaining such substances as fibrin in a state of chemical purity, and fit for an elementary analysis; we need not here repeat what has been already stated (in vol. i. p. 315) respecting the unfitness of fibrin for ultimate analysis, and (in vol. i. pp. 39 and 40) regarding the general cautions requisite in such cases.

With regard to the quantity of fibrin which we find in transudations, it is obvious, from what has been already stated, that it presents very great differences, although it is always somewhat less than that of the corresponding blood-plasma. This obviously only holds good with regard to fresh transudations; for when they have existed for some time in the living body, they may on the one hand be found to have been deprived of a great part of their water, or the fibrinous coagulum may have already passed into a state of cell-formation—an object to which other substances in the transudation, besides the fibrin, may be applied; in these cases we certainly meet with far more fibrin in the transudation than in the liquor sanguinis, if we calculate as fibrin all undissolved or insoluble matters.

No fibrin can be detected in those normal transudations which accumulate in some quantity in the animal body; as for instance in the moisture of serous sacs, the aqueous humor of the eye, the tears, the liquor amnii, certain dropsical effusions, hydatids, cutaneous vesicles (whether artificially excited or consequent on a skin-disease), or in secretions from the intestinal capillaries, as in the diarrhœa arising from catarrh or drastic purgatives, or accompanying cholera.

Those morbid secretions which are consequent on an acute inflamma-

<sup>1</sup> Müller's Arch. 1838, S. 95.

<sup>2</sup> Arch. gén. de Méd. Juin, 1842.

<sup>3</sup> Untersuch. z. Pathol. S. 106 u. 110.

<sup>4</sup> Journ. de Pharm., Nov. 1837.

<sup>5</sup> Eckstein's Handbibl. des Ausl. Heft. 4, S. 25-32.



tory process, and are accompanied by laceration of the capillaries and ulceration, have no claim to be reckoned amongst the transudations, seeing that they are not the products of a simple transudation; these are often very rich in fibrin, but in regard to their general constitution and certain of their constituents, they essentially differ from the simple transudations.

Like the fibrin, the *albumen* occurring in transudations is the same as we find in the blood and in other places; the difference which it exhibits in regard to the character and form of its coagulation are entirely dependent on the relations to which we have often alluded, and which are fully discussed in vol. i. pp. 295 and 297. Thus, in many physiological and pathological transudations, we find that casein-like albumen, which does not coagulate on heating, is precipitated by dilute acetic acid, and separates in the form of a superficial colorless membrane when its solution is evaporated; we need hardly repeat that this body is albuminate of soda, and possesses none of the essential characters of casein. Although casein has been often asserted to be a constituent of such transudations, and has even recently been declared (by Panum<sup>1</sup>) to be a normal constituent of the blood, I have never succeeded in finding any substance of this nature in such fluids excepting albumen rich in alkali.

In the normal transudations, as for instance in the liquor pericardii, in the fluids of the cerebral and spinal membranes, the liquor amnii, and all those fluids which contain only little albumen, we can always, with a careful examination, detect albuminate of soda; and the same remark applies to the fluid contained in the bullæ of pemphigus, and to the intestinal dejections in cholera. On the other hand, we occasionally, although rarely, meet with transudations from which all the albumen is precipitated on heating, in the form of small flakes; and those are still more rare which become very turbid on the addition of water, and gradually deposit a sediment of pure albumen; almost all albuminous transudations become, however, slightly turbid when very much diluted with water. Scherer<sup>2</sup> has especially directed attention to transudations of this kind; they are generally such as were not submitted to analysis till long after their separation, or such as are found in certain morbid processes, in which the alkali of the blood is diminished or has been saturated by the occurrence of an acid. It follows from these experiments of Scherer's, that the mere chemical analysis of transudations is in itself of little scientific value; and if we would draw any conclusion regarding the pathologico-chemical process from such an analysis, it is imperatively necessary that we should simultaneously institute a comparative analysis of the blood of the patient from whom the transudation was obtained. This is, moreover, one of the reasons why so very few of the analyses of morbid products at present in our possession can be applied to any scientific purpose.

The quantity of albumen in different transudations is extraordinarily variable; in some transudations, the amount is so small that some observers have believed it to be entirely absent, as, for instance, in the tears, in the aqueous humor of the eye, in the liquor amnii (in the last stage of pregnancy), in the fluid in the lateral ventricles and the spinal canal (in

<sup>1</sup> Arch. f. pathol. Anat. Bd. 3, S. 251-264.

<sup>2</sup> Pathol. Untersuchungen. S. 78.



the normal and in the dropsical state), and in the fluid of the cellular tissue in oedema of the extremities. If, however, albumen is never entirely absent in these fluids, its amount in other freshly transuded fluids never reaches that contained in the serum of the blood. It now becomes a question, whether there are any conditions inducing a more copious or a diminished transudation of albumen through the walls of the capillaries, so that certain general rules, if not laws, can be established, in accordance with which there may be an augmentation or a diminution of the albumen in the transudation.

The following is one of these rules:—*The quantity of albumen contained in a transudation is dependent on the system of capillaries, through which the transudation occurs.* We are indebted to the admirable investigations of C. Schmidt<sup>1</sup> for our knowledge of this rule, which is equally important in the elucidation of the mechanical metamorphosis of matter, and in the explanation of morbid processes; and at which he arrived by a series of carefully conducted parallel analyses of normal and abnormal transudations. Schmidt assumes, that the transudation from every group of capillaries contains a definite and constant quantity of albumen. He found the transudation in the pleura to be richest in albumen ( $=2.85\%$ ); that in the peritoneum considerably poorer ( $=1.13\%$ ); that within the cranial membranes yet more deficient in this constituent ( $0.6$ , or at most  $0.8\%$ ); and that of the subcutaneous cellular tissue the poorest ( $=0.36\%$ ). Schmidt found this proportion of the albumen to the effused fluid in the transudations of one and the same individual, who was suffering from Bright's disease; and he convinced himself by further investigations regarding the normal transudation of the cerebral capillaries and hydrocephalic effusions, that not only does the quantity of albumen always remain tolerably equal when there is an excess of the transudation, but also, when, after the removal of older effusion, a new transudation occurs through the same capillaries. In the normal cerebrospinal fluid of a dog, Schmidt found  $0.24\%$  of organic matter; in chronic hydrocephalus of a child, at the first and at a second paracentesis,  $0.156\%$  and  $0.179\%$ , and in acute hydrocephalus  $0.37\%$ ,  $0.649\%$ , and  $1.040\%$ ; in a pleuritic transudation, obtained by paracentesis,  $2.61\%$ ; in that obtained after death from the same person,  $2.85\%$ ; in the first peritoneal transudation, obtained by paracentesis,  $0.365\%$ ; in the second, from the same person,  $0.395\%$ . I collected  $33.8$  grammes of transudation from the pericardium of a perfectly healthy criminal within three minutes after his decapitation; it contained  $0.879\%$  of albumen, with  $0.093\%$  of other organic matter, and  $0.089\%$  of salts. In the fluid, in a case of hydropericardium ex vacuo (in pulmonary tuberculosis), I found  $1.543\%$  of albumen. In examining the dropsical transudations in the dead body of a drunkard with true and well-developed granular liver, I found, in the fluid of the pericardium,  $1.063\%$  of albumen; in that of the pleura,  $1.852\%$ ; in that of the peritoneum,  $1.044\%$ ; and in that of the cerebral ventricles,  $0.564\%$ . In a peritoneal transudation, in a case of cancer of the liver (where the liver extended two inches below the navel), I once found  $4.351\%$  of albumen, besides  $0.598\%$  of extractive matters, and  $0.890\%$  of salts; while, on the other hand, in hydræmia (consequent on chronic ulceration of the

<sup>1</sup> Charakteristik der Cholera. S. 145.



follicles of the large intestine), I have found only 1.127% of albumen, with 0.448% of extractive matters, and 1.014% of salts. In the transudation from the cerebral capillaries, in hydrocephalus ex vacuo (cerebral atrophy in an old man), I found 0.144%; in congenital hydrocephalus, 0.012%; and in hydrocele, 6.283%, 4.982%, 4.055%, and 3.410% of pure albumen.

Without quoting any additional results obtained either by myself or under my superintendence, and some of which support, while others are opposed to the law which Schmidt has attempted to establish, I will merely give a few numbers obtained by other chemists; in an effusion within the cerebral ventricles Berzelius<sup>1</sup> found 0.166%, Mulder 0.055%, and Tennant 0.303% of albumen; in a transudation within the peritoneum, v. Bibra<sup>2</sup> found 2.9%, Vogel<sup>3</sup> 3.3%, in one case and only 0.09% in another, Dublanc (like v. Bibra) 2.9%, Marchand 0.238%, and Simon<sup>4</sup> 0.84% of albumen; in a case of hydrocele the last-named chemist found 4.83% and v. Bibra 4.8%, and in œdema of the feet Simon found 0.70% of albumen.

If we compare the results of different analysts, it might seem at first sight that they are opposed to Schmidt's postulate, that the transudation of each individual group of capillaries has a special and a constant composition; but a closer examination of the relations accompanying these transudations renders it tolerably evident that this proposition is unquestionably established, but that, like all natural laws, it is modified in its results or actions by other valid laws, and that thus its direct recognition is not very obvious. We can, therefore, only demonstrate this proposition when we compare with one another the simultaneous transudations of different capillary groups *under identical conditions*. We then certainly find that the relative quantity of albumen is tolerably equal in the different transudations, but we must not hence conclude, as Schmidt seems inclined to assume, that the quantity of albumen in the transudation of each group of capillaries is, under all conditions, represented by a definite number; for different conditions may come into play, which exert an influence on the composition of the transudation. The transudation is not the result of merely a single factor; it depends not only on the thickness or the delicacy of the capillaries, but on the rapidity of the current of blood, and on the constitution of the blood itself. Even if there were not sufficient positive facts to establish the position that the composition of the transudation from the same capillary system varies under different conditions, we might *à priori* conclude that, on the one hand, when the current of blood in the capillaries is very slow, and there is great distension of their walls, the composition of the transudation will be very different from what it would have been under opposite conditions, and that, on the other hand, its composition, and consequently its amount of albumen, will vary extremely with the varying physical and chemical characters of the blood.

The capillaries also appear to vary in their capacity for transudation

<sup>1</sup> Lehrb. d. Ch. Bd. 9, S. 198.

<sup>2</sup> Chem. Untersuch. verschied. Eiterarten, S. 160 u. 170.

<sup>3</sup> Path. Anat. Th. 1, S. 16 [or English translation, p. 37].

<sup>4</sup> Med. Chem. Bd. 2, S. 582 [or English translation, vol. ii. p. 493].



in different stages of the development of serous membranes; thus, for instance, according to Vogt and Scherer,<sup>1</sup> the liquor amnii in the human subject contains more albumen and more solid constituents generally during the early than in the last stages of pregnancy. Vogt found 1.077% of albumen in the fourth month, and 0.667% after the sixth month; Scherer found 0.767% in the fifth month, and only 0.082% after the beginning of the ninth month; Mack found 0.370 and 0.264% in the liquor amnii at the full time. Three analyses of the liquor amnii, which were conducted by myself, coincide most nearly with those of Mack.

From the simple application of the few analyses which have hitherto been made, we may, by induction, establish the proposition, that the transudation *will be richer in albumen in proportion to the slowness with which the blood passes through the capillaries*. When the circulation is obstructed in the abdominal veins by the presence of large tumors, we find that the transudations contain a larger amount of albumen than in those cases in which the circulation of the blood in the veins is retarded by lesser mechanical obstructions, such as hepatic disturbances accompanied with contraction of the parenchyma of the liver, &c. When the disturbance in the circulation of the blood in one capillary system is so considerable, as is the case in inflammatory hyperæmia, the transudation will be far richer in albumen; and hence we find that all the fibrinous transudations are on an average far richer in albumen than the so-called serous ones. In the fluid of acute hydrocephalus we find, that while there is an absence of fibrin, there is less albumen than in many other serous transudations, but always a larger quantity than in chronic hydrocephalus, &c.

The constitution of the blood forms a third condition, which exerts an influence on the quantity of albumen, as well as on the general composition of the transudations; for *the poorer the blood is in albumen, the less of this substance will be present in the transudation*. C. Schmidt has, however, decisively shown, with reference to the dropsical accumulations in Bright's disease, where the blood is constantly rendered poor in albumen from the quantity of this substance carried off by the urine, that this diminution, when compared with the transudations in dropsy, arises from other causes. In the transudation dependent on the mechanical obstruction of the blood in the abdominal vessels, the blood at the same time being highly albuminous, we find more albumen (as in hepatic affections, heart-diseases, &c.) than in that variety which originates in hydræmic blood (as in Bright's disease, cancer, pulmonary tuberculosis, or after copious losses of the juices, &c.)

In considering the transudations, we must not overlook a circumstance to which we have elsewhere drawn attention, namely, that when the transudations stagnate for a prolonged period in a serous cavity, without being either resorbed or artificially removed, as is most frequently the case in hydrocele, ovarian dropsy, and other dropsical fluids contained in closed cavities, the aqueous and some portion of the saline parts are in general again absorbed, so that the fluid, on examination, appears to be far more concentrated, and richer in albumen, than is in general the case with such transudations.

<sup>1</sup> Zeitschr. f. wissenschaftl. Zoologie. Bd. 1, S. 88-92.



Even if we cannot anticipate that these propositions can be fully established in science until they have been confirmed by further and more systematically conducted investigations, they yet promise to throw some light on this obscure department of pathological chemistry, and to aid in associating into one distinct scientific whole those disjointed facts which have been concealed amidst a mass of imaginary crases and other chimeras of the same nature. Perhaps we may not be too sanguine, if we look forward to a period in the history of pathology, when these three factors shall yield results from which we may establish a numerical equation which shall express the pathologico-physical process of the transudation.

Although the chemical investigations of the transudations afford us some prospect of a nearer recognition of the mechanical interchange of matter in the healthy and the diseased animal body, they leave us wholly in the dark as to the chemical metamorphoses which these substances undergo during and after their transudation. This is especially the case in reference to those substances which are concealed amongst the *extractive matters*; as for instance, the protein-oxides, pyin, and other matters which probably belong to regressive metamorphosis. These extractive matters consist to a great extent of a substance which is soluble in water, but insoluble in alcohol, and which may be precipitated by basic acetate of lead. It resembles Müllder's tritoxide of protein, but exhibits a different composition when it is present in sufficient quantity to be submitted to an elementary analysis. The same is the case with the substance which is precipitable by acetic acid, and very frequently occurs in the older transudations. It seldom possesses the property, ascribed by Güterbock to pyin, of being soluble in acetic acid, but when we succeed in separating it from the albumen which is simultaneously precipitated by the acetic acid, and otherwise purifying it, it exhibits such a different composition, that we cannot even decide from the analysis whether or not it is a product of the oxidation of protein. This substance does not occur in fresh transudations.

The extractive matters are generally present in larger quantities in the transudations than in the corresponding intercellular fluid or serum of the blood. They are commonly more numerous in the older stagnating fluids than in those which have been more recently separated, and are relatively less considerable in the fibrinous than the serous transudations; whilst in the serum of the normal blood the ratio of the albumen (without fat) to the extractive matters is as 100 to 5, it is as 100 to 8 or even to 16 in fresh fibrinous transudations, and in fresh serous transudations it is as 100 to 12 or even to 30, and in the older serous ones, as 100 to 42, or even to 86. From hence we might conclude that these substances transude from the blood into the cavities in larger quantities than the albumen, and this is proved to be the case by the analyses of normal transudations, as for instance, of the fluid within the pericardium, the cerebral and spinal fluids, the liquor amnii, the tears, and the aqueous humor, in which the ratio rises to 100 : 300; indeed the quantity of albumen may be so much diminished as scarcely to be quantitatively determinable, although its presence may be qualitatively proved by the ordinary tests for the albuminates, as for instance, by Millon's (see vol. i.



p. 290). In general, however, the extractive matters present great variations in quantity, partly because they are somewhat increased by the chemical treatment employed for the albuminates, and partly because they stand in very various relations to the quantity of water transuded, either owing to the constitution of the blood, or to the peculiar structure of different systems of capillaries. Then, too, it must be borne in mind, that in the older originally fibrinous transudations, in which morphological formations have been developed, one portion of the albumen passes into these, whilst another part is converted into extractive substances, which may therefore be both relatively and absolutely augmented in the analysis. Hence it would be superfluous to give the various quantities of extractive matters assigned by our analyses to these transudations.

Scherer found in a dropsical ovarian fluid a "modification of *mucin*," precipitable by water and acetic acid. I have three times observed a similar body in the fluids of hydrocele.

Mack found 0.99% and 0.91% of extractive matters in the *liquor amnii* at the full term of pregnancy, Scherer only 0.06% at the same period, but 0.724% in that of a foetus in the fifth month.

We find only small quantities of neutral saponifiable and saponified fats in the transudations; but even here the nature of the capillaries through which these transudations pass is not without some influence, for the fluids of the capillaries of the cerebral membranes, of the pericardium, of the subcutaneous areolar tissue, as well as of the aqueous humor, are very poor in these substances; although here also, in certain pathological cases, they are often increased relatively to the albumen; but this is only the case when the fluid in question is very deficient in albumen. In transudations which are richer in albumen, the relation between the saponifiable and saponified fats differs little from that exhibited in the blood. We find, however, from a more exact comparison of the individual analyses, that the capillaries must possess a greater permeability for these fats than for the albumen. Thus, for instance, the amount of fat in the solid residue of fibrinous transudations is always somewhat greater than that in the solid residue of the intercellular fluid of the blood; and this probably contributes in some degree to the plasticity of the transudations, to the formation of pus-corpuscles, &c. The liquor amnii forms an exception to the general experience on this point; for in the latter months of pregnancy, when its albumen is diminished, it becomes very rich in fat, and indeed has been found to be actually turbid from the presence of fat-globules: this fat is, however, not a product of secretion of the amnion, but is secreted by the sebaceous glands of the foetus; in fact it is a portion of the vernix caseosa. Mack<sup>1</sup> found 0.125 and 0.013% of fat in the liquor amnii, and I found 0.098% at the full period.

The non-saponifiable fats or *lipoids*, cholesterin and serolin, usually occur in transudations in far larger quantity than the true fats: *cholesterin* is especially found in the fluid of ovarian dropsies, and even oftener in the fluid of hydrocele, in such quantity that these transudations present the appearance of opaque fluids in which glistening nacreous bands of crystals may be seen on agitation, or even occur as a

<sup>1</sup> Heller's Arch. Bd. 2, S. 218-224.



soft semi-fluid mass of cholesterin. As a general rule, transudations, and especially those of a normal character, are by no means so rich in cholesterin as to admit of a quantitative determination of this constituent; but from the microscopic examination of the ether-extract even of normal transudations, we may arrive at the certain conclusion that the amount of cholesterin in the fluid either exceeds, or at all events very nearly reaches that of the true fats. The capillaries generally have the power under certain, not yet accurately determined, conditions of allowing the transudation of cholesterin in larger quantity than other substances; for it is not only in the above-mentioned cases of dropsy that we find accumulations of cholesterin; the choroid plexus of the brain, which secretes a fluid that is very poor in fibrin, is not unfrequently found to be covered with an entire crust of minute plates of this lipid; and how many analyses are there of the transudations into the peritoneum and pleura, in which the quantity of cholesterin has been noted as strikingly great! Indeed we might almost believe that the walls of the vessels possess a peculiar attractive power for the cholesterin, when we reflect on the atheromatous process which is so common in the arteries, if these accumulations of cholesterin cannot be more simply (even if not completely) explained by the circumstance that water, albuminous substances, and salts, are more readily absorbed from the transuded fluid by the lymphatics, or some other means, than the cholesterin, or that by a process of partial absorption its solvent is taken up and removed, and that it is thus compelled to separate in a solid crystalline form in the cavity in which the transudation occurred.

In a hydrocele-fluid, which formed a tolerably consistent pulp, I found 3.041% of pure cholesterin (amounting to 38.202% of the solid residue), and in another fluid of the same nature 1.569%; Simon,<sup>1</sup> in a similar case, found 0.84% of cholesterin, with a little olein and margarin.

*Serolin*, which forms hexagonal or rhombic tablets, whose crystallographic determination has been given in the first volume, and which may be so readily distinguished from cholesterin and crystallizable fatty acids by its peculiar shape, always occurs with the cholesterin in the transudations, but seldom in any considerable quantity.

Since Pettenkofer's discovery of his admirable test for the detection of the *resinous acids of the bile*, many chemists who have investigated morbid transudations have met with these substances in dropsical fluids; and it was only to be expected that these substances, if they occurred in the blood, should also simultaneously pass into the transudations. In every case in which I have hitherto examined dropsical effusions dependent on affections of the liver, I have found in the alcoholic extract, if it has been previously extracted with ether, and usually also in the ether-extract, substances which gave the well-known reaction very distinctly and rapidly, so that they could not be confounded with olein. In dropsy from heart-disease (without any secondary affection of the liver) or from Bright's disease, I never succeeded in detecting these biliary matters. On the other hand, I was much surprised to find unquestionable traces of the resinous biliary acids, together with large quantities of cholesterin, in two cases of hydrocele, when neither by physical exami-

<sup>1</sup> Medic. Chem. Bd. 2, S. 582 [or English translation, vol. 2, p. 495].



nation of the patients, nor from the history of their cases, could I detect any evidence of an existing or previous hepatic affection. This circumstance must remain unexplained till further investigations are instituted.

I must not altogether omit to mention, that from the alcoholic extract of the liquor amnii, and still more from that of the vernix caseosa of an infant that had gone its full time, I obtained a substance which, although precipitable only by basic acetate of lead, gave no biliary reaction with sugar and sulphuric acid: the ammonia-salt of this acid crystallized under the microscope in broad plates.

That *bile-pigment* passes into the transudations, both normal and morbid, in cases of icterus, was long ago inferred from the characteristic color of such fluids, and has subsequently been placed beyond a doubt by chemical experiments. It is, however, remarkable that in the two above-mentioned cases of hydrocele, in which resinous biliary acids were found, traces of bile-pigment were also present, besides a very large amount of cholesterin. Its presence might have been very easily established with certainty, but it was not rendered perceptible until a part of the albumen had been precipitated from the fluid by acetic acid, when, on boiling, there was formed a green coagulum, and the supernatant fluid appeared of a somewhat deep-green color.

Heller has arrived at similar results in his investigation of various putrid, purulent, sanguineous hydrocele-fluids; but he also found uric acid, urea, margarate of soda, and glycocholate of soda in abundance.

It has been already mentioned (in vol. i. p. 258) that *sugar* is found in the serous exudations in diabetes, in the same manner as bile-pigment in icterus. After the discovery of this substance in healthy blood, it might be expected that it would likewise occur in the ordinary transudations, but there is no direct proof that this is the case, since the quantities which we obtain for analysis are generally too small to allow of any accurate search for sugar.

In a kilogramme and a half [or nearly three pints and a half] of the peritoneal transudation of a drunkard with granular liver (a quantity which would have been quite sufficient for the determination of sugar, if it had been present in the same proportion as in normal blood-serum), I sought in vain for this substance; but after what has been already remarked (see vol. i. p. 483), regarding the formation of sugar in the liver, it is probable that the production of sugar is interfered with in cases of hepatic disease, which might account for its not being found in this case.

We have already spoken (in vol. i. p. 154) of the occurrence of *urea* in normal and excessive transudations. Since this substance has been found even in the aqueous humor as well as in the liquor amnii, and has also been detected by C. Schmidt<sup>1</sup> in the fluid exudation in a case of chronic hydrocephalus in which no renal disease was present, we might fairly assume that it occurs in the circulating blood, and escapes through the walls of the capillaries in these parts with the water and other substances which permeate easily, and is then found in the exudations in a quantity corresponding to the amount of urea in the blood; indeed, if the functions of the lymphatics were disturbed, it might even accumu-

<sup>1</sup> Charakteristik der Cholera. S. 124.



late in larger quantity, since in all probability it passes through the animal membranes far more readily than other organic substances, or at all events as easily as the alkaline salts. Hence the reason why it is so frequently met with in the transudations in renal affections is simply this, that under these circumstances it accumulates in the blood in much larger quantities than usual, and such as admit of being easily detected.

Marchand<sup>1</sup> once found 0.42% of urea in a peritoneal effusion in a woman, which contained 4.78% of solid constituents.

Since urea is often found in such large quantities in the exudations from the capillaries, we should naturally expect that the other products of retrograde metamorphosis (whether as yet detected or not in the blood), as for instance, hippuric acid, creatine, uric acid, &c., would also occur there; but these, and such like substances, have at all events not as yet been recognized in such fluids by any analyst. It is more than probable that creatine occurs in the liquor amnii, for Scherer obtained from it, by means of chloride of zinc, a substance very similar to Pettenkofer's creatine and zinc compound.

In addition to the salts formed by the combination of the alkalies with fatty acids (the soaps), the transudations likewise contain other organic-acid salts; the alkali in them is certainly for the most part in combination with the albumen, but, as has been already mentioned, we sometimes find no albuminate of soda in the transuded fluid, and yet the ash is rich in alkaline carbonates: indeed, every transudation, if it only contains this alkaline albuminate, also contains other compounds of alkalies with organic acids, which dissolve readily in spirit, and impart to the alcoholic extract its well-marked hygroscopic properties. If the spirituous extract has been freed as completely as possible from fat and fatty acids, we yet always obtain carbonates on incineration. But what the acid is, and whether there are more acids than one, are points which cannot be determined in consequence of the small quantity of the substance or substances in question in the transudation, and even in its solid residue. We should be somewhat inclined to believe that this acid in combination with an alkali might be *lactic acid*, since this acid must at all events pass from the muscles into the blood, and must likewise be conveyed to the blood by the process of digestion. Those disturbances of the circulation on which excessive transudations depend, are usually associated with a diminished interchange of gases in the lungs, and consequently a less regular oxidation of the combustible constituents of the blood: hence it is very probable that under such conditions alkaline lactates make their way through the capillaries in excessive quantity, and that the absolute and relative augmentation of the alcoholic extract (as well as of its ash) in the transudation, as compared with the blood-serum, depends on its larger quantity of lactates. If the blood becomes acid, as Scherer<sup>2</sup> has shown to be the case in many forms of puerperal fever, it is very natural that the transudations should also contain a free acid; in these cases, Scherer has convinced himself, by direct analysis, of the presence of lactic acid. In a transudation of this nature he found 0.105% of free hydrated lactic acid.

We do not meet with true acid transudations, except when the blood

<sup>1</sup> Journ. f. pr. Ch. Bd. 11, S. 458.

<sup>2</sup> Untersuch. z. Pathologie. S. 147-194.



previously contains a free acid; for, in the first place, it is improbable that the walls of the capillaries should, during the act of simple transudation, possess the power of decomposing the salts of the blood into acids and bases, and that they should allow only of the transudation of the former; in the simple *transudations* no supplementary development of free acid appears, however, to occur; it is only when suppuration and similar processes have taken place in *exudations* that the fluid is observed to have an acid reaction; indeed, it is generally dependent on a process of fermentation set up in the fat.

Simon<sup>1</sup> once examined a specimen of the fluid of pemphigus which had a strong acid reaction; he considered the free acid to be the acetic, in consequence of its apparent volatility; this was doubtless an uncommon condition; the fat, in this case, as in ordinary pus, may undergo butyric fermentation; for all *vesicular cutaneous eruptions*, whether they are produced artificially by vesicants, or are the natural morbid phenomena of pemphigus, herpes, or eczema, have an alkaline reaction, and contain albumen, as Andral<sup>2</sup> had formerly observed, and belong to the simple transudations. It is only the vesicular cutaneous eruption, which is known as sudamina, which invariably presents an acid reaction; it, however, does not arise, like the other vesicular eruptions, in consequence of local congestion; the fluid within the vesicles in sudamina contains *no albumen*, and hence is not to be classed amongst the transudations. We shall return to the causes of this acid reaction when we treat of the sweat.

Heintz<sup>3</sup> has found a crystallizable organic acid, which sublimed without decomposition, and presented a very great similarity to succinic acid in the fluid of cysts containing echinococci (see vol. i. p. 77); as Des-saigne<sup>4</sup> has proved that succinic acid may be formed from butyric acid by oxidation, we need no longer regard the occurrence of succinic acid in the animal organism as extraordinary.

It may be readily inferred from some of the preceding observations that the *soluble mineral salts* transude through the walls of the capillaries in larger quantity than any organic matter; but a review of most of the good analyses of these exudations, in so far as the subject has been yet investigated, leads us to regard the following points as established: water in every case transudes in the greatest quantity; the fibrinous transudations which approximate most nearly to the plasma, in reference to their amount of solid constituents, contain almost constantly *rather less salts than the intercellular fluid*; while the average amount of mineral substances in the latter is about 0.85%, we usually find in fibrinous transudations from 0.73 to 0.82% of salts. In the true dropsical accumulations the proportion of the salts is, however, very different; such fluids contain an amount of salts often exceeding that which is found in normal blood-serum, the number sometimes rising to 0.86, or even to 0.95%; here, however, the general rule also holds good, that the transudation contains rather less salts than the *corresponding liquor*

<sup>1</sup> Med. Chem. Bd. 2, S. 579 [or English translation, vol. 2, p. 488].

<sup>2</sup> Compt. rend. T. 26, p. 650-657.

<sup>3</sup> Jenaische Ann. d. Physiol. u. Med. Bd. 1, S. 180-191.

<sup>4</sup> Compt. rend. T. 30, p. 50.



sanguinis; for in dropsy the blood is always rich in salts, as we have already seen in vol. i. p. 623. In proportion to the richness of the dropsical blood, so much the richer in salts is the transudation; the latter, however, always contains a fraction less salts than the former. This proposition can only be established by a careful comparison of all the analyses which we at present possess; but the careful investigations of Schmidt have rendered it certain that it may be regarded as a law which may be expressed by a general formula. Schmidt has, however, further shown that this rule presents an exception when, simultaneously with the transudation in the interior of the body, there is an elimination of albumen externally, that is to say, when albuminuria is at the same time present: in that case, a larger quantity of salts, and far less albumen transude through the capillaries of the peritoneum into its cavity than would have been the case if there were no external loss of albumen; hence in such cases the number representing the mineral salts often equals, and may even exceed, that of the organic matters.

A similar condition to that which we have just noticed may occur with regard to the amount of salts in the liquor amnii: in the fifth month of pregnancy we find, according to Scherer, 0.925% of salts with 0.767% of albumen; the albumen is here not lost, but is otherwise applied, and hence the considerable and extraordinary augmentation of the salts in the transudation of the amnion: towards the end of pregnancy the ratio of the albumen to the salts is still more unfavorable; in these cases there has been found only 0.37% of albumen with 0.92% of salts, and Scherer found actually only 0.082% of the former with 0.706% of the latter.

The relative proportion of the salts in the transudations through the intestinal capillaries in cholera, or in diarrhoea after drastic purgatives, is altogether peculiar; in these transudations the quantity of the salts is five, or even seven times as great as that of the albumen; at the same time they are richer in water than those of any other kind; there is here no direct proportion between the composition of the blood and that of the transudation, as in the dropsical effusions; but we rather observe that the fluids stand in an inverse relation to one another, the blood being poorer in water, poorer in salts, and far richer in albumen, than the effused fluid. (See our observations on the evacuations and the blood in cholera, vol. i. pages 539 and 634.)

The salts occurring in the transudations are precisely similar in their nature to those of the intercellular fluid, and they are found in almost exactly the same relative proportions to one another in the transudation and in the blood-serum; as in the latter fluid, the chlorides considerably preponderate over the phosphates, sulphates, and carbonates, and the soda-compounds over those of potash. A very important exception to this rule, in so far as the physiology of secretion is concerned, has been observed by C. Schmidt in the constitution of the salts which occur in the fluid within the lateral ventricles of the brain (the transudation from the choroid plexus). Whilst the transudation from the pia mater and arachnoid contains the salts in precisely the same proportions as occur in the fluids of other serous membranes, the mineral constituents here contain a great excess of potassium-compounds and phosphates, so that



the proportion of the potassium to the sodium, and that of the phosphates to the chlorides, approximates more nearly to that which is presented by the salts contained in the blood-cells. While (according to Schmidt) there are contained in the salts of the transudation from the peripheral cerebral capillaries 2·8% of potassium with 40·0% of sodium (a ratio almost identical with that which is presented by the salts of the serum), the salts of the transudation from the choroid plexus contain on an average 17·8% of potassium, and only 27·2% of sodium. In the same manner the constitution of the transudation within the lateral ventricles approximates to that of the blood-cells in regard to the chlorides and phosphates; while in 100 parts of the salts of the serum there are contained 5·6 of phosphoric acid with 45·2 of chlorine, Schmidt found 8·9% of phosphoric acid and 37·6% of chlorine in the salts in central hydrocephalus. Hence the cerebro-spinal fluid is not to be regarded as a mere *transudation* or filtrate from the blood, but as a peculiar *secretion* in whose formation the blood-corpuscles appear to take an essential part in so far as the salts are concerned.

We may further readily convince ourselves that *alkaline carbonates* are also present in the normal alkaline transudations, by placing fresh fluids of this kind which have been obtained by paracentesis in a vacuum, and as completely as possible removing the gas, then adding acetic acid without allowing the access of air, expelling from the serum the absorbed carbonic acid which has been liberated by the action of the air-pump, as well as by displacement with hydrogen gas, and determining it in the ordinary manner; in short, by applying the method which I<sup>1</sup> adopted for the determination of the combined carbonic acid in the blood.

In cholera, and after the use of drastic purgatives, the composition of the salts in the transudations—that is to say, in the intestinal dejections—differs essentially from that in ordinary effusions; here, according to the accurate investigations of Schmidt, the compounds of chlorine and sodium, preponderate over the phosphates and the potassium-compounds even to a greater extent than in ordinary transudations. On the other hand, transudations of any other nature that may accompany the cholera process generally present the opposite relation to the ordinary serous effusions; whilst, for instance, in other cases, the normal as well as the excessive transudations from the cerebral capillaries contain only a small amount of solid constituents, in which the mineral substances preponderate over the organic in ratios varying from 5 : 2 to 17 : 4 (or from 2·5 : 1 to 4·25 : 1), we find that in cholera the cerebral transudations are not only far richer in solid constituents, but that of these the organic actually exceed those of a mineral nature; amongst the latter the compounds of sodium and chlorine occur, however, in far less quantity than in ordinary transudations; indeed the potassium-compounds and the phosphates must preponderate the more, since the serum in cholera contains far more of these compounds than normal serum. Unfortunately, Schmidt had no opportunity of making an accurate analysis of the salts of the cerebro-spinal fluid in cholera, in order to prove by numerical results the preponderance of the phosphates and of the chloride of potassium in this transudation.

<sup>1</sup> Berichte d. k. sachs. Gesellsch. d. Wiss. Bd. 1, S. 96–100.



No *salts of ammonia* can be detected in normal and fresh transudations obtained by paracentesis (see vol. i. p. 403); and if some observers have believed that they had found them, this was dependent on the causes of error to which we have already alluded. Even in several secretions of long standing in the tunica vaginalis testis, I was unable to recognize ammonia with certainty. If indeed we attach any importance to the analyses of fluids actually becoming putrid, we might then always find ammonia; and, on the other hand, we must of necessity always find ammonia in the intestinal transudations, since the decomposition of such substances proceeds with such extraordinary rapidity in the intestine, that we must altogether abstain from analyzing them, if we wait till we can obtain them in their perfectly pure, native state. Ammonia must, however, be found, and indeed has been found by Schmidt in all transudations arising from blood containing ammonia or much urea (see vol. i. p. 634), and hence it is not uncommonly met with in dropsical exudations in albuminuria.

Finally, we may very readily convince ourselves that the transudations, like the animal fluids generally, contain free *gases*, by employing a simple gas-apparatus in communication with the air-pump. Amongst the mixture of gases that are evolved from the transudation, carbonic acid is found to preponderate, although the presence of oxygen and nitrogen may be recognized with certainty. From determinations which can certainly only be regarded as approximate ones, I obtained from fresh transudations discharged by paracentesis, on an average, a less quantity of gas generally, but always relatively more carbonic acid than from the fresh blood-serum of persons for whom venesection had been prescribed solely in consequence of plethora.

The apparatus which I employed for this somewhat superficial investigation was constructed in the following manner: Two flasks are united to one another by glass tubes and corks; in the lower one we place the fluid to be examined, and in the upper one, which is two-necked, we place pure almond or olive-oil; from the lateral tube there proceeds a glass-tube filled with oil to the bottom of a third flask; this last flask, whose bottom is covered with oil, is brought in connection with the air-pump. On now making a vacuum, the bubbles of gas which are developed from the blood rise into the upper flask (which stands reversed upon the lower one), and drive the oil through the communicating tube into the third flask; if now we allow air again to enter the last flask, the oil is only in part forced back into the upper flask; the bulk of the gases contained in it is diminished to the volume corresponding to the external atmospheric pressure. Since any resorption by the aqueous fluid in the lower flask is prevented by the oil, we may at all events form some idea of the quantity of gases which such fluids contain.

It is unnecessary to give a special description of the different methods which may be devised for the qualitative and quantitative analysis of the transudations, since the same rules hold here which we have fully noticed when treating of the "analysis of the blood" and of the individual animal substances, in their respective chapters in the first volume. We may, however, be permitted to make the single remark that here, as indeed in every investigation of an animal fluid, the microscopical analysis



must always precede the chemical. Thus, for instance, the presence of blood-corpuscles would at once destroy any claim that the fluid might otherwise possess to the character of a pure transudation; again, if the object itself be not pure, the results of the experiment must be in a corresponding degree worthless. The same observation equally applies if vibriones and other formations which accompany putrefaction are present. If none of these are to be observed, we may frequently perceive cells in the transudation, which resemble lymph-corpuscles or pus-cells. Without further investigation, they have, however, no more claim to be considered as pus-corpuscles, than those which are produced from mucous membranes; it is only when true pus is present (and in some cases it is very difficult to decide this point) that the object should be regarded as not a pure exudation. In transudations which contain no fibrin, the substances in suspension, as, for instance, fat, epithelial cells, cells in the process of development, and similar bodies, must naturally be separated as far as is possible from the fluid by filtration; if, on the other hand, coagulated fibrin be present, its absolute quantity cannot be determined with accuracy; we must further ascertain by microscopical investigations whether an excess or deficiency of morphological elements be present, and we must obviously take this circumstance into consideration in estimating the quantity of fibrin contained in the transudation.

The *quantitative relations* in which the various transudations, either in the normal or excessive state, are thrown off from the blood, are so various, that no general rule can be established even for each individual capillary system. They become, however, of the highest importance in relation both to the mechanical and the chemical metamorphosis of matter in the healthy and the diseased animal body; but here the amount of the transudation is only of interest in so far as the individual cases have reference to special conditions, and may accordingly be applied to the establishment of a more general view.

As in the preceding pages we have already sufficiently noticed the *genesis* of the transudation, in so far as we need here consider the general metamorphosis of matter, it only further remains for us to allude to the *physiological value* of the normal transudations, and the uses of the abnormal ones as channels for pathological processes (as after inwardly directed crises, &c.); but this is unnecessary, since the former pertains to purely physical physiology, and the latter are altogether beyond the domain of scientific investigation.

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## MILK.

This glandular secretion, which is peculiar to the mammalia, is generally of a white, but frequently of a bluish-white color, more rarely of a somewhat yellowish tinge, opaque, without odor, of a slightly sweet taste, and an alkaline reaction. Its specific gravity fluctuates, according to Scherer,<sup>1</sup> between 1.018 and 1.045, but in women is on an average 1.032 (Simon).

<sup>1</sup> Handwörterb. der Physiol. Bd. 2, S. 449-475.



As is well known, milk, when allowed to stand for some time, exhibits on its surface a thick, fatty, yellowish-white stratum, the cream, while the fluid below has become poorer in fat, and has, therefore, a greater specific gravity than fresh milk, and has likewise a more bluish-white color. When milk stands in a not very low temperature, it gradually begins to exhibit an acid reaction, remaining for some time thinly fluid, more especially after it has been repeatedly boiled. But if it has not been boiled, and the temperature be somewhat above the mean, and if there should be considerable electrical tension in the atmosphere, the acid will increase to so great a degree that the casein of the milk will be precipitated; that is to say, the milk will coagulate, become thick, and gradually be converted into a moderately thick pulp. The milk may be made to coagulate artificially by rennet, both when it has an acid as well as an alkaline reaction (see vol. i. p. 334). When exposed to rapid evaporation, milk becomes coated with a dense white membrane.

It would, of course, be superfluous to make any remarks as to the *mode of procuring* animal milk; it must, however, be observed, that it frequently is extremely difficult to obtain any considerable quantity of milk from women who are suckling. We need not, however, enumerate any of the well-known manipulations and methods, which are familiar to every practitioner, for procuring a sufficient quantity of milk to serve for a physical examination. The special forms of apparatus employed for this purpose are almost all based upon the principle of rarefaction or suction, but none appear so perfectly to fulfil their object as the one recently proposed by M. Lampérière.<sup>1</sup>

This apparatus is made of caoutchouc, in the form of a mouth, provided with lips, gums, and elastic cheeks, the latter being connected with the short neck of a small tubular retort, into which is introduced a glass tube, which, when necessary, receives the milk, either by the action of the woman herself, or by the aid of a small air-pump.

Fresh milk appears, on *microscopic* examination, as a clear fluid, in which fat-globules, the so-called *milk-globules*, are suspended, as in an emulsion.

These *milk-globules* differ considerably *in size*. The majority have a diameter of from 0.0012''' to 0.0018'''; and although they are rarely found to measure 0.0038''' in fresh milk, Henle states that he has found them to be 0.014'''; and, according to Raspail and Donné, they are even sometimes 0.044'''.

When examined under the microscope, without the addition of any chemical reagent, these globules exhibit no trace of any *investing membrane*, although its existence may very readily be demonstrated beyond all doubt, in two different ways. One method, which was suggested by Henle,<sup>2</sup> consists in observing, under the microscope, the action of diluted acetic acid on the milk. The milk-globules exhibit changes of form under these circumstances which they could not possibly experience if they were mere fat-globules, for they become much distorted, some appearing caudate, and others biscuit-formed. From the greater number there escapes a small drop, which appears almost like the nucleus of a

<sup>1</sup> Compt. rend. T. 30, p. 219.

<sup>2</sup> Allg. Anat. S. 942.



larger globule, and is soon displaced by another small fat-globule, which emerges from the milk-globule, and either combines with the larger globules, or is only made to project in such a manner, that the milk-globule exhibits a faint resemblance to a fermentation-fungus in the process of development. When treated with a less diluted acetic acid, the milk-globules become confluent. Mitscherlich's<sup>1</sup> method, which we described in detail in vol. i. p. 341, proves, in even a more distinct manner, the presence of a membrane round the milk-globules.

Occasionally also the milk exhibits certain morphological elements, which, from their invariable presence in colostrum (the first milk yielded after delivery), have been termed *colostrum-corpuscles* (the *corps granuleux* of French physiologists). They are irregular conglomerations of very small fat-globules, which are held together by means of an amorphous, somewhat granular substance. Their diameter varies, according to Henle, from 0.0063''' to 0.0232'', but may be considered on an average to be about 0.0111'''. The fat-granules of these masses are more easily dissolved by ether than those of the milk-globules; acetic acid and potash dissolve the granular combining substance, and scatter the fat-globules: an aqueous solution of iodine imparts an intense yellow color to the colostrum-corpuscles. There can, therefore, be no doubt that these molecules are merely very small fat-globules imbedded in an albuminous substance. There is no appearance either of a nucleus or of an investing membrane.

These molecules generally disappear on the third or fourth day after delivery, although they have been found as late as the twentieth day in perfectly healthy women. As a general rule, however, these corpuscles return whenever any disease supervenes after delivery, or in case the mother is attacked by any acute affection.

In all cases in which I examined the milk of women shortly after their confinement, or of nurses who were suffering from any acute disease, such as inflammations, acute exanthemata, typhus, &c., I always found colostrum-corpuscles, and, in addition to these, true granular cells, having a microscopically and chemically demonstrable investing membrane, and frequently also an obvious nucleus; the granules of these "inflammatory globules" were tolerably large, transparent, and rich in fat, resembling those which are so commonly observed in the grayish-black sputa of chronic catarrh (in the emphysema of old persons).

*Epithelial cells* and *mucus-corpuscles* are only incidental admixtures of the milk, and are, therefore, more frequently observed in morbid affections than in the normal condition.

*Fibrinous coagula* only occur when the milk contains blood.

*Blood-corpuscles* have rarely been found in the milk, and are only present in it in abrasions of the nipples, or in similar affections.

*Infusoria*, or some of the *lower forms of vegetation*, are occasionally found in cows' milk, especially in the so-called *blue-milk*. J. Fuchs<sup>2</sup> refers this coloring of the milk to the presence of an infusorium, which he terms *vibrio cyanogenus*; but Bailleul<sup>3</sup> ascribes it to a byssus.

My observations on this subject are limited to the ordinary manner in

<sup>1</sup> Göschel's Jahresber. Bd. 2, S. 19.

<sup>2</sup> Handwörterb. d. Physiol. Bd. 2, S. 470.

<sup>3</sup> Compt. rend. T. 17, p. 1138.



which the milk acquires this blue color. When freshly drawn, the fluid is generally perfectly white, assuming this peculiar blue shade of color on the formation of the cream, which exhibits pale blue specks, extending at first scarcely half a line deep, and appearing in detached groups upon the surface of the otherwise white fluid. These specks become darker, and gradually increase downwards and laterally, until they commingle. The curd which separates from the cream is colorless, and the bluish cream contains rod-like, colorless vibriones, similar to those described by Fuchs. I only once observed a distinct formation of byssus.

We have already become acquainted with the most important *chemical constituents* of the milk in our considerations of the organic substrata. This is especially the case with *casein* and *milk-sugar*, which have already been very fully treated of, not only in reference to their chemical properties, but also to their occurrence in variable quantities under different physiological and pathological conditions (vol. i. pages 263, 340). Knobloch<sup>1</sup> instituted a series of experiments upon one and the same cow in reference to the constitution of the milk at different seasons of the year, and according to the length of time during which each milking was continued. From these observations it would appear in reference to the amount of casein in the milk, in the first place, that its quantity is greater towards the close than at the beginning of each individual act of milking, whilst the quantity of water decreases; and in the second place, that the milk is poorer in casein on winter than on summer fodder. In winter the amount of casein and of salts insoluble in spirit rose during the milking from 7.07% to 7.08%, whilst in summer it varied from 8.40% to 8.67%. It still remains, however, for us specially to notice the third organic constituent of the milk, namely, the *fat* or *butter*. The fat of women's milk has not yet been subjected to any exact qualitative analysis, but the butter of cow's milk has been carefully analyzed by Chevreul,<sup>2</sup> and more recently by Bromeis<sup>3</sup> and Lerch.<sup>4</sup> Pure milk-fat is almost colorless, or at most is but faintly yellow; after being melted it solidifies at + 26°.5. It becomes soft and greasy at a temperature exceeding + 18°. One part of this fat dissolves in 28.9 parts of boiling alcohol of 0.822 sp. gr. It easily becomes rancid on exposure to the air, and then forms volatile fatty acids; hence it imparts a somewhat reddish color to moist litmus paper, even when in a comparatively fresh state. It is perfectly saponifiable, and yields, in addition to glycerine, margaric, oleic, capric, caprylic, caproic, and butyric acids, or in place of the two latter, vaccic acid (vol. i. pages 62-74). Bromeis calculated the composition of butter, from the quantity of the acids which he obtained from it, as equal to 68% of margarin, 30% of olein, and 2% of true butter-fat; but this calculation affords only an approximate representation of the composition of the milk-fat, since its constituents appear to vary considerably under different physiological relations.

The quantity of fat contained in milk appears to vary very considerably, for Simon<sup>5</sup> found in *women's milk* from 2.53 to 3.88% of butter; Clemm<sup>6</sup> and Scherer found on the fourth day after delivery 4.297%, on

<sup>1</sup> Kunst und Gewerbeblatt f. d. k. Bayern, 1851, S. 144-147.

<sup>2</sup> Recherches sur les corps gras. Paris, 1822. <sup>3</sup> Ann. d. Ch. u. Pharm. Bd. 42, S. 46 ff.

<sup>4</sup> Ibid. Vol. 49, p. 212.

<sup>5</sup> Die Frauenmilch u. s. w. Berlin, 1838. <sup>6</sup> Handwörterb. d. Physiol. Bd. 2, S. 464.



the ninth day 3.532%, and on the twelfth day 3.345%; Chevallier and Henry<sup>1</sup> found 3.55%, and Haidlen<sup>2</sup> 3.4 and 1.3%. Simon found in *cow's milk* from 3.80 to 5.10%, Herberger 3.89 and 3.75%, Chevallier and Henry 3.13%, Boussingault<sup>3</sup> 3.90%, Playfair<sup>4</sup> 4.90% (as the mean of nine observations made on the milk of the same cow), and Poggiale<sup>5</sup> 4.38% (as the mean of ten analyses). Clemm found 6.952% in *mares' milk*; Simon 1.21, and Peligot 1.29% in *asses' milk*. Chevallier and Henry found 4.2% in *sheep's milk*. Payen<sup>6</sup> found 4.08, Chevallier and Henry 3.32, and Clemm 4.251% in *goats' milk*. Schlossberger<sup>7</sup> found 2.65% in the milk of a buck; and in *bitches' milk* Simon first found 16.2, and afterwards 13.3%; while Dumas<sup>8</sup> found from 7.32 to 12.40%, and Bensch<sup>9</sup> 10.75 and 10.95%.

Simon found 5.00% of butter-fat in the *colostrum* of women's milk, and coincides with Boussingault in giving 2.6% as the quantity occurring in that of the cow. Chevallier and Henry found 5.0% in that of the ass, and 5.2% in that of the goat.

L'Heritier found, from a comparative analysis of the milk of two nursing mothers, aged twenty-two years, one of whom was dark and the other fair, that the milk of the former was richer in fat (containing 6.48 and 5.63%) than that of the latter (which contained 3.55 and 4.05%). This observation, which requires to be confirmed by further investigations, is the more remarkable, as the other organic constituents were considerably increased in the milk of the *brunette*.

L'Heritier<sup>10</sup> found from 1.62 to 1.70% of casein, and from 7.12 to 7.00% of milk-sugar in the *brunette*, and 1.00 and .95% of casein; and from 5.85 to 6.40% of sugar of milk in the *blonde*.

Peligot made the striking observation, which has recently been confirmed by Reiset,<sup>11</sup> that the milk which is last yielded during milking or artificial suction, is much richer in fat than that which is first drawn, although the composition of both portions, is otherwise the same. It was supposed from these observations, which were at first limited to the ass and the cow, that the milk lost some portion of its cream in the mammary glands, while the more watery and less fatty milk collected in the lower part of the udder; but as Reiset has made the same observations in respect to women's milk, which had been drawn in fractional portions from the breast, the cause can scarcely be dependent upon such simple mechanical relations as these.

Peligot found 6.45% of butter in the first third of the milk of an ass, 6.48% in the second, and 6.50% in the last portion. Reiset found precisely similar relations in the milk of two cows, provided a full period of four hours had intervened between both times of milking; for when the animals were milked after intervals of two hours only, there was no perceptible difference in the various portions of one and the same milking.

<sup>1</sup> Journ. de Pharm. T. 25, p. 333 et 401.    <sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 45, S. 273.

<sup>3</sup> Ann. de Chim. et de Phys. 3 Sér. T. 8, p. 98.

<sup>4</sup> Lond., Edin., and Dublin Phil. Mag. Vol. 23, p. 281.

<sup>5</sup> Compt. rend. T. 18, p. 505-507.

<sup>6</sup> Ann. de Chim. et de Phys. 1839, p. 144.

<sup>7</sup> Ann. d. Ch. u. Pharm. Bd. 51, S. 431.

<sup>8</sup> Compt. rend. T. 21, p. 708-717.

<sup>9</sup> Ann. d. Ch. u. Pharm. Bd. 61, S. 221-227.

<sup>10</sup> Traité de Chimie pathologique. Paris, 1842, p. 638.

<sup>11</sup> Ann. de Chim. et de Phys. 3 Sér. T. 25, p. 82-85.



When the collective milk of a cow yielded 4.5% of fat, the last portions of the milk were found to contain 7.63, 7.53, and 8.40% of butter. The milk of a nurse, aged 27 years (seven months after delivery), yielded more fat after the child had drawn the breast (on an average 5.54%) than before its application (on an average 3.24%).

According to Simon's investigations, the quantity of fat contained in woman's milk remains nearly the same throughout the entire *period of lactation*.

*The nature of the food* affects, at least in some degree, the quantity of fat contained in the milk. Boussingault<sup>1</sup> found that cows fed upon carrots, without the leaves of the plant, yielded milk containing 1.25% of fat, while the milk contained only 1.4% of butter when the food consisted of oats and lucerne. Playfair thought he could perceive an increase in the quantity of butter in the milk when the cows were fed on potatoes. The result of experiments made by Boussingault<sup>2</sup> on two cows was as follows: after feeding the animals on beet-root, the milk of one cow was found to contain 4.56%, and that of the other 3.42% of fat; when the food consisted of the after-crop of grass, the milk yielded 3.92 and 4.39%, and 3.97 and 4.63% when potatoes were used. Payen and Gasparin<sup>3</sup> found 3.53% of butter in the milk of a cow which had been fed in the ordinary manner, and 4.87% when the food consisted of maize-cake. Dumas found that the milk of bitches was on an average somewhat richer in fat when they had been fed on vegetable than on animal food.

A mere superficial mechanical investigation would be sufficient to show that the milk must be poorer in fat during disease; the fact has, however, been fully confirmed by some exact analyses made by Donné, Herberger, and Simon.

I found 3.39% of fat in a portion of cows' milk which became blue when the cream had formed. Three weeks after the disappearance of this phenomenon, the milk yielded 4.934% of fat, although the animal was fed on the same food.

No exact investigations have as yet been made on the *extractive matters* found in milk, or in reference to the different quantities in which they occur in different milk.

In reference to the *salts* of the milk, it must be observed, that the soluble salts consist of the chlorides of sodium and potassium, alkaline phosphates, and, in addition to these, of the potash and soda which are combined with the casein in the milk. The insoluble salts consist of the phosphates of lime and magnesia, which principally belong to the casein (see vol. i. p. 337). No sulphates or salts of ammonia are found in fresh milk (see vol. i. p. 398). Haidlen<sup>4</sup> found a little peroxide of iron in the ash of cows' milk.

The milk of women contains, according to the investigations of most observers, from 0.16 to 0.25% of salts, cows' milk from 0.55 to 0.85%, and the milk of the bitch from 1.2 to 1.5%.

The amount of the *soluble salts* in the milk is in general smaller than that of the insoluble phosphates. There occur about 0.04 or 0.09% of

<sup>1</sup> Ibid. T. 11, p. 433.

<sup>2</sup> Ibid. T. 12, p. 153.

<sup>3</sup> Compt. rend. T. 18, p. 797.

<sup>4</sup> Ann. d. Ch. u. Pharm. Bd. 54, S. 273.



soluble salts in the milk of women, and 0.21% of soluble and 0.28% of insoluble salts in the milk of the cow. According to Dumas, the milk of the bitch contains 0.71% of soluble and 0.77% of insoluble salts, when the food has been mixed, and 0.45% of soluble and 0.57% of insoluble salts, when the food consisted of animal substances. Bensch found in the milk of a bitch, which had been exclusively fed on meat, 1.252% of ash, of which 1.165 were phosphates of lime and magnesia.

The ash of cows' milk contains, according to Weber's analysis, conducted by Rose's method, 14.18% of chloride of potassium, 4.74% of chloride of sodium, and 23.46% of potash, and 6.96% of soda (combined with phosphoric, sulphuric, and carbonic acids). The ash of ox-blood, on the other hand, after the abstraction of the peroxide of iron, contains 38.82% of chloride of sodium, no chloride of potassium, 29.09% of soda, and only 11.44% of potash. This milk, therefore, independently of the absolutely small quantity of salts, contains a relatively less amount of soda compounds and alkaline chlorides, but a much larger quantity of potassium-compounds. In the ash of milk, we moreover find, according to Weber's analysis, 28.4% of phosphoric acid, while in the ash of the blood (according to the same analysis) there is only 7.74% of this acid, after deducting the iron. Finally, there is 17.34% of lime, and 2.20 of magnesia in the ash of the milk, while there is only 1.90% of lime, and 0.75% of magnesia in the ash of the blood (after a similar deduction of the peroxide of iron). Hence the milk exhibits a considerable excess of phosphoric acid and earths over the blood. The phosphoric acid present in the milk-ash is almost wholly tribasic. We shall in a future part of the work see the importance of these comparative numbers, in relation to the theory of the secretions and the metamorphosis of matter generally.

*Alkaline carbonates* are also present to some extent, if not in all kinds of milk, at all events in cows' milk. Thus, when two samples of fresh milk, one unmixed and the other treated with a little acetic acid, are placed under the receiver of an air-pump, and we produce a vacuum, the latter will be found to contain a much larger quantity of gas, that is to say, of carbonic acid, than the former.

*Lactic acid* is not contained in fresh milk, as we have already shown in vol. i. p. 98, and it only appears to be formed abnormally in the udders of graminivorous animals. The freshly drawn milk of herbivorous animals always exhibits a slight alkaline reaction, and is only rendered acid when the food of the animal has been scanty and poor in quality. It still remains for us to determine whether in these cases, the acid reaction invariably depends upon lactic acid, or, as may possibly be the case, on the presence of *acid phosphates*, or even on *butyric acid*. The milk of the bitch is, according to Bensch, neutral when the animal has been kept on vegetable food; whilst it is always acid when the food has been exclusively animal. This acid reaction is most probably owing to the acid phosphates, and more especially to superphosphate of lime. Mole-schott<sup>1</sup> found that the milk of two cows had a strongly acid reaction several days before and after calving during the winter.

Free *gases*, and more especially carbonic acid, can always be shown to

<sup>1</sup> Arch. f. physiol. Heilk. Bd, 11, S. 696-698.



be present in fresh milk, according to the method already described at p. 55.

Abnormal constituents have in general been but rarely found to exist in the milk, although our daily experience of the injurious influence exerted by the milk of some women on the children they suckle, and frequently by that of cows on the life of their calves, clearly indicates the existence of chemical metamorphoses in the milk, and the presence within it of certain abnormal substances. *Albumen* is the most frequent of these abnormal constituents of the milk; it is present in inflammatory affections of the mammary glands, when the milk contains blood and pus; and it is perhaps normally present in the contents of the lactiferous ducts in all periods except during lactation; at all events, Simon found 19.834% of a substance coagulable by heat in the fluid secreted by the udder of an ass, fourteen days before foaling. The colostrum of the cow coagulates on being boiled, but not when treated with rennet. We must not, however, assume that when the milk coagulates on being heated it necessarily contains albumen, for Scherer has obtained a casein from normal milk which coagulated by heat, while both Dumas and Bensch found that the milk of the bitch became pulpy, and was even almost completely coagulated on being heated, when the animal had been kept on vegetable food as well as when it was fed on animal matters, while on cooling it very frequently again became thinly fluid.

Marchand<sup>1</sup> found dissolved *hæmatin* in the milk of a diseased cow, without, however, being able to detect any blood-corpuscles under the microscope.

*Fibrin* occurs in the milk only when the latter contains blood; at least, as far as my own experience extends, it is never present except simultaneously with blood-corpuscles, or at least with *hæmatin*.

Rees<sup>2</sup> has found *urea* in the milk in Bright's disease.

Much was formerly written regarding the passage of foreign substances, as pigments, medicines, and poisons, into the milk, but we have no certain knowledge of any excepting iodide of potassium, which has been found in the milk of women by Peligot as well as by Herberger.

As in the case of the blood, it will hardly be irrelevant if after this notice of the normal and abnormal constituents of the milk, we enter into a brief consideration of the differences presented by this fluid when examined in relation to its general physiological bearings.

*Colostrum* generally appears as a turbid, yellowish fluid, similar to soap and water, having a viscid consistence and a strongly alkaline reaction. It passes more rapidly into lactic fermentation than normal milk, and it also constantly exhibits an excess of solid constituents both in women and animals, as we learn from the investigations of Simon, and of Chevallier and Henry. According to the last-named observers, this augmentation is most marked in the casein (in cows, asses, and goats). In women this increase principally affects the milk-sugar (according to Simon). Henry, however, finds much less sugar in the colostrum, and Simon less casein. Although a microscopical investigation and external appearances would seem to show that colostrum contains less fat, the

<sup>1</sup> Journ. f. pr. Chem. Bd. 47, S. 130-134.

<sup>2</sup> Guy's Hospital Reports, New Series, vol. i. p. 328.



contrary is proved by the results of most analyses. The colostrum is richer in fat than the corresponding milk. The cause of this striking phenomenon may perhaps depend upon the quantity of fat contained in the granular masses (*corps granuleux*). The colostrum contains more-over from two to three times more salts than the milk.

The colostrum of women yields, according to Simon, 17.2% of solid residue, and women's milk on an average 10.9%. The colostrum of the cow gives 16.0%, and the milk from the same animal from 14 to 15%; the colostrum of the ass yields, according to Chevallier and Henry, 17.16%, but asses' milk only 8.35%. The colostrum of the goat, according to the same analysis, contains 35.9%, and the milk 13.2%.

*Women's milk* is in general of a more bluish-white color than that of the cow or other animal, and is likewise sweeter in flavor. It has a strongly alkaline reaction, and turns acid less readily than other kinds of milk. Its specific gravity varies between 1.030 and 1.034, and it contains from 11 to 13% of solid constituents, amongst which there is on an average 3.5% of casein, and from 4 to 6% of sugar of milk. The casein in women's milk is less readily and completely precipitated by acids and by rennet, according to the concurring testimony of Simon and Clemm; the coagulum is also in general somewhat gelatinous and not so dense and solid as that of cow's milk, and therefore more easily digested by the child's stomach. The butter of women's milk is supposed to be richer in olein than that of cow's milk.

*Cow's milk* is in general of a pure or somewhat yellowish-white color. Its specific gravity varies, according to Simon, between 1.030 and 1.035, and according to Scherer, between 1.026 and 1.032. It contains on an average, 14% of solid constituents (varying between 12.9 and 16.5%). It contains more casein than women's milk (see vol. i. p. 340), and somewhat more butter, but less sugar of milk and far more salts, although this increase principally affects the insoluble salts belonging to the casein, with whose augmentation they are likewise increased.

*Mare's milk* is white, tolerably thick, with a specific gravity varying from 1.034 to 1.045 (according to Clemm it is 1.0203). It contains 16.2% of solid residue, a small proportion of casein (1.7%), but a large amount of fat (6.95%), and a considerable quantity of sugar of milk (8.75%).

*Asses' milk*, which is of a white color and sweeter than cows' milk, has a specific gravity which fluctuates between 1.023 and 1.035. It contains from 9.16 to 9.53% of solid constituents, of which from 1.6 to 1.9% is casein, from 12.1 to 12.9% butter, and from 6.8 to 6.29% sugar of milk; it is therefore far poorer in casein and butter than cows' milk, but richer in sugar of milk. This milk likewise very readily becomes acid, and easily passes into vinous fermentation.

*Goats' milk* is white, of a faintly sweetish taste, and a peculiar odor. Its specific gravity is in general about 1.036. It contains from 13.2 to 14.5% of solid constituents, amongst which from 4.02 to 6.03% are casein, from 33.2 to 42.5% butter, and from 4.0 to 5.3% sugar of milk. It is, therefore, poorer in casein than cows' milk, contains nearly the same, or perhaps a somewhat larger quantity of fat, and much more sugar of milk. When coagulated, the casein forms a dense mass.



*Sheep's milk* is thickish, white, and of an agreeable odor and taste. Its specific gravity varies between 1·035 and 1·041. It contains 14·38% of solid constituents, amongst which 4·02% are casein, 4·20% butter, 5·0% sugar of milk, and 0·68% salts. It appears from the single analysis instituted by Chevallier and Henry to contain somewhat less casein and butter, and more sugar of milk than cows' milk.

The only carnivorous animal whose milk has been analyzed is the *bitch*, and her milk, according to the investigations of Simon, Clemm, Dumas and Bensch, is somewhat thick, and on heating it becomes much thicker, even if it does not perfectly coagulate. When the animal has been kept on vegetable food, the milk is neutral, or has a faintly alkaline reaction. When animal food has been given, the milk exhibits an acid reaction, and has a specific gravity varying from 1·033 to 1·036. It then contains from 27·46 to 22·48% of solid constituents, of which from 8 to 11% are casein, and from 6·84 to 10·95% butter, besides a small quantity of sugar of milk. On mixed food bitches' milk contains more butter and also more sugar of milk. It is a singular circumstance, that on evaporating this milk, its sugar is found to be converted into grape-sugar (glucose), and the solid residue attracts a large quantity of oxygen from the air (Bensch.) The ash sometimes contains upwards of 93% of insoluble salts.

Although there can be no doubt that the *nature of the food* exerts an influence on the composition of the milk, it has not been shown in what manner this affects the individual constituents. From the experiments made on bitches, it would appear that a vegetable diet renders the milk richer in butter and sugar; while the solid constituents are augmented when a sufficient quantity of mixed food is given. Peligot found the milk of an ass most rich in casein when the animal had been fed on beet-root, whilst it was richest in butter when the food had consisted of oats and lucerne. Fat food increases the quantity of the butter. Bous-singault found the milk of a cow richer in casein when the animal had been fed on potatoes, than when other food was taken. Reiset found that the milk of cows which were at grass was much richer in fat than when the animals had stood all night in their stalls without food, but Playfair found on the contrary that the quantity of butter in the milk increased during the night as much as during their stall-feeding, but that the quantity of butter in the milk was considerably diminished by the motion of the animals in the fields—an observation which agrees more closely than Reiset's with every-day experience. Hay that has been cut and collected in a dry summer, yields a milk which is richer in butter than hay which has been cut in a wet season.

It follows from the experiments made by Simon on the milk of a woman who was suckling, that this fluid undergoes gradual alterations during the period of lactation. For while the quantity of the butter remains nearly the same, the casein increases as the child becomes more fully developed, at the same time that the sugar of milk gradually diminishes. The insoluble salts are increased simultaneously with the casein.

The alterations experienced by the milk from deleterious substances, mental and physical affections, and diseases, have been so imperfectly



investigated, that we can scarcely be said to know anything in relation to this subject. Herberger found that the milk of cows having the murrain, was richer in potash, and had a colostrum-like appearance. The milk becomes more watery in almost all morbid affections, and is then also especially poor in butter. In febrile affections it is frequently very acid.

Almost every experimentalist has adopted his own plan of *analyzing the milk*, but as scarcely any methods before Haidlen's can lay claim to accuracy, it is unnecessary to give a critical notice of them, and we will here simply draw attention to the difficulties which appertain to the quantitative analysis of milk, more than to that of many other animal fluids. These difficulties extend, however, to nearly all of its individual constituents, and mainly depend upon the following conditions:—While undergoing the process of evaporation, the milk becomes covered by the well-known casein-membrane, which during rapid evaporation is often broken by vesicles of steam, by which a portion of the fluid may spirt out and be lost. It is extremely difficult to dry the milk completely after it has once undergone evaporation, and indeed almost impossible unless a very small quantity of this fluid has been employed for the determination of the solid residue; for the dry casein, when penetrated by fat, forms a crust which is impermeable to water, and even to vapor. The casein is not perfectly thrown down from the solution by means of acetic acid (see vol. i. p. 340), since some portion may be extracted by alcohol as well as by water. When acetic acid is employed, the acid enters into combinations with alkalies, and augments the alcoholic extract in a manner which it is not easy to control, or even to estimate. The fat cannot be perfectly extracted from the simple residue of the milk, however long the latter may have been submitted to the action of ether. On evaporating sour milk, the sugar is in part converted into grape-sugar, or into an uncrystallizable syrup-like sugar. When milk is exposed to a warm temperature, the so-called extractive matters are formed in considerable quantity. It is more difficult to incinerate the residue of the milk than that of many other fluids. We are not yet able to make even an approximate determination of the investing membranes of the milk-globules.

Dumas and Scherer suggest, as a method for determining the casein with every possible accuracy, that the milk, after it has been evaporated in a water-bath or in a vacuum with sulphuric acid till it is nearly dry, should be treated with a little acetic acid, and then extracted with ether, alcohol, and water. In my opinion Haidlen's method (see vol. i. p. 340) is in many respects preferable to this, for the treatment of milk with definite quantities of sulphate of lime presents great advantages for evaporating and drying the fluid, and for determining the quantity of fat, independently of the circumstance that the casein is insoluble in all menstrua. Milk which has been treated with chloride of calcium, a solution of sulphate of lime, or, according to Haidlen's method, with dried gypsum, may easily be evaporated without experiencing any loss by the formation of vesicles of vapor; while at the same time the residue readily admits of being very perfectly dried, and then easily pulverized. Ether readily and completely extracts the fat, but alcohol does not remove any casein, either by boiling or after the fluid has cooled. A different



method must, however, be adopted for the determination of the solid residue, the salts, and the aqueous extract. The best mode of proceeding is to evaporate from 1 to 3 grammes of milk in a flat platinum basin, either in a vacuum or in a water-bath, and then to dry it in an air-bath at  $+120^{\circ}$ , or in a vacuum with the aid of a small sand-bath heated to  $120^{\circ}$ . The ash is best determined when a portion of well-dried residue is burnt in a platinum crucible with the co-operation of oxygen. Scherer's method is the only one by which the aqueous extract can be determined with any degree of accuracy.

We would refer to the observations already made (at p. 263 of vol. i.), for the method of obtaining a quantitative determination of the milk-sugar; simply remarking here, that acid milk must be neutralized before its evaporation, in order to obtain the milk-sugar in a crystallized state.

Dumas<sup>1</sup> observes that the milk-globules remain upon the filter when the milk has been treated with a concentrated solution of chloride of sodium. I have not been perfectly successful in this experiment, even when I have used freshly drawn milk.

Attempts have been made to invent instruments and methods for determining with promptness the goodness of the milk, in order to detect some of the numerous modes of adulterating cows' milk usually practised in large towns. These instruments, which are termed *galactoscopes* and *galactometers*, are designed to furnish an average determination of the quantity of fat contained in the milk, since the goodness of this fluid for ordinary purposes is estimated according to the amount of fat which it contains. The best known of these instruments is the galactoscope invented by Donn ,<sup>2</sup> which consists of two tubes that may be pushed into one another by means of a fine screw, each tube being closed at the opposite extremities by a plane of glass. The determination is made by ascertaining the thickness of the milk-stratum, through which the light of a taper may be detected; the opacity of the milk being usually regarded as a test of the quantity of fat contained in it. Areometric determinations, such as Jones, Chevallier and Henry, as well as Quevenne, have proposed for the determination of the density, and consequently of the goodness, of the milk, frequently fail in their object, while Simon's suggestion of employing a solution of tannic acid, of known strength, which precipitates butter and casein from the milk, may in many cases be open to deceptions. Moreover, Lamp rierre's<sup>3</sup> method of comparing the density of fresh milk with that of milk which has been filtered through paper, does not meet all the requirements of the case.

We are still very deficient in accurate determinations of the *quantity of this secretion* in women, but it must necessarily differ in accordance with the various relations of nutrition in the female while suckling. In women, the bodily constitution, the nature of the food, external relations, temperament, &c., must obviously influence the quantity as well as the composition of the milk. The quantity of the milk is, moreover, dependent upon its consumption, for in the early period of lactation, less milk is drawn from the breasts than subsequently, when the infant re-

<sup>1</sup> Arch. g n. de M d. Vol. suppl. 1846, p. 180.

<sup>2</sup> Compt. rend. T. 17, p. 588-592.

<sup>3</sup> Op. cit.



quires a larger amount of nutriment. Lampérière determined, by means of the apparatus described in p. 57, the quantity of milk secreted in definite times by a large number of women, and found, as a mean for each breast between 50 and 60 grammes in the course of two hours. If we were to assume that the secretion of milk proceeds at an equal rate during the twenty-four hours, then (taking 55 grammes as the mean) a woman might discharge 1320 grammes of milk in twenty-four hours from both breasts; according to this view, and assuming the mean weight of the female body to be 60 kilogrammes, there would be secreted every twenty-four hours during the period of lactation 22 grammes of milk for every 1000 grammes of weight.

We may calculate with tolerable accuracy the quantity of milk secreted by milch cows: according to the experiences of agriculturists, which coincide pretty closely with the results which Boussingault obtained in his experiments on the effects of different kinds of food, a cow yields on an average  $5\frac{1}{2}$  litres, or about 6 kilogrammes of milk in twenty-four hours; since on an average a cow weighs 580 kilogrammes, there are thus 10.4 grammes of milk secreted for each 1000 grammes weight of the animal.

With regard to the *origin* of the milk and of its constituents, we must refer to our observations on secretion in general. We need here only especially remark, that we cannot assume, as Chevreul and other chemists and even ourselves formerly did, that the constituents of the milk exist preformed in the blood. If we only adhere to the chemical view of the case, this much at all events seems established, that the presence of the leading constituents of the milk has not yet been recognized in the blood: we have already sufficiently shown, in p. 338 of the first volume, that all those reactions and phenomena from which it has been inferred that casein exists in the blood, either afford no certain proof that this is the case, or are altogether founded on error. The same is the case with the milk-sugar, which has never been recognized with certainty in the blood; the sugar of the blood, which we have especially found in the contents of the hepatic veins, and which C. Schmidt has detected in the whole mass of the blood, is fermentable; the sugar discovered by Scherer in the muscular juice, the inosite, is certainly not capable of undergoing fermentation, but in its other physical and chemical properties it differs essentially from milk-sugar; hence we may regard it as in the highest degree probable that no milk-sugar exists preformed in the blood, even if we do not deny that its augmentation or diminution in the milk is very dependent on the nature of the food. Dr. von Becker recently made several observations in my laboratory, which afforded the first experimental proof of a fact which had been long assumed. In his experiments on the resorption of sugar, he found, that in order to make sugar appear in the urine of rabbits, whose udders contained milk, it was necessary to introduce a much larger amount of that substance into the blood than in the case of male or non-suckling rabbits. In these cases there was also far less sugar in the blood than a comparison with other experiments would have led us to anticipate. The grape-sugar introduced into the blood must, moreover, have been very rapidly absorbed by the mammary glands in these cases. If these facts favor the view that the



sugar is formed in the mammary glands, the pre-existence of certain constituents of the butter in the blood is by no means opposed to it: for if we assume that the capillaries of the mammary gland allow of the passage of the fats in a different proportion from that in which they are contained preformed in the blood, as is quite possible from the phenomena which have been observed in transudation, it is obvious that these capillaries are perfectly impermeable to the cholesterin, which is so abundant in the blood, and transudes so readily; for no cholesterin is found in the milk. On the other hand, it is very questionable whether true butyric acid is contained in normal blood. Moreover, the salts do not pass into the milk in consequence of simple transudation; for on comparing the salts of transudations with those of the milk, we find that the chlorides do not preponderate to nearly the same extent in the latter as in the former, but that the potassium-compounds and phosphates are present in the milk in even larger quantities than in the blood-corpuscles: the preponderance of the insoluble phosphates in the milk-ash has been already specially noticed. But if we compare the soluble salts of the milk-ash with those of the intercellular fluid and of the blood-corpuscles (as for instance in the cow), it seems to follow as an almost necessary consequence that the blood-corpuscles take part in the formation of the milk, at all events in so far as the salts are concerned.

As when we treat, in this volume, of the process of secretion, we shall fully enter into the histological and physiological grounds which favor the view that there occurs a preliminary remodelling of the substances to be conveyed by the blood to the glands for secretion, we will here refer to that chapter, in which, after reviewing all the chemical results which have been described in the theory of the juices, the principle is fully established, that the main constituents of all true secretions, like those of the liver and the mammary gland, are first formed within the glandular organs themselves.

The physiological importance of the milk is so obvious, that it would be altogether superfluous to enter fully into the subject; but an accurate investigation of the influences which the individual constituents of this secretion, which Nature itself has provided as the type of normal food, exert on the infant, is of such great physiological importance, that one of the fundamental laws of physiological chemistry, the very turning-point of the metamorphoses of the animal tissues generally, is based upon it. For this reason we shall enter into a full consideration of this subject when we treat of the theory of nutrition, and shall, therefore, postpone all our remarks upon it for the present.

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## SEMINAL FLUID.

The seminal fluid, which is secreted by the testicles, and is usually mixed with the prostatic fluid, is viscid, tenacious, opalescent, colorless (only becoming yellow on drying), of a peculiar odor, considerably heavier than water, and of an alkaline reaction; when freshly discharged



it is gelatinous, but after some time it assumes a thin fluid consistence; a mucous sediment is formed when it is mixed with water; the mixture is not rendered appreciably more turbid by boiling, but alcohol induces perfect coagulation.

In animals, during the period of heat, the seminal fluid may be collected in comparatively large quantities from the vasa deferentia and the vesiculæ seminales; the latter, however, secrete an independent fluid, and hence we often find no true seminal fluid in them.

This fluid contains the most remarkable morphological elements which we meet with in the animal organism, the *seminal animalcules* or *spermatozoa*. These elements which, according to the unanimous evidence of physiologists, occur in the fruitful seed of all animals, have in most cases tolerably similar although distinguishable forms; there is a round, oval, or pyriform head, to which is attached a long filament gradually coming to a point. With regard to the dimensions of these singular formations, the head in man varies in breadth from 0.0007''' to 0.0013'', and in length from 0.0019''' to 0.0025'', while the filament or tail has a length varying from 0.0018''' to 0.0020''. The greatest peculiarity in connection with these structures is their apparently spontaneous motion, which for a long time led to the belief that they were infusoria; the continuous motion appears to be produced by the bending and rapid stretching of the tail from one side to the other, so that the molecule moves in a zigzag direction, following the course of its head. This power of motion is often retained for a long time if the semen be protected from evaporation, or when it is placed in tepid serum, urine, saliva, or mucus; if the seminal fluid be mixed with double its quantity of water, the filaments lose their power of motion, and become more or less rolled up (Henle,<sup>1</sup> R. Wagner.)<sup>2</sup> The motion is destroyed by decomposition of the semen, by spirits of wine, a solution of opium, and strychnine; the tail then generally remains extended. The spermatozoa are not readily destroyed by putrefaction; they are dissolved by concentrated but not by dilute solutions of the alkaline carbonates; the latter solutions, on the other hand, often render them more distinct under the microscope, by dissolving the coagula or mucus occurring between them. When carefully exposed to a great heat, they leave, according to Valentin, an ash, which retains their precise form.

There are likewise other morphological elements besides the spermatozoa which occur in the semen; in addition to scattered epithelial scales and mucus-corpuscles, R. Wagner also found finely granular, pale, sharply outlined molecules, the *seminal granules*, which vary in size from 0.0016''' to 0.01''; there are also minute fat-granules and molecular matter.

The *intercellular fluid* of the semen, which derives its origin less from the testes than from Cowper's glands, the seminal vesicles, and the prostate gland, gelatinizes after its discharge; Henle regards the gelatinizing substance as fibrin, while Berzelius compares it with mucus, although he does not regard the two as identical. This substance has been named *spermatin*; it is, however, probably nothing more than basic albuminate of soda, with which it coincides in most points; the

<sup>1</sup> Allg. Anatom. S. 949-958.

<sup>2</sup> Lehrb. d. spec. Phys. 3te Aufl. 1845, S. 49.



fluid does not become turbid on boiling; after evaporation, this albuminous substance becomes insoluble in water; a dilute alkaline solution redissolves the matter precipitated by the water, which is again thrown down on the further addition of concentrated solutions of the caustic alkalies or their carbonates; the solid residue of the fluid is only partly soluble in water, and partly also in alcohol; on the addition of acetic acid to the watery solution, a flocculent precipitate is thrown down, which redissolves in an excess of the acid, and is precipitable from this solution by ferrocyanide of potassium; this precipitate is soluble in concentrated nitric acid. Although all these properties coincide with those of albuminate of soda (see vol. i. p. 296), we must not hence conclude that this substance is simply albuminate of soda, but we are even less justified in assuming the presence of a special substance, spermatin, or even of ordinary fibrin.

Both the water-extract and the alcohol-extract of the seminal fluid doubtless contain albuminate of soda, as far as we can conclude from the investigations of Vauquelin; but we cannot decide whether in addition to this there are special extractive matters, as in the other animal juices, since the quantity of seminal fluid that can be collected is always too small for such investigations.

The salts of the serum may be easily recognized in the seminal fluid; we find, however, that the latter contains phosphate of lime, and especially phosphate of magnesia, in preponderating quantity; we can readily convince ourselves of the presence and quantity of the magnesian salt by placing semen between two glass slips which are united by varnish (in the same manner as microscopic objects are put up), and allowing it to decompose; we then observe the separation of innumerable crystals of phosphate of ammonia and magnesia amongst the uninjured spermatozoa; many have followed Vauquelin in assuming that these crystals are phosphate of lime, but this is obviously impossible, because the latter does not crystallize from organic solutions (and these crystals present no resemblance to apatite either in their form or in the mode of their formation). But independently of this we may readily convince ourselves, both by microscopico-crystallometric and by microscopico-chemical analysis, that these are crystals of the ordinary triple phosphate.

Vauquelin<sup>1</sup> found 6% of organic matter, 3% of earthy phosphates, and 1% of soda, and hence altogether 10% of solid constituents, in the semen.

With regard to the *analysis* of the semen, we have merely to follow the rules laid down for the investigation of the animal fluids generally; in the quantitative analysis we should, however, bear in mind, that by mixing the fresh object with a very dilute solution of ammonia, the separation of the organic matters from the actual fluid of the semen may be prevented, and hence probably a quantitative determination of the spermatozoa and other morphological elements of this secretion may be accomplished by filtration. In order to examine with accuracy the extractive matters of the semen, we should first dilute the fresh fluid with a little water, and neutralize with dilute acetic acid, and then filter, before commencing to evaporate, or to extract the residue with water and alcohol.

<sup>1</sup> Ann. de Chim. T. 9, p. 64.



In a medico-legal point of view the examination of the seminal fluid is of great importance. Much attention has recently been paid (by Remak,<sup>1</sup> Bayard,<sup>2</sup> and C. Schmidt),<sup>3</sup> to the characters which distinguish seminal fluid on clothes, linen, &c., from other dried fluids, and enable us to detect this secretion with certainty. The form of the spermatozoa is so characteristic, and so different from all other animal or vegetable forms, that on a microscopic examination they cannot be mistaken for any other structures. The diagnosis of semen in animal fluids, as for instance the urine, is extremely facilitated by the comparatively indestructible character of the animalcules. It is further worthy of notice that I have always found that urine containing semen very readily becomes alkaline, and that even when few animalcules are found, it throws down a mucous sediment of peculiar, finely laminated, and very transparent flakes. Hence the diagnosis of semen, is easy in every instance in which the object can be at once examined microscopically; in that case no chemical experiments are required, which unfortunately would fail in giving decisive results. It is a more difficult matter to prepare for microscopic examination semen that has been dried on linen or other textures. We omit any mention of the method adopted by Bayard for this object, since it is too circumstantial, requires a tolerably skilful analyst, and has other drawbacks; and we shall only give the very simple method recommended by Schmidt. His first direction is that we should ascertain on which side of the texture the spots are situated, for it is here only that we should find seminal animalcules; we can detect this side by its glistening surface when the light falls upon it, while the opposed surface appears dull and has a rough feeling. We then gather together the portion of linen on which the semen is found, and suspend it in a watch-glass half full of water; after four hours we warm the fluid having previously added a few drops of ammonia, while the portion on which the spots are situated still remain immersed; we then gently rub the surface, and afterwards examine with the microscope the fluid contained in the watch-glass.

According to Schmidt, seminal spots differ from all others, as for instance, those of the lochial discharge, vaginal mucus (whether syphilitic or non-syphilitic), pus, gonorrhœal matter, nasal and bronchial mucus, albumen, gum, fat, glue, or starch, in this respect, that the seminal spots become of a pale yellow color when kept near to the fire for one or two hours, while the form of the animalcules is not at all changed. Other substances when treated in this manner are either colored green (as for instance, vaginal mucus) or are not changed in color; spots caused by animal substances may be easily diagnosed, either by their morphological elements, or by the albumen, which can be detected after they are moistened. No one could mistake spots of mere fat, gum, or starch, for marks of the seminal fluid.

The *origin* of the semen and its *physiological importance* belong solely to histology and physiology; and we should be encroaching too much on

<sup>1</sup> Diagnostische u. pathogen. Unters. Berlin, 1845. S. 148-171.

<sup>2</sup> Ann. d'Hygiène publique. 1849. No. 43.

<sup>3</sup> Diagnostik verdächtiger Flecke. Mitau u. Leipzig, 1848. S. 42-48.



these departments if we were to enter more closely into these obscure subjects, on which chemistry has as yet thrown no light, and which it will probably never be able altogether to elucidate.

## THE FLUIDS OF THE EGG.

While investigations in reference to the egg and its morphological elements, its development, and metamorphosis, have led to the most brilliant discoveries in physiology, the composition and character of the animal egg and its constituents have met with little attention from the chemist, and perhaps not without reason, for other fields of inquiry, alike more accessible and more extensive, promised to yield a far richer harvest than could be anticipated from the investigation of this subject. An inquiry into the constituents of the egg is still deficient in those preliminary investigations, which are necessary for the cultivation of the subject in such a manner as to correspond to the general advance of science and the present stage of histological discovery. Thus, for instance, although our knowledge of the fats is undoubtedly much advanced, and has attained a certain decisive stage, we are still wholly ignorant of many of the animal fats and of their relations to the lipoids. Our physiological inquiries have, however, shown us that the fats participate largely in promoting the growth and metamorphosis of the egg. Considerable obscurity still attaches to the chemical investigation of the various matters containing phosphorus, which occur, as it would appear, with the same constancy in the egg as in the brain and spinal cord.

We have already frequently spoken of the deficiency of our knowledge of the protein-bodies. Inquirers have scarcely ventured till the most recent times to hazard a conjecture as to the presence of other non-nitrogenous matters, as for instance, sugar, in addition to the fats in the fluids of the egg.

Under the term "fluids of the egg," we also usually include those fluids which are coeval with the development of the embryo, but which we shall not take into consideration in the present place, since we treat of the liquor amnii under "Transudations," of the liquor allantoidis under "Urine," of the vernix caseosa under "Cutaneous Secretion," and of the gelatin of Wharton<sup>1</sup> under "Mucus."

As the eggs of most animals are either very small or cannot readily be obtained in any considerable numbers, those of the hen and of the carp are almost the only ones which have hitherto been examined. Since, according to Gobley's investigations,<sup>2</sup> the constituents of the eggs of both classes of animals are almost perfectly identical, we may assume

<sup>1</sup> [The gelatin of Wharton is the limpid fluid with which the cellular tissue, that unites the vessels of the umbilical cord with the amniotic investment, is impregnated.—G. E. D.]

<sup>2</sup> *Compt. rend. T. 21, p. 766-769; Journ. de Pharm. et de Chim., 3me Sér., T. 11, p. 409-417, et T. 12, p. 513; Journ. de Chim. Méd. T. 6, pp. 67-69.*



that an inference may with some justice be drawn as to the composition of the eggs of all other animals from that of the hen's egg.

It is well known that the eggs of most animals do not contain the same albuminous investment as bird's eggs, but simply a fluid corresponding to the yolk, and enclosed by a membrane. We will, therefore, begin by considering the yolk, the constitution of which we only know from our experiments on that of the hen's egg. The yolk of the hen's egg consists of a very viscid, thick, scarcely translucent fluid, which is either of a yellowish-red or of a sulphur-yellow color, devoid of odor, and of a faint but peculiar taste. When mixed with water it forms a white, emulsive fluid, imparts a blue color to reddened litmus paper, and solidifies on boiling into a very friable mass. It coagulates in cold alcohol, and yields when shaken with ether a reddish or amber-colored fat, whilst a viscid white mass separates.

On examining the yolk under the microscope, we find that it consists of a semi-fluid mass composed of very fine *granules* (whose diameters are too small to admit of being measured), amongst which there swim variously sized *yolk-corpuscles* and *fat-globules*. The latter are distinguished by a less intense yellow color, and by being covered with a layer of fine granules, whilst the yolk-corpuscles are surrounded by a membrane, which is, as it were, strewn with granules. When the yolk is acted upon under the microscope by hydrochlorate of ammonia, or other neutral alkaline salts, the granules almost wholly disappear, leaving only shining and sharply defined fat-globules, together with the somewhat distorted, oval, fusiform, or cucumber-like yolk-cells. The latter also exhibit a very faintly granular investing membrane. A similar distortion of the yolk-cells may be produced by dilute acetic acid, but this does not dissolve the suspended matter. But if the yolk be acted upon by concentrated acetic acid or a dilute solution of potash, the membranes of the yolk-globules likewise disappear, whilst a very finely granular substance alone remains visible, together with yellow-colored fat. The yolk-globules behave, therefore, precisely the same as the milk-globules (see vol. i. p. 341), the only essential difference being that the fat may be completely extracted from the yolk, even without the application of acetic acid, potash, hydrochlorate of ammonia, &c., although this may certainly be more rapidly effected by the application of hydrochlorate of ammonia or similar means. When we examine the yolk under the microscope, after the fat has been as far as possible removed by ether, we find that the minute granules are no longer scattered, but conglomerated into larger masses or aggregations, which are in a great measure dissolved by hydrochlorate of ammonia, acetic acid, and caustic potash, leaving only very fine, scarcely perceptible granules and flakes, which impart to the fluid a general opalescent or whey-like appearance.

I made numerous experiments, eight or ten years ago, on the constitution of the fluids of the egg, and the changes they undergo during the period of incubation, but deferred the publication of my observations, because the state of science at that time did not furnish the means of replying to the questions which I had propounded. I have unfortunately been prevented from repeating these experiments, which I the more regret, as the early observations of a mere beginner, conducted by



means of the imperfect methods then in use, are but ill adapted to aid in criticizing Gobley's recent experiments, which undoubtedly call for a rigid scrutiny in respect to several special points.

The ova of amphibia and fishes contain the so-called *yolk-plates*, or tablets, which have in part square, and in part other crystalline forms, and very frequently present a distinctly stratified appearance. Histologists (Bergmann) have long been acquainted with these bodies, and have usually regarded them as fat (stearin). Virchow<sup>1</sup> has recently submitted them to a more exact micro-chemical examination, and has shown that they cannot belong to any of the known fats, but very probably constitute a new substance, which has considerable similarity to the protein-bodies, especially in their relation towards nitric acid and Millon's reagent. According to Virchow these plates remain undissolved in ether and boiling alcohol, although they swell in both fluids, become pale, and sometimes burst into several pieces; the same observer found that they behaved in a similar manner towards acetic acid, dilute mineral acids and alkalies, chloroform, glycerine, &c. The square tablets thus become oblong, or often oval. They dissolve in concentrated acetic acid and caustic alkalies, merely leaving small membranous particles or larger pale flakes.

We are unable to determine the constitution of the spherical, cell-like fat-corpuscles of the yolk, as we have as yet neither the mechanical or chemical means necessary for the complete separation of the intercellular fluid.

They contain, as far as we are at present able to determine, scarcely anything but fat; which, however, is intermixed with the phosphorized matters of the yolk-fat. Such, at all events, seems to be the case, if we may judge by the following experiment. On repeatedly shaking the yolk with ether, we find that the portions of fat first extracted contain little or no substance yielding phosphoric acid, while those portions which have been the latest extracted by shaking the yolk with ether yield, on incineration, a very large quantity of the superphosphates of the alkalies and of lime. This difference in the quantity of phosphorus contained in the different portions of the fat is not observable when the yolk has been previously treated with hydrochlorate of ammonia, acetic acid, or potash. If the investing membranes of the yolk-globules were completely impervious to ether, this substance, when pure, would only extract fat free from phosphorus, whilst hydrochlorate of ammonia and similar substances would extract a fat containing phosphorus. (Even the milk-globules are not entirely impermeable, and are distorted by ether, although less fat is abstracted from them than from the yolk-globules when acted upon under similar relations.)

The pigments of the yolk form, together with the non-phosphorized and phosphorized fat, a principal part of the contents of these cell-formations, in which I have been unable to trace a nucleus or anything analogous to such a structure; at all events, when the yolk-cells have been treated with hydrochlorate of ammonia, they are invariably found to acquire a more intensely yellow color than the fat-globules which have no investing membranes. They certainly are generally much larger

<sup>1</sup> Zeitschr. f. wissensch. Zool. Bd. 4, S. 236-241.



than the latter, and must, on this account, also appear more highly colored: some of the fat-globules are, however, wholly devoid of color. According to these observations, the yolk-globules must occupy an intermediate place between the milk-globules and the blood-corpuscles; approximating most nearly to the former in their abundance of fat, and to the latter in the quantity of phosphoric acid which they contain, and in their ferruginous pigment.

Since we are as yet unable distinctly to define the differences existing between the *chemical constituents* of the yolk-globules and those of the intercellular fluid, we will merely take a general view of the respective elements of the yolk.

We have already spoken (in vol. i. p. 325) of *vitellin*, the most important albuminous constituent of the yolk. We did not then venture to depart from the ordinary view which regards the vitellin as a special kind of protein-body; but yet, however averse we are from making any assertion in reference to the supposed identity of similar bodies, we cannot withhold our opinion that the so-called vitellin is nothing but a mixture of albumen and casein. The amorphous, dark granules of the yolk consist of pure casein free from alkali, but which is as rich in phosphate of lime as ordinary casein. The true intercellular fluid of the yolk contains no casein, and simply dissolved albumen which is poor in alkali. It must be observed in the first place that it would be incorrect to maintain that the vitellin is coagulated by ether; for on repeating the experiment (as we have often done) by shaking the fresh yolk with ether and water, we find that under the fatty and yellow-colored stratum of ether, there is formed a white and somewhat viscid mass, which has erroneously been regarded as coagulated vitellin. When these flakes are collected on the filter, after the removal of the fat and the ether, and are rinsed as long as the fluid which passes through the filter exhibits any opalescence on being heated, there will remain a mass perfectly similar to the casein prepared according to the directions of Rochelder and Bopp, (see vol. i. pp. 337, 338), and which contains in addition to the true casein some portion of albumen which is very poor in salts. This albumen will be precipitated by diluting the yolk-fluid with water, precisely as we observe in the case of white of egg and blood-serum. This substance possesses all the properties ascribed to casein (vol. i. p. 333), as we find from its behavior towards acids and alkalies, and the alkaline, earthy, and metallic salts. We would simply observe that this substance dissolves even in very dilute solutions of hydrochlorate of ammonia, chloride of sodium, sulphate of soda, &c., leaving only a small residue (consisting of a little fat and of the investing membranes of the yolk-globules), which renders the fluid opalescent. Acetic acid renders this solution very turbid, and boiling has a similar effect in a less degree. The substance separated by boiling is the albumen, which had been precipitated by the dilution of the yolk with water, and which has been again dissolved by the hydrochlorate of ammonia, &c., at the same time with the casein. All these concurring similarities between casein and the substance of the yolk, would not, however, have led us to regard this substance as casein, if it did not further possess the property so peculiarly characteristic of casein, of *being completely coagulated by rennet*. Thus, for instance, if rennet



be added to this substance when dissolved in an extremely dilute solution of hydrochlorate of ammonia or soda, a dense casein-like coagulum will be formed in about two or three hours, at a temperature of about 30° C. As the sugar must have been entirely removed by washing, it cannot be supposed that this substance can in any way have contributed by its metamorphic action to the formation of this coagulum. One hundred parts of this substance in the dry state yielded 5.044 of ash, which consisted almost exclusively of earthy phosphates and carbonates.

In characterizing as casein this substance, which has hitherto been considered to be of a special nature, we do so with the reservation that this identity must be only conditionally accepted until we have better means of establishing the presence of casein, more especially as we know, on the one hand, that casein itself is probably a mixture of several substances (containing here, as in the milk, at all events the investing membranes of fat-cells), while, on the other hand, we can gain little or no information from elementary analyses as to the difference of identity of protein-bodies.

I found 13.932% of such casein in 100 parts of yolk-fluid (precipitated by acetic acid from a solution of hydrochlorate of ammonia). The quantity of matter insoluble in the solution of hydrochlorate of ammonia (the investing membranes) amounted only to 0.459%.

The *albumen* of the yolk is contained in the fluid that is obtained by washing the casein which is insoluble in pure water; on boiling, it coagulates in flakes—a proof that nothing is contained therein, but an albuminate, since in all other properties it resembles ordinary albumen, and is neither precipitated by acetic acid, nor coagulated by rennet. Of albumen of this nature, which is soluble in pure water, I found 2.841% in the fluid of the yolk; while of such as remained undissolved with the casein, and was only quantitatively determined after the precipitation of the casein by acetic acid, there was 0.892%. Prout found 17%, and Goble 15.76% of vitellin in the yolk; this vitellin consisting of a mixture of casein, albumen, and investing membranes.

In addition to the above-named protein-bodies, we find in the yolk both of fishes' and birds' eggs, a number of substances soluble in ether which are fats, or, at all events, on decomposition, yield acid and neutral fats, and contain in solution two pigments. The whole amount of these substances soluble in ether was found by Prout to be 29%, and by Goble to be 30.468%, while I found on an average, as much as 31.146%. Sulphur has not been found in the yolk-fat either by Goble or myself: neither the alcoholic solution of the yolk-fat, nor the water in which the fat has been warmed, reddens litmus.

In the examination of these fats, the first substances to notice are *olein* and *margarin*, whose quantity Goble estimates at 21.304%.

It has been generally assumed that *cholesterin* is present in the yolk, and Goble has even determined it quantitatively, and found that it amounted to 0.438%. The evidences of its presence are, however, not at all decisive, even though the fusing-point of the unsaponifiable fat obtained by Lecanu from egg-oil coincides with that of cholesterin, being 145° C. At all events, I have never been able to convince myself, by a measurement of the angles of the crystals which have been assumed to be



cholesterin, or by any other means, this liquid was actually present: the crystalline tablets of this substance form, for the most part, not rhombs, but compressed parallelopipeds, whose angles are different from those of cholesterin; while the cholesterin-tablets generally present re-entrant angles, in these elongated tablets the acute angles are obliquely truncated. These crystals separate on gradual evaporation from the ethereo-alcoholic solution in feathery groups. They fuse more readily than those of cholesterin. The circumstance of their appearing to dissolve readily in cold alcohol, when they are still mixed with yolk-fat, would afford no proof of their non-identity with cholesterin, since it is a well-known property of the latter to dissolve freely in cold alcohol, in the presence of oily fats and soaps.

I am still doubtful whether *margaric* and *oleic acids* are contained in fresh yolk-fat; they may be unquestionably detected in it after exposure for some time to the air. Gobley considers that both these acids, together with glybero-phosphoric acid, are formed by the decomposition of an indifferent matter, to which he has recently applied the term *lecithin*.

This *lecithin* has not yet been obtained by Gobley in an isolated and perfectly pure condition: it separates from the ethereal extract of the dry yolk, on the evaporation of the ether, in the form of a *matière visqueuse*, to whose investigation Gobley attaches a very great value, although most other fats, when similarly treated, yield a physically similar, although chemically very different *matière visqueuse*. I have been unable to discover any peculiarity in it; for all oleaginous fats yield, under favorable conditions, a similar mass, which consists essentially of margarin with a little olein. It is, however, true that the substance which contains the phosphoric acid occurs in that portion of the fat which first separates from the ethereal solution during evaporation. This substance, mixed with olein and margarin, and likewise with another matter, to which Gobley has applied the term *cerebrin*, is, according to his later researches, a perfectly neutral body, which, when treated with mineral acids or alkalies, both in its aqueous and alcoholic solutions, and even when the access of atmospheric oxygen is excluded, yields glybero-phosphoric acid, together with oleic and margaric acids. If in this process an organic be substituted for a mineral acid, the same action takes place, but less readily. Gobley found 8.426% of lecithin in the yolk of egg.

*Cerebrin* is obtained by treating the *matière visqueuse* with alcohol and an acid, and allowing it to stand undisturbed: it then separates as a white, soft mass, which corresponds with Fremy's cerebrie or oleophosphoric acid: it also is neutral, contains nitrogen and phosphorus, swells in water like starch, and fuses at a high temperature: in its isolated state it is insoluble in ether, dissolves readily in alcohol, and combines freely with metallic oxides; if it be again dissolved in spirit of wine, it loses phosphate of lime, and reddens litmus.

We shall treat more fully of these substances when we consider "the brain and spinal cord;" and, in order to avoid unnecessary repetition, we shall postpone to that chapter a notice of our own experiments and observations.

Two *pigments* were discovered by Chevreul in the yolk—a yellow and



a red one; both may be extracted with cold alcohol; the red one, which contains iron, is less readily soluble in ether than the yellow one, in which that metal is not present: when perfectly freed from fat, they appear to be all but insoluble in ether; neither of them has, however, been carefully examined.

Whether the organic acid which occurs in the yolk is *lactic acid*, is very doubtful; at all events, its presence is by no means established from the little that Gobley tells us on the subject.

Although Gobley has convinced himself that the constituents of the yolk which contain phosphorus are not in combination with ammonia, he yet assumes that *hydrochlorate of ammonia*, to the extent of 0.034%, is present in that fluid.

With regard to the *mineral substances*, we find in the ash of the yolk the ordinary salts of animal substances, but they occur in very different proportions from those in which we ordinarily find them. The compounds of potassium preponderate considerably over those of sodium, and, according to Poleck,<sup>1</sup> the chlorides are entirely absent; but, on the other hand, Rose and Weber<sup>2</sup> have more recently found that, at all events, some chloride of sodium (namely, 9.12% of the inorganic matters) can be detected in the yolk, if the organic matters have not been destroyed either by carbonization or by incineration. Only monobasic phosphates can be discovered in the ash prepared according to Rose's method, and in this Poleck found from 66.7 to 67.8% of phosphoric acid, and Weber 70.92%; a little peroxide of iron (1.45% of the ash), and a small quantity of silica (0.55% of the ash) were also found in the yolk-ash. If we call to mind the composition of the corpuscles, we cannot fail to be struck with the great analogy that exists between the nature of the salts occurring in the blood-cells and in the yolk; and we shall almost immediately see that, on the other hand, the composition of the salts in the white of the egg approximates in a similar manner to that of the salts of the serum.

We repeat that Gobley has found precisely the same substances, in almost the same proportions, in the eggs of fishes, which, like those of most animals, consist only of yolk, and are not surrounded with a special layer of albumen like birds' eggs.

In thirty hens' eggs I found 466.2 grammes of yolk; hence, an egg contains, on an average, 15.54 grammes of yolk; while Poleck obtained 427.361 grammes from twenty-nine eggs, according to which an egg would contain 14.75% of yolk. The amount of *water* in the yolk of fresh eggs is liable to considerable variations; it fluctuates from 48 to 55%. The *inorganic matters* in the yolk amounted, according to Poleck, to 1.523%.

We will here add, for facility of comparison, the quantitative relations of the *albumen* or *white* of hens' eggs. In thirty eggs I found 690.3 grammes of albumen, or, on an average, 23.01 grammes in each egg; Poleck found 719.742 grammes in twenty-nine eggs, and hence, on an average, 24.8 grammes in one. Moreover, the quantity of *water* in the white is very variable, fluctuating between 82 and 88%. On an average, I found 13.316% of solid constituents in the fresh white. The *inorganic*

<sup>1</sup> Pogg. Ann. Bd. 79, S. 155-161.

<sup>2</sup> Ibid. p. 398-429.



*constituents* amount to from 0.64 to 0.68% of the white; according to Poleck, to 0.65%. In the dried residue I found, on an average, 3.042% of fusible ash.

In the ash of the white the *soluble salts* preponderate considerably over the *insoluble*, while in the ash of the yolk the reverse is the case; the excess of the soluble salts in the ash of the albumen principally depends on the considerable quantity of chlorides, which amount to 50.45% (or according to Poleck to 41.92% of chloride of potassium and 9.16% of chloride of sodium). Soda, in combination with acids, occurs in the white in far greater quantity than in the yolk (amounting in the former, according to Poleck and Weber, to 23.04, and in the latter to 5.12, or at most, to 5.70%); while the proportions of the potash-salts are exactly reversed (for in the white we have 2.36, and in the yolk 8.60, or even 8.93% of potash). Phosphoric acid is only present in small quantity in the ash of the white, amounting to 4.83%; but carbonic acid (from 11.6 to 14.05%) and a little sulphuric acid (from 1.40 to 2.63%) are also present. Silica occurs in almost the same quantity in the ash of the white (0.49%) as in that of the yolk, but the peroxide of iron is present in smaller quantity (from 0.34 to 0.44%), and so also are the lime and magnesia (there being 1.74% of the former and 1.60% of the latter); while in the ash of the yolk the earths are six or seven-fold increased, with a great preponderance of the lime, there being 12.21% of lime and 2.07% of magnesia. All these relations point to a determinate object in the distribution of the inorganic matters amongst the cells and the inter-cellular fluid of the animal body—a point of view which we shall find to be highly important in the consideration of the history of development.

We may readily convince ourselves of the presence of *carbonates* in the white of fresh eggs, by placing a little of this substance under the microscope, and adding acetic acid; we may then often perceive an extraordinarily great development of gas. The quantity of these pre-formed carbonates appear, however, to be very variable, and is probably dependent on the longer or shorter time during which the egg has been exposed to the air; it is possible that the carbonic acid obtained from the atmosphere may abstract a portion of the base from the albuminate of soda.

Free *gases* are contained both in the white and in the yolk, as in all animal fluids.

According to my analyses, fresh white of egg contains 12.274%, and the dried white 92.293% of *albumen* (determined in accordance with the rules laid down in vol. i. p. 304). We must refer to vol. i. p. 299, for a notice of the difference between the albumen of the egg and of the blood-serum.

The white of egg is by no means free from *fat*, although this substance is only present in extremely small quantity. On examining fresh white of egg under the microscope, we discover at intervals small granules, with three or four projecting teeth or points, which are obviously composed of margarin. If further we extract dried white of egg with ether, we sometimes, but not always, obtain a light azure solution; the fat which remains after the evaporation of the ether consists of olein and



margarin, but also contains oleate and margarate of soda, if any alcohol has been present in the ether which has been used: it is precipitated from its alcoholic solution by acetate of lead; when isolated and incinerated, it leaves an alkaline ash which effervesces with acids.

We have already seen (in vol. i. p. 258) that the white of egg ordinarily contains normal *sugar*; from the determinations which have hitherto been made, it appears that in the dry residue of white of egg there is about 0.5% of sugar (as calculated from the carbonic acid developed after the induction of fermentation).

The number representing the *extractive matters* of the white after the deduction of the fat, the sugar, and the salts, is not large; I found 3.143% in its solid residue.

It is worthy of notice, that a little albuminate of soda passes over into the alcohol-extract as well as into the water-extract, if we do not previously neutralize the white, and hence we may readily obtain an apparently larger quantity of extractive matters; the acetic acid, in combination with the alkali of the alcoholic extract, should consequently be deducted in the determination of the extractive matters.

Although the white of egg is a substance that falls under our daily observation, there does not as yet exist any good *analysis* of it; for certain precautionary measures are requisite for its examination, which have not been sufficiently attended to. The gelatinous white, as we obtain it from fresh eggs, is not merely an albumen or an albuminate of soda swollen with water, together with some adhering fat and an admixture of soluble substances, but it likewise contains insoluble membranous parts; we here refer not only to the chalazæ, but also to the delicate, textureless, only faintly granular membranous structures which cross the white in various directions, and so enclose it that, even after its careful removal from the egg, it always retains the appearance of a tolerably consistent mass. These delicate membranes possess the same refractive power as the white that is enclosed within them; and hence they do not become visible till after the addition of water. It must not, however, be supposed that all the flakes which become separated on the admixture of water and white of egg, are merely these previously invisible membranes, for the albuminate of soda of the egg, like that of the blood-serum, separates by strong dilution with water into an albuminate rich in alkali, and into albumen poor in alkali; the latter increases the insoluble part of the albumen that has been modified by water. We may readily convince ourselves on this point, by the addition of a neutral alkaline salt, as for instance, chloride of sodium or hydrochlorate of ammonia, to albumen which has been thus treated, and has become almost white and opaque from the separated flakes; a very great part of the turbidity then disappears, and we can now perceive, on a microscopic examination, that the portion which still remains undissolved consists merely of the prolongations of the chalazæ and the membranous parts. Hence, in order to determine with accuracy the quantity of the true *albumen* in the white of egg, a quantity of the latter (perfectly fresh, and weighed in a closed vessel) must be carefully triturated in a mortar; the watered white of egg is then to be poured into a cylindrical glass, and to be diluted with fifteen or twenty times its



quantity of water. Without this very free dilution, the albuminous solution can hardly be filtered, and even then it will often not pass through the filter in summer at a high temperature, when formations of byssus and vibrones so readily occur. After the whole of the fluid has been placed upon the filter, it is advisable at once to treat the residue with an aqueous solution of hydrochlorate of ammonia, and then to thoroughly wash it. The hydrochlorate of ammonia not merely dissolves the albumen which was precipitated by the water, but it likewise has the effect of allowing the whole of the albumen to coagulate on subsequently boiling the filtered fluid; it supersedes the acetic acid that is generally recommended, since there are formed chloride of sodium and albuminate of ammonia, which latter parts with its ammonia on boiling, perfectly coagulates, and forms a coagulum which may be readily collected on a filter.

The *fat* of the white of egg, like the extractive matters and the sugar, must be detected and quantitatively determined by the methods which have been already described in their appropriate places.

The presence of preformed *alkaline carbonates* can only be determined by the same method which has been already described as applicable to the blood and to transudations (see p. 54); when they have been determined, we may readily find a means of calculating the quantity of alkali in combination with albumen. Unfortunately, however, in consequence of the varying proportions in which the alkaline carbonates, and the alkali in combination with albumen, exist in different eggs, the determinations that have been made are so various, that as yet we have not succeeded in determining a definite ratio of the alkali to the albumen, or of the alkaline carbonates to the albuminate of soda.

The analysis of the yolk also presents its difficulties, some of which cannot be altogether overcome. The yolk-corpuscles are the less easily separated mechanically from the rest of the fluid, in consequence of the simultaneous presence of free granules of undissolved vitellin and fat-globules. I have found the following to be the best method of proceeding with the analysis; as in the examination of animal fluids generally, we must first ascertain the amount of solid residue and of salts; the latter must, however, only be determined by Rose's method, since by the application of a strong red heat for the purpose of incinerating, we should unquestionably lose a portion of phosphoric acid. To determine with any degree of accuracy its albuminous constituents, the uninjured yolk must naturally be in the first place freed from adhering white, by repeated but quick rinsing. The fluid of the yolk, which must now be allowed to escape from its membrane and very readily dries, must be weighed and shaken with ether as long as it continues to impart the faintest yellow tint to that menstruum. The remaining watery albuminous fluid then forms a white semi-solid mass; this must be shaken with water, which takes up a great part of the albuminous matter; its quantity is determined by boiling; the fluid which is poured away from the coagulum is evaporated, and the residue is extracted with alcohol; and the quantities of the water-extract and of the alcohol-extract are thus determined; this, however, serves only as a check for the other method, according to which the quantity of the extracts is determined from the solid residue of the whole fluid.



A large proportion, however, of the albuminous constituents of the yolk, comprising the casein and some albumen devoid of alkali, remains undissolved in water; this portion is now to be treated with a dilute solution of hydrochlorate of ammonia, by which the yolk-granules which are visible under the microscope, the casein, and the albumen that has been precipitated by water, are dissolved. The solution of these substances is heated, which precipitates the *albumen*; and the casein-containing fluid, after the separation of the albumen by filtration, is then carefully treated with dilute acetic acid, which precipitates the *casein*; or conversely, the casein is first thrown down by acetic acid, and the albumen is subsequently precipitated by boiling, after the neutralization of the acetic acid by ammonia. In order, however, to remove all protein-matters from the fluid, it is necessary that the filtered fluid should be evaporated to dryness, and the residue freed from hydrochlorate and acetate of ammonia by rinsing with cold water. It is only further necessary to refer to the rule laid down in vol. i. p. 600, that all albuminous substances, after being thoroughly washed with water, should also be treated with boiling spirit, in order to remove any adhering matters which are insoluble in water, but soluble in alcohol. This is especially necessary in the case of vitellin, since this substance, when obtained in the above-mentioned manner, is seldom altogether free from fat.

The white flakes that are insoluble in the solution of hydrochlorate of ammonia, and consist for the most part of the *membranous investments* of the yolk-globules, must be washed with distilled water to remove the hydrochlorate, and must then be dried and weighed.

The *sugar* must be determined from the alcohol-extract (after it has been freed from fat), either by fermentation, or by Fehling and Trommer's method.

*Lactic acid*, even when it is actually present, occurs in such small quantity, that we can scarcely hope to be able to determine its amount.

To determine the quantity of the *fat* and of the *phosphorized matters*, we must evaporate the yolk-fluid and dry it at  $110^{\circ}$ , before we extract it with ether. An accurate separation of the different substances soluble in ether is at present impossible; we shall, however, refer somewhat fully to the methods of separating and quantitatively determining the phosphorized substances of the fats, of the salts of the fatty acids, and of certain lipoids, when we treat of the cerebral and nervous tissues, since the phosphorized matters there fall especially under our notice. We have already (in vol. i. p. 220) indicated the general method of distinguishing the neutral fats from the fatty acids, and of separating them from each other.

We refrain from offering any remarks on the *physiological importance* of the individual constituents of the yolk, since this subject will be fully noticed in the history of development. It is certainly no rash conclusion to believe that in the egg the animal substrata are deposited in a condition ready for the formation of cells and tissues, and to base our view of the metamorphosis of food into organized matters on the constitution of the egg and the development of the embryo in it. We should hence be guilty of useless repetition if we were, in this chapter, to discuss the importance of each individual constituent of the egg in relation to the history of development.



## MUCUS.

There is scarcely any animal fluid within the entire range of the theory of the juices that has been so little investigated, in a scientific point of view, as the mucus; and the reasons of this are sufficiently obvious. In the first place, the expression "mucus" has a very vague signification; for although the proposition has been advanced, that the secretion of the mucous membranes alone is to be regarded in the light of mucus, we yet find, that under certain conditions there is secreted in the animal organism a limpid, viscid juice, having all the characters of mucus, without however being secreted from a true mucous membrane with the so-called mucous follicles. We need here only refer to the mucous contents of certain cysts, which yield, according to the investigations of Virchow<sup>1</sup> and Rokitansky,<sup>2</sup> all the reactions which have been regarded as characteristic of normal mucus. Several colloid abnormal as well as normal structures, as, for instance, the gelatin of Wharton, become converted into a fluid, which cannot be distinguished by any reaction from normal mucous juice. Another and still more important ground for the silence of chemists in reference to the constitution of mucus is, that the normal mucus is always so filled or interspersed with morphological elements, that it cannot be obtained in a purely chemical condition. In the present state of analysis, we are unable to separate these structures from the actual mucous juice, and we cannot prosecute a satisfactory chemical investigation of this substance, except in those rare cases in which a mucous juice is secreted which contains few of these cells, either from their original scarcity, or from the facility with which they may incidentally be removed from the fluid. These cases, as we have already observed, are rare, and the question even then remains, whether the substance we are investigating is perfectly identical with the mucous juice. May we venture, on the strength of some few coincident reactions, to pronounce upon the identity of juices springing from such different sources, whilst we think ourselves justified in separating globulin from albumen, and vitellin from casein? Can we re-establish, by means of alkalies, certain combinations with albumen and fibrin, which will exhibit all the physical and many of the chemical properties common to mucus? What differences, moreover, exist in the properties and characters of perfectly genuine mucus, which has originated from different mucous membranes? We do not here refer to the acid or alkaline reaction, or to the admixture of different cells, but simply to the different capacity for exerting a digestive action with acids on animal substances. But even if the chemist should succeed in overcoming all these difficulties, his labors would be of no avail, in consequence of the impossibility of obtaining the fluid in a normal condition; for this juice is secreted in such small quantities on all the mucous membranes, as long as they continue in a normal state, that only the merest

<sup>1</sup> Verhandl. der Gesellsch. f. Geburtshülfe in Berlin. 1848. Bd. 3, S. 203.

<sup>2</sup> Zur Anatomie des Kropfes. Wien, 1849, S. 11, reprinted from first volume of Denkschriften der mathem. naturwiss. Classe d. kais. Akad. d. Wissensch.



traces of it can be obtained. We also know how easily the mucous membranes may become diseased, and how much the mucus differs in these cases from the normal secretion. Daily experience shows how rapidly the number of the so-called mucus-corpuscles increases with the slightest irritation of the mucous membrane; and we know from the researches of Julius Vogel, that an irritated mucous membrane secretes not only such corpuscles, but also an albuminous, coagulable matter, however much it may be disposed to form true transudations and exudations. A proper consideration of all these circumstances furnishes an excuse for the neglect of chemists towards a subject whose investigation is so desirable both in a chemical and a physiological point of view. Then, moreover, the question regarding the mode of formation of this juice has not been decided by physiologists; for whilst in most mucous membranes, special organs, the so-called mucous follicles, have been regarded as the source of the mucus, there are also mucus-secreting membranes, which are entirely devoid of these follicles,—as, for instance, those of the antrum Highmorianum, the frontal and sphenoidal sinuses, the cavity of the tympanum, the ovula Nabothi, the synovial sacs, and finally, abnormal formations, as hygroma, cysts, &c. Hence the source of the mucus cannot be referred, or at least, not exclusively, to the glandular organs of the mucous membranes. Tilanus<sup>1</sup> drew attention to the circumstance that all these membranes are invested with an epithelial layer, and that the epithelial cells are probably integral components of the mucous juice, which must therefore stand in a causal connection with these bodies. But it would appear from the observations of Virchow<sup>2</sup> and Rokitansky,<sup>3</sup> that the colloid matter of cysts of the thyroid gland, and of the liver, kidneys, and ovary, may be converted into a substance very similar to, or even identical with the mucus, no epithelium being present in it. In the same manner as permanent cartilage may be converted into gluten, the gelatin of Wharton is readily converted into mucus (Virchow).<sup>4</sup>

We will now briefly consider the various histological elements which are blended with normal and abnormal mucus.

Normal mucus is never free from the *epithelium* of the mucous membrane from whence it has originated, and may, indeed, be said to consist almost entirely of epithelium, which appears to be only held together by means of a pellucid juice. This is as much the case with the mucous membranes which are invested with pavement epithelium, as with those which exhibit the cylindrical or ciliated structure; the cilia of the latter are, however, in general thrown off, so that we can rarely find perfect ciliated epithelium even in abnormal secretions.

According to the assertions of several observers, *mucus-corpuscles* do not occur in normal mucus; but some of these bodies may always be found on carefully examining the expectoration from the mouth, the normal mucous cloudy sediment in the urine, or the solid excrements.

<sup>1</sup> De saliva et muco, spec. inaugur. Amstelodami, 1849, p. 56-75.

<sup>2</sup> Arch. f. path. Anat. u. Physiol. Bd. 1, S. 115.

<sup>3</sup> Ueber d. Cysten. Wien, 1849, S. 20, reprinted from the first volume of Denkschr. d. math. naturwiss. Classe d. kais. Akad. d. Wissensch.

<sup>4</sup> In a private communication.



Although the mucus-corpuscles, which have justly been regarded as abortive epithelial cells, exhibit no distinct differences, either in a morphological or even in a micro-chemical point of view, from the ordinary pus-corpuscles; yet it cannot be denied that it requires the aid of water, or acetic acid, to bring into view the nuclei both of the normal and sparingly dispersed mucus-corpuscles, and of those corpuscles which are secreted from the mucous membrane during catarrh; in this case, however, the nuclei present one or more fissures. The mucus in blennorrhœal discharges contains little epithelium, and consists almost solely of mucus-corpuscles which are suspended in a greater or less quantity of viscid intercellular fluid. No essential difference can be observed between it and pus, in so far as either the collective fluid or the cells are concerned.

In the so-called exudative, or croupous inflammations of the mucous membrane, we constantly find *fibrinous coagula*, which frequently bear the impress of the cavity, or canal, from which they have originated; and at other times appear in the form of small, fibrous flakes, interspersed with mucus- or pus-corpuscles. These bodies occur in the expectorated mucus in diphtheritis, pneumonia, Bright's disease, dysentery, and similar affections of the mucous membranes. In these cases *blood-corpuscles* are also found to be present.

When the inflammation of the mucous membrane has ceased, and an exudation of a croupous nature is no longer separated from the canal, certain changes generally occur, which in the ordinary course of the process give occasion to the formation of pus-corpuscles, and during the slower resolution of the exudation, tend to the development of the *inflammatory globules* or *granular cells*. Histology shows us that these morphological elements vary considerably in size and form. We would here, however, draw attention to the fact, that a species of such granular cells occurs in the mucus, and more especially in the bronchial mucus, without having been preceded by any croupous inflammation of the mucous membrane. (They occur, for instance, in the tenacious, thick mucus, which is expectorated in the chronic bronchial catarrh of aged persons.) Under such circumstances, there is only a small quantity of mucous juice in addition to the granular cells and masses, and rarely any other morphological elements; the granules of the cells are in general much larger than those of the usual inflammatory globules, and resemble the nervous tissue in their strong refracting power. In many respects they bear a resemblance to the *corps granuleux* of the milk. In addition to these, there occur concentrically striated corpuscles, which often present the size and form of the granules of potato starch, and greatly resemble them. They are probably identical with *Hassal's corpuscles*, found by Henle<sup>1</sup> under similar conditions.

It is well known that such sputa are often of a gray, or sooty color, exhibiting in many cases steel-gray, highly glistening cilia, which are visible to the naked eye. These cilia may be readily isolated by a needle or scalpel, and when brought under the microscope the appearance they present is simply that of closely crowded granular cells of the kind above described, except that they exhibit no trace of pigment-

<sup>1</sup> Zeitschr. f. rat. Med. Bd. 7, S. 411.



molecules, or of black, or dark-colored masses. I do not know how to explain this phenomenon, except on the supposition that all the light has been absorbed by the densely crowded and strongly refracting cells, in the same manner as we observe that many metallic sulphides which appear black when observed in masses by the naked eye, exhibit nothing more than a mass of strongly refracting globules, when seen in a finely comminuted form, under high magnifying powers. The black, sooty color has frequently been ascribed to lamp smoke, or to finely comminuted coal-dust, which has been inhaled; but although I have never been able to detect anything of the kind, I would not, on that account, deny that under certain conditions, as, for instance, in colliers, smiths, &c., coal-dust may become mixed with the bronchial mucus. Many of the experiments instituted in relation to this subject are hardly worthy of confidence.

Free *fat* occurs in almost every kind of mucus, either in the form of vesicles or of very minute granules, and either in mere traces or in large quantities.

*Molecular or elementary granules* are seldom absent from the mucous juice, but they are more decidedly observable when the mucus has originated in a diseased structure, as in tuberculosis or cancer, but more especially in typhus, in which the milk-colored sputa appear, when seen under the microscope, to be enveloped, as it were, in a veil of very fine granules. We still more frequently remark the presence of such granules in intestinal mucus, owing to the favorable conditions afforded for the separation of these molecules by the decomposition of albuminous substances.

*Intestinal and cellular formations* of various shape and size (Valentin's exudation-cells), as well as similar elements from the solitary and agminated glands, which are usually found within the mucous membranes, are of very frequent occurrence in morbidly secreted mucus.

*Vibriones, microscopic fungoid growths*, and similar organic particles, can only be considered as of incidental occurrence.

Amongst the chemical constituents of the mucus, *mucin* occupies the first place. The presence of this substance imparts to the mucus its most important properties; but, unfortunately, it has never yet been completely separated from the above-described morphological substances, neither has it been obtained pure and free from other chemical organic or inorganic matters. This may be one of the causes why different mucous juices often behave very differently towards individual solvents and reagents.

Mucin is generally considered as insoluble in water, and as distributing itself in a finely-comminuted state through the fluid in which it swells; occasionally, however, as Scherer<sup>1</sup> has observed, a mucus is found which actually dissolves in water, and may be separated by filtration from the morphological substances. The mucous juice does not coagulate when exposed to heat, but becomes in some instances more thinly fluid and more nearly similar to a true solution. Alcohol precipitates the mucin from the fluid in flakes and threads, while dilute acetic acid precipitates it in the form of viscid flakes; if it occurs as a gelatinous mass, it is converted

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 57, S. 196-201.



by the same acid into white threads or fibres. The flakes and fibres are insoluble in extremely dilute acetic acid, but they dissolve when treated with the concentrated acid and with the aid of heat. The mineral acids behave in a similar manner, precipitating the mucin when diluted, and again dissolving it very readily when employed in a concentrated state. Mucin, on the other hand, dissolves very readily in dilute alkalies, but much less speedily in concentrated solutions. Acetic acid precipitates a larger quantity from dilute than from concentrated alkaline solutions, which is owing to the circumstance, that mucin, if not entirely soluble, yet admits of being reduced to a gelatinous state in solutions of alkaline salts, when not too dilute. Acetate of potash prevents the mucin in these cases from separating perfectly into flakes. Gelatinous mucus is frequently, as it were, coagulated by water, which causes it to become denser, and to lose its translucent, gelatinous character. This change is very probably owing to the abstraction by the water of the alkali or alkaline salts to which it partially owes this gelatinous condition. Ferrocyanide of potassium does not throw down mucin from the alkaline or the acid solution. (When, as is frequently the case, the mucus is precipitated from the acetic-acid solution by ferrocyanide of potassium, albumen or some similar protein-body is probably present with the mucin.) When, on the other hand, mucus is boiled with concentrated acetic acid, it will be very copiously precipitated by ferrocyanide of potassium. Hot concentrated nitric acid colors it yellow, while it is changed to a blue color when heated with hydrochloric acid and exposed to the air. Tannic acid or basic acetate of lead gives rise to a considerable precipitate from the aqueous, weak alkaline mucous solution, whilst nothing beyond a faint turbidity is induced by alum, chromic acid, bichloride of mercury, neutral acetate of lead, and other metallic salts.

Several elementary analyses of mucus have been instituted, but they can scarcely afford us any aid in judging of the composition of the mucin, since the epithelium has been included in the substance examined. Scherer, who has alone succeeded to some extent in exhibiting a preparation in any degree fit for an elementary analysis, found, as the mean of three experiments, 52.1% of carbon, 6.97% of hydrogen, 12.82% of nitrogen, and consequently 28.11% of oxygen. No sulphur was found, but there was 4.114% of white ash, which contained some alkaline carbonates, in addition to a tolerably large quantity of phosphate of lime.

Scherer obtained this mucus from a sac between the trachea and the œsophagus, which was probably an abnormally dilated bursa mucosa. The mucus could be filtered when strongly diluted with water, so that the morphological substances admitted of being removed. The mucin was precipitated from the solution by alcohol, and was then repeatedly boiled in alcohol and ether.

We have already referred to the observation of Julius Vogel, which admits so readily of confirmation, that the mucus secreted in catarrhal irritation of the mucous membrane exhibits a varying quantity of *albumen*. There are also cases in which the normal mucus may contain albumen; and if we include under the head of mucus, as indeed we almost necessarily must, the mucous investment of the stomach, which



is intermixed with the gastric juice, we have a mucous juice, which constantly contains albumen (Buchheim).<sup>1</sup> I have seen the contents of the ovula Nabothi rendered turbid by heating. Tilanus always found albumen together with mucin in the synovia within the joints. The mucous fluid of colloid cysts contains varying quantities of albumen, as we learn from the reactions obtained by Virchow and Rokitansky.

The peculiar substance named *pyin*, which has frequently been found by Güterbock in pus, has been regarded by many observers as a constant constituent of mucus, and even as identical with mucin (Escholtz).<sup>2</sup> The erroneous character of such an opinion may, however, be readily seen on comparing the properties ascribed to the pyin found in pus with those of mucin.

*Fat* occurs only in very small quantities in normal mucus, although the quantity increases in proportion to the occurrence of albumen and larger quantities of mucus-corpuscles. Nasse<sup>3</sup> found 6.25% of a semi-solid, yellowish-white fat in the solid residue of the normal nasal secretion, whilst the same mucus contained only 4.448% of solid constituents.

The mucus likewise contains *extractive matters* soluble in water and alcohol, but they have not been very carefully examined. The quantity of these substances is no doubt increased by the glandular secretions which are mixed with the mucus in the stomach and intestinal canal, and in this manner the intestinal juice and mucus have frequently been identified with certainty. But the difference between the mucus and the glandular secretion effused upon the intestinal mucous membrane, ought to be strictly kept in view. We have already spoken (in vol. i. p. 508) of the intestinal juice.

The *free acids* frequently found in the mucus are included amongst the extractive substances. Andral<sup>4</sup> maintains that true, pure mucus is always acid in a normal state; but although this assertion may be true, it has not been proved, nor indeed would it be very easy to do so; for as we are not acquainted with any entirely pure mucus, which may possibly be wholly free from any reaction on vegetable colors, we may assert, in reference to every mucus which exhibits an alkaline reaction, that this property may be owing to certain admixtures, consisting either of pure transudations from the blood or of special glandular secretions. As may be readily conjectured, no careful investigation has as yet been made in reference to the nature of the free acid which occurs, amongst other instances, in the secretions of the mucous membranes of the mouth and the urinary bladder.

In considering the quantity of the *alkalies* contained in mucus, we must especially bear in mind that no inconsiderable portion of the soda is combined with true mucin, as was observed by Berzelius<sup>5</sup> in the secretion from the mucous membrane of the nose, and by Scherer in the abnormally generated mucus above referred to. Nasse also found alkaline carbonates together with carbonate of lime in the ash of the normal nasal secretion.

Mucus is very rich in *alkaline chlorides*, of which Berzelius found

<sup>1</sup> Dissert. inaug. Leips. 1845.

<sup>2</sup> Journ. f. pr. Ch. Bd. 29, S. 59.

<sup>3</sup> Lehr. d. Chem. 4 Aufl. Bd. 9, S. 531.

<sup>4</sup> Rust's Magazine, Bd. 10, S. 160.

<sup>5</sup> Compt. rend. T. 26, p. 650-657.



0.56% in fresh nasal mucus, and Nasse 13% in the dry residue of similar mucus, which, however, contained no cells.

Nasse found some alkaline *sulphates and phosphates*, together with earthy phosphates, in the ash.

Berzelius found 6.63% and Nasse 4.448% of solid constituents in the nasal mucus, and Scherer 11.299% in the above-described abnormal mucus. The latter observer likewise found 7.6% of ash in 100 parts of the solid residue.

Unfortunately, however, no attention has been paid in these analyses of the normal mucus to the relation existing between the potash and the soda. Yet the establishment of this relation is not wholly devoid of importance in the solution of the question, whether the blood-corpuscles take part in the preparation of the mucus as they do in that of most other secretions, or whether the mucus is formed solely from the constituents of the blood-plasma. I know of only one analysis of the kind suited to throw light on the subject, and this yielded more potash and less soda in the ash of the mucus than in that of the blood-serum; but as this mucus had been secreted during an acute catarrh, and besides being very rich in young cells (mucus-corpuscles), contained also some granular cells, it does not afford any conclusive evidence.

The *method* of analyzing mucus would be very simple, if it were not wholly impracticable, in most cases, to separate the true *mucin* from the *cells* which are intermixed with it. It is only in a few rare instances, as in the case investigated by Scherer, and already referred to, that the morphological elements can be collected on the filter by mixing the object with a large quantity of water, and rendering it capable of being filtered by repeated and continuous shaking. The mucin, however, instead of being distributed through the water, is in many instances converted into an apparently coagulated condition, this being more especially the case with catarrhal bronchial mucus, which becomes shrunk by the abstraction of the alkaline salts which had previously caused the mucus to present a swollen appearance. When the mucin is not soluble in water, the only method of determining it even in an approximate degree, is to filter the substance after it has been digested with highly diluted ammonia. Unfortunately, however, the mucin which has been dissolved by the alkali passes very slowly through the filter, in consequence of the obstruction presented by the gelatinous swollen epithelium. In many cases, therefore, this method proves insufficient for the separation of the mucin from the above-described morphological elements. If we succeed in removing the epithelium by filtration, the mucin may be precipitated from the neutral or weakly acid solution by spirit, and from the alkaline solution by dilute acetic acid; after this, the precipitate must be washed with hot spirit, and after being dried at a temperature of 120°, must again be washed with hot water, in order to remove all the mineral and organic substances which are insoluble in spirit. The waters employed in rinsing must then each be strongly concentrated, and immediately evaporated with the spirituous solution filtered off from the mucin, while the residue is extracted with ether, alcohol, and water.

When *albumen* is present with the mucin, which indeed it very generally is in the large quantities of the substance necessary for such inves-



tigations, the difficulty of the analysis is greatly increased. If the mucin were insoluble in water, which appears to be never altogether the case, the separation of the soluble albumen from the insoluble mucin might be very easily effected: but this is by no means the case, for the swollen, gelatinous, or apparently coagulated mucin only gives up the albumen to the water with difficulty, and after a long time. Hence it is necessary, if we would desire to attain a comparatively successful result, to distribute the mucus repeatedly in water, and after suffering it to form a deposit, to pour only the clear fluid upon the filter, repeating the process until the filtered fluid no longer exhibits any opalescence on heating; for the insoluble mucous residue cannot be collected on the filter until the albumen has been completely removed. The quantity of the latter substance may be determined by the ordinary rules, and a further separation of the mucin from the epithelium may then be effected by means of diluted alkalies.

If the substance named *pyin* occur in the mucus, or if the latter contain a substance not coagulable by heat, but precipitable by acetic acid, although not again soluble in an excess of this acid, the albumen, in case the fluid was not alkaline, must *previously* be precipitated by boiling, and its quantity determined, after which the pyin-like substance may be separated from the filtered fluid by acetic acid. In case, however, the mucous fluid is alkaline, this substance must first be precipitated by acetic acid, and then washed for some time, in order to remove any albumen that may have been precipitated from the solution by acetic acid; and after the filtered fluid has been carefully neutralized by ammonia, which generally imparts some degree of turbidity to it, it must finally be boiled.

The quantitative determination of the remaining organic and mineral constituents of the mucus may easily be conducted by following the rules already given.

We are necessarily unable to form any estimate of the *quantity* of mucus secreted by the different mucous membranes; and it would seem sufficient to draw attention to the view advanced by Valentin, that the secretion separated from the surface of many of the mucous membranes must be regarded as exceedingly small, or even absolutely nothing in the normal state. It can only be regarded as the result of special or general irritation, when any considerable quantity of mucus is separated from an apparently healthy mucous membrane;—a view which seems to derive confirmation from the circumstance, that normal mucus can never be obtained from the living body in quantities sufficient for chemical analysis, but must be scraped away from the mucous membrane of animals immediately after they have been killed. The liability to error presented by such means is too obvious to need further comment. It is probable that the secretion is seldom perfectly normal when present in excess in morbid affections of the mucous membranes, and that it is generally mixed, in these cases, either with a transudation or exudation. This is shown both by the microscopico-mechanical and the chemical investigation of morbidly secreted mucus.

We have already observed, in the beginning of this chapter, in reference to the *origin* of the mucus, that the seat of the formation of this



fluid is not limited to the mucous follicles, for we have already noticed several mucous membranes in which there was no appearance of any such glandular organs. Some facts, indeed, seem to warrant the conclusion, that the formation of mucus is not limited to a definite spot, or associated with any definite tissue. The conversion of Wharton's gelatin into a substance perfectly similar to mucus in respect to its physical and chemical properties, the gradual transition of the colloid mass of many cysts into perfect mucus, and its occurrence in many exudations proceeding from serous membranes, are facts which cannot be lost sight of in our consideration of the origin of mucus. Tilanus has drawn special attention to the circumstance, that epithelial structures are always present wherever there is true mucus. This observation might lead to the assumption, that the formation of mucus is connected with the development of certain cells, that is to say, that its production occurs simultaneously with the development of certain morphological elements. Two views here present themselves for our consideration; one of which is, that the albuminates of the liquor sanguinis become decomposed, under certain hitherto unknown conditions, into the substratum of the epithelial cells and into mucus, whence the latter substance might in some respects be considered as a secondary product of this cell-formation, so that the mucous juice in the mucus would hold the same relation to the epithelial cells as the spirituous fluid does to the yeast-cells in a mixture which has undergone fermentation. The other view, which seems to be supported by numerous observations made by Scherer and Virchow,<sup>1</sup> refers the origin of the mucus to a partial disintegration of the epithelial cells. All who have followed Frerichs in his observations on the metamorphosis of the cells within the gastric juice, or who have examined them by the microscope in the preparation of artificial gastric juice, will easily comprehend the gradual solution of the gastric cells and their conversion into a mucous fluid. Such a conversion of cells into a mucous substance would, therefore, at all events not be wholly without analogy. Scherer and Virchow, however, go still further and advance the opinion, based upon several pathologico-histological observations and chemical experiments, that certain colloid substances, and others adapted for the formation of urine, may be converted into mucus under certain conditions which still remain to be explained, and even without any cell-formation; and hence they regard the latter mode of development as associated with the existence of colloid or cartilaginous substances. This view is supported not only by the absence of epithelial structures in many mucus-containing cysts, but more especially by the frequently noticed conversion of the gelatin of Wharton into perfect mucus. It appears to us still to require accurate chemical experiments, to decide which of these two hypotheses deserves the preference. The elementary analyses which were made by Scherer on a single variety of mucous juice, unfortunately do not enable us to decide the question, both because the atomic weight could not be determined, and because we are still entirely deficient in an accurate analysis of the epithelial cells, the colloid substance, &c. It remains for us to hope that the investigating powers of men like Scherer may before long enrich science

<sup>1</sup>In a private communication.



with the knowledge necessary for elucidating a subject which is so intimately associated with the advancement of physiology.

The localities in which mucus occurs clearly demonstrate that it is especially designed to serve as a protecting medium to all the parts which are placed in a reciprocal connection with the outer world (Joh. Müller).

## CUTANEOUS SECRETIONS.

Although in a certain point of view we may regard the epidermis, the nails, hairs, feathers, and scales, as products of the secretion of the skin, these objects will find a more appropriate place in this volume, where we treat of histological chemistry. We shall, therefore, here only notice those two well-known secretions, the sebaceous matter and the sweat.

The *sebaceous matter* is secreted by those innumerable glandular structures, the *folliculi sebacei*, which are distributed over the whole skin; they are racemose, branching glandules, with flask-like or pear-shaped secreting vesicles (the saccules or acini) and a very narrow neck. There are simply two anatomical points to which we would here refer, seeing that they have a bearing on the further consideration of the sebaceous matter. The first of these points is, that these sebaceous glands are always entirely imbedded in the non-fatty corium, and, although they secrete fat, are never found lying in the fatty subcutaneous areolar tissue; the second is, that the great majority of these glands are grouped around the roots of the hairs, and that their narrow mouths open into the hair-follicles; it is only on the *nymphæ*, the *glans penis*, and the inner membrane of the *præputium*, that we find sebaceous glands independently of the presence of hairs; the glands on these parts have, however, a somewhat different formation, the acini or saccules being more rounded and grouped in a mulberry-like form. We might here also mention the racemose Meibomian glands, and the coiled and twisted tubular ceruminous glands, since we shall, in the present chapter, consider their secretions, in so far as our chemical knowledge of them at present extends.

Although the secretions of the above-named glandular organs by no means have a perfectly identical composition, and indeed probably, to a certain extent, contain very heterogeneous constituents, yet, in regard to many of their physical and chemical relations, they are at least as nearly allied as the transudations which were considered in a previous chapter. In order as much as possible to include the comparative physiology of the subject, we shall, at the same time, notice the composition of castoreum, which has been shown by E. H. Weber<sup>1</sup> to be essentially nothing more than the secretion from the innumerable preputial folds of the penis and clitoris of the beaver.

<sup>1</sup> Ber. d. k. sächs Gesellsch. d. Wiss. Bd. 2, S. 185-200.



In all these secretions, without a single exception, we find a larger or smaller number of morphological elements: all these glandular vesicles and ducts are invested with a fine cellular epithelium, and hence, on a microscopic examination, we find *epithelial cells* in all these secretions; we often, however, find more pavement epithelium from the external skin than delicate cellular structure from the interior of the gland.

In most of these secretions, and especially and invariably in those of the Meibomian and ceruminous glands, we find peculiar, oval, angular, or roundish *cells*, from  $\frac{1}{200}$ th to  $\frac{1}{140}$ th of a line in diameter, which, in addition to a pale nucleus with nucleoli, contain minute, dark, and clearly defined granules, and a few distinct fat-globules.

The sebaceous glands, like the mucous follicles, when in a state of inflammatory irritation, produce those primary cells to which we apply the terms *pus-cells*, mucus-corpuscles, &c. These cells are present in small quantity after even the slightest irritation of the skin and of the follicles in question, but especially in the thoroughly puriform fluids which are secreted in inflammatory affections of the external auditory meatus and of the Meibomian glands, in balanitis, in acne, and in similar cutaneous disorders, which for the most part have their seat in the hair-follicles.

The minute animal described by G. Simon,<sup>1</sup> the *acarus folliculorum*, is commonly found in the normal secretion of the sebaceous glands, as well as in the so-called *comedones*.

An *albuminous substance* is contained in all the secretions of the above-named glands; it cannot, however, be easily exhibited in the soluble form, since, in accordance with the method by which alone we can analyze these solid fatty matters, it is always separated in the insoluble state; hence we cannot determine whether it is most similar to casein or to albumen; it is obviously a protein-body from its behavior with acetic acid and ferrocyanide of potassium, with concentrated nitric acid, hydrochloric acid, &c. Esenbeck,<sup>2</sup> who had an opportunity of examining a mass contained in a very distended hair-follicle, found in the dry substance 24.2% of this albuminous substance; I<sup>3</sup> found 4.0% of it in the vernix caseosa of a tolerably full-sized foetus, 5.6% in human smegma præputii, and 2.9% in that of a horse, 2.4% in the semi-solid mass obtained from the fresh pouch of the beaver (after drying), and 5.8% in Canadian castoreum.

*Fats* and *lipoids* constitute the principal part of these secretions: the ether-extract in the above-mentioned case of Esenbeck's amounted to 26.2%, while in the vernix caseosa I determined it at 47.5%, in human smegma præputii (collected after several operations for phimosis) at 52.8%, in that of the horse at 49.9%, in the fresh castoreum of a German beaver at 7.4%, in Russian castoreum at 2.5%, and in a specimen from Canada at 8.249%.

Of the *saponified fats*, olein and margarin are found in considerable quantity in the ether-extract; but in none of the secretions which I have examined, including the cerumen, was there a trace of butyryn or

<sup>1</sup> Muller's Arch. 1842, S. 218.

<sup>2</sup> Gmelin's Handb. d. Ch. Bd. 2, S. 2155.

<sup>3</sup> Ber. d. k. sächs. Ges. d. Wiss. Bd. 2, S. 200-208.



of butyric acid to be detected, although, as we shall presently see, this acid is very frequently secreted by the sudoriparous glands.

Of *lipoids* I found in the smegma præputii a little cholesterin, besides a body soluble in ether and hot alcohol, and very similar to cholesterin, but not crystallizable; in the vernix caseosa I found only this substance, and could not detect any cholesterin.

No *phosphorized fatty bodies* were found either in the vernix caseosa or in the preputial secretion.

The alcoholic extract of these secretions consists for the most part of the *margarates and oleates of potash, soda, and ammonia*: here also no alkaline butyrates can be detected; the ammonia-soaps preponderate considerably in the preputial secretion.

In addition to the soaps, the alcohol-extract contains only a little organic matter which does not admit of further determination, unless a substance peculiar to a special secretion or some incidental matter happen to be present, of which we shall speak further presently.

Berzelius<sup>1</sup> obtained from the *cerumen* a fat which was soft, white, opaque, easily fusible, devoid of action on litmus, and when treated with potash, yielded an extremely fetid soap, which, on the addition of hydrochloric acid, deposited the fatty acids in the form of a white powder; these acids did not readily rise to the surface of the solution, and fused at about 40°.

Vauquelin found that the fat of human *hair* was oleaginous and colored, and that it contained sulphur.

The fatty *sweat* which adheres to undressed wool consists, according to Vauquelin,<sup>2</sup> chiefly of a potash-soap; while, on the other hand, Chevreul,<sup>3</sup> who has more recently examined it, found non-saponifiable fats containing neither sulphur nor nitrogen, one of which fuses at 60°, while the other is fluid at 15°; to these two fats he gave the respective names of *stearerin* and *elaerin*.

I found that the *alcohol-extract* in the vernix caseosa amounted to 15.0%, in the human preputial smegma to 7.4%, and in that of the horse to 9.6%.

The resinous constituents of the castoreum soluble in alcohol still require a more accurate investigation than they have yet received. The amount of these matters in castoreum is extremely variable; in a fresh German specimen I found 67.7%, in a smoked Russian specimen 64.3%, and in a Canadian one 41.34%.

In all these secretions I also found small quantities of matter soluble only in water, the organic portion of which did not admit of further determination. In the vernix caseosa I found that the water-extract amounted to 3.3%, in the human preputial smegma to 6.1%, and in that of the horse to 5.4%.

That portion of these secretions which is insoluble in water, alcohol, and ether, consists for the most part of the histological structures which have been already mentioned, and likewise of hairs; at all events, so far as the vernix caseosa is concerned, through which we always find a network of *lanugo* running. From this mass we may extract the above-

<sup>1</sup> Lehrb. d. Chem. Bd. 9, S. 536.

<sup>2</sup> Ann. de Chim. T. 47, p. 276.

<sup>3</sup> Compt. rend. 1840. No. 16.



mentioned albuminous substance, which, however, at all events, in part belongs to the cells.

We find only a small amount of soluble *mineral constituents*, namely, a little *chloride of sodium* and *hydrochlorate of ammonia*, with *phosphate of ammonia and soda*. *Earthy phosphates*, on the other hand, occur in considerable quantity; there being, according to my analyses, 6.5% in the vernix caseosa, 9.7% in the smegma præputii of man, and 5.4% in that of the horse.

From this sketch of the few experiments to which secretions of this class have been subjected, we may at all events draw this conclusion, that however different the position and the structure of the sebaceous glands may be, they secrete tolerably similar products.

It is sufficiently obviously that no great weight can be attached to the determinations of the *quantity of water* in these secretions; in order, however, to give some general idea of the amount of water that is present, it may be mentioned that in the vernix caseosa I found 66.98%, and John Davy<sup>1</sup> 77.87% of water, but that in the secretions of the sebaceous glands of animals living in the air, the quantity of water is far less in consequence of the continuous evaporation, although it is liable to great variations depending on external conditions.

We have now to mention a few substances which are to be regarded either as incidental admixtures or as constituents peculiar to individual secretions. Amongst these we must first mention a *bile-like substance*, which I found in the preputial secretion of man, the horse, and the beaver: as I have been unable to find it in the vernix caseosa, in the cerumen, or the secretion of the Meibomian glands of a scrofulous child, it appears to be peculiar to the hairless sebaceous follicles of the prepuce and the glans penis. It was obtained from the ethereal extract by extraction with water, and yielded, with sulphuric acid and sugar, the most beautiful biliary reaction; that this could not be fat, is sufficiently obvious from its solubility, as well as from the rapidity with which the reaction ensued; but whether the substance is identical with any of the products of decomposition of the biliary acids, is a question that must be decided by further investigations.

The *resinous constituents* of castoreum have been already mentioned. Wöhler<sup>2</sup> has shown that they contain *carbonic acid*, or *oxide of phenyl* ( $C_{12}H_6O_2$ ), which may be detected by the blue color it imparts to a pine-shaving saturated with hydrochloric (Runge) or nitric acid (Laurent). Since the resinous constituents of castoreum coincide in a remarkable manner with those of hyraceum (which, according to my investigations, can only be the dried intestinal excrement of *Hyrax capensis*), and since phenylic acid occurs in both these substances, it seems most probable that they are not products of the metamorphosis of tissue, or that they are any peculiar secretion, but merely derivatives of the resinous substances conveyed in the intestinal canal of the animal with its food.

*Benzoic acid* has been detected in castoreum by Saugier, Brandes, Batka, and Riegel; from certain experiments which I made on the con-

<sup>1</sup> Medico-Chir. Trans. 1844, p. 193.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 49, S. 360, and Bd. 65, S. 342.



tents of fresh pouches, I think it probable that *hippuric acid* is originally contained in this substance.

I found *benzoic acid* in the preputial smegma of a horse.

It is very doubtful whether *uric acid* occurs in castoreum, although Brandes believes that he has found it.

In the preputial secretion of herbivorous animals, there is little phosphate of lime, which seems replaced by *carbonate of lime*; this, at all events, is very abundant in castoreum. This salt may be easily recognized, by observing under the microscope the considerable development of gas which the residue, insoluble in ether, alcohol, and water, yields on the addition of acetic acid, and by noting the considerable turbidity that is induced in the fluid which is thus obtained, by the addition of oxalate of ammonia.

In fresh castoreum we can recognize with the microscope the well-known crystals of *sulphate of lime*, and in the preputial smegma of the horse, the octohedral forms of *oxalate of lime*. The presence of both salts may be readily confirmed by a few micro-chemical experiments.

The smegma præputii of the horse, which I obtained for analysis, was of a blackish-gray color, soft and plastic like wax, and somewhat viscid when fresh; but when dried, it was hard, almost brittle, and presented a glistening fracture.

Little remains to be noticed regarding the different methods of *analyzing* these secretions, both qualitatively and quantitatively, in addition to the ordinary general rules, and to the special remarks on the detection of each individual constituent.

The above-mentioned *albuminous substance* can be only approximately determined, since it can only be extracted by acetic acid from the residue of the matter that is left after extraction with ether, alcohol, and water; this acid, however, abstracts a little albuminous matter and a certain quantity of earthy salts from the cellular structures of the residue. I determined this matter in the following manner:—I dried the residue after its extraction with indifferent menstrua, and determined its weight; I then digested it for several hours in moderately dilute acetic acid, rinsed it, and after drying again, weighed it; the loss of weight indicated the sum of the matters extracted by the acetic acid; the acid solution was evaporated, and its residue, without any further treatment, was incinerated for the determination of the mineral matters; the weight of the ash was then deducted from the loss of weight which the residue had suffered from the acetic acid. I thus obtained the number representing the quantity of the albuminous substance contained in the secretion.

With regard to the *carbolic acid*, we have only further to add, that its presence is by no means so easily to be recognized as might be supposed from the above-named reactions; for, independently of the extremely minute quantity in which it occurs in castoreum, the application of pine or fir shavings, saturated with hydrochloric acid, is exposed to certain fallacies; for the shavings of these woods, after being acted on by this acid, readily assume a bluish-green color on exposure to the sun: hence it is necessary, before applying this test, to separate the carbolic acid as completely as possible from the resinous and fatty constituents



of the castoreum, which, however, in consequence of the slight solubility of carbolic acid in alcohol and ether, and its high boiling-point,  $187^{\circ}$  C., is altogether impracticable when only small quantities are present.

We have nothing to add to the observations contained in the first volume, regarding the method of detecting and separating the *lipoids* and *fats*, *hippuric*, *benzoic*, and *uric acids*, *oxalate of lime*, &c.

We have at present no means of determining the *quantity* of matter secreted by the sebaceous glands collectively, or by special groups of them; moreover, daily experience teaches us that the amount must be very variable in different individuals and under different physiological and pathological conditions.

With regard to the *origin* of this secretion, we must bear in mind (when further investigating it) that the fat of the sebaceous glands must either be derived directly from the blood of the capillaries coiling around them, or must be formed from other matters in the cells of these minute glands; for it is worthy of notice that almost all these sebaceous glands are, as it were, rooted in a tissue which is completely devoid of fat, and do not penetrate into the fatty cellular tissue beneath the corium; the *glans penis* is almost absolutely devoid of fat. The variously refracting granules, globules, and vesicles which occur in many cells, as, for instance, in those of the external auditory canal and of the Meibomian glands, so frequently appear to represent new progressive stages of development of the same object, that we are almost led to the conjecture that the fat peculiar to these secretions is primarily formed within these glands.

These glands yield a fatty investment to the hair and cuticle; Krause<sup>1</sup> regards it as definitely established that this secretion diminishes the hygroscopical property of the horny layer of epidermis and of the hair, and that it hence checks the too rapid evaporation of moisture, and the drying up of the deeper epidermic layers and of the corium.

Under the term *sweat* we include only the fluid secretion of the sudoriparous glands, without reference to the question, whether these glands are also the sources of the gaseous transpiration of the skin or not. The sudoriparous glands are thread-like, delicate, single tubes, not communicating with one another, which originate in a blind extremity in the fatty subcutaneous cellular tissue, where they form spirally twisted coils; they then make their way through the corium and the younger epidermic layers in a corkscrew-like or serpentine course, and finally open with a considerably contracted mouth in the cuticle. These tubular sudoriparous glands are always invested with an epithelium, which consists of roundish or oval-angular nucleated cells.

The sweat, as it collects in drops upon the skin of a person who is perspiring freely, is, as is well-known, a colorless, very watery fluid, with a rather saltish taste, and usually communicates a peculiar, more or less intense odor, which varies with the cutaneous surface from which it has exuded: in most cases it has a weak acid reaction; indeed it is only sweat which has been collected from the axillæ and the feet that is often found to be alkaline.

<sup>1</sup> Handwörterb. de Physiol. Bd. 2, S. 135.



It is very difficult to obtain a sufficient quantity of sweat for chemical analysis in order to ascertain its constituents. Thénard and other chemists have employed shirts saturated with sweat, and extracted the sweat from them by various solvents; but this is the least advisable method, since here there is always a larger or smaller quantity of sebaceous matter mixed with the sweat; perfectly clean sponges are generally used in this case in order to dry the skin which had been previously cleansed, but is again brought into a state of perspiration. In this way the above-mentioned error is certainly much diminished, but it is not altogether avoided; for we still find in the sweat a very large number of epithelial scales, to which a little of the sebaceous secretion always adheres. The best method is that which was adopted by Anselmino,<sup>1</sup> who enclosed his arm in a glass cylinder that was rendered as air-tight as possible, and was thus able, in the course of five or six hours, to collect about a tablespoonful of sweat.

The sweat contains only a very small amount of solid constituents; Anselmino, whose method of proceeding is certainly the best that has been yet adopted, found that the solid non-volatile constituents varied from 0.5 to 1.25<sub>g</sub>.

The principal constituent of the sweat, that is to say, the substance which, next to the water, occurs in the largest quantity in this fluid, is, according to the experience of all observers, the *chloride of sodium*. *Phosphate of soda* is not found in sweat, and the *sulphate* only rarely (Simon),<sup>2</sup> while, on the other hand, the presence of *salts of ammonia* is very obvious (Berzelius);<sup>3</sup> the ammonia in the sweat is not only combined with hydrochloric acid, but also with organic acids; indeed it probably exists as carbonate of ammonia in alkaline sweat.

*Earthy phosphates* and a little *peroxide of iron* are constantly found in the sweat; they are, however, probably dependent on the admixture of epithelial cells with the fluid under examination; it is only in consequence of the assumption that lactic acid is contained in the sweat, that it has been also assumed that phosphate of lime exists in a state of solution in it.

It must still remain very doubtful whether the *fat* which is found in the sweat proceeds from the sudoriparous glands, or, whether it only depends on the admixture of a little of the secretion of the sebaceous glands. The fat of sweat that has been collected in the ordinary manner has, in point of fact, precisely the same physical and chemical properties as the fat of the sebaceous glands, as I have convinced myself by an examination of the very profuse perspiration of woman after delivery. Krause<sup>4</sup> has, however, shown, by a very admirable experiment, that, in reality, the sudoriparous glands themselves secrete true fat (together with butyric acid, &c.) It is well known that there are no sebaceous glands on the palm of the hand or the sole of the foot; Krause removed the fat and any loose epithelial scales from the palm of the hand by ether and friction, and then covered a square inch of it with a pad

<sup>1</sup> Tiedemann's Zeitschr. Bd. 2, S. 321-342.

<sup>2</sup> Handb. d. med. Ch. Bd. 2, S. 326-336 [or English Translation, Vol. 2, pp. 101-111].

<sup>3</sup> Lehrb. d. Chem. Bd. 9, S. 390-397.

<sup>4</sup> Op. cit. p. 146.



of filtering paper, from which all fatty matter had been removed by ether; this pad was firmly attached to the hollow of the hand, and retained there for one night, being securely guarded from external impurities; a gentle perspiration was induced towards morning; the paper, on being submitted to the action of ether, then yielded a fat which, in addition to margarin, contained an oily matter which rendered tissue paper distinctly transparent.

We may further readily convince ourselves of the presence of *butyric acid* in the sweat, by extracting with spirit textures thoroughly impregnated with sweat—as, for instance, stockings, flannels, and other parts of the dress that have been worn next the body—and distilling the extract; we then saturate the acid distillate with potash, evaporate, and decompose the salt with sulphuric acid, when a most distinct odor of rancid butter is developed; I even succeeded in obtaining the baryta salt, but the small quantity of irregular crystals was insufficient to enable me to prove with certainty by micrometrical measurement, that the salt was butyrate of baryta. If we can form an opinion from the odor of different kinds of sweat, it is very probable that caproic and metacetic acids, which are closely allied to butyric acid, are also present; in many diseases, especially such as are accompanied by an acute exanthematous eruption, there is often a singularly strong smell of metacetic acid. Anselmino and Simon have also detected *acetic acid* in sweat by its smell; since this acid, if it actually occur in the sweat, is always associated with other volatile acids of this group, it cannot be determined with certainty by any of the known tests for acetic acid: it is only by experimenting with very large quantities that we can form a decided opinion regarding the existence of acetic acid in sweat; we think it not improbable that it occurs there. Berzelius considers that *lactic acid* is the free acid of the sweat, and that it likewise is in combination with the ammonia; Berzelius has, however, not operated on such quantities of sweat as to have enabled him to determine this acid with his ordinary accuracy. Since, according to my investigations, the secretion of the sebaceous glands, even after saponification, yields either no volatile fatty acids, or, at most, very small quantities of them, the above-mentioned volatile acids must of necessity pertain to the secretion of the sudoriparous glands.

The *extractive matters*, which afford so much annoyance to the chemist, are of course present here; from the facility with which the sweat decomposes, it is even more difficult to arrive at any definite conclusion regarding its extractive matters than regarding those of many other animal fluids. Although we cannot recognize amongst these substances any material which possesses the properties of a protein-body, a *sulphurous matter* must be contained in the sweat; for if we keep fluid sweat in a closed glass, we find that a considerable quantity of sulphide of ammonium is formed as soon as decomposition commences.

The observations which have been made by physicians regarding the qualitative and quantitative changes which the sweat undergoes in diseases are of so uncertain a character, that we must hesitate in basing any conclusions on them. Such observations and conclusions as the following,—namely, that as the sweat of persons who perspire very



copiously, as, for instance, of rheumatic and arthritic patients, has a very distinctly acid reaction, therefore rheumatism and arthritis depend on a lactic-acid dyscrasia or diathesis,—might have been well spared in medicine. We need hardly observe that the increased acidity is in such cases dependent upon the concentration of the sweat by evaporation.

Anselmino maintains that he detected *albumen* in the “critical” sweat of a patient with acute rheumatism.

*Urea*<sup>1</sup> has not yet been found in the sweat; but it may probably occur there in cases in which the blood is richer than usual in this substance, and in which there is a very copious secretion of sweat.

Wolff<sup>2</sup> thought that he had once detected *uric acid* in the dried sweat from the forehead of a patient with calculus.

Every physician must have had opportunities of observing that certain *pigments* sometimes occur in the sweat of patients; thus the body-linen of jaundiced persons who perspire freely, sometimes assumes a yellow color. Blue and red pigments have also been observed in the sweat.

It has been shown by the experiments of Milly, Jurine, Ingenhous, Spallanzani, Abernethy, Barruel, and Collard de Martigny,<sup>3</sup> that *gases*, and especially *carbonic acid* and *nitrogen*, are likewise exhaled with the liquid secretion of the sudoriparous glands. According to the last-named experimentalist, the ratio between these two gases is very variable; thus, in the gas developed after vegetable food there is a preponderance of carbonic acid, and after animal food an excess of nitrogen; Abernethy found that on an average the collective gas contained rather more than two-thirds of carbonic acid, and rather less than one-third of nitrogen. When the process of perspiration is especially active, as, for instance, after strong bodily exercise, less gas is on the whole exhaled.

With regard to the *method of analyzing* the sweat, we have scarcely anything to add to the remarks already made (in various parts of the first volume) respecting the determination of the individual constituents contained in this secretion; we must, however, especially recollect that its volatile constituents can only be accurately determined by a careful examination; and again it must not be forgotten that the sweat very easily decomposes, and gives rise to the secondary formation of ammonia.

Numerous, and undoubtedly very careful, investigations have been made regarding the *absolute quantities* of the substances which are thrown off in a definite time by the sudoriparous glands and the skin generally. We shall postpone any notice of those investigations which, from the time of Sanctorius to that of Scharling, have simultaneously included the cutaneous and the pulmonary transpiration, and have estimated their sum collectively, till we treat of the respiratory process. Cruikshank, Abernethy, Dalton, and Anselmino, attempted in various ways to determine the amount of the cutaneous secretion; the most important, however, was that which Anselmino adopted, of determining the

<sup>1</sup> [Urea has been found in the sweat of healthy persons by Landerers (see Arch. f. Chem. u. Mikros. Bd. 4, p. 196), and by Schottin, a pupil of Lehmann's, in cases of renal disease (see Schmidt's Jahrb.) Bd. 74, S. 9.—G. E. D.]

<sup>2</sup> Diss. inaug. sing. cas. calculositatis. Tüb. 1817.

<sup>3</sup> Journ. de Physiol. T. 11, p. 1.



amount of the perspiration given off by a single extremity or by a known extent of cutaneous surface, and then calculating how much would be given off by the whole surface of the body; but independently of the circumstance that the other data for our calculation depend for the most part on very uncertain assumptions, no great weight can be attached to the final result. The argument *ex parte in totum* here holds good even to a less extent than in any other case, in consequence of the unequal distribution and unequal development of the glands (as, for instance, in the axillary region); and finally, the cutaneous surface, when enclosed, can hardly discharge its functions in the same manner as when it communicates freely with the atmosphere.

The calculations founded on the very laborious investigations of Seguin<sup>1</sup> should lead us nearer to the truth, although the non-volatile constituents of the skin have not been here included in the calculation. Seguin obtained absolute numbers from the amount of matter transpired by the skin, by weighing his body in such a manner that he determined the loss of weight which the body experienced when the respiration and perspiration are unimpeded, and then compared this with the loss of weight which the body underwent when the perspiration was retained in an air-tight case. It appears from these experiments, that the mean amount of the cutaneous is to that of the pulmonary transudation as 2 : 1, a ratio to which the still more carefully conducted experiments of Valentin also lead us, if we deduce it, as Krause<sup>2</sup> has done, from the sum of the quantities of water and carbonic acid expired by the lungs in twenty-four hours, and from the loss of weight which occurs during the same period from pulmonary and cutaneous transpiration. Valentin<sup>3</sup> found, by weighing at intervals of three days, that on an average his body lost 1246.93 grammes in twenty-four hours from cutaneous and pulmonary transpiration; from his measurements of the quantities of water and carbonic acid that are expired, as contrasted with the quantity of inspired oxygen, it followed that in the same time Valentin lost on an average 455.18 grammes; hence the perspiration in twenty-four hours amounted to 791.75 grammes, and the ratio of the perspired to the expired matters was as 9 : 5. Notwithstanding that the calculations founded on his experiments led to almost the same results as those of Seguin, Valentin<sup>4</sup> regards it as altogether impossible that more matters should be eliminated by the cutaneous perspiration than by the pulmonary exhalation; I agree, however, with Krause, in thinking that the above ratio is in all probability the true one. It appears to me that we in no degree detract from the full importance of the respiratory process, in considering that the loss of weight occasioned by pulmonary exhalation only happens to be so small because at the same time there is a great absorption of oxygen, which is not the case with the perspiration. If, for instance, we compare the quantities of the carbon and hydrogen eliminated through the lungs in twenty-four hours with the carbon and hydrogen of the perspiration (which, however, owe their oxidation for the most part to the oxygen absorbed by the lungs), the ratio becomes considerably modified and much more in favor of the pulmonary exhalation, the sum of the weights of these elements in the cutaneous transpi-

<sup>1</sup> Ann. de Chim. T. 90, p. 52-88 et 413-580.

<sup>2</sup> Lehrb. d. Physiol. d. Menschen. Bd. 1, S. 714.

<sup>3</sup> Op. cit. p. 144.

<sup>4</sup> Ibid. p. 582.



ration being to that in the pulmonary exhalation as 24 : 13. Hence there is nothing so extraordinary in the ratio assigned by Seguin, as to induce us to doubt that it approximates to the truth.

According to Brunner and Valentin<sup>1</sup> there are about 10·4 grammes of carbon, and according to Vierordt 1·5 of hydrogen, expired every hour in the form of carbonic acid and water. If we assume that the 51·95 grammes, which is the hourly amount of perspiration, according to Valentin, consist of 0·93 of a gramme of carbonic acid (as Abernethy asserts), 0·31 of a gramme of nitrogen, and 50·71 grammes of water, there would be 0·25 of a gramme of carbon, 0·92 of a gramme of nitrogen, and 5·57 grammes of hydrogen, removed by the perspiration in an hour. Hence the separation of non-oxygenous elements through the lungs would be to that through the skin in the ratio of 11·9 : 6·75, which corresponds pretty closely with that of 24 : 14. If we compare the quantity of the oxides exhaled from the lungs with that of the oxides in the cutaneous transpiration, we find that the two quantities are almost perfectly equal; for in the course of one hour there are exhaled from the lungs 51·53 grammes of carbonic acid + water, and from the skin 51·95 grammes of the same oxides, together with nitrogen.

We possess very few, and, from the nature of the case, very inaccurate determinations regarding the quantities of the sweat which are secreted under special relations, as, for instance, during strong bodily exercise, after abundant draughts of water and being enveloped in blankets, in the vapor-bath, &c. The only observations bearing on this point to which we will refer, are those of Berthold,<sup>2</sup> which were made in a vapor-bath, and therefore under circumstances in which the sweat that was thrown off could not evaporate, and also where water could not easily be given off by the lungs; Berthold found that after he had remained half an hour in the vapor-bath, he had lost a pound and a half in weight; since the carbonic acid exhaled from the lungs is nearly replaced by the inspired oxygen, we may fairly assume that an adult man in a vapor-bath loses about 25 grammes of sweat in a minute.

According to Abernethy, there are about 412 cubic inches of carbonic acid exhaled from the skin of a full-grown man in twenty-four hours.

Krause calculated that in the course of twenty-four hours there are excreted by the sweat of an adult male 791·5 grammes of water, 7·98 of organic and volatile matters, and 2·66 of mineral substances.

Physiologists have long held different views regarding the *sources* of the cutaneous transpiration, some maintaining that the whole of the cutaneous transpiration and sweat arise solely from the sudoriparous glands, while others assert that an elastic fluid permeates the epidermis. We shall revert to this subject, in so far as it falls within the scope of our inquiries, when we treat of the mechanical metamorphosis of matter.

The *importance* of the cutaneous transpiration is so obvious to every one, that we might readily believe that its objects would be sufficiently manifest; yet the most we can do is to frame hypotheses on the subject. One of the undoubted uses, although not the principal object, of the cutaneous transpiration, is to regulate the temperature of the animal body. Although there is a perfect correspondence of physical laws and

<sup>1</sup> Arch. f. phys. Heilk. Bd. 2, S. 373-417.

<sup>2</sup> Müller's Arch. 1838, S. 177.



physiological experiments in so far as this function of the perspiration is concerned, it has in general been somewhat over-estimated; because, on the one hand, the external temperature is almost always below the temperature of the body, and hence the evaporation of fluids is not required to cool the organism from the surface inwards, and because, on the other hand, the activity of the lungs, by which the blood is almost directly cooled, fulfils this object in a far higher degree. It is generally believed that the transpiration is the medium through which certain substances are eliminated, whose retention, in cases of suppressed perspiration, might give rise to various morbid conditions. The most superficial observer cannot fail to perceive the extremely injurious consequences that often follow even a partial suppression of the transpiration, and hence the analysis (which is always imperfect) of the chemical constituents which the skin separates, not only fails to give us any conclusion, but it might probably lead us to the erroneous view that this function of the skin may be perfectly replaced by the kidneys, for the constituents of the sweat are collectively contained in the urine. We should, however, obviously be drawing too general a conclusion, if we were led from the investigations of chemists to ascribe a less importance to the cutaneous transpiration. When we can directly refer individual groups of symptoms to affections of the peripheral nerves, induced by rapid cooling, there follow a group of sequelæ, which we cannot help ascribing to the retention of certain deleterious substances. In the present imperfect state of zoo-chemical analysis in reference to the volatile odorous matters, we may readily believe that the substances of this nature, which always occur more or less abundantly in the sweat, induce definite changes in the metamorphosis of the blood as well as in the functions of the individual organs, and thus occasion the various forms of diseases arising from chill; many, however, of the volatile matters pertaining to the *materia medica* and to toxicology, when introduced into the mass of the juices, even in extremely minute quantities, induce the most urgent morbid phenomena. There is no secretion—not even the very analogous pulmonary exhalation—in which we find such various and penetrating odorous substances as in the cutaneous transpiration. Strongly odorous matters, as for instance, balsam of copaiva, musk, ether, the dead-house smell, &c., when taken into the system, are not only given off with the flatus and the pulmonary exhalation, but also by the cutaneous transpiration. Hence it would seem as if the skin, like most other organs, provided for the separation of certain peculiar matters, and thus fulfilled a special object in the economy of the animal organism.

As a natural sequence, we should here notice the pulmonary exhalation, but the positive results of the investigations that have been hitherto made in relation to this subject, are so intimately connected with those undertaken to elucidate the process of respiration, that we must run the risk of being charged with procrastination or want of clearness, if, from a love of systematic arrangement, we should boldly separate from one another investigations undertaken with a single idea.

[Favre,<sup>1</sup> who asserts that he has operated on 40 litres (or 8·8 gallons)

<sup>1</sup> *Compt. rend.* T. 35, p. 721-723; and *Arch. gén. de Méd.* 1853, 5<sup>e</sup> Sér. T. 2, pp. 1-21.



of sweat, maintains, that after prolonged sweating the secretion becomes neutral, and finally alkaline; Lehmann, however, was unable to confirm this observation; it is to be regretted that Favre has not stated how he collected this enormous quantity.

The solid constituents amount, according to Schottin,<sup>1</sup> to 2.26%, while according to Favre they do not exceed 0.443%. In these 2.26% of the solid constituents of normal sweat, Schottin found 0.42% of epithelium and insoluble matters. In 100 parts of the ash of the sweat he found 31.3 parts of chlorine, combined with 28.2 of sodium and 11.1 of potassium; the ratio of the potassium to the sodium in the ash was as 15.7 : 27.5.

In the ash of the sweat from the feet he found 4.1% of phosphate of lime, and 1.4% of phosphate of magnesia and oxide of iron. Moreover, in two closely coinciding analysis of the ash of sweat from the feet and arms, he found 5.5% of insoluble and 94.5% of soluble mineral constituents.

The organic acids of the sweat were never strictly investigated until Schottin undertook the examination of this fluid: he has demonstrated with the greatest certainty the presence of *formic* and *acetic acids* in it. Lehmann considers it singular that the formic acid should preponderate so much, as seems to be the case, over the other volatile acids; the acetic acid was in far smaller quantity, and butyric acid was present in new traces.

For a long time the presence of *lactic acid* in the sweat was regarded as an accepted fact; but Lehmann failed in detecting any trace of it in the sweat either of puerperal women or of persons suffering from gout or rheumatism, and it was unquestionably proved that this acid was not present in the sweat collected by Schottin. Favre, who seems to have entirely overlooked the presence of volatile acids in the sweat, maintains, however, that he has not only demonstrated the existence of this acid by the exhibition of its zinc-salt and elementary analysis, but that he has determined the actual quantity of the lactate of potash and soda in the sweat at 0.0317%.

Favre further believes that he has discovered a new nitrogenous acid in the sweat, to which he has given the name of *hydrotic* or *sudoric acid*. From two elementary analyses of its silver-salt he assigns to it the formula  $C_{10}H_8NO_{13}$ .

With regard to the presence of *urea* in the sweat, Favre regards it as a normal constituent, and he thinks that it is upon its presence or that of a similar substance that the readiness with which the fluid becomes alkaline depends; but notwithstanding the most careful search, Schottin failed in detecting it, either in the normal sweat generally, or in the sweat of the feet which so soon becomes alkaline. Schottin, however, made the interesting observation (see foot-note to p. 101) that in *uræmia* (especially when occurring in cases of cholera) considerable quantities of urea pass into the sweat.

We sometimes find the bodies of persons who have died from cholera coated with a thin bluish layer, which on closer examination is found to consist of a fine powder, composed for the most part of urea.

Lehmann was unable to detect any trace of *sugar* in the sweat of a

<sup>1</sup> Arch. f. physiol. Heilk. Bd. 11, S. 73-104.



diabetic patient, who, contrary to the general rule, perspired very copiously in a hot summer.

Schottin has instituted several very admirable experiments on *the passage of several matters into the sweat*, and from these it would appear that *benzoic acid*, and also succinic and tartaric acids, pass very rapidly and unchanged into the sweat. Iodide of potassium was not detected in the sweat until it had been taken for five days (half a drachm daily). When salicine was taken, neither this substance itself nor any of its known products of decomposition, could be detected in the sweat. Quinine, taken to the amount of 12 grammes, did not pass into the sweat. After the ingestion of much *sugar of milk*, neither a saccharine matter nor lactic acid appeared in the sweat.

It would be very interesting to decide, whether the benzoic acid found by Schottin in the sweat is produced from the decomposition of hippuric acid by the sweat, or whether the acid is separated unchanged by the sweat-glands without being previously converted into hippuric acid (as when it is separated by the urine). As cinnamic acid would appear from the discovery of Marchand and Erdmann to be separated by the kidneys as hippuric acid, this question might apparently be determined by an examination of the acid that appears in the sweat after the use of cinnamic acid; for if, instead of the latter, benzoic acid should appear, it would tend in some degree to favor the opinion that the cinnamic acid was first converted into hippuric acid, from which the benzoic acid was then produced. If, on the other hand, cinnamic acid were found in the sweat, it would afford greater probability to the view, that the benzoic acid found in the sweat could not have been converted into hippuric acid before its excretion. Unfortunately, however, the quantity found in Schottin's experiments was no more than sufficient for a microscopico-chemical examination, but the microscope could not settle this point definitely, owing to the great resemblance between the crystalline form of these two free acids and of their salts.—G. E. D.]

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## URINE.

If there were any branch of zoo-chemistry from which physiology and medicine might reasonably have expected to reap any certain knowledge in reference to the vegetative processes in the animal body in health and disease, it was assuredly the urine. For if the physical properties and changes exhibited by this secretion, under different conditions, had even attracted the attention of the ancients, and led them to the knowledge of a number of highly significant, although unexplained facts, the subject could not fail from its accessible nature, early to become a matter of inquiry on the revival of scientific investigation. The readiness with which the urine might be obtained, necessarily facilitated the labors of experimentalists in a greater degree than is the case with most other objects submitted to analytical investigation. Hence the early inquirers, whose attention was chiefly directed to the observation of animal phe-



nomena, made the elucidation of this subject a special object of their investigations. Men such as van Helmont, Boerhaave, and others, who excelled in all branches of the sciences cultivated in their age, instituted several very admirable experiments with the urine; while those who aided in establishing modern chemistry, amongst whom we may instance Cruikshank, Fourcroy, and Vauquelin, have left us tolerably perfect analyses of this highly compound fluid. At the beginning of the present century, the analysis of the urine was one of the earliest investigations of Berzelius, and it still ranks, after a period of fifty years, as an index of the composition of this fluid, as well as a type of the mode in which an analytical inquiry should be conducted. Modern investigators have devoted themselves, with all the ardor and enthusiasm of a newly-created or revived science, to the chemical examination of the urine, and hence modern literature is overcharged with works on the subject. We have here no lack of systematic inquiries, conducted from physiological, or pathological, points of view, or of individual analyses which have been undertaken with reference to some point of pure chemistry, or for purposes of special diagnosis. In the place of any such deficiency, we have so vast an accumulation of such labors, that one might be disposed to believe, judging by its bulk, that the study of the urine was the most complete portion of physiological chemistry. In how far such a belief is confirmed by fact, we leave the reader to determine from the following pages.

It is scarcely necessary to observe that the urine, when considered from a physiological point of view, must be regarded as a fluid secreted by the organism from definite organs—the kidneys—and containing certain soluble, nitrogenous, and saline substances, which have either become effete through the metamorphosis of animal matter, or have been conveyed into the animal body, but are injurious to the animal functions.

On examining normal human urine, we find that, when in a fresh state, it is of a lighter or deeper amber color, and has a bitter saline taste. When freshly passed, and while it retains the temperature of the body, it is perfectly clear and transparent, and has a peculiar, faintly aromatic odor. It is always somewhat heavier than water, although its density never rises above 1.03 (in the normal state). It distinctly reddens litmus paper, although not always with equal intensity. When the urine is kept in a clean vessel, it does not decompose so rapidly as has generally been supposed, especially when it contains a considerable amount of solid constituents. In urine, shortly after cooling, particularly if it be concentrated, and after it has remained for a long time in the bladder, as, for instance, in morning-urine, a light, cloudy film becomes formed, which gradually sinks to the bottom. The acid reaction gradually increases when the urine is kept for some time at a mean temperature, and yellowish-red crystals, which are even discernible to the naked eye, are then deposited in the mucous sediment, and on the sides of the vessel. In this condition the urine may often continue unchanged for several weeks, without undergoing further decomposition; if, however, the urine be very dilute, and the temperature rises above the mean, a different process from that of acid fermentation is observed speedily to



occur. The urine is then found to be covered with a thin, fatty, shining, and frequently iridescent membrane, fragments of which gradually sink to the bottom. The mucous sediment is then interspersed with dirty yellowish-white flakes, the urine acquires a pale color, its reaction becomes alkaline, and it begins to develop a nauseous, ammoniacal odor. The reddish-yellow crystals are replaced by white granules, which are intermixed with colorless, strongly refracting, prismatic crystals.

The urine of carnivorous mammalia differs little from that of man. It is perfectly clear, generally of a much lighter, almost straw-colored hue, and strongly reddens litmus paper. The urine of herbivorous animals, on the contrary, is usually turbid, and in some cases even exhibits a decided sediment of a dirty yellow color. It has a nauseous, sweetish odor, and an alkaline reaction.

The urine of birds and amphibia—animals in whom the ureters open into the rectum—is gelatinous, semi-fluid, and translucent, when freshly discharged; it rapidly dries in the air, and is then converted into white, cheese-like, crumbling masses.

The normal urine contains fewer *morphological constituents* than any other animal fluid, although the peculiarly formed *pavement epithelium* of the urinary passages, and more especially of the bladder, are never wholly absent. Virchow has drawn attention to the different forms of the epithelium of the bladder, which sometimes resembles three-toothed clamps, within which portions of the ordinarily shaped pavement epithelium are enclosed. The appearance of such cells in the urine is only of rare occurrence; they are found connected together, when the urine exhibits an abundant supply of epithelium, which had been peeled off within the urinary tubes; this is frequently the case after scarlatina, and less constantly after erysipelas.

The mucous sediment of normal urine is found, on a careful microscopical investigation, to contain well-formed *mucus-corpuscles*, having a simple, lenticular nucleus. These bodies occur in increased quantities even on slight irritations of the mucous membrane of the bladder, and, still more constantly, in vesical catarrh and pyelitis, when the urine often deposits a considerable, and apparently purulent sediment. In gonorrhoea, the mucus-corpuscles arising from the urethra are distinguished from those of the bladder and the remainder of the urinary tract by their greater size, and by their vitreous and but slightly granular appearance.

Among the different molecules of morbid urine which have been recognized by the aid of the microscope, special attention has been directed to the *tube-like, or cylindrical bodies*, investigated by Nasse,<sup>1</sup> Henle,<sup>2</sup> and Simon.<sup>3</sup> On attempting to classify them by their texture, we find that they admit of being divided into three kinds: the first class embracing those tube-like formations, which appear to consist of the epithelial investment of the tubes of Bellini; they are tolerably regular cylinders, to which the small cells and nuclei appear to adhere in a somewhat honeycomb arrangement. These cylinders do not in general occur excepting in the desquamative stage of acute exanthemata, and at the

<sup>1</sup> Correspondenzbl. rh. u. Westph. Aertze. 1843, S. 121.

<sup>2</sup> Zeitschr. f. rat. Med. Bd. 1, S. 60 u. 68.

<sup>3</sup> Müller's Arch. 1843, S. 26.



commencement of every inflammatory irritation of the kidneys. The second class of these cylinders consists of fresh exudation, which is formed within the tubes of Bellini, whose shape it retains, and consists of cylindrically granular parts, enclosing blood-corpuscles and pus-corpuscles, and consisting apparently of fibrin; at all events they dissolve pretty readily in alkalis, while the enclosed corpuscles are partly destroyed and partly distributed in the fluid. As these are true croupous exudations, they necessarily appear in all the inflammatory renal affections which are usually included in the acute form of Bright's disease. There is, however, frequently a third form of these tubes, which occur in the shape of hollow cylinders with walls, which are so perfectly hyaline that they cannot easily be detected under the microscope, unless by modifying the light. They are frequently compressed together, or plaited as it were, and even in some cases coiled round their axes. They generally occur only scattered in the chronic forms of Bright's disease, as, for instance, in fully developed fatty degeneration of the kidneys. When treated with potash, they disappear, leaving only a fine, granular substance. An epithelial cell, or a rudiment of it, may often be observed in this species of cylinders, which I can scarcely regard as anything but the *membrana propria* of the urinary ducts. Acetic acid causes them to disappear, but I have been unable to discover by washing with water, or by neutralization with acids, whether they have actually been dissolved, or have only swelled up, and have thus attained the same refracting power as the surrounding medium. They must not be confounded with the above-described croupous cylinders of fibrin.

*Spermatozoa* are generally present in the urine after nocturnal emissions, or the act of coition, and they are also believed to occur in the somewhat rare affection of spermatorrhœa. They are not unfrequently found in the urine of typhous patients; although in these cases there may probably have been previous erection with a discharge of semen, yet in this disease, they would sometimes appear to have passed from the urethra into the bladder, since they have been found attached to its mucous membrane in the bodies of persons who have died of typhus.

*Elongated mucus-plugs*, which appear, when examined under the microscope, to consist of mucus-corpuscles arranged in rows, are frequently met with after gonorrhœa, and the so-called *goutte militaire*.

*Blood-corpuscles* are of frequent occurrence; and, as may be conjectured, they may originate from very different sources. They occur in small quantities in inflammations of the kidneys and urinary passages, but more especially in Bright's disease, in all the stages of which they have been found. If the urine be acid, the blood-cells remain for a long time without being decomposed, or at most become somewhat jagged; they are usually somewhat swollen, and approximate to the spherical form, being in general paler than in their ordinary condition, although still characterized by a strongly defined outline. The salts contained in the urine are probably the cause of their not assuming the nummular arrangement.

Large accumulations of *fibrin* only occur in the urine in acute inflammations of the kidneys or urinary ducts, and then always in association with blood-corpuscles.



When the urine is not perfectly fresh, it is found on examination frequently to contain certain organized matters, which may be classed among vegetable substances, or infusoria. These are gradually developed in the acid urine, and more especially in the mucous sediment, from which, as it would appear, there are formed certain microscopic *filamentous fungi*, which are very similar to the *mykoderma cerevisiæ*, differing only in being considerably smaller ( $\frac{1}{280}$  to  $\frac{1}{330}$ "), having a spherical rather than an oblong shape, and a distinct eccentric, round nucleus. They appear to be developed precisely in the same manner as the yeast-fungi; when the urine begins to lose its acid reaction, they may be observed upon the surface of the fluid, and probably contribute towards the formation of the membrane with which it is frequently found to be covered. The more complex vegetable organisms are not formed until the urine has begun to be alkaline; when we may observe numerous confervoid filaments, with or without spores, which often form a dense network, whose separate threads are commonly seen to extend over the whole field of view, even when examined with low powers.

*Infusoria* may always be detected in the urine after it has become alkaline: the form usually present is the ordinary filamentous or rod-like *vibrio* (*vibrio lineola* ?), although moving molecular specks are also observed, which Höfle<sup>1</sup> regards as the *monas termo* of Ehrenberg.

We have already mentioned, at p. 527, that Heller seems on one occasion also to have found the *sarcina ventriculi* of Goodsir in the urine.<sup>2</sup>

We now pass to the non-organic formations of chemical substances which occur in the urine, and which give rise to the urinary sediments when present in large quantities; amongst these the ordinary amorphous *urate of soda* occupies the principal place. We have already noticed this substance at length, at p. 194 of vol. i., where we also referred to the occurrence of *urate of ammonia*, in the form of dark globular molecules studded with fine needles, in urine that has become alkaline.

The prismatic crystals of the *phosphate of ammonia and magnesia*, occur only in neutral or alkaline urine; this substance was also noticed at p. 382 of vol. i.

The octohedral crystals of *oxalate of lime*, which are found in small quantities in the normal urine, and in greater abundance in certain morbid conditions, have also been described in vol. i. pp. 50–54.

The crystals of *cystine*, described in vol. i. p. 164, constitute a less frequent spontaneous sediment of morbid urine.

*Urea* occupies the first place amongst the *chemical constituents* of the urine, both because it exceeds in quantity all the other solid constituents of this fluid, and on account of the important part which this body plays amongst the *detritus* of the metamorphoses of animal matter, both in a physiological and in a chemical point of view. All these relations have already been fully considered in vol. i. pp. 143–156.

A similar observation may be made in reference to the *uric acid* present in the urine (vol. i. pp. 182–200).

<sup>1</sup> Chem. u. Mikr. Nachträge, S. 159.

<sup>2</sup> [Heller has since recorded a second case. See Arch. f. Chim. u. Mikros. New Ser. Bd. i. S. 30. A case has also been met with by Dr. Mackay. See Bennett's "Introduction to Clinical Medicine," 2d ed. p. 96.—G. E. D.]



We have already stated in our description of the chemical and physiological relations of *hippuric acid* (see vol. i. pp. 173–182), that this acid must be regarded as a normal constituent of human urine.

Liebig's discovery that the nitrogenous and crystallizable bodies, known as *creatine* and *creatinine*, which are contained in the fluid of the flesh, also occur in the urine, induced us to enter into a full consideration of these substances in the first volume. (See pp. 126–133.)

We have already spoken, in vol. i. p. 99, of the occasional presence of *lactic acid* and lactates.

We treated at pp. 283–286, vol. i., with all possible brevity, of the *extractive* and *coloring matters* of the urine; and as it would only lead to confusion, if we were to notice the numerous and fruitless observations which have been made on this subject, we will leave this question for the present, in the hope that it may speedily be elucidated by the scientific exposition of some able inquirer. We must, however, observe that the extractive matters occur in very variable quantities in the urine, more especially during disease, although it may also be the case in health during different physiological relations. Thus, for instance, Scherer<sup>1</sup> found that children, in relation to their bodily weight, excrete far more extractive matter through the urine in 24 hours than adults. He found that the sum of the excretion was 0.346 of a gramme in the 24 hours for every kilogramme's weight of a child, while in the case of an adult it was only 0.156 of a gramme for every kilogramme's weight. Scherer, moreover, made a very remarkable observation on an insane person, who, although he had scarcely taken any nourishment for four weeks, yet discharged a large quantity of extractive matters, exceeding even the amount of the urea; thus, for instance, he excreted 9.48 grammes of urea and 10.59 grammes of extractive matters in the 24 hours. There is, however, one substance concealed in these extractive matters, to which the attention of chemists has been specially drawn by Scharling.<sup>2</sup> This substance is contained in the ethereal extract of the urine, where it occurs mixed with pigment, with a fatty matter, and with volatile fatty acids. Unfortunately, however, all attempts to obtain this substance in a perfectly pure state for the purpose of investigation have hitherto failed. This body, to which Scharling gave the name of *oxide of omichmyl*, resembles resin, fuses in boiling water into a yellowish oil, and dissolves in alcohol, ether, and alkalies. It must, for the present, remain undetermined whether the acid reaction depends upon some acid associated with it, or whether it appertains to the oxide of omichmyl. When dry it smells like castoreum, but when moist it has a somewhat urinous odor, and when treated with oil of turpentine it developes a violet-like fragrance. It is decomposed by heat. On treating it with chlorine gas, Scharling obtained a substance whose composition was  $= C_{14}H_5ClO_4$ , and, therefore, perfectly isomeric with chloride of salicyl. It must, however, still remain an open question, whether the oxide of omichmyl is actually precipitated, and the above-described substance is a simple hydrogen-compound,  $C_{14}H_6O_4$ , of the chloride analyzed by Scharling, this compound being isomeric with salicylous

<sup>1</sup> Verhandl. d. phys.-med. Ges zu Würzburg. Bd. 3, S. 187–190.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 42, S. 265.



acid; for it might easily be the product of decomposition of a more complicated compound. Unfortunately, the above-described body was unfit for an elementary analysis, as it could not be exhibited in a perfectly pure state. This oxide of omichmyl did not yield the same reaction as the salicyl-compounds, when treated with nitrate of iron.

*Mucous juice*, as already mentioned, always occurs in the normal urine, although it is often present in very small quantities. It exhibits all the properties which are ascribed to the mucous juice generally (see p. 87 of this volume).

We have already (see vol. i. p. 51) shown at length that *oxalate of lime* must be regarded as a normal constituent of the urine, in which it occurs in increased quantities during certain physiological and pathological conditions.

The *chlorides of sodium and potassium* occur in very variable quantities in the urine, as has been already stated (in vol. i. p. 387). Hegar<sup>1</sup> has recently instituted experiments, under the direction of Julius Vogel, on eight persons, for the purpose of ascertaining the fluctuations in the amount of chlorine in the urine: the following are the results of these investigations; the mean amount of chlorine in the urine is 10.46 grammes in the 24 hours, although the quantity varies very considerably in different persons. In the afternoon the secretion of chlorine is at the maximum (although not immediately after dinner), in the night it sinks the lowest, and again rises in the morning. Bodily exertion increases the excretion of chlorine; indisposition diminishes it somewhat rapidly. The secretion is augmented by drinking water, but it is afterwards proportionally diminished. When chlorine-compounds are taken after fasting, the secretion remains for some time less than it would otherwise have been. Even when no chlorine-compounds are introduced into the system from without, a little alkaline chloride is still separated with the urine. When more than the usual amount of chlorine is taken up, the secretion is simply augmented for a short time; but, on the whole, less chlorine is excreted by the urine than is taken up; the excess of chlorine must, therefore, be eliminated by some other channel. It only remains for us to observe, that the quantities of the alkaline chlorides are diminished in an extraordinary degree under certain pathological conditions; this being especially the case whenever copious transudations or exudations have been separated from the blood within a short period of time; but it is remarkable that this diminution is frequently only observable when we take into comparison the quantity of the alkaline chlorides discharged with the urine in twenty-four hours; this occurs, for instance, in acute dropsy, the acute form of Bright's disease, in copious diarrhoea, in cholera, and typhus. On the other hand, the diminution of the metallic chlorides is frequently so considerable in inflammations accompanied with very copious exudations, that nitrate of silver will scarcely induce any decided turbidity in the urine when first discharged. This was observed by Heller,<sup>2</sup> first in pneumonia, and after-

<sup>1</sup> Ueber die Ausscheidung der Chlorverbindungen durch den Harn. Inauguralabb. d. med. Fac. zu Giessen vorgel. 1852.

<sup>2</sup> Arch. f. Chem. u. Mikros. Bd 4, S. 516-526. [We may also refer the reader to a Memoir by Dr. Beale, "On the Diminution of the Chlorides in the Urine, or their absence from that fluid, in cases of Pneumonia," in the Transactions of the Med. Chir. Soc. for 1852, Vol. 35.—G. E. D.]



wards in other considerable inflammations. Redtenbacher<sup>1</sup> has, however, seen in 80 cases of pneumonia that the amount of the chloride of sodium fell to a minimum; at the crisis of the disease nitrate of silver actually yields no precipitate in acidified urine; with the decrease of the inflammatory process the chlorides again gradually increase. Even after the use of hydrochloric acid, Redtenbacher was unable to detect any chlorine in the urine of persons affected with pneumonia. According to the same observer, the chlorine disappears for a short time from the urine during relapses in pulmonary tuberculosis. In acute rheumatism, capillary bronchitis, and typhus, the chlorine frequently, although not constantly, disappears from the urine for a short time.

We have already spoken in vol. i. p. 399, of the amount of sulphates present in normal urine. Observations have been instituted in reference to the fluctuations occurring in the amount of sulphuric acid present in the urine; among these analyses, those of Bence Jones<sup>2</sup> and of Gruner,<sup>3</sup> conducted under the direction of Julius Vogel, deserve special notice; the following were the results which were obtained: an adult (whose bodily weight is 60 kilogrammes) discharges on an average 2.094 grammes of sulphuric acid in 24 hours (Gruner). The amount of excreted sulphuric acid rises during the period of digestion, falls somewhat in the night, and is at its minimum in the forenoon (Gruner and Jones). Active bodily exercise and mental excitement seem alone able to influence the increased secretion of sulphuric acid in the urine; moderate exercise does not influence it (Jones and Gruner). Fasting does not diminish the excretion of sulphuric acid, at least during the first 24 hours. This secretion is increased for a short time, but afterwards proportionally diminished, by copious draughts of water (Gruner). Sulphate of soda, potash or magnesia, is perfectly eliminated by the urine in 18 or 24 hours after it has been taken (Gruner and Jones). The amount of sulphuric acid in the urine also increases after the administration of sulphur. In the meanwhile, this phenomenon is not constant, and may, perhaps, depend upon the amount of exudation that is formed. It is certain that this deficiency of the alkaline chlorides in the urine is of very short duration; indeed, I have never found it continue longer than three days. The quantity of the chloride of sodium rises, according to Heller, above the normal mean on the beginning of the resorption of the inflammatory exudation; but, although this may be possible, or even probable, it has certainly not as yet been proved; for, as we shall soon see, the method recommended by Heller does not afford the means of ascertaining the normal quantity of the chloride of sodium, or even of detecting a small excess above the average.

We have already spoken (in vol. i. p. 398) of the presence of *alkaline sulphates* in the urine; and it, therefore, only remains for us to state, that Heller has also attempted to investigate the fluctuations in the quantity of sulphates contained in morbid urine, by his method of applying baryta salts to urine which had been previously acidified. From

<sup>1</sup> Ber. d. kais. Ak. d. Wiss. zu Wein. 1850.

<sup>2</sup> Philosophical Transactions. 1849, pp. 252-260.

<sup>3</sup> Die Ausscheidung der Schwefelsäure durch den Harn. Inaug.-Abh. der med. Fac. zu Giessen vorgel. 1852.



these observations, he thinks he has found that the sulphates increase in the urine in inflammatory diseases proportionally to the degree of inflammation which is present.

I did not succeed in confirming Heller's statement in three successive series of experiments which I made on the urine discharged in the course of twenty-four hours by one pleuritic and two pneumonic patients. Relatively, the urine certainly contained more sulphates than in its normal state: that is to say, in 100 parts of inflammatory urine (whose specific gravity was increased) there were more sulphates than in 100 parts of the normal (specifically lighter) fluid of the same patient after his perfect restoration. There were from 4.512 to 5.842 grammes of the sulphates of potash and soda (all the potash being calculated as combined with sulphuric acid) discharged by these patients during the twenty-four hours, whilst the urine discharged after recovery during the same period yielded from 4.974 to 6.582 grammes of the sulphates. Heller found the sulphates of the urine diminished in chlorosis, neuroses, chronic diseases of the kidneys, and in affections of the spinal cord; but, as the urine is generally very highly diluted in these diseases, we may conjecture that Heller, in estimating the volume of precipitated sulphate of baryta, may not have taken into account the large quantity of water in the urine. In one case of decided chlorosis, I found that 6.247 grammes of the sulphates of potash and soda were discharged in twenty-four hours.

The normal urine contains *acid phosphate of soda*, and not the basic phosphate, as asserted by Heller,—a fact that has been clearly shown by Liebig.<sup>1</sup> (See vol. i. p. 395.)—Careful investigations have been instituted by Breed<sup>2</sup> and by A. Winter,<sup>3</sup> in reference to the amount of phosphoric acid in the urine. The mean of several experiments on different individuals showed that there were eliminated in the 24 hours from 3.765 to 5.180 grammes (Winter), or 3.732 grammes (Breed). An increased use of fluids slightly raises the number of the excreted phosphoric acid (Breed), but according to Winter this is only observable in the first three or four hours. In the night very much more phosphoric acid is eliminated than in the morning, although then even less than at noon (Winter). The amount of excreted phosphoric acid rises very considerably after taking food (Breed and Winter). This salt increases and diminishes, according to Heller, in nearly an equal ratio with the sulphates; Bence Jones,<sup>4</sup> however, once found them to be considerably diminished in a case of cerebral inflammation.

The *phosphates of lime* and *magnesia* occur in very various quantities in the normal urine; but where the food has been mixed, there are generally about 1.093 grammes of the earthy phosphates discharged by the urine in the twenty-four hours. The quantity of this salt in the urine depends in a great degree upon the nature and quantity of the food partaken of; that is to say, a much larger amount is secreted when the food is purely animal than when a vegetable diet is used. Thus, in my

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 50, S. 161–196.

<sup>2</sup> Ibid. Bd. 78, S. 150–152.

<sup>3</sup> Beiträge zur Kenntniss der Urinabsonderung bei Gesunden. Inauguralabh. d. med. Fac. zu Giessen vorgel. 1852.

<sup>4</sup> Philos. Transactions for 1846, p. 449.



own case, while I continued for twelve days to live solely on animal food, I discharged, on an average, 3.562% of phosphates in the twenty-four hours. The quantity of phosphate of lime is often found to be considerably diminished in the urine of pregnant women, as Donné<sup>1</sup> has very correctly stated, and this is especially the case from the sixth to the eighth month of pregnancy; at the same time, the quantity of the lime is scarcely diminished. Here also the nature of the food may have exerted a special influence on the quantitative relations of the earthy phosphates in the urine, as may be seen from analyses of this secretion in its morbid state. In those acute diseases in which, on account of an antiphlogistic diet, only small quantities of animal food are taken, the secretion of the phosphates is very much diminished, as compared with that of the urea in the normal state. Heller, who has made important observations on the variations in the quantity of the phosphates, considers that they are increased in rheumatism and diseases of the ear, and diminished in acute and chronic spinal affections, neuroses, and in acute and chronic diseases of the kidneys.

If any evidence could be drawn from one observation, I might be induced to believe that there is an excessive secretion of the earthy phosphates by the urine in rachitis. A thoroughly rachitic child, aged four years, discharged by the urine, which was very acid and contained oxalate of lime, as much as 0.496 of a gramme of the phosphates in twenty-four hours; whilst another child of the same age, and who, like the first, had been fed principally upon milk, with some meat and white bread, secreted 0.345 of a gramme in the same period.

*Iron* is very commonly present in small quantities in the urine, although it is sometimes absent in this fluid in healthy persons. There has been much difference of opinion as to whether or not the urine in chlorosis contains iron; but this question might easily have been settled, if more practicable methods had been employed for detecting the iron. According to my own observations, iron occurs in the urine, of chlorotic patients as well as in that of healthy persons, although it may in some cases be entirely absent; as the urine in chlorosis is generally poor in solid constituents, it is necessary to employ a large quantity of this secretion in order to detect its presence. It is, however, worthy of notice, that after the use of ferruginous preparations, whether employed in chlorosis or any other disease, iron may be detected in fresh urine, either directly by the ordinary reagents, or only in small quantities in the ash of the urinary residue. I have been unable to determine the relations which induce such an increased activity in the resorption of the iron as to enable larger quantities of it to pass into the urine.

A small quantity of *silica* may also be found in the urine, as was shown by Berzelius (see vol. i. p. 384).

The urine likewise holds in solution gases, namely, *carbonic acid* (Marchand),<sup>2</sup> with a little nitrogen. Both admit very readily of being exhibited by the method described at p. 55 of this volume.

The quantity of *water* in the normal urine is so exceedingly different, even under purely physiological conditions, that no definite estimate can

<sup>1</sup> Gaz. Méd. de Paris, 1841. No. 22, p. 47.

<sup>2</sup> Journ. f. prakt. Ch. Bd. 49, S. 250.



be made of it. The quantity of water which permeates through the kidneys is entirely independent of the quantity of solid urinary constituents which are simultaneously secreted; although, according to Becquerel's observations,<sup>1</sup> which I am able perfectly to confirm, large quantities of water may simultaneously carry off a large amount of solid constituents with the urine; that is to say, when large quantities of water have been drunk, more solid constituents are generally carried off by the urine in the twenty-four hours than when but little drink has been taken. Falk<sup>2</sup> has instituted very careful investigations in reference to the same subject, and has obtained very opposite results; but three experiments are not sufficient to warrant us in regarding this question as finally settled. According to Falk's observations, water is eliminated in about six hours after it has been taken, while a certain quantity of urine is eliminated in a fasting state, even when no water has been introduced into the organism. But the quantity of water which passes off in the urine depends upon such various reasons, that the causes of its diminution and increase in this fluid cannot always be determined, even under purely physiological relations. These controlling causes are more especially the quantity of water drunk, or absorbed, in the bath, the nature of the stools, and the more or less copious transpiration which again depends upon the external temperature, the degree of moisture of the atmosphere, bodily exercise, and many other internal and external causes.

Some interesting experiments on the influence of the injection of water into the blood simultaneously with bloodletting, have been made by Kierulf,<sup>3</sup> in Ludwig's laboratory. It would appear from these observations, that a considerable attenuation of the blood generally gives rise to a secretion of albumen through the kidneys, followed by hæmaturia, which, however, is probably not accompanied by laceration of the capillaries of the kidneys. The rapidity with which the urine was secreted bore no proportional relation to the amount of water contained in the blood.

Much obscurity long prevailed as to the cause of the *acid reaction* of the normal urine, which was originally referred to lactic and even to acetic acid; but this subject has at length been set at rest by Liebig, who has shown that the acidity of normal urine can alone depend upon acid phosphate of soda. Thus, for instance, when ordinary phosphate of soda (which, as is well known, yields an alkaline reaction) is dissolved in water, and the solution is gradually treated with uric acid, which exerts no reaction on vegetable colors, a fluid is obtained, which, on heating, reddens litmus paper, and on being cooled deposits a white crystalline powder, which exhibits under the microscope the most beautiful groups of prismatic crystals of urate of soda. Since so extremely weak an acid as uric acid can abstract from the phosphate of soda a portion of its base, we can hardly deny that stronger acids, such as hippuric, lactic, and sulphuric acids, may, immediately after their formation by the metamorphosis of animal matter, convert neutral phosphate of soda

<sup>1</sup> Sémeiotique des Urines, &c. Paris, 1841.

<sup>2</sup> Arch. f. physiol. Heilk. Bd. 12, S. 150-155.

<sup>3</sup> Mitth. der naturf. Ges. zu Zurich. Juli 1852.



into an acid salt, in which form it then passes into the urine, together with the already formed sulphate, lactate, and hippurate of soda. If this mode of explanation be applied to the acidity of every species of urine, freshly discharged urine would not saturate a larger amount of base than would correspond with the quantity of phosphate of soda which it contained. The observations necessary for determining this question are not, however, so easily conducted as one might at first sight suppose; for when the urine has been treated with so much alkali that its reaction is neither acid nor alkaline, there must obviously still remain the acid phosphate of soda in the solution; for the neutral phosphate of soda has an alkaline reaction, and, therefore, the acid salt cannot be neutralized whilst the urine continues to exhibit no reaction towards vegetable colors. On this account, I have endeavored to determine the quantity of the free acid in the urine by the following method: I precipitate the urine with an excess of chloride of barium, and after boiling the precipitate with a very weak solution of sulphuric acid, determine the weight of the sulphate of baryta. I next digest equal quantities of urine with freshly precipitated carbonate of baryta until the acid reaction has entirely disappeared, and after acidifying the filtered fluid with a little acetic acid, precipitate by means of chloride of barium. This precipitate also is boiled in an extremely dilute solution of sulphuric acid, and then weighed; the quantity of the latter is far smaller than that of the sulphate of baryta first weighed, and this difference between the two weights gives the quantity of sulphate of baryta necessary to yield a sufficient amount of base to saturate the free acid contained in the urine. Hence we may easily calculate from the chemical equivalents the amount of the free acid or of the acid phosphate of soda. If this method did not lead us to calculate a larger quantity of acid phosphate of soda in the urine than it would appear from another mode of analysis there actually existed, the acid reaction would depend solely upon the acid phosphate. Although this was not unfrequently the case, I found still oftener that the opposite condition existed in healthy as well as in morbid urine; that is to say, a comparison of the baryta salts commonly yielded a higher number for the quantity of the acid phosphate of soda than was found by direct analysis to be present, and hence there must, in most cases, be some free organic acid present in addition to the acid phosphate of soda, or some other acid salt which reddens litmus paper. We must, however, beware of drawing too hasty a conclusion in reference to this subject, for the acidity of the urine often increases so rapidly after its discharge, owing to the formation of lactic or acetic acid, that the excess of free acid observed in the above-mentioned experiments may perhaps be owing to the lactic acid formed after the urine has left the body. On the other hand, we frequently find such an excess of free acid in morbid urine, compared with the phosphate of soda, that this mode of explanation is no longer applicable. The acid reaction of the urine depends, therefore, in many cases, on the presence of hippuric and lactic acid no less than on that of the acid phosphate of soda. If, moreover, the latter substance alone were present in the urine, the phosphates of lime and magnesia could only be dissolved in it either as acid phosphates or by means of another free acid. But if, in this calculation of the free acid from the



precipitated baryta salts, the earthy phosphates had been included in the weighing, the result always remained the same; or, in other words, there was more free acid than could be accounted for from all the acid phosphates of the urine. The water-extract of the urine commonly exhibits an acid reaction, notwithstanding repeated rinsing with alcohol, solely owing to its contained acid earthy phosphates, which must be present wherever lactic or hippuric acid constitutes the acidifying principle of the urine.

The fluctuations in the amount of free acid in the urine during health have been made a special object of attention by Bence Jones<sup>1</sup> and A. Winter.<sup>2</sup> A. Winter found that an adult of average bodily weight (67 kilogrammes) discharged in the 24 hours as much free acid as would correspond with 2.304 grammes of oxalic acid. (The amount of the free acid was determined by means of a solution of ammonia of known strength.) It appeared, moreover, from the experiments of both these observers, that during the period of digestion, that is to say, in the afternoon hours, the quantity of the free acid was at its mean; it attained its maximum during the night, and fell far below the mean during the forenoon. It would appear from the experiments of Jones, that the diminution of the free acid was more decided after the use of animal food than after the use of mixed food, and more especially of a vegetable diet, which is the more remarkable, since we know that a purely vegetable diet gives a very faint acid or even an alkaline reaction to the urine, whilst the latter becomes very acid after the use of animal food (see my investigations on the urine under different modes of diet), this being the case, as Bernard has observed, even in herbivorous animals, which usually discharge an alkaline urine. Nevertheless, these observations, which are in direct opposition to our own experiments, deserve to be more carefully investigated.

The spontaneous decomposition of the urine stands in the closest relation to the formation of its sediments, and even to the formation of the urinary concretions, as Scherer<sup>3</sup> has shown by several beautiful observations. We will next direct our attention to the almost normal sediment of the urine, which, as we have seen in vol. i. pp. 194-197, consists essentially of urate of soda, and commonly occurs under very different physiological and pathological relations. This sediment is often formed as soon as the freshly discharged urine cools, and hence we might be disposed to believe that its occurrence indicated nothing more than such an increase of the urate of soda that the latter could no longer be held in a state of solution in the urine at the ordinary temperature. This view is supported on the one hand by the fact, that such rapidly formed sediments of urate of soda are often completely dissolved on the addition of less concentrated urine, and on the other, by all these sediments becoming again dissolved as soon as the urine is heated to 50 or 60° C. But it hardly requires the aid of the thermometer to trace the connection between the fall of the temperature and the deposition of a sediment, to convince ourselves that, in most cases, the turbidity and the formation of a sediment in the urine occur long after the temperature of

<sup>1</sup> Philosophical Transactions. 1849, pp. 235-251.

<sup>2</sup> Op. cit.

<sup>3</sup> Ann. d. Ch. u. Pharm. Bd. 42, S. 171, and Untersuch. z. Pathol. 1843, S. 1-17.



the fluid has become identical with that of the surrounding atmosphere ; thus a period of eight, ten, twelve, or even twenty-four hours, often intervenes before the deposition of the precipitate of urate of soda. The analysis of the urine shows, moreover, as Becquerel specially noticed, that a non-sedimentary urine very often contains a much larger quantity of urates than a sedimentary one. The separation of urate of soda must, therefore, depend upon some other cause than on the mere decrease of the temperature of the urine. The simplest induction leads us to assume that some alteration must occur in the urine when it is exposed to the atmosphere, which it does not experience within the bladder, and which is independent of a mere diminution of temperature. This alteration must, therefore, originate in some metamorphic process effected by the atmosphere in one or other of the constituents of the urine. The following facts induce us to regard the colored extractive matter, or the extractive pigment of the urine as the substance which causes a large quantity of the urate of soda in the urine to remain in a state of solution, and which by its metamorphosis gives rise to the separation of a large portion of this urate. We know that this coloring extractive matter combines especially with the urates, whose properties it essentially modifies. I have elsewhere<sup>1</sup> shown that it is this extractive substance which hinders the urate of soda, when a warm solution is suffered to cool, from separating into the well-known groups of crystals ; for if we add to a solution of urate of soda, which had deposited beautiful colorless bundles of crystals on cooling, some of the extractive matter of the urine which is soluble in alcohol, this salt loses its capacity for crystallization, and the same corpuscles are deposited in the cooling solution, which are generally found, although not in a crystalline form, to be separated from the urine, and which, moreover, occur in a smaller quantity, as may be seen by the naked eye, independently of weighing. Any one, moreover, who has collected on a filter this spontaneous urinary sediment, must have noticed that the metamorphosis of the pigment exerts a direct influence on the entire constitution of the urate of soda. On examining the deposit upon the filter, the bright-red or even scarlet color assumed by the sediment strikes the observer very forcibly ; but on examining it more attentively, either through the microscope, or after we have attempted to dissolve it in hot water and to filter it, a number of the most beautiful crystals of uric acid will appear, of which not a trace can be discovered in the portion of the urine which was not filtered, and whose sediment, from not having been exposed to the action of the air, exhibited no redness. All these appearances certainly indicate that the pigment of the urine, which, according to Duvernoy<sup>2</sup> and Scherer, participates in the separation of uric acid, may also contribute to the formation of the ordinary sediment of urate of soda. Even if we are not disposed to regard the extractive matter as a simple solvent, according to the above view, we might yet assume that the neutral urate of soda was dissolved in fresh urine that was very rich in uric acid, whilst a little acid might be formed by this metamorphosis of the pigment, which might extract an equivalent of base from the simple urate of soda,

<sup>1</sup> Götschen's Jahresber. 1844. Bd. 2, S. 26.

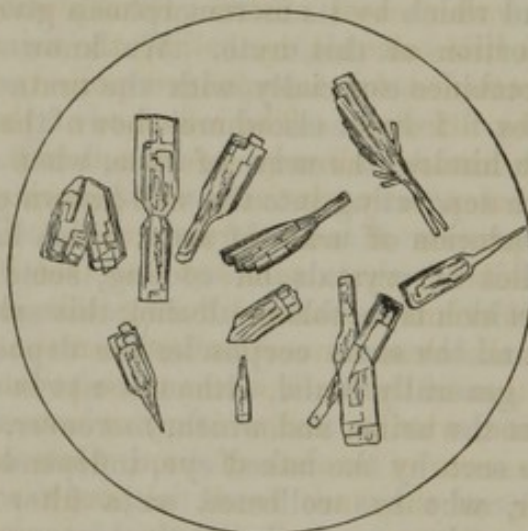
<sup>2</sup> Unters. über d. menschl. Urin. Stuttgart, 1835.



and thus give rise to the formation of the bi-urate. (See vol. i. p. 185.) This view is corroborated, in the first place, by the fact that this ordinary sediment certainly does consist of the bi-urate of soda, and in the next, by the fact that in the above-described experiment, in which the sediment had been collected on the filter, and it was then attempted to dissolve it in hot water, the filtered fluid did not exhibit an alkaline reaction, although a large portion of crystalline uric acid free from soda remained upon the filter. It requires, however, further experiments to elucidate this much-neglected department of zoo-chemistry.

It must be observed, that Scherer has demonstrated, almost beyond a doubt, by means of several striking experiments, that the metamorphosis of the pigment exerts a great influence on the formation of the *sediments of uric acid*. (For the chief varieties of the forms of uric acid see figs. 13 and 14, page 191, and fig. 23.) We have already shown, in

Fig. 23.



Fan-shaped aggregates of tabular crystals of uric acid, rather less often met with in urinary deposits.

vol. i. p. 196, that, except perhaps in lithiasis, sediments composed of free uric acid never occur in freshly passed urine, nor can they be generated by the mere cooling of the urine. Hence I can only regard uric acid sediments as products of the decomposition of the urine after its removal from the animal organism. The different kinds of urine vary solely in respect to the rapidity with which any one kind of morbid, or normal, urine undergoes acid fermentation sooner than another, and thus gives rise to the formation of the insoluble sediments of uric acid. Scherer was the first who recognized and attentively followed this process of *acid urinary fermentation*. Every normal, non-sedimentary urine, when exposed to the ordinary atmospheric temperature, begins, after a longer or shorter period, to separate uric acid, and to exert a stronger reaction on litmus paper; we may, moreover, convince ourselves most strikingly of the increase of free acid in the urine by the volumetric method, which corresponds to the alkalimetric. Faintly alkaline urine, such as is passed after vegetable food which is rich in alkalies, or after several doses of acetate or tartrate of potash, acquires, after a short time, an acid reaction, which increases so much under favorable conditions, that any



turbidity, which may have arisen from the separation of earthy phosphates, disappears, and crystals of uric acid are separated. Scherer, and subsequently to him, many other observers, have noticed that jaundiced, brownish-yellow, faintly acid urine becomes strongly acid, and that, in place of this color, it assumes a green tint, owing to the peculiar action of the free acid on the bile-pigment.

The duration of the acid fermentation of the urine extends, according to Scherer, to four or five days, although in a temperature of from 10 to 20° C., I have seen the acid of the urine increase for two or three weeks, and then often not disappear until after a period of six or eight weeks. Scherer explains this process on the supposition that the mucus of the bladder is a fermenting body, and that the extractive pigment is the substance metamorphosed into lactic acid. I have, however, frequently observed, as Liebig had previously done, that acetic acid is also present. Scherer's view derives support from the fact that the acid fermentation of the urine may be impeded, or interrupted, by most of the conditions which in other cases obstruct fermentation, as, for instance, by the addition of a little alcohol, by boiling the urine (when the formation of an acid is retarded for a prolonged period), and finally, by removing the mucus by filtration. The influence of the latter is also obvious, from the circumstance already mentioned at p. 110, that a species of fermentation-globules, or yeast-fungi, are generated in and from the mucus during the process of acid fermentation. I must again draw attention to the possibility that *oxalate of lime* (see Figs. 1 and 26) may be formed, or, at all events, separated during this process of fermentation; at all events, the close connection between the separation of uric acid and the formation of this salt, seems to be proved by the fact that most samples of urine, whether sedimentary or non-sedimentary, exhibit no trace of the presence of oxalate of lime, when examined under the microscope, as long as they are fresh, although some of the known crystals of oxalate of lime may be detected as soon as the uric acid crystals are formed. Indeed the abundance of such crystals in morbid urine is proportional to the rapidity with which acid fermentation is induced, and the consequent early deposition of free uric acid.

From the fifth day to the second or third week after the discharge of the urine, the free acid begins gradually to diminish; *confervæ* and *algæ* are then observed, in addition to the filamentous fungi in the sediment and on the surface of the urine, when examined under the microscope. The urine finally becomes neutral, the yellow crystals of uric acid disappear, or in their place, we find the well-known crystals of phosphate of magnesia and ammonia, either in the form of large, colorless pyramidal prisms or in small radiated groups of needles or larger prisms. (See Figs. 24 and 25.) The urine becomes alkaline, acquires a most abominable odor, and is covered with whitish-gray membranes, which swarm with innumerable vibriones and monads, in addition to vegetable products. The color of the uric acid sediment is, with few exceptions, yellow, like its microscopical crystals, but when the deposit is *white*, it exhibits not only the crystals of triple phosphate, infusoria and fungi, but also the brownish-black, round clusters of urate of ammonia, studded



on all sides with sharp needles. (See Fig. 25.) The urine effervesces strongly with acids; the fluid then scarcely exhibits any yellow color, the pigment being consequently for the most part destroyed.

The *alkaline urinary fermentation* occurs, under certain partially unexplained relations, even before the completion of the acid fermentation, and sometimes even within the bladder. Normal urine passes more or less rapidly into the alkaline fermentation when the temperature exceeds  $20^{\circ}$  C.; this change is effected very readily when the urine has been kept in unclean vessels, and almost at once when mixed with urine which has become alkaline, even when the quantity added is so small as hardly to saturate the free acid of the fresh urine. We may, therefore, conclude that here, as in other kinds of fermentation, there is a special alkaline fermenting substance present, which, we believe with Scherer, can only be sought in the changed urinary mucus, and in the microscopical organisms contained in it. This mode of explanation is not only in accordance with the views which chemists now hold regarding the processes of fermentation, but it is likewise further confirmed by certain results of clinical experience. We have found that an alkaline urine which effervesces with acids is most constantly and distinctly observable in primary or secondary affections of the mucous membrane of the bladder. In the former case there either exists inveterate vesical catarrh or complete suppuration of the walls of the bladder in consequence of cancerous tumors or other secondary products; in these cases the secretion of mucus is abnormal, the mucous juice which is secreted in increased quantity, possessing none of the ordinary properties of urinary mucus, and being decomposed with extraordinary rapidity. In the latter case the mucous membrane of the bladder, at most, suffers only indirectly; as, for instance, in affections of the spinal cord, accompanied with paralysis of the extremities and of the bladder; and if the vesical mucous membrane retain its perfect integrity, the mucus secreted from it cannot be thrown off on account of the deficient contractility of the bladder, but adheres to it, and begins to be decomposed to such a degree that it induces alkaline fermentation almost at once in the urine as it drops from the ureters, so that even in incontinence of urine, where the fluid had been retained only a short time in the bladder, it is both alkaline and ammoniacal when passed. Catarrh of the mucous membrane of the bladder is, however, only a secondary affection.

Scherer assumes from these facts, that the vesical mucous membrane may also acquire a condition within the bladder by which it predisposes the extractive matter to the formation of acid. This must undoubtedly be admitted to exist in the calculous diathesis, in which an acid urine is secreted with preformed crystals of uric acid; but the assumption of a mucus which is already modified before it leaves the bladder, does not appear to me to afford a satisfactory explanation in those frequent cases of febrile urine in which this secretion, when freshly discharged, exhibits a moderately acid reaction, and contains only urate of soda; for, independently of the circumstance that in those febrile or inflammatory affections in which we can scarcely assume the presence of any derangement of the mucous membrane of the bladder, or the existence of a mucus which has been modified within that organ, it frequently happens



that one kind of freshly passed urine does not turn acid very quickly, nor is uric acid immediately separated from it, whilst urine which had been passed only two hours before may exhibit these properties in a very high degree. This phenomenon might be ascribed to the prolonged retention of a more concentrated urine, which might irritate the mucous membrane of the bladder, if the reverse were not occasionally observed, that is to say, if we did not sometimes find that one specimen of urine turns acid very readily and speedily, although another specimen, passed a couple of hours previously, may not exhibit the same properties for a prolonged period. We must here seek for the causes of the more rapid acidification of the urine in the constitution of the fluid secreted by the kidneys, that is to say, in the special condition of individual substances formed by the metamorphosis of matter during its modifications in fever, and perhaps more especially in the quantitative increase and the qualitative alterations of the urinary pigment.

Scherer has, moreover, endeavored to show that these processes of fermentation, in so far as they occur within the bladder, contribute largely towards the *formation of calculi*.

Fig. 24.



Urinary deposit of phosphate of magnesia and ammonia with mucus corpuscles from catarrh of the bladder.

Fig. 25.



Urinary deposit of triple phosphate (phosphate of magnesia and ammonia), and urate of ammonia in alkaline fermentation. In paralysis of lower extremities.

Thus, for instance, it depends solely upon the character of the vesical mucus, and upon the nature of the fermentative process induced by it, whether the urinary concretion that is formed consist of uric acid, earthy phosphates, or urate of ammonia. The varying conditions of decomposition at different periods of the disease, that is to say, the gradual qualitative and quantitative change of the secretion of the morbidly affected mucous membrane, may afford an explanation of the formation of urinary calculi whose various layers have a different composition. Scherer thus seeks for one of the most important causes of lithiasis in a degeneration of the secretion of the vesical mucous membrane—a mode of explanation which derives support from the chemical investigations of urinary concretions as well as from medical experience. The majority of these uri-



nary concretions contain a clot of mucus as a nucleus, whence it would appear that the mucus generally affords the first formative basis for the concretions ; then, moreover, the inner layers of most calculi contain uric acid, whilst the outer ones contain earthy phosphates or urate of ammonia ; a trace of uric acid, if nothing more, may always be detected in the nucleus of the concretion. Every uric acid concretion aids, by irritating the vesical mucous membrane, in increasing its own size by the deposition of phosphates or of the urates of ammonia and of lime ; whilst it is obvious, from the formation of calculi, that at the commencement of their deposition mucus must almost always be present, and there must at the same time, be a tendency to the separation of uric acid,—in short, an acid urinary fermentation. The uppermost layers of most urinary calculi show that, at the time of their deposition, an alkaline ferment was present, and that its action had already been established in the urine. All who have examined the constitution and formation of numerous urinary concretions, more especially of the larger ones, must be led almost involuntarily to the adoption of Scherer's view. Even the mulberry calculi, which undoubtedly contain a very large proportion of oxalate of lime, but probably never consist solely of this substance, furnish additional corroboration in support of this mode of explanation, for they always contain a large quantity of uric acid, and frequently constitute the nucleus of larger earthy concretions.

Fig. 26.



Urinary deposit of uric acid, urate of soda, and oxalate of lime, from urine of a patient recovering from typhus fever.

This admirable and simple mode of explanation, which harmonizes with the established views of the decomposition of organic substances, derives considerable support both from the chemical analysis of concretions as well as from medical experience, however widely it may deviate from the ordinary opinions of physicians who adhere to the idea of lactic, uric, and phosphatic diatheses. In the mean time it would be extremely difficult to prove that uric acid concretions owed their existence solely to a modification of the vesical mucus ; for, as we have already observed, in speaking of sedimentary formations, there must be some controlling



cause in the composition of the renal secretion, which in one case may facilitate and in another hinder the formation of concretions. There remain, probably, many other points which require to be investigated before we can explain all the phenomena relating to the formation of concretions, or hope to arrive at a scientific interpretation of the different forms of development of urinary calculi.

We will now proceed to the consideration of those urinary constituents which are *conveyed to the body from without*, and which, after remaining only a short time within it, *pass into the urine*, either wholly unchanged or in a slightly modified form. This subject, which is of the highest importance in the study of the metamorphosis of animal matter, was long since investigated by Wöhler,<sup>1</sup> and more recently by the same observer in conjunction with Frerichs.<sup>2</sup> Although it may appear somewhat illogical to notice the substances which, according to the experiments made in relation to this subject, do not pass into the urine, the present seems a fitting place to collect those facts which may serve as a positive basis for a theory of the formation of the urine, and aid in elucidating the internal mechanism of the zoo-chemical metamorphosis of matter.

It may be assumed as a general proposition, that such substances (not belonging to the nutrient matters) as are easily soluble in water, and exhibit no tendency to enter into insoluble combinations with the organic or inorganic matters of the animal body, alone pass into the urine. On this account, most of the soluble alkaline salts, as nitrate of potash, borax, iodide of potassium, bromide of sodium, alkaline silicates, chlorates, carbonates, &c., are found unchanged in the urine. But in order that substances should pass unchanged into the urine, it is necessary that, in addition to solubility, and the incapacity for entering into insoluble combinations, they should possess another character, namely, that of being already perfectly oxidized, or that of having no tendency to oxidation and decomposition generally. Thus, for instance, sulphide of potassium is a very readily soluble substance, which is not disposed to enter into insoluble compounds even with the matters within the animal body; but owing to the readiness with which it becomes oxidized, this substance does not pass into the urine unchanged, but in the form of sulphate of potash, unless too large a quantity have been introduced into the body. Many substances which enter into insoluble combinations with animal matters, as, for instance, with the albuminates, only pass into the urine when they have been conveyed into the organism in large quantities; hence Orfila found that the heavy metals, which are not in general separated by the kidneys,—namely, gold, silver, lead, bismuth, antimony, and arsenic,—might be detected in the urine, if administered in very large doses, but were commonly found to be present only in the liver and its secretion, and, consequently, also in the solid excrements, when they had been given in relatively small and frequently repeated doses.

Many organic substances undergo the same alterations in their passage through the animal organism which have been artificially produced by chemists; and this is especially the case with those organic matters which have been decomposed into different substances by the application of

<sup>1</sup> Zeitschr. f. Physiol. Bd. 1, S. 305-328.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 65, S. 335-349.



certain oxidizing agents; there are even many soluble substances which become so perfectly oxidized in the blood, that neither they nor any of their products of decomposition can be recognized in the urine. Many others, on the contrary, which readily part with their oxygen, lose a portion of it in their passage through the animal body, and very probably in the *primæ viæ*, which causes them to appear in the urine in lower stages of oxidation.

We have already seen (in vol. i. p. 54) that after the use of drinks containing a large quantity of *carbonic acid*, the amount of the oxalate of lime in the urine is increased; but we must here observe, that we have found, from positive experiments, that the free carbonic acid of the urine is also very considerably increased by their use. After the use of champagne, the urine contains 52<sub>0</sub> of its volume of gas, and after that of Bavarian beer, 68<sub>0</sub>.

It has been observed both by Buchheim and myself, that Seltzer water did not produce the same effect as beer in the act of fermentation, or as sparkling wine, which may probably be owing to the circumstance noticed by Couerbe,<sup>1</sup> that when the pressure is removed from Seltzer water, it only retains one volume of gas, and probably loses a large portion of its acid by eructation after it has entered the stomach; whilst, on the contrary, champagne gives off only one half volume of its four volumes of condensed carbonic acid. It must be observed, however, that this transition of the carbonic acid from those highly carbonated drinks, or from alkaline bicarbonates, into the mass of the blood and the urine, is only very distinctly manifested when the substances in question are taken on an empty stomach. Buchheim has proved this to be the case, by repeated experiments on himself. A development of gas necessarily takes place as soon as food is introduced into the stomach, as we may readily comprehend from known physical and chemical grounds, and which is plainly manifested by eructations, and frequently also by flatulence, even enabling us in some cases to determine by percussion of the abdomen in what part the fluid containing the carbonic acid is in contact with the intestinal contents.

The *alkaline carbonates* obviously reappear, from what has been already stated, in the urine, although a portion of them must have been saturated by the acid juices of the stomach and intestines. It would be interesting to determine how much alkaline carbonate is necessary in order to induce the secretion of a neutral or faintly alkaline urine in man under definite conditions. Buchheim, who for some time instituted experiments of this nature on himself, found that even with reference to food and general dietetic relations, the quantity of alkali necessary for this purpose was extremely variable; this, however, is easily explained, when we consider how many causes there are which, in a greater or less degree, influence the acidity of the urine, and which are altogether beyond the control of the experimenter.

The ammonia of the *ammoniacal salts* passes for the most part unchanged into the urine.

Bence Jones<sup>2</sup> believes that he has convinced himself, by numerous

<sup>1</sup> Journ. de Pharm. T. 26, p. 321.

<sup>2</sup> Philosophical Transactions. 1851, pp. 321.



experiments, that after the use of ammoniacal salts (he employed the carbonate, tartrate, and hydrochlorate of ammonia), nitric acid might always be detected in the urine, and consequently that the power of oxidation possessed by the organism is so great, that the nitrogen of the ammonia is oxidized into nitric acid. I regret that this observation must be regarded as so far erroneous, that the method employed by Jones for the discovery of nitric acid must necessarily yield a reaction which is similar to that of nitric acid. Jones decomposed about four ounces of urine with half an ounce of concentrated sulphuric acid, and distilled two-thirds of the fluid in a retort; in the fluid thus yielded by distillation, Jones thought he might determine the amount of nitric or nitrous acid by Price's method (which is a mixture of starch, iodide of potassium, and hydrochloric acid). In some experiments which I made, I certainly found that the distilled fluid, when treated with iodide of potassium and hydrochloric acid, turned starch blue. In the meanwhile it would seem chemically incomprehensible how nitric acid, if it really were present in the urine, could pass unchanged from it during its distillation with sulphuric acid; we need only observe that in this concentration of the fluid, the chloride of sodium, as well as the supposed nitrate in the urine, will be decomposed by the sulphuric acid, and that nitrous acid must be formed together with free chlorine, but the former is at once decomposed into nitrogen and water, on being brought in contact with urea; the undecomposed nitric acid, if any could be present, would also be decomposed on boiling. Now it is easy to see that sulphurous acid, by which, as is well known, hydriodic acid is decomposed, passes into the receiver, and thus probably induces this supposed nitric-acid reaction. The following results were obtained from the experiments which were made in my laboratory by Jaffé, one of my students, for the purpose of verifying this proposition: ordinary urine, when no ammoniacal salts had been taken, was found to yield this reaction when treated by Bence Jones's method; this reaction, however, did not occur when the distillate had stood for some time in the air, in which case the sulphurous acid had become converted into sulphuric acid. The distillate, even after the most careful distillation with sulphuric acid, always yielded, with chloride of barium, a precipitate which was insoluble in acids and much water, but this precipitate is not formed when the urine has been treated with phosphoric instead of sulphuric acid, and then distilled. The distillate which was obtained after the application of phosphoric acid, does not exhibit this supposed nitric-acid reaction even when the urine has been previously treated with some drops of nitric acid. Jaffé modified this experiment in various ways, but the methods we have already given are sufficient to show that the presence of nitric acid in the urine cannot be proved by Jones's method, even when it occurs in moderate quantities, and that Price's method for detecting nitric acid is altogether inapplicable when sulphurous acid is present. We must, therefore, for the present, leave the somewhat improbable view of the conversion within the organism, of ammoniacal salts into nitric acid, as a subject requiring further investigation before it can be regarded as settled.



[Dr. Bence Jones<sup>1</sup> has defended his former views in a memoir recently read (June 15, 1854) before the Royal Society, "On the Oxidation of Ammonia in the Human Body." In this paper he describes a series of experiments, from which it results—

1st. That in Price's test sulphurous acid produces exactly the opposite effect to nitrous acid, and even hinders nitrous acid from liberating iodine from hydriodic acid.

2d. That phosphoric acid, when mixed with urine containing nitre, and distilled very low, does liberate nitrous acid; though when used instead of sulphuric acid, it does not enable the nitrous acid to be detected so readily as when the latter acid is employed.

"Hence (he observes) the experiments performed in Professor Lehmann's laboratory by Herr Jaffé,<sup>2</sup> do not invalidate Price's test for nitrous acid in the way Professor Lehmann supposes; and by again repeating some of my former experiments, I still arrive at the conclusion that when ammonia is taken into the body, nitric acid may be detected in the urine, but that the quantity which can be made to appear is so small that the most delicate method is required for its detection. This, however, is no proof that a much larger quantity may not be lost in the process for obtaining it from the urine."—G. E. D.]

*Iodine* combines very rapidly with alkalies in the animal body, and then appears as iodide of potassium in the urine.

*Soluble baryta salts*, although they are so easily decomposed by sulphates, phosphates, and carbonates, yet, if given in sufficient doses, reappear, according to Wöhler, in the urine.

*Ferridecyanide of potassium* reappears in the urine as ferrocyanide of potassium.

*Sulphocyanide of potassium*, even when administered in small doses, may very soon be detected in the urine.

It appears from the investigations of Wöhler, that most of the *organic acids* pass unchanged into the urine, when they are introduced into the system in a free state; he experimented with oxalic, citric, malic, tartaric, succinic, gallic, and salicylous acids.

*Tannic acid* is converted, in its passage through the animal organism, into gallic acid.

The observation made by Wöhler, that *benzoic acid* is separated from the animal body by the urine in the form of hippuric acid, has been confirmed by Ure,<sup>3</sup> Keller,<sup>4</sup> and many other observers.

The organ from whence the benzoic acid in this case obtains the elements of fumaramide (see vol. i. p. 182) cannot at present be decided with certainty; Ure believes that after the use of benzoic acid, the hippuric acid is increased in the urine at the expense of the uric acid, and that it consequently assimilates a nitrogenous group of atoms, which in its absence would have been applied to the formation of uric acid: hence he recommends physicians to employ benzoic acid against the uric acid diathesis. Unfortunately, however, Wöhler and Keller could not detect any diminution of the uric acid after the use of benzoic acid; and Booth

<sup>1</sup> Proceedings of the Royal Society, vol. 7, p. 94.

<sup>2</sup> Journ. f. pr. Chem. Bd. 59, S. 238.

<sup>3</sup> Pharm. Trans. vol. 1, No. 1.

<sup>4</sup> Ann. de Ch. u. Pharm. Bd. 43, S. 103.



and Boye<sup>1</sup> arrived at the same conclusion. Garrod, on the other hand, believes that he has constantly found a diminution in the quantity of urea in the urine after the administration of benzoic acid; but neither Simon's investigations nor my own confirm this view. In four observations in which I examined the twenty-four hours' urine after the administration of large doses (two drachms) of benzoic acid, I failed in any case to detect a marked diminution of any of the nitrogenous constituents; experiments of this nature are, however, so difficult to execute, and the daily sum of the individual nitrogenous constituents is so fluctuating, that no conclusions should be drawn from such investigations; thus, for instance, it would be extremely rash to conclude, from the apparently negative result of the examination of the urine, that the benzoic acid abstracted nitrogenous matter from the substances designed for cell-formation.

If the close affinity that exists between benzoic and hippuric acids in some degree elucidates the production of the latter from the former in the metamorphosis of the animal tissues, the result obtained by Erdmann and Marchand<sup>2</sup> is the more striking, namely, that cinnamic acid,  $C_{18}H_7O_3.HO$ , in its passage through the animal organism assimilates nitrogenous matter, and escapes in the urine as hippuric acid.

There are various ways in which we may suppose that the conversion of cinnamic into hippuric acid may take place: it may either lose four atoms of carbon and two atoms of hydrogen, in order to be first converted into benzoic acid (for  $C_{18}H_7O_3 - [4C + 2H] = C_{14}H_5O_3$ ), or by the assimilation of ammonia and the separation of water there is formed cinnamide ( $C_{18}H_7O_3 + H_3N - HO = C_{18}H_9NO_2$ ), which has only to take up four atoms of oxygen in order to form water and hippuric acid ( $C_{18}H_9NO_2 + 4O = 3HO + C_{18}H_8NO_5.HO$ ).

It is worthy of notice that *cuminic acid*, which is so closely allied to benzoic acid, does not resemble benzoic and cinnamic acids, in combining with nitrogenous matter within the animal organism, but passes unchanged into the urine; hence in its behavior it resembles salicylic acid (hydride of salicyl) which is even more nearly applied to benzoic acid.

Wöhler and Frerichs have convinced themselves by experiments on several rabbits and dogs, that *uric acid*, whether introduced into the stomach or injected into the veins, is decomposed in the animal body in precisely the same manner as by peroxide of lead; the urine is at all events found to be far richer in urea and oxalate of lime after the administration of the acid.

We are indebted to Wöhler for one of the most important discoveries in physiological chemistry, namely, that the neutral salts formed by the combination of the alkalis with vegetable acids, are oxidized in the animal organism in precisely the same manner as if they were burned in oxygen gas: alkaline carbonates pass into the urine and render it alkaline; it consequently becomes turbid from the separation of earthy phosphates, and naturally effervesces with acids. That the conversion of the alkaline salts of the organic acids into carbonates takes place in the blood, might have been *a priori* concluded; but I have convinced

<sup>1</sup> Medical Times, November, 1845.

<sup>2</sup> Journ. f. pr. Ch. Bd. 35, S. 307-309.



myself, by the injection of an alkaline lactate into the jugular vein of dogs, that the change takes place with extraordinary rapidity, and that an alkaline carbonate very soon appears in the urine (see vol. i. p. 97). The same experiment has been made by others. It is, however, a singular circumstance, and one that requires further investigation, that in different persons, even under, apparently, precisely similar conditions, the period that elapses before the urine becomes alkaline, after the administration of these salts, is very various, and that in different cases very different quantities of these salts are necessary to render the urine alkaline. From the experiments of a young chemist, whose urine constantly became alkaline even after the use of a few baked plums, I was led to observe that in many persons who are living on a mixed diet, the urine becomes alkaline in two or three hours after swallowing half a scruple of acetate of soda, whilst in others who are living on a purely vegetable diet, two drachms of acetate of soda never succeeded in rendering the urine alkaline. From numerous experiments on healthy persons, and observations on patients who had taken alkaline acetates and tartrates, I could only deduce the following certain conclusions; when the salts in question exert a purgative action, the urine does not readily become alkaline; in fact, it seldom becomes alkaline at all under these circumstances; as might be expected, the urine of persons living upon animal food does not so readily become alkaline as that of persons living on vegetables and those on an antiphlogistic diet: if, however, the febrile affection be accompanied by a very acid urine, then it naturally follows that the urine is longer in becoming alkaline; hence two febrile patients might be taking the same doses of these salts, and the urine in one case might be alkaline, and in the other it might remain distinctly acid. In one and the same person living on the same kind of food, the urine may become alkaline after a dose of these salts, if he remain quiet; but may retain its acid reaction after an equal dose, if he take strong bodily exercise. Hence we should be far from the truth if we believed that these points were thus cleared up; for a very small amount of observation at the bedside would suffice to convince us that we are far from being able to comprehend why, in special cases, the urine remains acid, or why it becomes alkaline. We must generally assume it as an undoubted fact, that the metamorphosis proceeding in the blood during the continuance of the morbid process tends, in a greater or less degree, to the formation of acid; and hence that in one of the cases, a smaller quantity of the vegetable salt is necessary to saturate the free acid of the urine than in the other case. The alkalinity of the urine during the use of vegetable diet appears, however, to be by no means solely dependent on the alkali contained in the organic salts of the food; for I have seen my own urine, which usually has a strong acid reaction, remain alkaline for eighteen hours after the use of food altogether devoid of nitrogen and alkalies, as, for instance, milk-sugar, starch, and fat. Magendie<sup>1</sup> injected a solution of starch into the jugular vein of a rabbit that fasted for three days, and whose urine was acid, clear, and rich in urea; the urine almost instantaneously underwent a complete change, becoming alkaline, turbid, and poor in urea. Bernard<sup>2</sup> injected

<sup>1</sup> Compt. rend. T. 23, P. 191.

<sup>2</sup> Ibid. pp. 536-537.



a solution of grape-sugar into the veins of a dog and of a rabbit; the urine of both animals was thus rendered alkaline and turbid from the separation of earthy salts, while, under similar conditions, a solution of cane-sugar exerted no such action on the urine, but was carried off unchanged by that secretion. From these facts, we may undoubtedly conclude that the alkalinity of the urine of graminivorous animals does not solely depend upon the vegetable alkaline salts contained in the food. Bernard, moreover, found that the urine of dogs, which in the normal state is acid, becomes alkaline as soon as these animals are kept strictly upon vegetable food; and conversely, that the urine of rabbits, which under normal conditions is alkaline, becomes acid as soon as animal food has been introduced into the stomachs of these creatures, or a decoction of flesh is injected into their veins. From the experiments which Bernard instituted on herbivora, whose urine after the abstraction of all food, was clear, of an amber-yellow color, and strongly acid, it follows that the pure metamorphosis of tissue in the animal body, like a purely flesh diet, induces the secretion of a limpid, acid urine. Finally, Bernard believes that he has discovered that the pneumogastric nerves exert an influence on the reaction of the urine; thus, for instance, he saw that the alkaline urine of animals fed upon vegetables became acid after the section of both these nerves—a result whose accuracy I feel justified in doubting, having myself performed a similar experiment on a rabbit: rabbits are, however, by no means well adapted for such experiments; as far as my experience goes, these animals often secreting an acid urine without any apparent reason for so doing.

*Quinine* may be easily rediscovered in the urine after the use of moderate doses.

*Urea*, according to the experiments of Wöhler and Frerichs, passes unchanged into the urine.

*Theine* and *theobromine* cannot be rediscovered in the urine: since both these substances occasion intense excitement of the vascular and nervous systems, I am unable to decide whether the augmentation of the urea discharged in twenty-four hours, which I observed to occur, was dependent on the decomposition of these nitrogenous matters or upon the stimulus communicated to the entire organism.

*Aniline*, as it would appear from the experiments of Wöhler and Frerichs, does not reappear in the urine.

No direct experiments have been made with other organic bases in reference to their transition into the urine.

*Alloxantin* appears, from the experiments of Wöhler and Frerichs, to be converted in the animal body into urea and other substances; they found neither the substance itself, nor alloxan, in the urine of persons who had taken five or six grains of it.

*Thiosinamine* does not pass unchanged into the urine; in its place we find sulphocyanide of ammonium; hence it undergoes the same decomposition in the body as we can artificially produce by soda-lime. (W. and Fr.)

*Allantoine* does not pass into the urine, nor does it induce any augmentation of the oxalate of lime, as might have been expected; since it is decomposed artificially by alkalies into oxalate of ammonia (see vol. i. p. 161).



*Amygdalin* cannot be rediscovered with certainty in the urine. (W. and Fr.)

Ranke<sup>1</sup> found that after the use of *amygdalin* considerable quantities of formic acid passed into the urine, an observation which I thoroughly confirmed in my experiments on the injection of amygdalin, into the veins. The action of amygdalin, when injected into the blood, is therefore never injurious, since no prussic acid is formed.

*Salicin* generally undergoes a change corresponding to oxidation in the organism; and it is only when taken in very large quantity that a portion of it passes undecomposed into the urine. The experiments instituted by myself as well as by Ranke<sup>2</sup> on the metamorphosis of salicin, give the following results: after the introduction of salicin into the body by the mouth, we find in the urine not only salicylous and salicylic acids, but also saligenin, while no sugar and no phenylic acid can be detected. The salicin must be for the most part decomposed in the blood, for whenever I have injected a solution of this substance into the jugular vein in rabbits, substances were found in the alcohol extract of the urine which yielded, with the persalts of iron, the blue color corresponding to saligenin and salicylous and salicylic acids.

*Salicin* undergoes the same decomposition in the animal organism that is induced by oxidizing agents. Salicylous acid<sup>3</sup> is found in the ethereal extract; it might be supposed that the salicin is decomposed in the animal body, in the same manner as by emulsin, into sugar and saligenin, and that it is only on the evaporation of the urine that the latter is converted by the free acid which is present into salicylous acid; since, however, no substance in the animal body acts upon amygdalin in the same manner as emulsin, it is by no means probable that salicin undergoes the last-named mode of decomposition.

I could not detect the presence of *asparagin* in the urine.

*Phlorrhizin* has not been rediscovered in the urine.

*Volatile oil of bitter almonds* (free from prussic acid) seems first to be converted into benzoic acid (without giving rise to any symptoms of poisoning), and then appears as hippuric acid in the urine. (W. and Fr.)

*Quinone* is decomposed in the animal organism. (W. and Fr.)

*Benzoic ether* causes an augmentation of the hippuric acid in the urine. (W. and Fr.)

According to Wöhler most pigments and many odorous matters pass unchanged, or only slightly modified, into the urine; as, for instance, the coloring matters of indigo, madder, gamboge, rhubarb, logwood, red beet, and whortleberries, and the odorous constituents of valerian, garlic, asafoetida, castoreum, saffron, and turpentine. Wöhler could not rediscover the following substances in the urine: Camphor, resins, empyreumatic oil, musk, alcohol, ether, cochineal, litmus, sap-green, or alcanna.

Another point worthy of notice is the *rapidity with which many substances pass through the animal organism*. We may generally assume that the rapidity with which a substance reappears in the urine is directly proportional to its solubility, and inversely proportional to the amount of change which it undergoes in the animal organism. This

<sup>1</sup> Ibid. Bd. 56, S. 17.

<sup>2</sup> Journ. f. pr. Chem. Bd. 56, p. 1-11.

<sup>3</sup> Handwörterb. der Physiol. Bd. 2, S. 15.



rule, however, has many exceptions, amongst which we may especially mention iodide of potassium—a substance which is so easy of detection, even in extremely minute quantities; according to some observers it may be detected in the urine in from four to ten minutes after it has entered the mouth. I have only been able to observe this in a man in whom the posterior wall of the bladder, with the opening of the ureters, lay exposed; in other persons it often did not appear in the urine till after a period varying from three-quarters of an hour to five hours, while, on the other hand, it was very soon to be detected in the saliva (see vol. i. p. 424). After the ingestion of from two to three drachms of bicarbonate of potash, I have found, in experiments on several persons, that the urine became neutral in from thirty to forty-five minutes, and alkaline in the course of an hour. Lactate of soda taken to the extent of half an ounce, rendered normal urine alkaline in half an hour; on injecting similar quantities of the same salt into the jugular veins of dogs, their urine became strongly alkaline after five, or at the longest after twelve, minutes.

There is great diuresis in dogs after this operation if we provide them with plenty to drink; the loss of blood, even when small, seems to excite their thirst, while, on the other hand, the alkaline carbonate that is formed probably actually hastens the secretion of urine. Hence it is in general very easy to observe the time at which such urine becomes alkaline.

Erichson<sup>1</sup> observed the period of the transmission of soluble and coloring substances into the urine in a man with extroversion of the bladder, probably the same person who had been travelling about Germany; after administering forty grains of ferrocyanide of potassium, he saw it reappear within two minutes in the urine: the ferrocyanide of potassium and other substances which were tried, appeared less rapidly in the urine when the experiments were made shortly after meals.

I have recently observed in the same individual that the urine was expelled in nearly alternating jets from the two ureters four minutes after he had taken half an ounce of acetate of potash, while the urine became alkaline in the course of seven minutes. In the meanwhile it ought to be observed that the constitution of the individual probably exerts some influence on the rapidity with which such substances are transmitted into the urine, and that in this patient the rapidity may have been unusually great. I certainly have never found, in any of the numerous experiments conducted in my laboratory, that such substances as iodine, ferrocyanide of potassium, and alkaline carbonates, passed so rapidly into the urine as in either of the older or more recent observations made on this person.

The period during which a foreign body remains in the animal organism is extremely various; here also it depends upon the solubility of the substance in question, and especially upon its chemical nature, whether a longer or a shorter time be required for its elimination. Substances of easy solubility are, as a general rule, rapidly removed from the body by the urine; thus I have seen the alkaline reaction of the urine disappear in as short a space as ten hours after a dose of two drachms of acetate of potash, while once after a dose of three drachms of bicarbonate

<sup>1</sup> Lond. Med. Gaz. June, 1845.



of soda, it remained alkaline for three days. The idiosyncrasy of each individual patient appears, however, to exert an influence on these relations. This is best observed in experimenting with iodide of potassium; in some persons no trace of this substance can be detected in the urine twenty-four hours after a dose of ten grains has been taken, while in others its presence may often be recognized after three days, both in the urine and also in the saliva. Substances which enter into insoluble chemical compounds with animal matters, are eliminated from the body only very slowly, and usually less through the urine than through the intestinal canal; metals, as is well known, are found after a very long time in the liver and in other parts.

We now proceed to the consideration of those *substances which usually only occur in morbid urine*.

Although an extremely large number of observations have been made regarding the occurrence of *albumen* in the urine, it has only been found to be constantly present in certain affections of the kidneys. Since we have possessed a more accurate knowledge of those forms of renal disorder which we know as Bright's disease, it has been established as a result of experience that albumen is always present in the urine in this affection, although its quantity may be so small that it may appear to be altogether absent. In the chronic form of Bright's disease the amount of albumen in the urine is often considerably diminished, if any acute or inflammatory disease be simultaneously present. The quantity of albumen in Bright's disease is, however, sometimes so considerable that, on heating, the whole fluid solidifies into a yellowish-white coagulum. We cannot mention any other disease in which albuminuria is a constant symptom. Albumen is, however, very frequently present in the urine in all those diseases with which uræmia is associated, and particularly in scarlatina and other acute exanthemata, and most especially in cholera. Bright's granular degeneration of the kidneys is, however, very often present with uræmia, so that these diseases appear to owe their albuminous urine solely to the access of Bright's disease; there are, however, numerous cases, as for instance of scarlatina and erysipelas, in which albumen is only transitorily present in the urine for one or two days, and is accompanied by the epithelial cylinders, which have been already described. In these cases there is merely *simple renal catarrh*, in which as in catarrhal affections of all other mucous membranes, there is desquamation of epithelium and a secretion of mucus.

In *dropsies*, at least in their more advanced stages, albumen is often found in the urine without the simultaneous existence of degeneration of the kidneys; in these cases there are two ways in which we can explain the manner in which this substance escapes from the renal capillaries; either the blood has already become so hydræmic that it not merely transudes through the capillaries of the peritoneum, of the subcutaneous cellular tissue, and of other organs, but also of the kidneys themselves, and that consequently some albumen is thus added to the substances which are ordinarily separated by the kidneys; or we may assume that those organic diseases of the thoracic or abdominal organs, which occasion a stasis of the circulation in the capillaries and veins of the abdomen, and thus give rise to copious transudations, also set up a similar



condition in the capillaries and veins of the kidneys, by which an effusion of albumen into the urinary canals is induced. Meyer<sup>1</sup> has made some beautiful experiments on rabbits which support this latter view. On compressing with a ligature sometimes the renal vein on one side and sometimes the inferior vena cava, by which the increased hydrostatic pressure of the blood must dilate the renal capillaries, he always found albumen in the urine collected after the operation; and on tying the renal vein on one side he only found albumen in the urine that escaped from the exposed ureter of the side on which he operated, and here it was very abundant.

*Organic diseases of the thoracic and abdominal organs* sometimes occasion an escape of albumen through the kidneys, without, however, the simultaneous occurrence of any dropsical transudation; here the albuminuria probably only arises from the above-mentioned causes.

If, in consequence of any affection of the urinary passages, *blood*, or true *pus*, should find its way into the urine, it is obvious that that fluid must then become albuminous.

When albuminuria occurs in association with *hectic fevers*, *diabetes*, *diseases of the spinal cord*, &c., this symptom is dependent either on the watery character of the blood, or, as is sometimes the case in diabetes, on an actual lesion of the kidneys.

The cases are by no means rare in which persons with only *slight fevers*, and unaffected by any other serious disorder, for a short time secrete a urine that is more or less albuminous (Becquerel,<sup>2</sup> C. Schmidt,<sup>3</sup> and others). Since we sometimes meet with cases in which the urine is albuminous when there is perfect health, and no cause can be assigned for its presence (Simon,<sup>4</sup> Canstatt,<sup>5</sup> Becquerel,<sup>6</sup> and others), we are entitled to believe that some persons are specially predisposed to this affection, that is to say that the facility with which the albumen escapes is dependent upon a peculiarity of their organization. We must here also notice the transitory occurrence of albumen in the urine during pregnancy (Rayer,<sup>7</sup> Becquerel).<sup>8</sup> As the œdema of the lower extremities is closely allied to a varicose condition of the veins, so the overloading of the bloodvessels in the abdominal organs during pregnancy is probably a more efficient cause than any other of the transudation of the albumen into the kidneys.

We have already spoken of the occurrence of *fibrin* as an abnormal morphological constituent of the urine; and we remarked that it was always found in cases of hemorrhage into the urinary passages. Urine is, however, occasionally observed in which only the intercellular fluid of the blood appears to have transuded; in some of these cases the fibrin becomes separated, after the emission of the urine, either as a gelatinous mass, or in granular clots or threads (Prout,<sup>9</sup> Nasse,<sup>10</sup> Pickford,<sup>11</sup> Heinrich).<sup>12</sup>

<sup>1</sup> Arch. f. phys. Heilk. Bd. 3, S. 116-119.

<sup>2</sup> Sémeiotique des urines, &c. P. 134

<sup>3</sup> Charakteristik der Cholera. S. 117.

<sup>4</sup> Lehrb. d. med. Chem. Bd. 2, S. 382 [or English translation, Vol. 2, p. 184].

<sup>5</sup> Pathologie. 2 Aufl. Bd. 2, S. 182.

<sup>6</sup> Op. cit., p. 324.

<sup>7</sup> Maladies des Reins. T. 2, p. 579.

<sup>8</sup> Op. cit., p. 394.

<sup>9</sup> On the Nature and Treatment of Stomach and Renal Diseases. 1848, p. 46.

<sup>10</sup> Unters. z. Physiol. u. Pathol. Bonn. 1835. S. 215.

<sup>11</sup> Arch. f. phys. Heilk. Bd. 6, S. 85.

<sup>12</sup> Rhein. Monatsschr. f. Aertze. Bd. 1, S. 24.



*Casein* has been particularly found in the so-called milky or chylous urine: I have frequently had occasion to remark in the preceding pages, how difficult it is to distinguish casein from basic albuminate of soda and other protein-bodies. I have never been able to detect true casein in urine; but in all the analyses of chylous urine, instituted by Chevallier,<sup>1</sup> Blondeau,<sup>2</sup> Rayer,<sup>3</sup> Bouchardat,<sup>4</sup> Golding Bird,<sup>5</sup> and others, the evidence of the presence of casein is by no means established with scientific accuracy; for if it were, we must believe in a perfect metastasis of milk to the kidneys. It is, however, an unquestionable fact, that there do sometimes occur in the urine certain protein-bodies whose properties do not coincide with those of any known protein-compound, and whose modifications cannot be solely dependent on their admixture with the urinary secretion. Thus, for instance, Bence Jones<sup>6</sup> found a peculiar albuminous substance, together with the well-known tubular casts, in the urine of a man suffering from osteomalacia and from a renal disease; this substance was characterized by its solubility in boiling water; when precipitated by nitric acid it redissolved on the application of heat, but again separated on cooling; with acetic acid and ferrocyanide of potassium it behaved precisely as a protein-body, as also with concentrated hydrochloric acid, forming with it a brilliant purple solution; moreover, its elementary analysis showed that its composition was altogether analogous to that of the protein-bodies; it contained 1.1% of sulphur, which could be very easily recognized on treating it with potash, &c. The urine contained 6.7% of this substance, which cannot possibly be regarded as either albumen or casein, at all events until we are able by the addition of certain substances either to convert albumen or casein into this substance, or it into them; it presents too many points of difference to allow of our regarding it as a modification of any of the known protein-compounds.

*Fat* is comparatively rarely found in the urine, if we exclude the admixture of fatty matter that often arises from the external generative organs of women. In the older medical literature we often read of fatty urine, in which the fat collected as an iridescent film upon the surface; but in the great majority of cases these membranes must have consisted of the crusts of earthy phosphates and confervoid filaments, which have been already described, and not of fat; for these crusts are often singularly like a coating of fat, which latter I have never observed on the urine. In more recent times Nauche<sup>7</sup> has regarded this membrane as a characteristic sign of pregnancy, and has instituted a number of experiments, which, however, only lead to a negative result. The *kyestein* is nothing else than the formation of crystals of triple phosphate, and fungoid and confervoid growths, which takes place when the urine becomes alkaline, as has been described in p. 121; but whether or not this membrane and the flocculent precipitate which is subsequently formed from it be actually a characteristic symptom of pregnancy, it cannot be denied that such a membrane, or, more correctly, the rapid alkalinity of the

<sup>1</sup> Journ. de Chim. méd. T. 4, p. 179.

<sup>2</sup> Ibid, Vol. 4. p. 41.

<sup>3</sup> L'Expérience. 1838. No. 12.

<sup>4</sup> Journ. de Connaiss. méd. Août, 1843.

<sup>5</sup> Lond. Med. Gaz. Oct. 1843.

<sup>6</sup> Ann. d. Ch. u. Pharm. Bd. 67, S. 97-105 [and Philosophical Transactions for 1848, p. 55]

<sup>7</sup> Journ. de Chim. méd. 2 Sér. T. 5, p. 64.



urine, is more frequent in pregnant women than in other cases; the urine of pregnant women is, as a general rule, very watery, and hence more readily undergoes alkaline fermentation; it further contains more mucous, protein-like substances than other urine, and this is a second reason why it more readily becomes alkaline and presents a tendency to the formation of this membrane. Hence Nauche's view is not altogether devoid of foundation; but every one must have observed that the urine of pregnant women, especially when they have been living chiefly on animal food, very often does not possess this property, and, on the other hand, that the limpid urine of hysterical and chlorotic women, as well as faintly acid and albuminous urine, may present precisely the same phenomena that have been regarded as peculiar to pregnancy.

Fat, however, sometimes occurs in perfectly normal urine. I found that it was constantly present, although in small amount, in the urine of tortoises (*T. græca*); Frerichs<sup>1</sup> commonly found it in the urine of cats, and the subsequent carefully conducted investigations of Lang<sup>2</sup> confirmed this observation. The latter observer also detected a small amount of fat in human urine, especially after the use of fatty food; and the various experiments which were made by him on cats, as well as on men, leave no doubt that the occurrence of fat in the urine is frequently to be referred to the food. Whether, however, this is the sole cause of the occasional appearance of fat in the urine of healthy animals, appears from the observations which I have made on the urine of tortoises and on the kidneys of the deer, to be a matter of considerable doubt. The amount of fat appearing in normal urine is, however, very small, even after a very abundant use of fat, as is shown by the very careful quantitative determinations made by Lang. This observer generally found no more than about 0.11% of fat in the solid residue of the urine of cats which had been fed on fatty flesh; in human urine he found, in one instance, 0.2% in the solid residue.

I have never observed true milky or chylous urine in which the turbidity and coloration were owing to fat. Urine of this kind owes its peculiarity to an excess of suspended pus-corpuscles, which, in all the cases hitherto observed, originated in the kidneys, and were not owing to vesical catarrh. Whenever this kind of milky urine is actually found to be rich in fat, it may be owing to the presence of milk added, as in Rayer's case,<sup>3</sup> for the sake of deceiving the physician. Bence Jones<sup>4</sup> has recently examined with care, a case of this kind of chylous urine, and the following are the results at which he has arrived: the urine contained from 0.7 to 0.8% of fat, associated with which there were, however, also albumen, fibrin, and normal blood-corpuscles; the greatest amount of fat was found in the urine after digestion, although the blood was not found to be richer in fat.

Neither motion nor rest exerts any influence on the amount of fat in the urine, although it may affect the above-named abnormal constituents of that secretion. No change could be perceived in the kidneys (on

<sup>1</sup> Die Bright'sche Nierenkrankheit. u. deren Behandl. Braunsch. 1851, S. 154.

<sup>2</sup> De adipe in urina et renibus diss. inaug. Dorp. Liv. 1852, pp. 6-46.

<sup>3</sup> Traité des maladies des Reins. T. 1, p. 159.

<sup>4</sup> Philosophical Transactions. 1850, pp. 651-660.



dissection) by the naked eye, and they were not examined by the microscope.

It is in chylous and milky urine that the largest quantity of fat is found, where it occurs suspended in globules as in the chyle and milk. Unfortunately, very little is known regarding the forms of disease with which such urine is associated.

The occurrence of fat in albuminous urine is a symptom of more importance; it has been already mentioned (in vol. i. p. 228) that fat may be expected to be present in fatty degeneration of the kidneys; my own experiments on the urine in Bright's disease have not as yet confirmed this expectation; free fat-globules are, however, sometimes found in the urine, but it is never easy to decide whether they actually pertain to the urine, or, whether they are mere foreign admixtures; and the difficulty is increased by the very small quantity in which they always occur. In the latter stages of Bright's disease we sometimes, however, find individual tubes which appear to be filled with small globules or granules of fat, and present a striking resemblance to the *tubuli contorti* of fatty kidneys. In such a case it would be quite possible to diagnose fatty degeneration of the kidneys from an examination of the urine.

By instituting a very careful examination, we may also sometimes find fat-globules in the urine in diseases which are accompanied with rapid emaciation; as, for instance, in certain diseases of the liver, and in those conditions with which hectic fever is associated.

We need hardly observe that *sugar* occurs in diabetic urine; it is, however, the quantity of sugar that is present which constitutes the characteristic sign of diabetes mellitus. It has been generally believed that sugar is also often found in urine which is not diabetic (Lersch,)<sup>1</sup> but no very great weight should be attached to such an opinion, for the methods which have been employed for the discovery of sugar are open to many fallacies; even Trommer's test, when applied with every possible precaution, may give no decided reaction, even when sugar is unquestionably present in urine; while conversely it may, in inexperienced hands, easily lead to the belief that sugar is present when in reality it is absent. It has been already mentioned (in vol. i. p. 257), that Prout and Budge have found sugar in the urine of gouty and dyspeptic persons, and that I detected it in the urine of a woman shortly after delivery; and I have the greater reason for believing that the results of these observers are correct, from the circumstance, that I have very recently found sugar (by applying the method described in vol. i. p. 252) in the urine of a man with very acute gout.

We have already spoken, in the first volume, of the amount of *sugar* in the urine, under different physiological and pathological conditions. I must, however, here additionally remark that, contrary to my earlier experiments and the more recent observations of Uhle, sugar occasionally passes into the urine after the use of highly saccharine food. C. Schmidt<sup>2</sup> had, indeed, made an experiment of this nature on a cat, and Bernard had been led from his observations to maintain a similar view, but the experiments made under my direction by Dr. Von Becker were the first to convince me that under at least apparently similar relations,

<sup>1</sup> Baier. medic. Correspondenzbl. 1846. S. 534.    <sup>2</sup> Charakter. d. Cholera. S. 167.



sugar is quite as often absent as present in the urine of rabbits after the use of highly saccharine food (carrots), or after the injection of solutions of sugar into the stomach of those animals. Certain relations which exert a general influence on the secretion of urine, appear, moreover, to exercise a special action on the urinary secretion. Thus Dr. Von Becker observed in several experiments that rabbits, into whose stomachs a concentrated solution of sugar had been injected, did not exhibit sugar in the urine unless the urinary secretion was very abundant; these animals continued perfectly well even when as much as 60 grammes had been injected in the course of three hours. Other rabbits, however, which exhibited morbid symptoms, or which speedily died in consequence of excessive filling of the stomach and intestines (as far as the transverse colon) with saturated saccharine solutions, voided very little urine containing no sugar whatever. It would appear, therefore, that sugar does not readily pass into the urine when the quantity of the secretion is diminished. It is worthy of remark that only from 0.336 to 0.348% of sugar was found in the blood of those rabbits which retained their healthy appearance and liveliness, whilst as much as from 1.03 to 1.20% of sugar was found accumulated in the blood of those animals which apparently suffered after the injection of sugar, and which secreted only small quantities of urine that was either very poor in sugar, or entirely free from that substance. It would appear, therefore, that when the quantity of sugar in the otherwise normal blood exceeds 1%, the other limit is reached at which no sugar passes into the urine, and at the same time the urinary secretion is then reduced to the minimum.

Numerous cases have been recorded in which *abnormal pigments* have been found in the urine; the color of the brick-dust sediments in febrile urine is unquestionably not dependent on the normal urine-pigment, although it may possibly arise from its oxidation; at all events, we very often see the ordinary urinary sediment (urate of soda) on the filter, of a deep brick-dust or scarlet color; it has not been further examined; and at different times it has received the various names of *rosacic acid*, *uroerythrin*, and *purpuric acid*. Blue, green, violet, and black pigments are, upon the whole, of rare occurrence in the urine. We have already spoken (in vol. i. p. 284) of the pigments which Heller has exhibited from the urine; unfortunately, however, his experiments were so incomplete, that the very existence of such pigments as *uroxanthin* and *urrrhodin* is still doubtful; the one whose existence is most clearly established, and which admits of the most accurate examination, is the crystallizable *uroglaucin*, which has also been artificially obtained by Alois Martin<sup>1</sup> and by Scherer, by the action of nitric acid. This uroglaucin may possibly be contained in the blue, violet, and black urine of the earlier observers, and is probably identical with the pigment named *cyanurin*. Heller's assertion that the urine in Bright's disease and in cholera very often assumes a blue color on the addition of very concentrated nitric acid, may be very easily put to the test; as far as my own experience goes, it is only when uræmic symptoms have manifested themselves, that this peculiarity of the urine is generally observable.

[For much additional information on the *abnormal pigments* of the

<sup>1</sup> Arch. f. Chem. u. Mikros. Bd. 4, S. 191-196.



urine, we may refer to the Memoirs of Dr. A. H. Hassall,<sup>1</sup> read before the Royal Society, on June 16, 1853, and June 15, 1854, "On the frequent occurrence of indigo in human urine, and on its chemical, physiological, and pathological relations;" of Dr. Harley,<sup>2</sup> "On the coloring matters of the urine;" of Virchow,<sup>3</sup> "On the pigments in the urine;" of Heller,<sup>4</sup> "On uroerythrin as a constituent of the urine in diseases;" and of Kletzinsky,<sup>5</sup> "On uroglaucon, considered as an oxide of indigo."—G. E. D.]

The presence of the *biliary acids* in the urine is by no means so rare as has generally been supposed. Pettenkofer himself once detected them, by means of his own test, in the urine in a case of pneumonia; it is worthy of notice, that they are often present in only very small quantity, or are altogether absent, in well-marked cases of icterus, even when the urine abounds in bile-pigment, while a urine which contains very little pigment is often found, on a careful investigation, to be comparatively rich in the biliary resinous acids. Cholic acid is, however, by no means invariably present in the urine in cases of pneumonia; indeed, it is comparatively seldom found in that disease. I have not been able to discover these substances in the urine in any other disorder, unless (as is often the case with pneumonia of the right side) there was a decided affection of the liver.

We have nothing to add to the observations already made (in vol. i. p. 282) regarding the occurrence of *bile-pigment* in the urine.

We must similarly refer our readers to vol. i. pp. 156 and 163, for all that need be stated regarding those comparatively rare substances, *xanthine* and *cystine*.

We have already noticed the pathological conditions under which *carbonate of ammonia* may occur in the urine.

*Sulphuretted hydrogen*, although in most cases formed in the same manner as carbonate of ammonia, has been occasionally found in the urine in cases of tuberculosis and rubeola by Chevallier,<sup>6</sup> Höfle,<sup>7</sup> and Heller.<sup>8</sup>

*Butyric acid*, which was first detected in the urine by Berzelius,<sup>9</sup> is only rarely present in it either in health or disease. The occurrence of this acid does not seem to be associated with any definite form of disease; I have more frequently met with it in the urine of pregnant women than in that of non-pregnant women, or men.

Berzelius submitted to distillation urine that had been treated with sulphuric acid, saturated the acid distillate with baryta water, filtered, and obtained on evaporation a crystalline saline mass, which, on the addition of sulphuric acid, developed much butyric acid. On repeating the experiment, and submitting very large quantities of urine to such treatment, I never obtained more than traces of butyric acid; but on examining the urine of a woman who was not suckling (who was living on very low diet, and had little appetite), on the third, fourth, sixth, and ninth days after delivery, I obtained, by merely extracting the solid

<sup>1</sup> Proceedings of the Royal Society. Vol. 6, p. 327, and Vol. 7, p. 122.

<sup>2</sup> Pharm. Journ. Nov. 1852.

<sup>3</sup> Arch. f. pathol. Anat. Bd. 6, S. 259.

<sup>4</sup> Arch. f. Chem. u. Mikrosk. 1853, S. 361.

<sup>5</sup> Ibid. p. 414.

<sup>6</sup> Journ. de Chim. méd. T. 1, p. 179.

<sup>7</sup> Medic. Ann. Bd. 11, S. 415.

<sup>8</sup> Arch. f. Chem. u. Mikrosk. Bd. 3, S. 24.

<sup>9</sup> Lehrb. d. Ch. Bd. 9, 424.



residue with ether, an acid fat which had the odor of butyric acid, and exhibited the ordinary properties of that substance: on then dissolving in water the residue that had been extracted with ether, adding sulphuric acid, and following the directions of Berzelius, I obtained a fresh quantity of butyric acid. This urine which contained butyric acid was always somewhat turbid and of a dirty yellow rather than an amber color.

*Ammoniacal salts*, such as the hydrochlorate of ammonia, phosphate of soda and ammonia, and phosphate of magnesia and ammonia, do not occur in fresh urine, although their presence there has been often asserted. The experiments which prove the non-existence of ammonia in fresh urine have been described in p. 404 of the first volume. We have there also remarked that the efflorescence which is observable on evaporating a drop of urine under the microscope, depends neither upon hydrochlorate of ammonia, or phosphate of soda and ammonia. When, on the other hand, ammonia can be distinctly recognized in fresh urine after its evaporation, it must be the product of some decomposition. We have already alluded to the facility with which urinary pigment undergoes alteration, and thus hastens the decomposition of the urea. Any one, by repeating the following experiment which I devised, may readily convince himself that the presence of ammonia in even the most carefully evaporated urine affords no proof of its presence in the fresh secretion; for if we evaporate perfectly fresh urine in a retort at the lowest possible temperature, we always find ammonia in the distillate, while the concentrated urine that is left in the retort often reddens litmus paper more strongly than before. In this case the acid phosphate of soda exerts a decomposing action on the urea or on the pigment (probably on both), and there is formed phosphate of soda and ammonia, which, as is well known, evolves ammonia at a temperature of  $100^{\circ}$ , and again becomes converted into acid phosphate of soda; hence it exerts a continuous decomposing action on these nitrogenous matters during evaporation, and thus the urine may retain its acid reaction, while a large amount of an ammoniacal fluid passes over into the receiver. If we boil acid phosphate of soda with pure urea, or with the alcoholic extract, after freeing it from all bases and from ammonia by sulphuric acid, and saturating the sulphuric acid with potash or soda, we may readily satisfy ourselves of the correctness of this mode of explaining this singular phenomenon. On treating urine that has been concentrated by freezing with bichloride of platinum and alcohol, there is a precipitation of chloride of platinum and potassium, but no precipitation of platinum and ammonium; on adding caustic potash to such urine, the precipitate, when examined with the microscope, does not exhibit the well-known star-like groups of laminae of basic phosphate of ammonia and magnesia, but merely amorphous matter; and further, no ammonia can be detected in this precipitate by any chemical test.

It is universally known that ammoniacal salts occur in morbid, alkaline human urine; but we also sometimes find ammoniacal salts in the acid urine of patients, as I have convinced myself in examining the perfectly fresh acid urine of typhous patients. It is, however, extremely difficult to determine the quantity of ammonia with any moderate degree



of accuracy, whether we apply bichloride of platinum according to Liebig's<sup>1</sup> method, or magnesian salts, as recommended by De Vry,<sup>2</sup> since urine of this nature has generally a great tendency to decomposition, and no conclusion can be deduced from a single specimen; for in the determination of the ammonia, it is necessary to employ the urine collected in a definite period. On this account also it is difficult to decide in what forms of disease we especially find acid urine to contain ammonia.

The following is De Vry's method of determining ammonia quantitatively in urine. Fresh urine is treated with bicarbonate of soda in order to remove the earths, is filtered, and sulphate of magnesia is then added to it; in consequence of the presence of phosphate of soda in the urine, the addition of the sulphate of magnesia causes a precipitation of phosphate of magnesia and ammonia, from which we must calculate the ammonia. There are, however, two points to be borne in mind, if we would wish to obtain accurate results by this method; the first is, that the bicarbonate of soda throws down some ammonia with the magnesia; and the second is, that it is possible that there may not be sufficient phosphate of soda in the urine to combine all the ammonia with the magnesia, and to precipitate them. Both these difficulties may, however, be readily overcome; the former, by determining the magnesia in the precipitate thrown down by the bicarbonate of soda, the latter, by the addition of an excess of phosphate of soda (Berzelius).<sup>3</sup>

The occurrence of *nitric acid*, which Prout<sup>4</sup> and Wurzer<sup>5</sup> believed that they had discovered in brickdust sediments, is very doubtful; for the methods of analysis which they employed might very easily deceive them.

In considering the *analytical methods* which have been employed, or suggested, for the examination of the urine, we find ourselves upon one of the most unpromising fields of inquiry within the whole domain of physiological chemistry. Our remarks as to the time and labor that have been lost in examining the analyses of the blood, apply with still greater force to most analyses of the urine. For these very analyses have been the means of throwing so much disrepute on the zoo-chemical investigations of true chemists, that they have been classed in the same catalogue with the much-condemned analyses of old and modern drugs. We will only add a few remarks to what has been already stated in the first volume, in reference to the modes of discovering, and the methods of determining, individual constituents of the urine.

But if pathology has hitherto reaped only little advantage from analyses of the urine, the fault rests less with chemists than with physicians, who obviously can benefit little, or nothing, from even the best analyses of the urine, as long as they continue in error as to the actual results which may be obtained from such investigations. Till they learn to comprehend the questions they would submit to the chemist, they cannot obtain the desired reply from pathological chemistry. As long as the physician thinks he may employ chemical reagents as mere diagnostic instruments, like the stethoscope and the pleximeter, he will acquire but little information from a chemical investigation of the urine,

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 50, S. 195.

<sup>2</sup> Ibid. Vol. 59, p. 383.

<sup>3</sup> Jahresber. Bd. 17, S. 628.

<sup>4</sup> Op. cit.

<sup>5</sup> Op. cit.



which conducted on such principles will necessarily rank amongst the most slovenly experiments.

With respect to the *purely diagnostic investigation of the urine* it may be observed that the application of the microscope, and some few chemical reagents will, in general, afford all the necessary means for answering the questions commonly demanded in chemical inquiry. If the urine be acid, the microscope may reveal, as we have already seen, mucus or pus-corpuscles (in the erroneously-termed chylous urine, such, for instance, as is almost constantly found to accompany pyelitis), epithelium, spermatozoa, casts from the tubes of Bellini, blood-corpuscles, &c., and in addition to these urate of soda, oxalate of lime, and cystine; if the urine be alkaline, a microscopical investigation will easily enable us to ascertain that the fluid contains only phosphate of magnesia and ammonia, urate of ammonia, and other morphological elements.

In order to distinguish *urate of soda* from uric acid in a sediment, by the aid of the microscope, the urine should not be heated, for this would dissolve the urate of soda, as has been mentioned in vol. i. p. 194.

If an apprehension be entertained of mistaking the molecular masses of urate of soda for other molecules under the microscope, a few drops of hydrochloric acid should be added to the object, when rhombic crystals of uric acid will be formed. (Acetic acid often acts imperfectly or very slowly.)

In order to avoid confounding certain crystalline forms of the *triple phosphate* with *oxalate of lime*, a little acetic acid should be added to the microscopical object, as directed in vol. i. p. 50.

The hexagonal tablets of *cystine* may readily be, and probably often are, confounded with the analogous forms of *uric acid*. They may, however, easily be distinguished under the microscope, on the addition of acids; since the crystals of uric acid, which are generally yellow in color, are insoluble in them, whilst the crystals of cystine (which are generally colorless) very rapidly dissolve in them. We have already spoken in vol. i. p. 164 of the chemical means of recognizing cystine.

Other substances, such as *urea*, *hippuric acid*, *uric acid* (when it is not contained in the sediment), *albumen*, *sugar*, *the biliary acids*, and *bile pigment*, can only be chemically recognized in the urine by the methods which we have already considered in the first volume.

We have already noticed the mode of detecting *butyric acid*, certain abnormal *pigments*, and *ammonia*.

With a view of determining the average quantitative relations of certain inorganic constituents, the same reagents are generally employed which are used in their qualitative analysis; thus, for instance, in order to detect an excess or a deficiency of hydrochloric, phosphoric, and sulphuric acids, and lime, in the urine, nitrate of silver, acetate of lead, chloride of barium, and oxalate of ammonia are usually directly added to separate specimens of urine—a mode of proceeding which can scarcely be justified, even in a medico-diagnostic investigation. Care should at all events be taken to bring the different samples of urine which are to be compared with the normal secretion to the same degree of density by concentration, since it is by this method only that a comparison can be



made between the volumes of the precipitates. Such a method would, however, consume more time than observers are willing to expend on the inquiry, although it must be obvious that such a comparison of the volumes of the precipitates cannot in itself lay claim to the slightest degree of accuracy. How many substances may not be contained in the precipitated metallic salts, even where nitric acid has been most carefully employed for the recognition of the chloride of silver or the sulphate of baryta? May not numerous organic substances be precipitated by the metals from the urine, more especially when it is in a morbid condition? How is it possible to decide regarding the density of the urine from its color, or in this manner to determine the excess, or diminution, of these substances? Physicians should be cautious, lest they may be led into new errors by these superficial chemical tests, when they have only just liberated themselves, by physical and anatomical investigations, from older misconceptions. It would, however, be going too far, were we to attempt wholly to avoid these misapplied methods, in entering upon a scientific examination of the urine. Thus, for instance, in attempting to ascertain the increase, or diminution, of the phosphates in any disease, we might, after collecting the twenty-four hours' urine, and keeping it as cool as possible, add ammonia in order to remove the earths and the greater part of the uric acid, and then treat the filtered fluid with sulphate of magnesia. The first precipitate after exposure to a red heat would show the amount of the earthy phosphates, and from the second we could calculate the phosphate of soda. If we wish to ascertain the quantity of lime separated with the urine in a certain time, it would be sufficient to precipitate the filtered urine with oxalate of ammonia (provided the urine be acid), and after the oxalate of lime has been washed according to the usual methods of analytical chemistry, to expose it to a red heat, weigh it, and thus calculate the quantity of the lime. If we precipitate acidified urine with a baryta salt, we may approximately determine the quantity of sulphuric acid; but if we follow all the prescribed rules, we shall, after exposure to a red heat, obtain a carbonaceous sulphate of baryta, which after the combustion of the carbon will exhibit an alkaline reaction or develope bubbles of air, when treated with acid. A similar remark may be made in reference to the determination of the chlorine in the urine by direct precipitation.

The method of determining the potash in the urine by bichloride of platinum would, for reasons which remain to be explained, be almost equally devoid of exactness with the modes of determination already referred to.

It must be observed in reference to the qualitative investigation of the urine, that it is very instructive to allow this fluid to stand for a prolonged period, and to examine it from time to time with the microscope, since the nature of the physical alterations, the rapidity with which they occur, and the changes observed in the reaction on vegetable colors, yield, as we have already seen under the head of Urinary Fermentation, considerable information as to the presence of such ingredients or characters of the urine as could not be chemically detected.

More importance has been attached to the determination of the *specific gravity* of the urine than it actually possesses in a scientific point of view,



or than it merits from the methods employed in determining it. In fact, the determination of the specific gravity of the urine is of less importance than that of any other animal fluid. We may regard it almost as a law, that the blood and most other animal fluids, have always a tendency to maintain a definite specific gravity, which is necessary for the fulfilment of their functions. The fluctuations in the specific gravity of these fluids are, therefore, very inconsiderable, and hence it is the more important to notice great variations in them. The case is altogether different in respect to the urine, whose concentration is almost invariably changing; indeed, it seems to be the special function of the kidneys to maintain the other animal juices in their normal state of admixture and in their proper degree of concentration; at one time there being an excess of salts carried off with the *detritus* arising from the metamorphosis of tissue, at other times, more or less water. We have already shown what numerous and different external and internal conditions control the quantity of water which passes through the kidneys, and we can therefore derive but little instruction from a knowledge of the specific gravity of the urine, while we remain in ignorance of the conditions which exist in individual cases.

It may be asked, however, will not the specific gravity of the urine aid us at the bedside in arriving at important conclusions regarding the course of the morbid process, or even in recognizing the disease? But, notwithstanding the use of the highly vaunted *urinometer*, which has been constructed in various forms and according to different principles, we do not find that the more accurate determination of the specific gravity of the urine has thrown any great light upon the morbid processes in question. Nor indeed was this to be expected, for it is far more difficult to draw any scientific conclusions from the density of the renal secretion in the diseased organism than in health. But may it not be objected, that the specific gravity of the urine may aid in the diagnosis of diabetes mellitus? This very question shows that the importance of determining the density is ideal rather than real, for the specific gravity of diabetic urine, even when the disease has been diagnosed, is frequently not greater than that of other urine; even when diabetes is fully established, that is very frequently the case; so that the color and reaction of the urine, and the quantity daily discharged, must be taken into account in forming a diagnosis from the urine alone. But surely it would be much better at once to apply one of the simple tests; for sugar, if found to be present, would have a higher diagnostic significance than all the other characters together. Why should a bad method be employed when a good one is at our disposal? The urea diathesis assumed to exist by English physicians, may perhaps be diagnosed from the specific gravity of the urine; as yet, however, this disease has not, so far as we know, been observed on the continent, and, indeed, we almost doubt if it ever will be, for a disease which consists of a mere metamorphosis of all the tissues into urea, without any special anatomically demonstrable organic lesion, is not credible on physiological grounds. How rapidly this supposed chronic affection would run its course, if such masses of urea passing daily through the urine were the *detritus* of the tissues, and not, as is



probably the case, merely the result of a good digestion of large quantities of animal substances!

The specific gravity of the urine has never been determined on account of its absolute value, but always solely with the view of determining the quantity of solid constituents and water contained in this fluid. It was supposed that the residue of the urine might readily be determined from its specific gravity, and for this purpose Fz. Simon,<sup>1</sup> Becquerel,<sup>2</sup> and G. Bird,<sup>3</sup> have attempted to establish formulæ from which, when the specific gravity was given, the solid residue of the urine might be determined. The complete inapplicability of such formulæ, which I have shown by my own experiments,<sup>4</sup> has recently been most completely demonstrated in a large number of investigations made by Chambert<sup>5</sup> on the urine of healthy persons. These experiments prove that there does not even exist any definite proportion between the quantity of salts in the urine and its density, and much less that any such connection exists between the organic matters and the density of the fluid. A comparison of the numbers yielded by the formulæ of these three observers will suffice to show the remarkable differences in the results. These differences are clearly exhibited by the following simple illustrations; thus, for the urine whose specific gravity is 1.010, Becquerel gives 1.650%, Simon 1.927%, and Bird 2.327%; for a specific gravity of 1.020, the first gives only 3.300%, the second 4.109%, and the last 4.659%, &c. If this enormous difference in the results depend upon the different methods adopted by the several observers for the determination of the specific gravity as well as of the solid residue, it is evident from Becquerel's tables, in which the specific gravity is only increased about  $\frac{1}{1000}$ th part and the urinary residue about 0.165%, that a progression which is so much at variance with all the laws of physics cannot be correct. It would be necessary to expound the principles of physics, were we to attempt, in the present place, to explain why two or three kinds of urine may have the same specific gravity, and yet differ in the quantities of their solid constituents, and why, conversely, samples of urine which contain similar quantities of solid constituents, might yet differ so considerably in density. In order, however, fully to show the impracticability of this method, we need only refer to the remarks made in vol. i. p. 409, in reference to the determination of the specific gravity as a means of controlling the chemical analysis. It is obvious, from Schmidt's positive investigations, that a definite progression in the specific gravity which may be expressed numerically, cannot correspond with that of the increase of the solid constituents; and that in the analysis of the urine, Schmidt's mode of determining the specific gravity, *as a volumetric check* on the chemical determinations, possesses only a fictitious accuracy. The reasons of this uncertainty consist partly in our ignorance of the coefficient of condensation of many of the constituents of the urine, which are present in very variable quantities, and partly on the utter impossibility of determining the quantity

<sup>1</sup> Beiträge z. med. Ch. u. Mikrosk. Bd. 1, S. 77 u. 143.

<sup>2</sup> Semeiotique des urines, &c. P. 33.

<sup>3</sup> London Medical Gazette. New Ser. Vol. i. p. 138.

<sup>4</sup> Schmidt's Jahrb. Bd. 47, S. 5.

<sup>5</sup> Recueil des Mémoires de méd. et pharm. milit. T. 58, p. 358.



of some of the substances contained in the urine, even with a moderate degree of accuracy.

Although we regard it as entirely out of place in a work on physiological chemistry, to enter more fully into the methods of determining densities, or to pass an opinion upon their value, since these are subjects which should be learnt from physics, or at all events from practical chemistry, we cannot forbear making a few remarks, which may prove serviceable to those who have been unable to form any opinion regarding the numerous determinations of densities with pathologico-chemical literature is over-burdened. The ordinary means employed for the determination of the specific gravity of animal fluids are, the areometer, the hydrostatic balance, and the direct weighing of equally large volumes of distilled water and of the fluid in question. We need hardly repeat an observation which we have already made more than once, that the areometer gives only approximately correct results, even when it has been graduated for a definite temperature, and is in other respects well made. It would, however, be wholly at variance with the principles of areometry, if we were to expect to arrive at even a tolerably accurate result, if we applied the areometer to fluids containing any solid particles in suspension. Even if such approximate determinations may suffice in the case of analyses of the urine, they should be discarded in all other animal fluids; for if the specific gravity is to be anything beyond a mere appendage to the analysis, its approximate determination will simply furnish a means of error. Our remarks naturally apply to all the other methods in use for determining the densities of fluids, and even with greater force, in so far as they justify us in expecting more accurate results than those which can be furnished by the areometer.

Among the different areometers, there is only one which deserves any special notice; but this instrument, which is constructed by Alexander,<sup>1</sup> of Munich, yields, according to my experience, much more accurate results than one might be disposed to expect, *à priori*, from its construction. It is arranged in the following manner: Two parallel graduated glass tubes, both open at one end, and communicating with each other at their other ends, at which is a small syringe, are introduced, the one into water, and the other into the liquid to be examined. The air in the tubes is now slightly rarefied by means of the syringe, when by comparing the elevation of the water and of the other liquid in the tubes, the ratio of the specific gravities is given. This is the best of all the instruments for rapidly determining the density, as the influences of the temperature and of atmospheric pressure are here almost eliminated.

The *hydrostatic balance with a glass sinking-ball* generally yields more accurate results than the areometer; but yet, notwithstanding every precaution, it does not admit of the exactness presented by the direct weighing of volumes. The defects in this method depend principally upon the irremediable loss of a portion of the water of the animal fluid by evaporation, and more especially upon the circumstance that the balance gives a much less accurate result when the glass ball is weighed in water or in an animal fluid than when it is weighed in the air; and on this account fluids that are at all viscid, such as blood-serum, should not be

<sup>1</sup> Polytechn. Centralb. 1847. Heft. 6, S. 361.



treated by this method; defibrinated blood cannot be examined in this manner, for we often find that even the addition of one or two centigrammes does not affect the beam of the balance. Even if the unavoidable adhesion of vesicles of air to the glass did not render this mode of determination unsuitable for the blood, its employment in the case of a fluid in which solid particles are irregularly distributed, appears, from well-known physical grounds, to be wholly irrational.

The ordinary method of determining the specific gravity by the *direct weighing of equal volumes* in glass flasks is the best, but its value may unfortunately be very considerably diminished if it be not conducted with a care and attention which many medical chemists scarcely seem to think necessary, excepting in the case of elementary analyses. It is not sufficient in this method to weigh the empty and carefully dried flask, to determine its weight when filled with water, and finally with the fluid to be examined, for several calculations will be required to make the necessary corrections, on account of differences in the thermometric and barometric relations. It must further be borne in mind that the weighing is not conducted in a vacuum, and that the specific gravity alone possesses any value when it has been reduced for a vacuum. This is easily effected when the specific gravity of the glass and the coefficients of expansion of the air and water are known; and the calculation may be very considerably shortened by the use of logarithms, or of a couple of algebraic equations.<sup>1</sup>

But in how few of the numerous determinations of the density of animal fluids has it been thought necessary to employ all these precautions! No one, however, who compares the results obtained with and without these corrections can deny their necessity. Then, moreover, we very rarely find the mode of determination indicated in the notice of the specific gravity, although the knowledge of the method employed is quite as important here as in the case of the numerical results of the analysis. How can we place entire confidence in the technical mode of conducting such a determination, when this essential part of the calculation of the specific gravity has been neglected? We can hardly expect that an experimentalist who neglects to attend to the influences of temperature and the degree of expansion of the different media employed in these measurements, should regard all the other necessary precautions; amongst which, we may enumerate the following as points worthy of attention. In every experiment for the determination of volume, we should use freshly-boiled distilled water; the glass should be held and dried with some non-conducting substance, and care should be taken to avoid all contact with heated or perspiring hands; all vesicles of air should be excluded as far as possible, and the glass cover or plate should be moistened before it is placed upon the flat surface, in order to remove any adhering air; and the flask should be dried with some cleaner substance than ordinary linen or strips of paper, which may give rise to great inaccuracy.

The practice of drying the flask by means of a wire wrapped in linen

<sup>1</sup> We would refer those who may be ignorant of the mode of constructing the necessary formulæ, to any of our best Manuals of Physics, and especially to Berzelius's *Lehrb. d. Ch.*, 3d Ed. Vol. 10, p. 285, and to C. Schmidt's *Entwurf einer Untersuchungsmethode thierischer Säfte*.



or paper, is not only laborious and tedious, but may, at the same time, give rise to slight errors; on which account, it is better to place the flask over sulphuric acid in a vacuum, which accomplishes the proposed purpose very rapidly and effectually; or, after the flask has been placed in the sand-bath, the air must be suffered to pass through it, as in smoking, by means of a tube running along the bottom of the vessel. By these methods, which are familiar to all chemists, the faintest breath may be observed upon the exterior or interior of the glass. We simply refer to this well-known operation, in order to show those less familiar with this apparently simple method, how much care and attention are required for the mere determination of the specific gravity of a fluid.

Having already offered these remarks on the methods of determining the specific gravity, it may not appear superfluous to observe that we have been induced to adopt this course on two different methodological grounds. The first, which has already been noticed, refers to the necessity for the utmost accuracy where we are desirous of imparting any scientific value to our determinations of density as a controlling test of the chemical analysis, and as a means of comparison with the specific heat and the refractive and polarizing powers; since, without such precaution, the scientific object of the inquiry could never be attained. The method alone is not all that ought to be considered, since the mode of its application is of even greater importance; for whilst one person may obtain very incorrect results in weighing with the most accurate balance, another may contrive to arrive at the best determinations by means of an inferior balance, provided the weights are accurate. Thus, too, the second reason which has led us into some diffuseness, is obvious from our previous observations, and consists in this: that we should regard all average estimates of density which are prosecuted simply by way of appendage to the chemical analysis, or for the purpose of roughly determining the quantity of water in a fluid, as entirely superfluous, and a mere waste of time and labor, which might have been expended upon some of the numerous questions of science which still require elucidation.

In passing to the consideration of the *quantitative analysis* of the urine, we need only observe generally, that in all investigations of the urine, in which the quantitative relation of the secreted urinary constituents is to be ascertained, the collective fluid which has been passed within a definite period (as, for instance, twenty-four hours) should be selected for analysis, and its composition compared with that of other normal or morbid urine which has been passed within the same period of time; or in case this method is not practicable, or is otherwise unsuited to the object of the investigation, the quantity of water should be wholly disregarded, and the proportions of solid constituents to one another should be made the object of investigation (that is to say, the constituents should be calculated for 100 parts of solid residue). So much has already been said in reference to the necessity of this point in a rational investigation of the urine, as insisted upon in Becquerel's and my own observations,<sup>1</sup> that it would be alike uninteresting and superfluous to revert to the reasons which led us to establish this rule, more especially as it must be

<sup>1</sup> Journ. f. pr. Ch. Bd. 25, S. 1-21, and Bd. 27, S. 257.



obvious from all that has been, and still remains to be, mentioned concerning the urine. It may, however, seem as if we were too strenuously insisting upon this very important point; for this rule by no means entirely precludes the analysis of any other urine besides that which has been collected in twenty-four hours. For, independently of the fact that the analysis of the entire quantity of urine discharged from the bladder at one time, is not only admissible, but even highly desirable, when considered in a scientific point of view, we may derive accurately scientific and purely physiological results by adopting a method I have elsewhere recommended, of comparing together the different solid constituents in the urine, without restricting the examination to the twenty-four hours' urine. The comparison of the numbers representing the solid constituents frequently gives very unexpected results, which cannot be obtained from a mere comparison of the complete analysis of the twenty-four hours' urine, or of any other urine. By way of illustration, we will simply refer to our remarks in vol. i. p. 487, in which we showed that we had been enabled, by a comparison of the solid constituents of hepatic venous blood with those of portal blood, to arrive at several conclusions which could not have been obtained independently of this mode of calculation, but which are very important, and throw considerable light on the metamorphoses effected in the liver, the physiological import of the hepatic function, and the rejuvenescence of the blood. This is even more essential in respect to the investigation of the urine, since water in general plays a far less important part, or, at all events, does not stand in so definite a relation to the solid constituents here as in other animal fluids,—a remark which applies equally to daily urine and to any individual specimen. Indeed it would be wholly illogical to insist that analyses should be rigorously limited to the twenty-four hours' urine, since such a method could not fail to lead to errors and misapprehensions. We need hardly remark, that in acute diseases the character and composition of the urine may change very considerably in the course of twenty-four hours; and this is not only the case in typhus, measles, &c., but sometimes also in inflammations running their ordinary course. Thus it not unfrequently happens in pneumonia, that a urine is passed in the morning, which either already exhibits an alkaline reaction, or becomes alkaline in a very short time, whilst the urine discharged three or four hours later may have an acid reaction, and exhibit an increase of acidity on standing. Now, when such different kinds of urine are mixed, we can hardly be said to be conducting a very strict, or even rational, method of investigation.

In conducting an analysis of the urine, special attention must be devoted to its evaporation and the drying of its residue; and here again we encounter other difficulties, which differ from those presented by similar modes of investigation, as, for instance, in evaporating and drying milk. I have convinced myself by direct experiments<sup>1</sup> that, in *evaporating* the urine, its decomposition will be directly proportional to the duration of the evaporation; and I have already drawn attention to the fact that the urine always develops ammonia during its evaporation, although it may retain its acid reaction. It is, therefore, very important

<sup>1</sup> Op. cit.



to let this evaporation be effected as rapidly as possible, when it is unavoidably necessary to do so by heat; and this observation is especially applicable when the collective twenty-four hours' urine is evaporated, since in this case the urine is rendered more susceptible of decomposition from prolonged standing. Slow evaporation has, however, the effect of causing the urine to be decomposed with extraordinary rapidity, as we may see from the fact that urine which has been thus collected and mixed together will, in four out of five cases, contain no hippuric, but only benzoic acid. The urine always becomes slightly decomposed when evaporated by heat, in whatever manner this may have been accomplished; but the following method is, I think, the best adapted to hinder, as much as possible, this decomposition. The urine should be introduced into a wide tubular retort, and whilst the evaporation is proceeding on a sand-bath near the boiling-point, atmospheric air, or hydrogen gas, should be continually passed over the evaporating surface. The distillate will then always be ammoniacal, although not to such a degree as if the evaporation were accomplished without the employment of a current of air. The quantitative determination of the solid residue cannot, however, be obtained by this method, which simply serves for the preparation of the extract from which the urea and the other constituents of the urine may be quantitatively determined.

I regard the following as the only correct method of ascertaining the quantity of the solid residue: small quantities of the fluid (see vol. i. p. 408) should be placed in a vacuum with sulphuric acid, care being taken in exhausting the air that the urine does not boil, and is not allowed to bubble; from ten to fifteen grammes may in this manner be very readily evaporated in a shallow basin. The application of heat, as, for instance, of the air-bath, is, however, even more objectionable for *drying* the residue than for evaporating the urine; the urinary residue commonly forms a tough, extract-like, and very hygroscopic mass, and hence several precautions are here required, besides those which were noticed in vol. i. p. 305, for drying animal substances. In the first place, the urinary residue ought only to be dried in a vacuum at a mean temperature, because it invariably becomes decomposed on the application of heat, although in some cases more than others. When the urine is heated on an air-bath, as, for instance, at about 90 or 100° C., it always becomes enveloped in an atmosphere which contains ammonia, but which regains its ordinary condition when the air has been frequently changed, and a corresponding loss of weight may be observed on each repeated weighing. The process of weighing is here attended with the greatest difficulties, since the urinary residue is almost more hygroscopical than that of the bile; and on this account the precautions there indicated, or some other means, must be employed to hinder the increase of weight which may be induced by the attraction of water during weighing. It is of little use to place sulphuric acid or chloride of calcium within the case of the balance; but, instead of the shallow evaporating basin, a wide vessel may be employed, having a ground-glass stopper or glass plate, which, immediately after the drying and before the weighing, should be attached to the evaporating vessel. We certainly cannot hope to effect a perfect drying of the urinary residue without the application of artificial heat;



but we may, at all events, obtain results by this method which admit of being compared with one another, and which would be unattainable if we employed heat.

*Alkaline urine*—that is to say, urine containing carbonate of ammonia—is very ill adapted for quantitative analysis. If, therefore, it is deemed necessary to analyze it, it must be neutralized before it is evaporated, or, what is still better, acidified, by means of a definite quantity of dilute sulphuric acid, which must subsequently be accounted for in the analysis.

We have already spoken, in the first volume, under their respective heads, of the various methods adapted for the quantitative determination of *urea*, *uric acid*, *hippuric acid*, *sugar*, *albumen*, *oxalate of lime*, &c. Nor have we much to add in reference to the quantitative determination of the *mineral constituents* of the urine beyond what we have already stated of analyses of the ash in vol. i. pp. 368–407. In case we do not wish to adopt Rose's method of determining the ash, the process of carbonizing and incinerating the residue of the urine may be considerably facilitated by adding to the urine, before its evaporation, a quantity of nitric acid nearly equivalent to its urea; by this means nitrate of urea is formed, which becomes decomposed on evaporation into carbonic acid and nitrate of ammonia, and escapes, during further concentration, in the form of water and nitrous oxide. Much time is gained by this method, for the substance which constitutes the larger portion of the urinary residue, and which yields a very large quantity of carbon on exposure to a red heat, is in this manner almost entirely eliminated. It might be feared that a portion of the alkaline chlorides would thus be decomposed either by the nitric acid or the nitrous oxide; but from the direct experiments which I have made with this and with the ordinary method, I find that there is no loss of chlorine unless we add so much nitric acid that slight explosions occur on exposing the solid residue to a red heat. But it is not possible, even by this method, to consume the urinary residue so entirely as only to leave a white ash, if we keep in view that we are attempting a quantitative analysis, and have regard to the vapors of phosphorus and chlorine which escape on intense heating. On account of the presence of soluble and fusible salts, the carbonaceous residue of the urine can scarcely ever be perfectly incinerated, for the particles of carbon become invested by means of the fusible salt with a crust, which protects them from the action of oxygen. As this is the case even with very small quantities of the urinary residue, I regard the following method as the best adapted for quantitatively determining the mineral constituents of the urine: the carbonaceous ash must be weighed with the caution necessary in the case of hygroscopical bodies, and after being washed with water, must be filtered; and the residue on the filter, whose weight in the dry state has been previously ascertained, must be again weighed. The difference of weights gives the amount of the mineral substances dissolved by the water; the insoluble parts may now be easily incinerated, and their quantity thus determined. The further analysis must then be completed by the ordinary methods.

The combustion of the carbon by oxygen in a platinum capsule seems to me, at all events in the case of the urine, to be altogether unsuitable,



on account of the volatilization of the chlorine, and even of sulphuric and phosphoric acids.

Chambert's<sup>1</sup> method is the best adapted for a continuous series of determinations of the mineral substances of the urine. The evaporation of the urine must be effected in the following manner: a tube, two centimetres in width is provided, at its lower extremity, with a glass tube, twice bent at right angles, and terminating in a sphere; this sphere again opens into a minute drawn-out glass tube, whilst the upper part of the wide tube passes into a small glass tube into which a cock is inserted. This apparatus is filled with urine, and so secured to the stage of a Berzelius's spirit lamp that the opening of the glass sphere is brought immediately over a heated platinum crucible. By means of the cock we may regulate the access of the air, and the corresponding dripping of the urine into the crucible. Chambert allows the urine to escape so slowly, that one drop is suffered to evaporate before another succeeds it. In this manner 100 or 110 grammes of urine may be evaporated in the course of an hour and a half. Loss by spirting may be tolerably well prevented by carefully and uniformly regulating the escape of the fluid. The layer of carbon which speedily invests the crucible does not amount to the twentieth part of that obtained by the ordinary method.

In order to effect the combustion of the residuary carbon, distilled water should be suffered to drop on the glowing carbon from the same reservoir in which the urine was previously contained; the combustion of the carbon will go on with tolerable rapidity at those points with which the water comes in contact, owing to the well-known decomposition of this fluid at a red heat; but as some carbon will always adhere to the walls, it must repeatedly be removed, and more water allowed to drop upon it. The experiment does not gain in accuracy by this method, but the combustion is effected with greater rapidity. Hence we may perceive that, although this analysis is very applicable in certain cases, it cannot, for many reasons, lay claim to any great degree of exactness.

The *volumetric method* is on many accounts to be preferred to determinations by weight, in the analysis of the urine. This method has not only the advantage over weighing of being more rapidly accomplished, which is especially desirable in the case of urine-analyses, in which, for the most part, a large series of observations are necessary for the attainment of reliable results, but it has the further advantage of rendering all long-continued evaporation unnecessary, and this is a great advantage, in consequence of the decomposition of the urine, which this process always induces. This method, after having been for a long time employed in testing metals, has been adopted by Liebig in the analysis of the organic juices. We have already considered in detail (vol. i. p. 254) Fehling's method of determining the sugar in the urine. The following method for determining the amount of *phosphoric acid* in the urine was recommended to Breed by Liebig.<sup>2</sup> A solution of perchloride of iron, of definite strength, is added to acid urine, or to urine which has been acidified with acetic acid, until no more phosphate of iron is separated; the quantity of phosphoric acid in the urine is then calculated

<sup>1</sup> Recueil des Mémoires de méd. et de pharm. militaire. T. 58, p. 328.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 78, S. 150.



from the volume of the iron-solution which has been employed. The solution of the perchloride of iron is prepared by dissolving 15.556 grammes of iron in *aqua regia*, and then carefully evaporating the solution to dryness in a water-bath, in order to remove the excess of free acid without decomposing and volatilizing any part of the perchloride of iron. The residue is dissolved in 2000 c.c. of water; 1 c.c. of this solution will precipitate 0.010 of a gramme of phosphoric acid (that is to say, 10 millegrammes). In the place of this solution we may employ one of undetermined concentration, the strength of which may be tested by a solution of phosphate of soda, whose amount of phosphoric acid has been previously determined. The solution of perchloride of iron must not, however, contain any of the protochloride. In order to ascertain whether all the phosphoric acid has been precipitated, and there is a trace of perchloride of iron in excess, we must moisten a slip of paper saturated with ferrocyanide of potassium with a drop of the urine to be tested; if the excess is considerable it will be detected by the formation of Prussian blue. Here, as in all cases in which this method is employed, the quantity of the substance to be determined in a previously determined volume of the urine, is ascertained from the volume of the test-fluid which has been expended in the experiment.

We may proceed in a perfectly similar manner in the determination of the *chlorine* and *sulphuric acid* in the urine; but here we must acidify the urine with nitric or hydrochloric acid, and bear in mind that, notwithstanding the free acid, organic matter, combined with oxide of silver or baryta (as, for instance, uric acid, &c.), is precipitated, although perhaps only in very small quantities, together with the chloride of silver and sulphate of baryta, and hence rather more chlorine, and especially more sulphuric acid, is always calculated than the urine actually contains.

Liebig<sup>1</sup> has suggested a very ingenious method for determining volumetrically the amount of *urea* in the urine, which is closely connected with a chemical fact that he has recently discovered,<sup>2</sup> namely, that if bichloride of mercury in solution, and bicarbonate of potash in excess, be added to a solution of urea, we obtain a compound of urea and mercury,  $\overset{+}{U} + 4 \text{ Hg O}$ , which is perfectly insoluble in water. This method has, further, this advantage, that we simultaneously determine the amount of *chlorine* in the urine. The following are the main steps in the process. In order to remove the phosphates and sulphates of the urine, a definite quantity of the fluid is mixed with half its volume of a fluid, containing 1 volume of a saturated solution of nitrate of baryta to 2 volumes of a saturated solution of caustic baryta. We take about 15 c.c. of the filtered alkaline fluid (which consequently contains for every 3 volumes 2 volumes of urine), and then, without neutralizing it, we add from a burette a solution of nitrate of mercury of known strength, as long as any precipitate is formed. The mixture must be well stirred during this process. The precipitate is the above-mentioned compound of urea and oxide of mercury,  $\overset{+}{U} + 4 \text{ Hg O}$ . When a few

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 85, S. 289-328.

<sup>2</sup> Ibid. Bd. 80, S. 123.



drops of the turbid fluid are poured into a watch-glass, and one drop of a solution of carbonate of soda is added, the mixture soon becomes yellow when treated with an excess of the solution of mercury, but it remains white when the solution of mercury is insufficient to precipitate all the urea. Very different methods may of course be employed for the preparation of the test-fluid (of nitrate of mercury); Liebig has, however, proposed a very simple method for this purpose, which consists in treating nitrate of mercury, in place of the bichloride, with phosphate of soda; if, however, a solution of common salt, of known concentration, be added to a mixture of these salts before the precipitate of the phosphate of mercury is rendered crystalline, the quantity of the oxide of mercury may be very easily calculated from the volume of the chloride of sodium necessary for its resolution (for one equivalent of chloride of sodium necessarily corresponds to one equivalent of the phosphate of mercury). We may, however, at once obtain a solution of chloride of sodium suited for the purposes of these experiments, when we consider that a solution which is saturated between the temperatures of  $0^{\circ}$  and  $100^{\circ}$  constantly contains 27% of salt.

The method of determining the amount of *chlorine* in the urine is based upon the fact that, on the one hand, urea may be precipitated by the nitrate but not by the bichloride of mercury, and, on the other hand, that the nitrate becomes converted into bichloride of mercury when brought in contact with chloride of sodium. In order, therefore, to find the amount of chlorine in the urine, a definite volume of it should be decomposed with the solution of baryta; the urine which is filtered from the precipitate should then be treated with nitric acid until it is completely neutralized, and the solution of the nitrate of mercury poured upon it until the precipitate no longer dissolves on being stirred (that is to say, as long as bichloride of mercury is formed). The quantity of the bichloride of mercury, or of the chlorine, contained in the urine may be calculated from the volume of the solution of mercury which has been used.

*The amount of the secretion of urine* exhibits greater fluctuations than the secretion of any other organ. So many of the most varied external and internal conditions here come into play, that it would be impossible to estimate them perfectly, either for special or general cases. Although we may form to ourselves a tolerably correct idea of the more remote influences acting upon the secretion of urine, and of their extent, we are still very deficient in the knowledge of the more immediate conditions which influence this secretion and regulate the variations in its amount. The science of physiology more especially feels the want of those chemical investigations, which might elucidate the relation of the character and composition of the blood to the secreted urine, although we are not deficient in isolated facts confirming the proposition which had been *a priori* advanced, that the constitution as well as the amount of the urine must depend upon the existing constitution of the blood. In the meanwhile it cannot be overlooked, that the chemical character of the blood cannot be the exclusive cause of all or any of the modifications in the urine, but that the mechanism of this secretion, as well as the condition of the nervous system, must be included amongst the immediate agents



of the secretion of the urinary matters from the blood, and therefore must control the amount of the secretion. Whilst it is only recently that the view has been generally admitted, that the most essential constituents of the urine exist preformed in the blood, it has even been attempted to refer the process of the secretion to purely dynamical relations, depending upon the nervous system. No sooner was the fundamental law of endosmosis established, than it was supposed that the transmission of the urinary constituents into the "tubuli uriniferi" might be referred to this process; but a more thorough investigation of the laws of endosmosis sufficiently demonstrated that endosmosis alone was insufficient to afford an explanation of the mechanical processes involved in the secretion of urine. Ludwig<sup>1</sup> made the first successful attempt to establish a theory for the mechanical part of the process of the urinary excretion in the kidneys. Whichever view one may incline to in reference to the terminations of the urinary canals, it must be admitted that the principal part of the secretion from the blood is effected in those singular coils of vessels, the Malpighian bodies. It would appear, however, from the measurements of most histologists, that the capillaries leading from the Malpighian bodies are of a smaller diameter than the vessels constituting the bodies themselves; hence it follows from the laws of hydraulics that there must be a greater pressure against the walls of the latter, by which means, according to Ludwig, the water passes through them, and the true urinary constituents are introduced into the "tubuli uriniferi." The collected urinary fluid, which is so rich in water, is further impelled through the "canalicula contorta" by the fluid which is subsequently exuded from the blood; here, however, these small vessels are surrounded by a network of vessels originating in the "vasa efferentia," and here an endosmotic interchange seems so far probable, that the more concentrated blood of the different vessels is necessarily brought into contact with the thin urinary solution, from which it again abstracts water, and thus leaves the urine more concentrated.

Ludwig advances the following grounds, in addition to the anatomical arrangement of the kidneys, in support of this view. According to him, his view explains why the urine never exceeds a certain degree of concentration; why a rapidly secreted urine is in general very much diluted, whilst urine which is more slowly secreted, is generally more concentrated; why the amount of urine increases as the quantity of the excretory matters of the blood is augmented; and finally, why no more fluid passes from the kidneys, after the solid constituents of the urine have been excreted in the kidney.

As Ludwig's whole theory rests essentially on the difference in the pressures of the blood, he has directed his attention to the more thorough elucidation of the influence of this relation upon the urinary secretion. Whilst Kierulf endeavored, under his direction, to ascertain the influence of the character of the blood, especially its amount of water, Goll<sup>2</sup> made the mechanical question the subject of a series of very

<sup>1</sup> Handwörterb. d. Physiol. Bd. 2, S. 637-640.

<sup>2</sup> Ueber d. Einfluss des Blutdrucks auf. d. Harnabsonderung. Inaug.-Abd. der. med. Fac. zu Zürich vorgel. 1853.



admirable observations. From his labors we may conclude with certainty, that the lateral pressure in the arterial system of the kidneys exerts a very important influence on the urinary secretion. Thus, for instance, on irritation of the *nervi vagi*, as well as when the vascular system is deficient in blood, that is to say, during conditions in which the tension in the arterial system is diminished, the urinary secretion was found to be very considerably diminished, whilst this secretion was greatly augmented during an increased tension of the blood in the arterial system, when this condition was induced by the tying of some of the larger arteries. It was further shown, that in addition to this well-attested influence of the pressure of the blood, other causes exerted a modifying action on the amount of the secretion. But as it was further proved, that even where the constitution and pressure of the blood were the same, the excretion of urine from the two kidneys was never parallel (for either the right or the left kidney secreted more than the other), other relations, as for instance, the influence of the kidneys upon the contractile fibres of the renal tissue, and the yet unknown relations of the constituents of the blood to the permeability of the walls of the bloodvessels and urinary canals, will still have to be taken into consideration.

It is obvious from the above remarks, that the composition of the urine in certain physiological and pathological conditions can only be correctly determined when the quantities of the urinary constituents daily secreted by the kidneys can be compared together. We will, therefore, in the first place give the *quantitative relations* which occur under different conditions in the collective urine which has been secreted within definite periods of time.

Lecanu<sup>1</sup> found that sixteen persons of different ages and sexes, but who all received a due supply of mixed food, passed in twenty-four hours from 525 to 2271 grammes of urine; while Becquerel found that the mean daily quantity passed by four men was 1267.3 grammes, whilst that by four women was 1371.7 grammes. Chambert, who made twenty-four observations on men between the ages of twenty and twenty-five years, found that the daily quantity of urine varied from 685 to 1590 grammes. In experiments which were, for the most part, made in the summer, I discharged, during a fortnight's strictly regulated diet, from 898 to 1448 grammes of urine daily; during twelve days, on which I lived exclusively on animal food, from 979 to 1384 grammes; and during a twelve days' course of vegetable diet, from 720 to 1212 grammes.

Winter found that three youths discharged respectively the average quantities of 1672, 1702, and 1933 c. c. of urine in 24 hours, the extremes being 910 and 3340 c. c.

Scherer found that a child, aged three years and a half, discharged 755 grammes; a boy, aged seven years, 1077 grammes; a man aged twenty-two years, 2156 grammes; and a man, aged thirty-eight years, 1764 grammes in 24 hours.

Now if we reduce these and certain other determinations to the weight of the body as a standard, it follows from Winter's experiments, that a man for every kilogramme's weight discharges an average quantity of

<sup>1</sup> Journ. de Pharm. T. 25, p. 681 et 746.



25.9 grammes of urine (the maximum being 46.8, and the minimum 14.0 grammes). According to Scherer, a child for every kilogramme's weight discharges 47.4 grammes, while the corresponding quantity in an adult is only 29.5 grammes; further (according to Schmidt<sup>1</sup>) a cat during an abundant flesh-diet (108.755 grammes of fatty meat) discharges in 24 hours 91.036 grammes of urine for every kilogramme of its weight; on a less abundant flesh-diet (44.118 grammes of meat) 53.350 grammes of urine; on 75.938 grammes of meat 71.570 grammes of urine; and on 46.154 grammes of meat (without any drink) 26.454 grammes of urine; a kitten which consumed daily 83.769 grammes of meat, discharged 60.455 grammes of urine.

We have already spoken of the dependence of the *quantity of water* which is separated by the kidneys, on the amount of drink that has been taken, and on the degree of transpiration. Unfortunately we have as yet no accurate experiments to demonstrate the influence which each of these physiological causes exerts on the amount of water that is separated by the kidneys. The facts communicated by Julius Vogel,<sup>2</sup> who, for 189 days, weighed all the food and drink that were taken by a person on whom he was experimenting, show how much other influences, besides the fluids that have been taken, modify the quantity of water in the urine. Whilst on some days scarcely the third part of the fluids that had been taken were carried off by the urine, on other days the quantity of the urine equalled that of the drink, or even exceeded it by one-twentieth, or even one-tenth. The largest quantity of water was unquestionably discharged by the kidneys after the use of a cold bath; here there was not only suppressed transpiration, but water was absorbed from without.

It appears, from the observations of Chambert, that shortly after a meal, less water, both absolutely and relatively to the solid constituents, is separated with the urine. Closely allied to this point is the first of the questions propounded by Lecanu, whether, when the kidneys are secreting an excess of water after copious drinking, they, at the same time, separate an excess of solid constituents; Lecanu answers this question in the negative, although my own experiments lead to an opposite conclusion, as do also those of Chossat<sup>3</sup> and Becquerel.

This is obviously a question to be settled by bedside experience; we can hardly, however, agree with Becquerel in believing that it will explain the mode of action of many diuretics.

Before proceeding to enumerate the quantities of the solid constituents of the urine which are daily secreted, I must not omit to mention the very great differences between the statements of those who have investigated this subject. This difference depends only in a very slight degree on the different methods of chemical investigation and calculation; it is mainly due to the individuality of the different persons, we might almost say of the different nations, on whom the experiments had been instituted. On comparing the urinary analyses that have been made by experimentalists in the three great nations, we perceive that, generally

<sup>1</sup> Verdauungssäfte und Stoffwechsel. S. 304.

<sup>2</sup> Wagner's Physiol., S. 264 [or English translation, p. 421].

<sup>3</sup> Journ. de Physiol. T. 5, p. 65.



speaking, far the least solid constituents are found in the urine of the French, and that they are especially deficient in urea and uric acid, that the Germans very far exceed the French in these respects, while again the English pass even larger quantities than the Germans. One of the principal grounds of this difference is, no doubt, to be sought in the difference of diet, and in the varied modes of life of the three nations. It is well known that the French take very little animal food, and live generally with great moderation, while the English use highly seasoned animal food so abundantly that Prout<sup>1</sup> not unfrequently met with specimens of urine from which nitrate of urea at once crystallized on the addition of nitric acid,—a circumstance that would hardly occur to a genuine German urine, to say nothing of French specimens. From statistical data it appears that any given number of Londoners eat six times as much animal food as an equal number of Parisians. Besides the nature of the food, there are doubtless other, although probably less influential causes for such differences, as, for instance, the general mode of life in other respects, the climate, &c.

With regard to the *solid constituents* which are daily separated with the urine, the following are the final results obtained from several series of experiments: Becquerel found (from experiments on four men and four women) that 39.52 grammes of solid matter are, on an average, secreted daily by the kidneys of men, and 34.31 grammes by those of women. While living on a mixed diet, I discharged, on an average, 67.82 grammes in twenty-four hours; on an exclusively animal diet, 87.44 grammes; on a vegetable diet, 59.235 grammes; and on non-nitrogenous food, 41.68 grammes. Lecanu found that men secreted far more solid matters by the kidneys than women, old men far less than women, children eight years old more than old men but less than women, and lastly, children four years old even less than old men. According to Scherer's<sup>2</sup> determinations, a child, aged three years and a half, excreted in twenty-four hours 26.13 grammes of solid matter with the urine; a boy, aged seven years, 32.40 grammes; a man aged twenty-two years 47.97 grammes; a man aged thirty-eight years 71.23 grammes; and an insane patient, aged fifty years, who was starving himself, 23.69 grammes.

It is obviously to be expected, that the quantities of solid constituents which are separated by the kidneys should be very variable. Thus it is manifest, that whenever the metamorphosis of matter is more active than usual, and after the expenditure of bodily force, or an abundant supply of food (especially nitrogenous matters), and in certain diseases associated with a considerable wasting of certain organs, the quantity of the matters excreted with the urine will be considerably augmented, without reference to the excretion of water. But further investigations are still required to elucidate scientifically the relations of dependence of the quantity of those substances on their original conditions, and more especially on the simultaneous physical and chemical constitution of the blood. The cases are far more frequent in which there is a diminution

<sup>1</sup> [We are not aware that Prout has described any cases in which he has seen *healthy* urine undergo this change.—G. E. D.]

<sup>2</sup> Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 3, S. 280-290.



in the excretion of solid matters through the urine, as for instance in those diseases in which the metamorphosis of matter is either partially or generally altered. It is, therefore, in the latter cases especially that more frequent opportunities have presented themselves of gaining a more intimate knowledge of these conditions, and their direct and indirect effects. Thus, for instance, it has been generally found that in Bright's disease, the normal constituents decrease to an extraordinary degree, which may be readily explained by the loss of unchanged nutrient matters (albumen in this disease). As soon, however, as a more active metamorphosis of matter is induced by the occurrence of febrile excitement or an inflammatory process, the constituents of the urine are again excreted in the normal, or in an increased quantity, while there is at the same time a diminution of the albumen (Scherer).<sup>1</sup> As we observe in Bright's disease, so also we learn from direct experiments, that after the artificial *augmentation of the salts of the blood, the normal constituents of the urine are considerably diminished.*

We may here add a few remarks on the recent investigations which have been made regarding the quantity of *urea* that is secreted under different conditions. According to Scherer's observations, a child excretes 0·810 of a gramme in twenty-four hours for every kilogramme of its weight, and an adult only 0·420 of a gramme; while, according to Schmidt, a cat when eating daily 108·755 grammes of fat meat, excretes 7·663 grammes of urea for every kilogramme of its weight; when taking 44·118 grammes of meat 2·958 grammes of urea; when taking 75·938 grammes of meat 5·152 grammes of urea; and when taking 46·154 grammes of meat 3·050 grammes of urea. Hence a cat living on a flesh-diet forms and separates by the kidneys on an average 6·8 parts of urea for every 100 parts of flesh which it consumes. If all the nitrogen of the food were separated as urea, rather more urea would of necessity be excreted than corresponds to the above mean numbers. For 100 parts of flesh contain, according to Schmidt's analyses, 22·83 parts of muscular substance and tendon; and 100 grammes of albuminates + collagen = 16·11 of nitrogen (with 53·01 of carbon, 7·02 of hydrogen, 22·86 of oxygen, and 1·00 of sulphur); hence these 100 parts of nitrogenous matters must yield 34·52 parts of urea (which contain 16·11 of nitrogen). Hence 100 parts of flesh (corresponding to 22·83 of albuminates + collagen) yield according to this calculation 7·88 parts of urea. A cat during eighteen days' inanition excreted on an average 2·11 grammes of urea in twenty-four hours for every kilogramme's weight.

With regard to the *extractive matters* Scherer found that a child aged three years and a half, excreted in twenty-four hours (when living on a mixed diet) 2·17 grammes of extractive matters; a boy, aged seven years, 3·88 grammes; a man, aged twenty-two, 24·335 grammes; a man, aged thirty-eight years, 20·484 grammes; and an insane patient, aged fifty years, who was starving himself, 10·59 grammes.

The *fixed salts* discharged with the urine in twenty-four hours, were determined by Scherer as follows: in the child, at 10·98 grammes; in

<sup>1</sup> Pathologische Untersuchungen.



the boy, at 10·23 grammes; in the young man, at 23·627 grammes; in the middle-aged man, at 29·919; and in the man who was starving himself, at only 3·62 grammes.

In addition to what has been already remarked regarding the individual amounts of the various organic matters, we have only to add, that according to the recent investigations of Hegar, Gruner, and Winter, an adult man excretes in twenty-four hours for every kilogramme of his weight 0·064 of a gramme of phosphoric acid (the extremes being 0·096 and 0·043 of a gramme); and 0·032 of a gramme of sulphuric acid. According to Schmidt's investigations, a cat when living on 108·7 grammes of flesh excretes 0·267 of a gramme of sulphuric acid for every kilogramme of its weight; when living on 44·12 grammes of flesh, 0·106 of a gramme; when living on 46·15 grammes of flesh, 0·084 of a gramme; and when living on 76 grammes of flesh, 0·078 of a gramme.

We have already spoken, in the first volume, of the proportions in which the most important of the solid constituents of the urine stand to one another, as well as of the quantities which are daily secreted. (See vol. i. p. 150, for urea; p. 192, for uric acid; and p. 179, for hippuric acid.)

According to Becquerel, the daily amount of *extractive matters* (that is to say, of the organic matters exclusively of the urea and uric acid) averages 11·738 grammes in men, and 9·655 grammes in women; while living on a mixed diet, the quantity of these matters which I daily secreted, amounted to about 13 grammes.

The quantity of the *fixed salts* varies extraordinarily in different persons, living different modes of life. The following are the daily quantities of fixed salts which were discharged in the specimens of urine analyzed by Lecanu—

	The average.	Fluctuations between
In men, . . . . .	16·88 grammes.	9·96 and 24·50 grammes.
In women, . . . . .	14·38 “	10·28 “ 19·63 “
In children, . . . . .	10·05 “	9·91 “ 10·92 “
In aged persons, . . . . .	8·05 “	4·84 “ 9·78 “

According to Becquerel, the mean quantity of fixed salts daily secreted by the kidneys in men is 9·751 grammes, and in women 8·426 grammes; while Chambert, from analyses of the urine of twenty-four young men, fixed it at 14·854 grammes, its limits being 23·636 and 6·993 grammes. In my own urine, I found that while living on a mixed diet, the average quantity was 15·245 grammes, the extremes being 17·284 and 9·652 grammes.

Lecanu found that the quantities of phosphate of lime which are daily given off by the kidneys varied between 0·029 of a gramme and 1·960 grammes. I have never observed such great fluctuations either in my own urine, or in that of other healthy persons, during an ordinary or even an exclusively animal or vegetable diet. The influence of the food upon the quantity of earthy phosphates in the urine is, however, undeniable; while, living on a purely animal diet, I found that my urine contained nearly three times as much earthy phosphates as when living on a mixed diet. The urine of young children, like the allantoic fluid of calves, contains only very small quantities of phosphates, but a comparatively large amount of sulphates. It is probably for some similar



physiological reason that pregnant women secrete far less phosphate of lime with the urine than non-pregnant ones,—a fact that has been previously mentioned.

These few illustrations are sufficient to indicate the numerous conditions on which the quantities of the urinary constituents and their various proportions to one another are dependent, and to show the caution we should exercise in forming an opinion on the nature of a specimen of urine or in drawing any conclusions on the point, unless we have numerous analyses of different urines collected under similar conditions.

The next point which it is necessary for us to notice is the difference in the urine *in the two sexes*. From the experiments of Lecanu and Becquerel, to which we have already alluded, it appears that the chief difference is, that the urine of women contains more water and less urea and salts, even in relation to the other solid constituents; that is to say, women discharge absolutely more water and far less urea and salts than men, while the quantity of uric acid appears to be about the same in both sexes.

The urine of women in a state of *pregnancy* presents certain marked peculiarities, of which the most distinguishing, namely, the formation of the substance called kyestein, has been already noticed in p. 136. Becquerel found that the specific gravity during pregnancy never exceeded 1.011. According to Lubanski,<sup>1</sup> such urine contains less than the ordinary quantity of free acid, and is frequently neutral or even alkaline; as far as my own experience goes, it is, however, always acid when freshly passed, if the women are in good health, but during the latter months of pregnancy it very readily becomes alkaline, since it then generally becomes more aqueous. We have already alluded to the relative and absolute diminution of the phosphate of lime in the urine of pregnant women.

We are indebted to Lecanu for most of our knowledge regarding the influence which the different *periods of life* exert on the constitution and the quantitative relations of the urine. It appears generally from his observations, that men in the vigor of early adult life, when the metamorphosis of tissue is proceeding most actively, secrete the largest quantity of solid constituents with the urine; that women secrete somewhat less, and children and aged persons still smaller quantities. The period of life appears to exert no influence on the quantities of the uric acid and of the salts. From certain experiments, it would appear that the urine of very young children contains relatively more hippuric acid and far less phosphate of lime than the urine in more advanced life.

Of all the physiological conditions, the food is unquestionably that which exerts the most marked influence on the constitution of the urine. We have already spoken, in various parts of this work, of the influence which special substances contained in the food exert on the acid or alkaline reaction of the urine, and on some of its constituents. In the prolonged series of experiments, to which I have often alluded, I have attempted to ascertain the influence which varieties of diet (animal, vegetable, and non-nitrogenous) exert on the character of the urine generally, and on its special quantitative relations. The most essential results may be

<sup>1</sup> Ann. d'Obstetr. &c. 1842, p. 235.



seen at a glance in the following tabular arrangement. While living on a mixed diet and adhering as closely as possible to the same dietetic conditions, I made the analysis of the collected urine; while living on a purely animal diet (almost exclusively on eggs), I made twelve observations, and a similar number while living on a purely vegetable diet; and while living on a perfectly non-nitrogenous food (fat, milk-sugar, and starch) I made two analyses; and independently of the variable quantities of water, the following were the mean quantities (in grammes) of the other substances which were discharged in the twenty-four hours' urine:

	Solid constituents.	Urea.	Uric acid.	Extractive matters and salts.
On mixed diet, . . . .	67.82	32.498	1.183	12.746
On an animal diet, . . .	87.44	53.198	1.478	7.312
On a vegetable diet, . . .	59.24	22.481	1.021	19.168
On a non-nitrogenous diet,	41.68	15.408	0.735	17.130

From these researches we may draw the following general conclusions:

(1.) The solid constituents of the urine are very much increased by animal food, while they are considerably diminished by a vegetable diet, and still more so by a non-nitrogenous one.

(2.) Although the urea is a product of the effete and decomposed tissues of the animal organism, the quantity in which it occurs in the urine depends in part upon the nature of the food that has been taken; during a highly nitrogenous animal diet, the quantity of urea is absolutely increased, while, on a vegetable as well as on a positively non-nitrogenous diet, it is absolutely diminished. Moreover, the relative quantity of urea, as compared with the other solid constituents of the urine, increases, or diminishes, with the nature of the food. During a mixed diet, I found that in my own urine the ratio of the urea to the other solid constituents was as 100:116; during an animal diet, as 100:63; during a vegetable diet, as 100:156; and during a non-nitrogenous diet, as 100:170.

(3.) The quantity of uric acid in the urine depends much more on other conditions, and possibly on other substances introduced into the organism, than on any peculiarity of diet. The differences observed during these observations were too small to allow of our concluding that the nature of the food exerted any essential influence on the formation of uric acid.

(4.) When the protein-compounds, and, consequently, the nitrogen of the animal food, are absorbed in excess in the intestinal canal, that portion of them which is not applied to the reproduction of the consumed tissues, undergoes metamorphosis, and, at last, is again rapidly separated by the kidneys in the form of urea and uric acid. It is only through the kidneys that the animal organism gets rid of any excess of nitrogen which may be absorbed.

(5.) The sulphates and phosphates which are discharged correspond very nearly in quantity with the nitrogenous matter that has been taken, that is to say, with the protein-compounds, which contain sulphur and phosphorus; after the almost exclusive use of protein-compounds, the quantity of these salts in the urine is considerably increased.

(6.) It follows from these propositions, that the other organic consti-



tuents of the urine, that is to say, the extractive matters, must be very much diminished during an animal diet; we find, from our investigations, that after the use of vegetable food, there is an absolute (not a mere relative) augmentation of such substance—a proof that vegetable food contributes largely to the formation of the extractive matters of the urine. Further, after the use of animal food, the physical properties of the urine precisely resemble those of this secretion in the carnivora; that is to say, the secretion is of a very light amber-yellow tint or almost straw-colored, has a strong acid reaction, and appears either to contain no lactic acid, or only a very small quantity, while, according to Liebig's experiments, it also appears to be perfectly devoid of hippuric acid. On the other hand, after a course of vegetable diet, a very great portion of the free acid is lost, and during a non-nitrogenous diet it altogether disappears: it contains a larger amount of dark-colored extractive matter, and hence is of a brownish-red tint; it is also somewhat turbid, from the separation of earthy phosphates, or at all events, readily becomes so on boiling; it almost always contains alkaline lactates, with oxalate of lime; according to Liebig, it is tolerably rich in benzoic acid; as is obvious, from the preceding table, I have never found the uric acid completely absent.

The influence of *indigestible or highly seasoned food, of alcoholic drinks, &c.*, on the augmentation of the uric acid in the urine, has been already noticed in vol. i. p. 194.

The fact that, after prolonged fasting, the urine becomes strongly acid, and poor in solid constituents, but that it always contains some urea, has been already mentioned, and is in part numerically demonstrated in vol. i. p. 151.

It follows, from my own and Simon's experiments,<sup>1</sup> that after *violent bodily exercise* far less water is separated by the kidneys, but that the quantities of free acid, of urea, of phosphates, and of sulphates, in the twenty-four hours' urine, are increased, while those of the uric acid and of the extractive matters are diminished.

It is scarcely necessary to mention that the quantity of water separated by the kidneys must be influenced by *the season of the year, the climate, and the atmospheric temperature*; for the most superficial observer can notice this in his own person. Julius Vogel has, however, definitely proved it, by weighing daily for six months the urine that was discharged by the same individual. I believe that my experiments (noticed in vol. i. p. 193) completely overthrow the opinion maintained by Fourcroy, Marcet, and Schultens, that prolonged *sweating* increases the quantity of uric acid in the urine.

The urine first passed after the night's rest, the *urina sanguinis*, is, as is well known, of greater density, a darker color, and a somewhat stronger acid reaction, than that which is passed during the day. The quantities of this *morning urine* vary with the amount of drink that has been taken before retiring to rest. Independently of the smaller quantity of water which it contains, I can detect no difference in the ratio of its constituents to one another. The nature of the food exerts a certain amount of influence on the morning urine; at all events, while

<sup>1</sup> [We may also refer the reader to Percy's experiments on this point, recorded in p. 169 of the second volume of the translation of Simon's Animal Chemistry.—G. E. D.]



living on animal food, I found it comparatively even more concentrated than the urine passed during the day; even after living for only a single day on purely animal food, I found that on the addition of nitric acid to the urine passed on the following morning, nitrate of urea was at once separated.

Another kind of urine, that, namely, of *digestion*, or the *urina chyli*, was formerly regarded as a distinct variety, to which much weight was attached; in those who do not drink much at, or after, their meals, it is somewhat denser and more colored than that which is passed at other periods of the day; it is, however, not so colored or so dense as the morning urine.

Chambert's experiments, which appear to have been very carefully conducted, do not altogether coincide with my own: the differences are, however, such as may be readily explained by surrounding circumstances. Chambert invariably found the urine of digestion denser and richer in salts than the morning urine; the greater or lesser transpiration during sleep, and the varying amount of drink taken at meal-time, afford the simplest clue to these differences. Moreover, Chambert found that the inorganic constituents of the urine stand in a direct proportion to the quantity of salts taken in the food.

In the twenty-four hours' urine Chambert found on an average 1.3024% of salts, in the urine of digestion 1.6394%, and in the urine discharged between waking and breakfast 0.9332%, while in the urine soon after drink had been taken, the maximum was only 0.2113%.

In animals, at all events, in the *mammalia*, the influence of the food is reflected in the constitution of the urine. We will now proceed to notice the urine of animals, classifying them according to the nature of their food.

Unfortunately, our knowledge of the urine of the *omnivora* is confined to that of man and the *pig*. The urine of the latter animal has been examined by Boussingault<sup>1</sup> and Von Bibra;<sup>2</sup> it is perfectly clear, almost devoid of odor, distinctly alkaline, effervesces with acids, and becomes turbid on boiling, which converts the earthy bicarbonates into simple carbonates, which, consequently, become precipitated; it does not contain ammonia; neither Boussingault nor Von Bibra could discover either uric, or hippuric, acid in it; but Boussingault has shown that in all probability it contains alkaline lactates. Phosphates occur only in very small quantity in it, but sulphates and chlorides are tolerably abundant. The specimens of pigs' urine examined by these chemists contained from 1.804 to 2.086% of solid constituents, in which from 0.29 to 0.49 were urea.

The urine of *carnivorous animals* differs only slightly from that of man; when freshly passed, it is of a light yellow color, of a disagreeable odor, a nauseous bitter taste, and an acid reaction; it very soon, however, becomes alkaline. Vauquelin,<sup>3</sup> Gmelin, Hünefeld, and especially Hieronymi,<sup>4</sup> have examined the urine of lions, tigers, leopards, panthers, hyænas, dogs, wolves, and bears. Urea is present in the urine of these

<sup>1</sup> Ann. de Chim. et de Phys. 3 Sér. T. 15, p. 97-104.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 53, S. 98-112.

<sup>3</sup> Ann. de Chim. T. 82, p. 174.

<sup>4</sup> Jahrb. d. Ch. u. Phys. Bd. 3, S. 322.



animals in large quantities, and may be separated in a state of great purity, since only little pigment is present: uric acid is only present in it in very small quantity; Landerer,<sup>1</sup> however, found 1% of uric acid in the urine of the hedgehog (*Erinaceus europæus*).

The urine of the *herbivora* is very different from that of the *carnivorous* animals and of man. This secretion has been examined in the case of elephants, rhinoceroses, camels, horses, oxen, goats, beavers, rabbits, hares, and guinea-pigs; it is generally of a yellowish color, very turbid, of an offensive odor, and is always alkaline; it certainly resembles the urine of the *carnivora* in often containing much urea, but it differs from the latter in containing a considerable amount of alkaline and earthy carbonates, and of a fatty and odorous matter, in the perfect absence of uric acid, and in its extremely small quantity of earthy phosphates. According to Boussingault, lactates are always present.

The *urine of the horse* has been more carefully studied (by several chemists) than that of any other animal of this class; like that of man, it varies with the nature of the food; when freshly passed, it is usually turbid and of a pale yellow color, but on exposure to the air it very soon assumes a dark-brown tint; in the course of my experiments I have sometimes found it tolerably clear, and it then had a strong alkaline reaction; besides alkaline bicarbonates, it contains in solution a very little of the bicarbonates of lime and magnesia, which separate from the fluid on boiling; it often, however, has a faintly acid reaction, and then we have true *urina jumentosa*, from the deposition of earthy carbonates. Bibra often found great and altogether unaccountable differences in the urine of horses fed in precisely the same manner. The potash in this urine naturally preponderates considerably over the soda. In the sediment of horses' urine I have always found the most beautiful crystals of oxalate of lime in very considerable quantities. Bibra, however, in examining the sediment of a horse's urine, found also a special organic substance, which he could not accurately examine, in addition to the carbonates of lime and magnesia. Attempts have been made to explain the occasional presence of benzoic acid, which is assumed sometimes to take the place of hippuric acid in horses' urine under certain physiological, or pathological, conditions; it is, however, I believe, now established beyond all doubt that the view originally supported by Liebig, regarding the frequent occurrence of benzoic acid in the urine of horses, is correct (see vol. i. p. 84). In the urine of diseased horses I have likewise always found hippuric acid, if it was examined while still fresh. No traces of the salts of ammonia can be detected in horses' urine. Sometimes in examining horses' urine we find that in place of hippuric acid there is a nitrogenous, uncrystallizable, resinous matter, which has not yet been accurately examined. (C. Schmidt.)

In the urine of a diseased horse I found so large a quantity of lactate of potash, that the lactic acid could be combined with lime, magnesia, and oxide of zinc, and could be recognized with certainty by its salts.

It stands to reason that the characters of the urine must vary extremely during the diseases of animals. I extract, by way of illustration, the following examples from my note-books. A very lean, badly

<sup>1</sup> Arch. f. Ch. u. Mikros. Bd. 3, S. 296.



conditioned Wallachian horse, fourteen years old, had suffered for a week from pneumonia of the right side; the urine was of a very pale-yellow color and scarcely at all turbid; it was viscid and somewhat ropy, was strongly alkaline, but did not effervesce on the addition of acids; it remained yellow on evaporation, contained only very little hippuric acid, &c. Another Wallachian horse, thirteen years old, was suffering from acute glanders; it was fed, as was the horse in the previous case, upon bran, hay, and straw; the urine was of a well-marked reddish-brown color, was faintly alkaline, and contained a very considerable sediment of the carbonates of lime and magnesia; the fluid, after the removal of the sediment by filtration effervesced strongly with acids, became of a reddish-brown and almost of a black color on evaporation, contained a large quantity of hippuric acid, &c. A very powerful cavalry horse, seven years old, and fed upon hay, oats, and straw, passed a brownish-yellow, very alkaline urine, which contained only a small amount of earthy carbonates; the same horse, when fed upon oats and straw, without hay, discharged urine which was very turbid from the presence of earthy carbonates, whose reaction was scarcely alkaline, and which, when filtered, did not effervesce with acids.

The *urine of cattle* has been frequently analyzed by Boussingault and v. Bibra. On examining it shortly after its discharge, I have always found it clear, of a bitter taste, a pale-yellow color, and with a strong alkaline reaction: it contains much sulphate and bicarbonate of potash and magnesia, but very little lime; according to Boussingault, it contains no phosphates, very little chloride of sodium, but on the other hand, a large amount of lactate of potash; according to v. Bibra, the quantities of urea and hippurate of potash are liable to great variations, even when the feeding and external conditions remain unchanged. I have always found oxalate of lime in the sediment, but, like Boussingault, I have never been able to detect ammoniacal salts in the fresh urine of oxen. This urine generally contains from 8 to 9% of solid constituents, of which from 1.8 to 1.9% are urea. The hippuric acid varied, according to v. Bibra, from 0.55 to 1.20%. Boussingault found free carbonic acid gas in it, in addition to alkaline bicarbonates.

The *urine of calves* differs very much from that of cattle, and approximates more in its composition to the allantoic fluid of the foetus. It appears from the investigations of Braconnot and Wöhler,<sup>1</sup> that the urine of calves, as long as they are sucking or are fed on milk, is almost colorless, clear, devoid of odor, of very little taste, and with a strong acid reaction, which it does not lose even on evaporation. Wöhler's discovery, that allantoine is the principal organic constituent of this urine, has been already noticed in p. 162 of the first volume. According to Wöhler, it appears, further, to contain urea and likewise *uric acid*, in the same proportions as they occur in normal human urine; hippuric acid, on the other hand, cannot be discovered in it. It contains a very considerable amount of phosphate of magnesia and of the potash salts, but only very small quantities of the phosphates, sulphates, and soda salts. Braconnot also found in calves' urine an organic matter

<sup>1</sup> Nachr. d. k. Gesellsch. d. Wiss. zu Göttingen. 1849. No. 5, S. 61-64.



which was soluble in alcohol, precipitable by tannic acid, dissolved on boiling, but again separated on cooling. Lastly, this secretion does not contain even 1% of solid constituents; according to Braconnot, they amount to 0.62%.

The *allantoic fluid* of the foetal calf has, as yet, only been carefully analyzed by Lassigne;<sup>1</sup> from his observations, it seems to possess precisely the same properties and the same composition as the urine of the calf, while still living on milk.

We have already mentioned that the urine of *rabbits*, as well probably, as that of other herbivorous animals, becomes acid, and assumes almost all the properties of the urine of the carnivora, when these creatures have been kept fasting for a long time, or have been compelled to digest animal food.

*Hyraceum* appears, from Reichel's analysis, to be at all events very much mixed with the urine of the animal (*Hyrax capensis*): but from a microscopical and chemical examination, to which I exposed a specimen of this substance, whose therapeutic value was to be tested, I convinced myself that it consists solely of the solid excrement of this creature; I found in it the remains of plants and vegetable fibres, together with isolated prosenchyma cells and spiral vessels, which rendered it more than probable that the vegetable matters had passed through the intestine, and were not either accidentally or intentionally superadded after its discharge; it was only on the outer surface that fragments of the skeletons of insects could be detected, stamped, as it were, upon it: in addition to a very large amount of resinous matters and carbolic acid, this mass undoubtedly contained biliary matter; but no urea, or uric, or hippuric acid could be discovered.

The urine of *birds*, which for the most part forms a whitish investment to the solid excrements of these animals, consists essentially of urates, and especially of the bi-urates of ammonia and lime; Coindet maintains that he has found urea in birds' urine.

The urine of *serpents*, which is often discharged independently of the solid excrement, is at first pulpy, but soon becomes solid and dry; it consists for the most part of alkaline bi-urates, a little urea, and earthy phosphates.

The urine of *frogs* is fluid; it contains urea; chloride of sodium, and a little phosphate of lime.

The urine of *tortoises* has been examined by Magnus, Marchand, and myself. (See vol. i. pp. 179 and 193.) I found the urine of *Testudo græca* to possess the following properties and composition: when the animals had taken no food for a long period, they discharged (when lying on their backs) a very pale yellowish-green clear urine, with a distinctly acid reaction; on cooling, it deposited a white sediment, which redissolved on the application of heat; when they had not fasted for a long time previously, they discharged a neutral or faintly alkaline, tolerably clear urine, which exhibited no turbidity on cooling. The spontaneous sediment dissolves only partly in boiling water, the bi-urates of ammonia and lime remaining undissolved, while the bi-urate of soda dissolved. The presence of hippuric acid could always be detected with

<sup>1</sup> Ann. de Chim. et de Phys. 1 Sér. T. 17, p 301.



great facility in the urine of these animals by either of the methods described in vol. i. p. 178.

Besides urea and the above-named substances, I also found a crystallizable organic matter, that was insoluble in absolute alcohol, but dissolved in alcohol of 82%; but in consequence of the small quantity in which it occurred, I could not minutely investigate it. Fat was always present in appreciable quantity. The acid sedimentary urine contained from 3.014 to 3.584% of solid constituents; the average amount of the ash of the solid residue was 52.5%; when burnt white, it contained no carbonates, but only phosphates and sulphates with chlorides; it further contained more potash than soda compounds.

The excrements of *insects* consist, for the most part, of the remains of the tissues which have served them for food, but they also contain materials which are nowhere else found than in true urine, even when no definite organ for the elaboration of this secretion can be detected in them.

It has long been known that the red *excrements of butterflies* contain a very large amount of alkaline urates, and the fact has been recently confirmed by Heller. I have found that the intestinal contents of butterflies that have been sucking honey often contain free uric acid in very beautiful crystals. The red pigment of the excrement is an oily body, which, when placed in water, separates in minute drops; in addition to these substances, a little phosphate and oxalate of lime are also present in these excrements.

In the *excrements of caterpillars*, vegetable fibre is naturally the preponderating constituent, but they also contain large quantities of chlorophyll and starch; the latter is found not only in the globular form, but also in the peculiar baton-like shape in which it occurs in the Euphorbiaceæ. These excrements are especially rich in oxalate of lime, which is not produced directly from the ingesta; for I have found them in the biliary tubes of caterpillars. Although the intestinal juices and the contents of the stomach of caterpillars have always a very strong alkaline reaction, the excrements are for the most part neutral, and indeed sometimes have an acid reaction. In the latter case, we often find that they contain very beautiful crystals of uric acid; the uric acid, however, generally only appears in very small quantity in the excrements of caterpillars. Different parts of plants, as, for instance, the spiral vessels, may be very distinctly observed in these excrements, which are so poor in nitrogen that, as an average of three analyses, I found only 0.362% of this element in the matters discharged by the silkworm, while the leaves of *Morus nigra* contained 4.560%.

We have already spoken, in vol. i. p. 160, of the occurrence of guanine in the excrements of spiders. Seeing that this substance is present here as well as in guano, it is not improbable that guanine may also occur in the excrements of birds and in those of most insects, especially since the researches of Will and Gorup-Besanez<sup>1</sup> have rendered it probable that this substance is also present in the green organ of the crawfish.

*Guano*, that much-prized article of commerce, which is the product of

<sup>1</sup> Gel. Anzeigen. d. k. bair. Ak. d. Wiss. 1848. S. 825-828.



the slow decomposition of the excrements of certain sea-fowl, has been very frequently analyzed, and has been found to be very variously composed according to the place from whence it was obtained; its principal constituents are guanine, urate of ammonia, oxalate of ammonia, phosphate of lime, phosphate of magnesia and ammonia, and oxalate of lime; we likewise find the remains of vegetable substances; and there is one variety which contains the most beautiful siliceous shields of infusoria pertaining to the Bacillariæ.

We now proceed to the changes which the urine undergoes in disease; and we will first notice the characters which are impressed upon the secretion in *fever*, that is to say, in that group of symptoms which accompany almost all acute diseases. Febrile urine is generally more deeply colored than usual (being of a red or reddish tint) has a stronger odor, a higher specific gravity, and a more decided acid reaction. As long as the fever continues, less than the normal quantity of urine is generally secreted by the kidneys, and the urine appears concentrated, because the diminution of the water of febrile urine is relatively more considerable than the diminution of the solid constituents.

The constant characters of such urine are the relative and absolute diminution of the inorganic salts, and the obvious augmentation of the uric acid or urates. The diminution of the salts was always observed by Becquerel and Simon; it was the latter chemist who first discovered that the loss principally fell on the chloride of sodium. Even when febrile urine does not deposit the ordinary sediment of urate of soda, it is always absolutely and relatively richer in uric acid than other urine. The urea is generally somewhat diminished, as Becquerel first demonstrated; Simon holding the opposite view. The extractive matters are usually somewhat increased. Lactic acid may very often be detected with chemical certainty in urine of this nature.

In contrast to febrile urine Becquerel has distinguished an *anæmic* urine. Such urine, which depends upon a deficiency of blood, and occurs in various forms of debility, contains far less urea and uric acid than normal urine; the diminution of the salts, as compared with the quantity usually secreted, is inconsiderable; the salts are consequently increased in relation to the organic matters; moreover, the extractive matters only differ slightly from the physiological average. This variety of urine is especially observed after repeated venesections, and in chlorosis.

If we endeavor to name and distinguish the constitution of the urine in individual diseases, in accordance with the present condition of pathology, and to collect and arrange the results of the numerous investigations which have been made on this subject during the last twenty years, we are led to the unexpected and discouraging conclusion, that all our knowledge regarding it is alike incomplete and obscure. The innumerable analyses of morbid urine have induced many physicians to believe that the study of the character of the urine in diseases was the most complete section of pathological chemistry,—an error which has been promulgated, whether consciously or unconsciously, even by chemists. Where are we to seek the reason of a fact at once so mortifying and discouraging to the pathological chemist? In reply, it may be answered, that



there are several grounds on which we might explain the want of success which has so frequently attended the most earnest endeavors of numerous able inquirers. It has already been frequently noticed, both here and elsewhere, that the methods employed in these investigations were not of such a nature as to justify the establishment of those conclusions and general propositions which were deduced from the results of the analysis; in the methodological introduction to the first volume, we drew attention to the errors, and the different causes which have given rise to these false deductions. A truly scientific examination of the urine is, however, associated with numerous obstacles and difficulties, and failure may thus frequently attend our efforts, even when all the methods have been employed which present themselves for the prosecution of such an important investigation. The object of such inquiries is obviously that of ascertaining the general properties of the urine and its especial composition in any one definite form of disease; for the urine, even in health, and still more in disease, is of so variable a nature, that in many cases it is impossible to determine whether the alterations noticed in its condition actually arise from a morbid process, or only from incidental influences. If we carefully observe the changes which often occur in the urine in the course of the same day, not merely in typhus or any abnormally developed acute exanthema, but also in inflammations which are running their ordinary course, we shall clearly see that the urine is regulated much more closely in accordance with the transient condition of the organism, external influences, and simultaneously manifested groups of symptoms, than by the nature of the morbid process. Thus the albumen in the urine in Bright's disease is considerably diminished, and may even almost disappear, if the chronic form of this disease is associated with an affection giving rise to inflammatory fever. The urine which is so characteristic of this form of disease, loses almost all its distinctive properties, and assumes, both in a qualitative and quantitative point of view, the character of inflammatory febrile urine. It appears to us, therefore, to be more rational to limit our examination of the composition of the urine to certain morbid conditions and individual groups of symptoms, and to compare together the various analytical results thus obtained, instead of attempting to extend similar observations to different forms of disease. This method of proceeding is exemplified in the numerous analyses of the urine conducted with such extraordinary perseverance by Becquerel; for the results of these admirable observations prove less that certain groups of diseases are associated with definite alterations in the proportions of the solid constituents, than that most diseases are attended by very considerable fluctuations in the composition of the urine, depending more upon incidental individual phenomena than upon any special morbid process. Although the blood may not unfrequently undergo more marked changes from secondary causes than from any essential, morbid process, it retains a stronger impression of these modifications than the urine. This difference may probably depend upon the blood preserving the capacity, even in a morbid condition, of throwing off effete matters, if not by the kidneys, by some other medium, whilst the urine retains everything that may have been incidentally generated in the blood and conveyed to the kidneys.

But although these and many other relations may have opposed the



efforts of inquirers to discover any constantly recurring properties and admixtures of the urine in individual acute diseases, it might have been hoped that more promising results would have rewarded their labors in the case of chronic disorders, where the change of symptoms is not so rapid as in acute forms of disease. But here, too, our expectations are not realized, chiefly because the deviations from the ordinary composition of the urine are in general more inconsiderable in these conditions than the modifications which depend upon purely physiological relations, such as the nature of the food and other dietetic relations generally. In reply to the question, whether we have actually discovered any distinctive characters in the urine of tuberculous, cancerous, or arthritic patients, it must be admitted that although numerous conjectures have been suggested which bear the semblance of affording empirical results, we have acquired no facts based upon scientific and exact observations. Thus, for instance, according to Donné, the urine in tuberculosis exhibits a viscid mass of honey-like consistence after evaporation, when seen under the microscope; but has not a similar appearance been observed in other urine? According to some observers, arthritic urine is characterized by an abundance of uric acid; according to others, by a deficiency, or even an absence, of this constituent. Although this striking discrepancy may be referred to the vagueness of the term Arthritis, and to an error of medical diagnosis, hundreds of instances might be enumerated in which results scarcely less discrepant have been established by one and the same observer.

We have here enumerated substances which only occur abnormally in the urine. Are not these characteristic of individual pathological processes? Albumen, fibrin, oxalate of lime, &c., are not characteristic of specific groups of diseases, but merely of individual processes or groups of symptoms accompanying disease; we have already endeavored to show the numerous conditions which may influence the transition of albumen into the urine, and that these relations may occur in the most various forms of disease. The once prevalent idea that albuminuria was a specific disease, instead of being only a symptom of different diseases, is not entirely exploded.

But there likewise exist abnormal substances in the urine, which differ so widely from the substances commonly contained in that fluid, or in the animal organism generally—as, for instance, red, green, and blue pigments, crystalline and xanthine—that they would appear to indicate the existence of some definite pathological process or some specific form of disease. Such may indeed be the case, but all who have observed the occurrence of these matters must be aware that none of these rarely observed substances have been found to appertain to any special form of disease.

Amidst the confusion which prevailed in pathological chemistry as to the composition of the urine in special diseases, the ingenious idea suggested itself to certain inquirers of inventing entirely new diseases in accordance with the constitution of the urine, and the nature and quantity of the various substances which it contains, instead of determining the composition of the urine with reference to the disease. These diseases were named the uric and oxalic acid diatheses, the urea diathesis,



&c. Observers thus fell into the same errors of which the older physicians had been accused ; namely, that of classifying diseases in accordance with individual symptoms, instead of grouping them in natural families based upon distinct processes rather than symptoms. As we have already frequently expressed our dissent from the assumption of any such diatheses, it would be superfluous again to revert to the subject. But, in opposition to this, it might be asked, is not diabetes mellitus a diathesis ? and is it not generally assumed to be a special disease ? According to our view, this phenomenon is only a symptom, standing in a causal connection with a definite series of symptoms, in the same manner as many other symptoms are also associated with their respective phenomena. Thus, if in consequence of any anomaly in the metamorphosis of animal matter, from a mechanical or physiological obstruction, the conversion of the sugar in the blood should be impeded, it will be very rapidly separated by the kidneys, as Bernard, Kersting, and myself have proved by direct experiments ; this separation cannot, however, be effected, as we have already seen in experiments on animals, without the abstraction of a large quantity of water ; the blood becomes poor in water, and hence arises the thirst, the suppressed cutaneous transpiration, and the parchment-like skin of diabetic patients. We almost invariably find, on examining the bodies of patients who have died from diabetes, that certain pathologico-anatomical changes are present ; but how widely do these differ in character ? As is well known, tubercles are frequently present in the lungs in diabetes, and also, in some cases, affections of the abdominal organs, the spinal cord, &c. Sugar in the urine is therefore as much an incidental, inconstant accompaniment of tuberculosis as albumen in the urine is of dropsy ; the former, like the latter, seems always associated with definite conditions, such as we have endeavored to explain in the case of the albumen present in the urine in dropsy, but which we are unable to explain in the case of the sugar contained in the urine in tuberculosis. Dropsy, however, is as much a mere group of symptoms as tuberculosis ; and we must leave it to a future era in medicine to classify diseases in families and species according to definitely expressed chemico- and physico-physiological processes, instead of grouping them according to individual pathologico-anatomical or chemical characteristics.

After our remarks upon the constitution of the urine in the recognized groups of disease, we think it would be superfluous to enter upon the further consideration of the properties and composition of the urine, or the changes which this fluid experiences in every individual disease ; for we have already, as far as the present state of science permitted, classified the alterations occurring in the morbid urine, in accordance with chemical modes of arrangement. We must leave this subject for the present, trusting that the attempts which will be made in this volume to discover the physiological processes in the healthy and diseased animal organism from the positive results of physical and chemical investigations of the animal tissues and juices, may contribute towards the establishment of definite characteristics of the urine as a means of classifying families and groups of diseases.

Owing to the want of systematic investigation of normal and abnor-



mal urine, and the inconsiderable progress made in organico-chemical analyses, a very high value was formerly attached to the analyses of urinary concretions, and of calculi generally. When considered from a scientific and pathological point of view, we are as unable to admit the idea of a Lithiasis as of the above-mentioned diatheses; it lies entirely beyond the scope of our inquiries. Moreover, the little that admits of being said regarding the formation of these concretions may be readily inferred from the observations we have already made in reference to urinary fermentation. (See p. 123.) The analysis of these concretions falls either entirely within the department of inorganic chemistry, or will be found in the descriptions of the methods of zoo-chemical investigation, considered in different parts of this work. Those who are familiar with zoo-chemistry need hardly be referred to the copious monographs on urinary calculi with which our literature abounds. But if the practical physician should in this case, as probably in many others, be disappointed in not finding in these volumes all that he had been led to anticipate from the importance attached to the facts derived from pathologico-chemical inquiry, he must remember that the newly-sown seed cannot at once blossom and bear fruit, and that years must pass before the anticipated harvest can be reaped. Truly scientific, physiological, and pathological results can only be deduced from the study of physiological processes, of which we propose to treat in this volume.

We ought, indeed, in accordance with the entire plan of this work, to enter fully both into the consideration of the origin of the urinary constituents and the physiological importance of the urinary secretion; but we abstain from doing so, because the subject here referred to will either be treated of in our remarks on Histo-chemistry (the chemical theory of the tissues), or fall so entirely within the department of the chemical and mechanical metamorphosis of matter, that we must defer their consideration until we enter upon the study of that subject.

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## HISTO-CHEMISTRY.

The theory of the chemical nature of the animal tissues is a department of physiological chemistry which as yet has been very little cultivated; and the reasons of this unsatisfactory state of our knowledge are too obvious to require any detailed exposition. We will, therefore, simply observe, that the most important obstacle to the chemical investigation of the tissues is, that their elements are too intimately combined or associated with one another to admit of their being prepared for chemical analysis by a previous mechanical separation. This separation of the various elementary tissues which are deposited among, penetrate between, and envelope one another, is rendered the more difficult by the circumstance that with scarcely an exception they are equally insoluble in the ordinary indifferent menstrua employed by chemists. If we have recourse to the stronger or more energetic solvents, as for instance, acids



or alkalies, we have seldom any assurance that the dissolved substance is the (otherwise) unchanged histological element, and that the portion remaining undissolved is in reality a simple chemically pure material; indeed, in the majority of cases, there cannot be a doubt that the chemical constitution of the tissue on which we are experimenting is entirely changed by such reagents.

Various means have been attempted with the view of submitting the animal tissues to chemical investigation. The first analyses, having any claim to accuracy, had for their object the determination of the elementary composition; in the Giessen laboratory, Scherer, and subsequently others of Liebig's pupils, instituted elementary analyses of several of the tissues, after purifying them by means of the ordinary indifferent menstrua from any soluble admixtures that might be present. If in the present advanced state of our knowledge we are compelled to regard such analyses as irrational, since many of the analyzed tissues, which were then considered by histologists to be simple, may be now seen by the most superficial microscopic examination to be composed of various morphological elements, yet such investigations must be considered as fully equal to the requirements of science at that date. Chemists were then attaching a high value to the existence of protein, and were striving to ascertain the metamorphoses which it underwent in its conversion into the tissues, and the relations that existed between the chemical constitution of the individual tissues, and the composition of the main constituents of the blood. Moreover, a special value should be attached to these analyses from the circumstance that they form the earliest foundation for the construction of the statistical method, which in the hands of Liebig and others has proved so important an adjunct to chemical physiology (see vol. i. p. 27). We should, however, be falling into great error if we were to regard the results of these analyses as strictly accurate expressions of the composition of the tissues in question. The subcutaneous cellular tissue, tendon, horn, &c., are not elementary tissues; for they are composed of various morphological elements, combined together in varying quantities.

This fact induced Mulder to decompose, by means of acid or alkaline solvents, even those tissues which were regarded by histologists as simple; and to attempt to deduce conclusions regarding the morphological arrangement of the various elements or the chemical composition of the original object from the nature of the products of decomposition, by tracing these backwards to their origin. In this manner hair, horn, the nails, tortoise-shell, elastic tissue, &c., were examined either by himself or under his superintendence. Although these investigations led to many interesting results, they did not yield to histologists the information that was expected; for independently of the circumstance that the substances which were examined were not sufficiently defined in their character, and were unfit for an accurate chemical investigation, or even for an exact elementary analysis, the method itself was as imperfect as that to which we previously referred; too little importance was attached to morphologically different constituents of tissues, and hence this method yielded strikingly similar or identical results for very differently constructed (or mechanically composed) objects,—a circumstance which must invalidate



the claim of the chemical analysis to accuracy, and which was itself in part based on the attempt to establish a more intimate ideal connection between the results of the elementary analyses and the hypothetical formula of the yet more hypothetical protein.

Mulder himself was by no means unconscious of the imperfections of this method, and endeavored in union with Donders to approach this somewhat inaccessible department of science in a totally opposite direction. The tissues to be examined were exposed to the action of various chemical reagents, and the changes which their texture underwent were observed under the microscope, with the view of deducing from them conclusions regarding the differences in chemical constitution. This course was, however, first adopted by J. Müller, who was led by it to several results of much value in relation to physiology and general anatomy. Several observers followed with more or less success the path which he had thus marked out; but their investigations (unfortunately for us) had reference more to the histological than to the chemical side of the inquiry. Histology has already derived the most important aid from this method, since the reagents which we apply to microscopical preparations are no longer limited to dilute acetic acid, tincture of iodine, or, at most, perhaps a little ammonia. It was by means of microscopico-chemical analysis that the structure of the different horny tissues was first clearly exhibited; who could formerly have established with such precision that nails, cows' horn, and whalebone are composed of aggregations of individual cells, from the most careful tracing of their developmental history? Would the axis-cylinder of the nerve-fibres have remained so long unperceived, or at all events a subject of doubt, if at an earlier period we had been more familiar with micro-chemical investigations? Chemical appliances have often afforded most important service to histology, even when not promoting our knowledge of the chemical constituents of the tissues. We shall, therefore, be warranted in assuming that the progress of histo-chemical inquiry will be satisfactory, when micro-chemical investigation is directed and regulated by the results of micro-chemical analyses; the micro-chemical relations of a tissue serve to indicate the course that must be pursued in order to lead to a successful investigation of the chemical constituents of the tissue, and of its composition.

These are, as we conceive, the points of view from which, in the existing state of science, histo-chemistry ought to be investigated; and in accordance with these ideas, we have attempted to give a sketch of the mode in which it should be treated.

We need hardly remark, in connection with these histological objects, that the chemist has to deal solely with the elementary tissues; for the coarser or finer admixture of cells, fibres, &c., which we find congregated even in the tissues still deemed simple by many histologists, cannot in themselves constitute the object of a chemical investigation; we should, for instance, regard it as altogether inexpedient to devote special sections of this volume to the consideration of the smooth muscular fibres of the intestine, the contractile tissue of the *tunica dartos*, the middle arterial coat, &c. We know that these tissues are composed of very various histological elements, and that there occur in them, interwoven



in many forms and proportions, fibres of connective tissue and nucleated fibres, or ordinary elastic tissue, with the fibre-cells which are common to all contractile organs. The admirable inquiries of Kölliker have indeed shown us that these fibre-cells constitute the most essential element in all the contractile tissues, and his results have been almost as decisively confirmed by chemical investigation as by the certain physiologico-physical test of magnetic electricity. Hence we should not regard the middle arterial coat, or even the walls of the bloodvessels themselves, as subjects for histo-chemical research, but we should rather attempt to ascertain, under the head of "fibre-cells," the chemical character of the substance that is common, and at the same time peculiar, to all contractile tissues. At the present day it would be highly inexpedient to devote special sections to the chemical constituents of the eye, the chemical constitution of the brain, &c. We are, however, as yet unable to limit histo-chemistry very strictly to the consideration of the pure elementary tissues, for we must still speak of nervous tissue, of the striped muscular tissue, &c., although very different morphological and chemical elements are associated in them; for unfortunately, we have not yet made sufficient progress to enable us properly to distinguish from one another the elementary parts of these compound tissues, and we are consequently obliged to limit histo-chemistry to the mere determination of the chemical characteristics of the morphological elements of the tissues.

Although every one who directs his attention to histo-chemistry must be familiar with the normal histological characters of the tissues, and although every one who would propose engaging in histological investigations must be thoroughly familiar with the present state of general anatomy, we have notwithstanding deemed it expedient to introduce a sketch, short though it may be, of the conformation of the individual tissues. In accordance with this view, we have endeavored to indicate, in the shortest possible terms, the morphological relations of each elementary tissue, its admixture with other textural elements, and its occurrence in the various organs of the animal body.

While it cannot be denied that chemical investigations of the tissues, if they are to lead to any valuable result, must be intimately associated with histological examinations, so on the other hand the first step towards a chemical recognition of the textural elements can only be taken through the aid of micro-chemical reactions. We will, therefore, begin the consideration of "histo-chemistry proper," with a description of the changes which we observe with the microscope in the texture of each tissue after the application of various reagents, limiting ourselves, for the most part, to the results obtained by personal observation. There is no department of physical science in which personal observation is more necessary for the purpose of forming a correct judgment than in micro-chemistry. Our judgment regarding surrounding objects or phenomena, of which we obtain cognizance only through the sense of sight, is exposed to numerous sources of error: we know that in making observations with the microscope we are deprived of many aids which, under other circumstances, would assist us in forming our opinion regarding the objects we perceive, and we especially miss this assistance in forming our judgment regarding the changes which microscopical



objects undergo under the influence of chemical reagents; thus, for example, many histological elements swell and become as imperceptible to the eye as if they were actually dissolved, whilst in reality they are simply reduced by the reagent to a gelatinous condition in which their refractive power corresponds with that of the surrounding fluid; and it not unfrequently happens that the membrane or fibre that had become invisible may be again brought into view by repeated washing with water, or by careful saturation of the acid or base that had been employed, thus affording evidence that it had not been dissolved in the reagent. After the application of other reagents, parts often become visible which previously could not be perceived; it is then often impossible to distinguish whether these objects actually existed previously and were only very transparent, or whether they were produced by the application of the reagent. In such cases it is often impossible to arrive at any certain conclusion; we know, for instance, that histologists are not yet fully agreed as to the nuclei which appear so abundantly in the corpuscles of frogs' blood that has stood for some time, some maintaining that they exist preformed in the fresh circulating blood, and others holding the opposite view.

Again, many reagents induce coagulation of the intestinal juice in mixed tissues, and in this way not only obscure the form, but occasion such contractions and alterations of outline of one or other of the parts, that it often becomes extremely difficult to distinguish to which of the tissues that are thus intermingled the filaments or granules, that are observed, belong. These, and similar relations, make it extremely difficult to form a judgment regarding the effect of the action of chemical reagents on the tissues, and, indeed, often render it impossible to arrive at any definite result. We might adduce many examples of apparently very simple questions regarding which the best histologists are even now at variance (as, for instance, whether nucleoli are or are not contained in the nuclei of certain cells, and whether these nucleoli, when they are unquestionably present, consist of fat or of some other matter). To show that we have not overrated the difficulties of micro-chemical investigation, are there not many who even now deny the pre-existence of an axis-cylinder in the nerve-tubes? and do we not find such distinguished observers as Mulder and Donders holding the apparently very erroneous view that the axis-cylinder visible within nerve-tubes that have undergone change consists essentially of fat?

It is hardly necessary to remark that perfect familiarity with the microscope, and an accurate acquaintance with all the auxiliaries employed in its use, and with all its sources of fallacy, are indispensably requisite for the successful pursuit of micro-chemical investigations. The various means of checking error which have been recommended by such experienced observers as Jul. Vogel,<sup>1</sup> Schleiden,<sup>2</sup> Hugo Mohl,<sup>3</sup> Purkinje,<sup>4</sup> and others, in ordinary microscopical inquiries, are required in a still higher degree in micro-chemical researches.

<sup>1</sup> Anleitung z. Gebrauch des Mikroskops u. s. w. Leipz. 1841.

<sup>2</sup> Botanik, Methodol. Einleitung. Leipz. 1849.

<sup>3</sup> Mikrographie u. s. w. Tübingen, 1846.

<sup>4</sup> Wagner's Handwörterb. d. Physiol. Bd. 2, S. 411-448.



It must also be borne in mind that the application of chemical reagents demands the observance of many precautions, the necessity of which has been only recently perceived. Formerly it was the ordinary practice to allow the chemical reagent to flow on the microscopic preparation, and to observe its direct action on the morphological elements of the object under examination. Donders<sup>1</sup> has, however, correctly shown that it is very often necessary to submit the tissue we may be examining to the prolonged action of the chemical reagent—an action not merely of hours but of days. We regard both modes of proceeding as absolutely necessary for an accurate examination. In association with Messerschmidt,<sup>2</sup> I long ago directed attention to the fact, that even in objects which are easily penetrated—as, for instance, pus—the solution of the chemical reagent only very gradually makes its way into the mass of the object, and acts very unequally on the parts that are differently situated; and consequently that the microscopical appearance may often give occasion to very different interpretations. Hence Donders especially recommends that the tissues should not be submitted to microscopical investigation until they have been exposed for a longer or shorter period to the action of the chemical agent in a somewhat disentangled or carefully prepared state. In this way the final result of the action may be much better observed than by any other means, and the altered parts are seen with perfect clearness. In the meanwhile, although the result may be sufficiently obvious, it may often be far from easy to decide in what manner the change has been brought about, and what parts especially undergo solution, contraction, or gelatinization. If we merely observe such preparations without tracing the action of the chemical reagent upon them under the microscope, we soon see how readily we may fall into error. Hence in every case it is expedient when examining a preparation, at the same time to observe the direct action of the same reagent on it. In the latter proceeding there are various means by which we may be assisted in accurately observing the direct action of the chemical reagent; thus, for instance, Henle recommends that a hair should be introduced between the slide on which the object is placed and its cover, in order to regulate the flow of the test-solution, and to retard its action on the preparation, which is often extremely rapid; linen or cotton threads may often be more conveniently used, provided they are not affected by the reagent. One's own experience is, however, a better guide than any written directions in successfully carrying out experiments of this kind.

Another point of much importance in micro-chemical researches, which has been often neglected even in recent times, and which has been strongly insisted upon by Donders and myself, is attention to the strength of the solutions employed in micro-chemistry. A disregard of this rule frequently led in earlier times to the most discrepant statements regarding the action of various reagents on blood and pus-corpuscles, and at the present day we may possibly ascribe to the same cause the very different assertions that have been made regarding the action of various chemical matters on certain tissues. We shall presently see, for instance, what different effects are produced on muscular

<sup>1</sup> Holländische Beiträge. 1846, S. 39.

<sup>2</sup> Arch. f. physiol. Bd. 1, S. 225.



tissue by extremely dilute, moderately dilute, and concentrated hydrochloric acid, and what different consequences result from the application of alkaline solutions of various strengths to similar objects. Whilst the chemist throws together organized parts, crushes the organic mass in a mortar, and then most laboriously attempts to fish out the individual constituents, always, however, carefully paying attention to his chemical reagents, and the manner in which they should be applied, the micro-chemical inquirer has often followed a totally opposite course; he may have observed the alterations in form which the object has undergone, while he has not sufficiently attended to the nature of the chemical reagents he has employed; indeed, they sometimes seem to be selected at hap-hazard, and are of such a nature that they cannot lead to chemically serviceable results, their application being so irrational in a chemical point of view that, let their action be what it may, no conclusive results can be expected from them. These remarks lead us to another point in micro-chemical analysis, to which we should pay the most serious attention, and by the neglect of which we lose many most important results.

It is obvious that micro-chemical reagents should be applied for other purposes than merely for the object of studying the changes of form which the elementary tissues undergo, and of investigating their minute structure, or of determining whether this or that histological element be the more nearly allied to that hypothetical substance, protein, or whether it rather falls into the very vague category of "gelatigenous tissue," or whether it be altogether different from either. Micro-chemical investigation must be pursued with the same aims as every other chemical manipulation, that is to say, it must be directed to the elucidation of the chemical constitution of the object under consideration, and must indicate the direction to be followed in our advance towards the goal of our inquiries. But this point will not be attained as long as we content ourselves with employing this or that reagent at random, and are satisfied with observing the alteration of form which it induces, and with ascertaining in what group of chemical substances this or that part of a tissue should be classed. Micro-chemistry must rather furnish us with the means of extracting from the tissue to be examined one chemical constituent after another, and of thus rendering them more accessible to further chemical investigation. We believe that the following pages present some striking illustrations of the advantages of this application of micro-chemistry, which has first indicated the method of investigating the chemical nature of the textures by the separation of the less essential parts interwoven with them; it will thus throw some light on the constitution of parts like the brain, which have hitherto defied all the efforts of pure analysis.

If we glance at the somewhat numerous micro-chemical reactions which have been observed in the different tissues, we shall find that they have rather excited our hopes than fulfilled our expectations. The large number of reagents often scarcely differing in their actions, and their unsystematic accumulation, show clearly enough that this branch of science has as yet been little cultivated, and is but ill adapted to lead us to any explanatory facts. But the cause of the unsatisfactory nature of the



efforts hitherto made to advance histo-chemistry by means of micro-chemical experiments, is to be referred less to the inefficiency of our micro-chemical agents, than to the imperfect development of general zoo-chemistry or the theory of the animal substrata. We cannot, however, hope to make great or brilliant progress in the chemical knowledge of the tissues until chemists shall have succeeded in throwing light upon the protein bodies, until better analytical methods are discovered for the distinction and separation of these widely differing, although in some respects analogous substances, or until some more reliable methods can be adopted for the establishment of less hypothetical formulæ than those hitherto employed—as, for instance, in the case of albuminous substances. The protein hypothesis has frequently served as the *πρῶτον ψεῦδος* for giving scope to hazardous conjectures on the nature and formation of the tissues, as well as on the entire metamorphosis of matter in the animal body. We have, therefore, abstained as far as possible from giving the artificial formulæ and equations by which it has been attempted to exhibit an ideal connection between the composition of the different tissues and their origin and metamorphosis, since it appears to us that science in its present undeveloped state more especially demands caution in the indulgence of fanciful hypotheses. A cautious reserve in this respect is more especially called for from those pathologists who imagine that a pathological histo-chemistry may be hurriedly built up on a few insecure props, and who have obscured the few exact chemical facts which we possess regarding morbid tissues with their own nebulous hypotheses.

If, however, we could extend to histo-chemistry our inherent tendency to general abstractions, we may consider the general proposition (laid down in vol. i. p. 36), that the physiological importance of a substance is dependent on its chemical constitution, as being equally well established, in so far as our experience goes, in regard to the tissues; for we merely express the simple result of positive experience, and the inductions deduced therefrom, when we assert that *the chemical nature of the tissues invariably corresponds with their functions*. It has been long known that those tissues which are of service in the animal body almost solely from their physical properties (their hardness, toughness, elasticity, &c.), contain as their most essential basis a substance which on boiling yields gelatin; we further know that those textural elements which are remarkable for a high degree of elasticity, as the nucleated fibres of connective tissue and the true elastic tissue, present a perfectly similar chemical relation; and as we gradually develop the subject of histo-chemistry, we shall have convincing evidence that those tissues which exhibit special vital activity—those, namely, which, in addition to a slight but very perfect elasticity (Ed. Weber), possess the power of contracting in consequence of certain influences transmitted through the nerves—contain as a matrix and essential constituent, one and the same substance, muscle-fibrin or syntonin; here we must place the fibre-cells of those tissues which are specially known as “contractile,” and of smooth muscle, and the cylindrical fibres of striped muscle. The arrangement and the chemical character of the substrata constituting the nervous system, confirm rather than oppose the above proposition, and afford a new proof that the material substrata of the tissues are always constructed in chemical conformity with their vital functions.



There is one more circumstance which must not be left altogether unnoticed, and which probably stands in a nearer connection with the above subject than might at first sight be supposed; we refer to the fluids permeating and bathing the tissues. We have already seen that there are great differences in the chemical character and composition of the fluids moistening the different classes of tissues, the peculiarities of the fluid being apparently closely connected with the chemical constitution of each individual tissue. We find, for instance, that the lower elementary tissues, such as exert a mere physico-mechanical action, are moistened by a fluid which scarcely differs from the serum of the blood, and in general closely resembles the transudations described in this volume. On the other hand, the tissues which are capable of a vital contraction, and, consequently, the fibre-cells and muscular-fibres are surrounded by a fluid which is altogether different from an ordinary transudation; in the first place this fluid is distinguished, in all contractile tissues without exception, by the presence of a certain amount of free acid; further, the phosphates and potash-salts predominate here over the chlorides and soda-salts (which preponderate in the transudations); and, lastly, there occur in this fluid a number of substances which, hitherto at least, have not been recognized in the blood and transudations. It may probably depend upon the different modes of action of the fibre-cells (in the contractile tissues and in smooth muscles) and of the muscular fibres (in the striped muscles), that the acid interstitial juice in the former case always contains casein with albumen, whilst, in the latter case, it contains no casein, but several other substances peculiar to itself alone. Unfortunately these relations afford us as yet mere points of view from which we may get glimpses of the connection between the chemical composition and the function of the tissues, or at most a few new advanced points from which we may hope by further investigations to promote the physiology of the animal tissues.

The preceding remarks will sufficiently elucidate the course which we intend to pursue in treating of the chemical relations of the animal elementary tissues. We first notice the *micro-chemical reactions*. In the present very imperfect state of micro-chemistry a logical arrangement and subdivision of these reagents is out of the question, and hence their number is far greater than it would otherwise be. Although many of these reagents act in a very analogous manner, and others again do not yield very definite results, we shall, nevertheless mention them in detail, as we are of opinion that in a rapidly advancing and comparatively new department of science every fact, however unimportant, should be retained, since we do not know what significance it may subsequently attain. Moreover, no accumulation of facts can do harm.

Basing our remarks for the most part on the micro-chemical reactions, we shall next proceed to the investigation of the chemical properties and composition of the individual substances which may be extracted or isolated from the tissues, without any essential change in their composition. We shall then notice the parenchymatous juices which permeate the tissues, provided they exhibit any peculiar chemical relations. Without entering deeply into the purely physiological relations of the individual tissues, we shall then consider the question whether anything defi-



nite, regarding the physiological function of the tissue, can be deduced from its chemical constitution, in so far as it is yet known.

Finally, we shall endeavor, at the conclusion of each subject, to form, as it were, a basis for an introduction to a more general chemical analysis from the results obtained by the micro-chemical investigations. If our previous remarks on the chemistry of the tissues have failed to demonstrate the great deficiency of our knowledge in this department, the analytical results will afford conclusive evidence that we are still very far from being able to clothe histo-chemistry in a rational garb, or to represent in a scientific form the morbid changes of the tissues.

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## OSSEOUS TISSUE.

Were we to consider the constitution of osseous tissue only from a chemical point of view, without reference to its histological conformation we should scarcely arrive at anything like a correct idea of bone. We must, in the first place, bear in mind that this substance which was formerly included amongst the simple tissues, has not only a somewhat varying, but also a complicated texture, in which, as in the tissues of a higher order, vessels and nerves enter, and in which, as in other tissues, nutrient matter (or plasma) and effete materials are met with. Without entering minutely into the structure of osseous tissue, we must at all events remark that this substance—whether pertaining to the flat or the long bones—is penetrated by numerous cavities and canals, which in the fresh bone are not empty, and, in the dry, contain at least the non-volatile constituents of the former contents. These cavities in the bones are not merely those which are perceptible to the naked eye, as for instance, the great medullary canal in the centre of the cylindrical bones, and the cellular spaces of the spongy bones, and the nutritious foramina; in addition to these more obvious solutions of continuity, there are two different kinds of minute canals, one being much smaller than the other, and both perforating the true osseous substance. The larger of these sets of tubules, which have an average diameter of 0.01–0.05''' (Kölliker),<sup>1</sup> and are known as the Haversian canals, or *canaliculi medullares*, form a network in the more compact osseous tissue, and open (1) externally on the outer surface of the bone, and (2) internally, on the walls of the medullary cavities and spaces. The substance, however, which is surrounded by these spaces, is by no means to be regarded as the matrix of bone—as a perfectly continuous tissue, for we find in it a third group of tubules by which the bone is converted into a thoroughly porous substance. It is these tubules which were formerly regarded as the special morphological elements of osseous tissue, and were known as the bone-corpuscles and *ductuli chalcophori*: they are empty spaces, which, on examining dried sections of bone under the microscope by transmitted light, are such conspicuous objects from their black color,

<sup>1</sup> Mikrosk. Anat. Bd. 2, S. 278.



or rather their opacity. These elongated lenticular bone cavities, which have, according to Kölliker,<sup>1</sup> an average length, breadth, and thickness of 0.01"', 0.004"', and 0.003"' respectively, send out innumerable intercommunicating offshoots (the above mentioned *ductuli chalcophori*), and convert the matrix of the bones into a most porous material.

All these cavities, which we find in macerated and dried bones, are filled in fresh bones with various tissues and materials which do not pertain to the osseous matrix—the true object of chemical examination. It is well known that the large cylindrical cavities of the tubular bones are filled with marrow, of which we shall speak presently; this marrow is also found in the cancelli of the apophyses of the cylindrical bones, and in the cavities of the spongy substance of the flat and short bones, but is not contained in the dense cortical substance; hence it does not penetrate into the Haversian canals, which only exist there. While the marrow consists of a little connective tissue, and some vessels intermingled with the true medullary matter, the Haversian canals contain only bloodvessels and the nerves pertaining to them.

With regard to the bone-corpuscles and their prolongations, it was held, until very recently, that, as their name indicated, they consisted essentially of calcareous salts, or, at all events, were filled with them. This error, which was first exposed by Bruns and Bowman, and afterwards more fully by Kölliker, was one into which it was the more easy to fall, because, on the one hand, these air-containing spaces refract the light in its passage from the osseous matrix into these cavities in such a manner that these parts appear perfectly dark in consequence of the deviation of the rays, and thus resemble opaque objects, such as we often find (in another form) in morbid concretions, and because, on the other side, it is only with difficulty and by a very slow process that these empty spaces and passages can be filled with fluids. (The best fluids for this purpose are the oils and balsams.)

Virchow and Donders, and more recently Hoppe,<sup>2</sup> have shown the extreme probability that these bone-corpuscles and their prolongations are not simple excavations in the bone, but that they are lined by a membrane, by finding that after the prolonged ebullition of pieces of bone (the tegumentary bones of the sturgeon) the corpuscles, with their prolongations, remained perfectly intact after the solution of the matrix. Drummond<sup>3</sup> maintains, as Kölliker had previously done, that a nucleus is constantly present in the bone-corpuscles.

The easiest method of demonstrating that the bone-corpuscles and their prolongations are cavities, is to apply a little pure turpentine or Canada balsam to the edge of a long thin slip of bone (which, after perfect drying, serves the best to exhibit these parts) and to examine it under the microscope; we then perceive the dark bone-corpuscles and their prolongations very gradually become light, by slowly absorbing the turpentine, and thus losing their strong refractive power.

These minutest cavities or pores do not contain air in the fresh moist substance; they must be filled with a fluid whose refracting power is not very different from that of the matrix of bone, as is obvious from the in-

<sup>1</sup> Mikrosk. Anat. Bd. 2, p. 291.

<sup>2</sup> Arch. f. pathol. Anat. Bd. 5, S. 176.

<sup>3</sup> Monthly Journ. of Med. Science. Vol. 14, p. 285.



vestigation of fresh or thoroughly moistened osseous tissue; hence a deposition of calcareous salts within them is out of the question. No examination has as yet been made of the contents of these pores and cavities in fresh bones; it must, however, suggest itself to every one, that this system of most minute cavities which communicates on all sides with the Haversian canals (the vascular cavities of the bones) must take up the transudations from the vessels (the nutrient fluid) and reconvey the effete particles in a state of solution into the Haversian canals. If we could succeed in collecting the contents of these minute tubes in a state of purity (which is by no means impossible), we should thus have an opportunity of chemically examining a perfect physiological plasma.

We perceive, from this short notice of the different systems of cavities which penetrate bone, and of the variety of their contents, that even in analyzing bones that have been long and carefully macerated, we are dealing with not only the true osseous substance, but with other matters, as, for instance, the remains of the contents of the various canals, &c.

But before proceeding to the chemical consideration of the bones, we have still to determine the question whether the true matrix (independently of the contents of these canals) is a thoroughly homogeneous mass, that is to say, whether, morphologically considered, it exhibits a perfectly homogeneous continuity, and whether in a chemical point of view, it can be regarded as a perfectly uniform material, that is to say, as a chemical compound of certain proximate constituents.

The matrix of bones is found on a careful microscopical examination to be far from perfectly homogeneous. In the first place, on examining well-prepared transverse sections, we perceive a number of concentric circles surrounding the section of each Haversian canal. These circles are true lamellæ, varying in thickness from 0.002 to 0.005''' (Kölliker).<sup>1</sup> Besides these lamellæ connected with the Haversian canals, there is also a general system of such plates which correspond to the outer and inner surface of the bone, and are parallel to these surfaces. (Kölliker's Fundamental Lamellæ.) Associated with these and interspersed here and there in the interior of the bone between the lamellæ of the Haversian canals, are isolated groups of parallel lamellæ. (Kölliker's Interstitial Lamellæ.) These are most distinctly seen in sections of bone that have been carefully treated with dilute hydrochloric acid; but they may also be recognized in incinerated bone. But even the individual lamellæ, independently of the very minute tubules occurring in them (the bone-corpuscles with their prolongations), are not by any means homogeneous: we remark in them an extremely fine punctated appearance, depending on the presence of innumerable pale granules of nearly uniform size (according to Kölliker, about 0.0002'''). Kölliker is inclined to regard these granules as identical with the angular corpuscles which Tomes found in the fragments of incinerated and crushed bone, and he considers it not improbable that the true osseous tissue, or the matrix of bone, consists entirely of an intimate admixture of granules firmly combined with one another. If this supposition should be con-

<sup>1</sup> Mikrosk. Anat. Bd. 2, S. 288.



firmed by further investigations, we could hardly conceive a juxtaposition of these granules without an intervening substance: and even if this view regarding the minute structure of osseous tissue should not be confirmed, the granular appearance would always militate against the homogeneity of osseous tissue.

The chemical, like the physical relations of osseous tissue, indicate that in the minutest particles of it there is a very intimate blending of the textural elements, but not a true mixture (or chemical combination) into a homogeneous substance. It may be inferred from the results of Hoppe's experiments, to which we have previously referred, that the bone-corpuscles and their prolongations are invested by an albuminous membrane insoluble in boiling water.

Further, it is an old-established fact that almost all the earthy constituents may be extracted by dilute acids from a bone, without affecting its form, or even destroying its minute structure; in the same way the form and structure of a bone remain unchanged when we remove the organic matter from it, either by calcination or by careful boiling with dilute alkalis. These two facts might at first seem to be in favor of the view that the osseous tissue is homogeneous, and that there is an actual chemical combination between its organic and inorganic matters; but when we consider that the very numerous analyses of bone which have been already published do not lead to the inference that there is a definite proportion between the organic and inorganic matters, but on the contrary, that the proportions vary extremely in accordance with the physiological conditions,—and further, when we bear in mind that the cartilage may be removed from bone even by the weakest agents, as for instance, by boiling with water in a Papin's digester, or by an extremely dilute solution of potash,—we feel at all events that we have grounds for doubting that the matrix of bone is a chemical compound of earthy and organic matters; and we are strengthened in these doubts by observing that the minute points grow pale or entirely disappear in osseous substance treated with dilute hydrochloric acid.

As we have already spoken, in the first volume, of the individual constituents of osseous substance, we need here only observe in reference to its qualitative composition, or rather, in reference to that of bones in general, that the most essential organic constituents are gelatigenous cartilage (vol. i. p. 360) and fat (vol. i. p. 222), while the inorganic are phosphate of lime (vol. i. p. 373), phosphate of magnesia (vol. i. p. 381), carbonate of lime (vol. i. p. 378) and fluoride of calcium (vol. i. p. 383). In addition to these main constituents, the bones also contain substances which must be regarded as incidental or unessential constituents of osseous substance. Thus the alkaline sulphate in Bibra's cases<sup>1</sup> (see vol. i. p. 398) should probably be regarded as for the most part the product of the incineration of the bones. With regard to the other soluble salts that can be extracted by water or spirit from fresh pulverized bones after the removal of their fat, we possess no investigations which enable us to decide the question whether the chloride of sodium, carbonate of soda, &c., are at all events in part peculiar to the matrix of bone, or

<sup>1</sup> [See the foot note in page 190.]



whether they only belong to the blood which can never be thoroughly removed, or to the fluid contents of the bone-corpuscles and their prolongations. Precisely the same may be said of the organic substances which may be extracted from pulverized bone by digestion with mere water, or more thoroughly (together with the earthy salts) by dilute hydrochloric acid. Even the fat which we have enumerated amongst the main constituents can only occur in extremely small quantity in the matrix of bone. For the small quantity of fat (from 1 to 3%) which we find in bones that have been as thoroughly as possible cleaned and macerated, must be chiefly marrow from the cavities of the spongy portions of the bones, and only a mere trace can arise from the matrix: we, moreover, find from the investigations of the most distinguished histologists, that the marrow does not pass into the Haversian canals of the compact osseous substance. Hence it is only by the analyses of bones which have been well macerated and deprived of their fat that we can hope to arrive at any definite conclusion regarding the constitution of the osseous matrix.

The bone-cartilage, obtained by prolonged digestion with dilute and frequently changed hydrochloric or nitric acid, occurs in its moist state as a tolerably elastic, yellowish, translucent substance, which perfectly retains the form of the portion of bone from which it was obtained. When dried, it becomes very hard, but only slightly brittle. When it has been so often extracted with a weak acid solution that the latter no longer exhibits any traces of dissolved lime, the cartilage leaves very little or a mere trace of ash on incineration. We have already mentioned that neither Marchand nor von Bibra could recognize any difference between the elementary composition of this cartilage and of the glutin obtained from it or from tendons or connective tissue. The analyses of thoroughly pure bone-cartilage and of glutin coincide so accurately with one another, that notwithstanding their somewhat high atomic weights, we must regard these substances, if not isomeric, at all events, as polymeric, although we always find a little sulphur in the former, which is absent in the latter. Bibra<sup>1</sup> has made the interesting observation, that in fossil bones in which the organic substance is still retained, the cartilage is converted into a glutin-like substance or into true glutin. After freeing these bones in the ordinary manner from their earthy constituents, it was found that the residual cartilage fused at a temperature at from 37° to 40° into a thoroughly gelatinous mass, which swelled up in water into a trembling jelly. This only took place, according to Bibra, in true fossil bones, and not in those which were obtained from ancient graves. We shall postpone the description of the characters of the cartilage which occurs in bones before true ossification takes place, till we treat of cartilage generally. Neither Bibra,<sup>2</sup> Ragsky,<sup>3</sup> or any other chemists have found any essential alteration in the cartilage of diseased bones; in all cases the cartilage was converted by boiling with water into a substance perfectly similar to glutin.

As we have already described in considerable detail (in the first vo-

<sup>1</sup> Chem. Untersuch. über die Knochen u. Zähne. 1844, S. 399. <sup>2</sup> Op. cit. p. 319.

<sup>3</sup> Rokitansky's Handb. d. pathol. Anat. Bd. 2, S. 205 [or English Transl. vol. 3, p. 182.]



lume) the individual mineral constituents of bones, and the varying quantities in which they occur, we shall here merely present the reader with a general scheme representing the constitution of compact osseous tissue, as deduced from the best analyses :

Phosphate of lime, . . . . .	57
Carbonate of lime, . . . . .	8
Fluoride of calcium, . . . . .	1
Phosphate of magnesia, . . . . .	1
<hr/>	
Mineral constituents, . . . . .	67
Cartilage, . . . . .	33
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	100

The fluctuations in the proportions of the individual constituents are by no means inconsiderable under different physiological conditions, as has been already shown in the first volume. The differences which the different bones of one and the same individual exhibit are especially interesting. Von Bibra has especially elucidated this point by the most conclusive results. With regard to the proportions between the organic and inorganic matters, Rees has, next to Bibra, most distinctly shown that the bones of the extremities are in general richer in earths than those of the body; of the former the humerus and femur contain somewhat more than the other cylindrical bones; the cranial bones contain about the same quantity of earths as the cylindrical ones, while the metatarsal and metacarpal bones have a closer affinity in this respect to the bones of the trunk. The ribs and the clavicles contain on an average rather more organic substance than the vertebræ; those of the pelvis approximate very closely in this respect with the last-named bones. The carbonate of lime appears to be entirely dependent upon the quantity of the phosphate of lime in the different healthy bones of the same individual; at all events, Bibra found that in the most diverse bones of the same animal, the carbonate and phosphate of lime always stood in nearly the same ratio. Moreover, it would appear from the observations at present in our possession, that the quantity of magnesia in the different bones rises and falls with that of the phosphate of lime. The short bones always contain, according to von Bibra, more fat than the cylindrical bones, even where the former have been as completely as possible freed from spongy substance. The quantity of water contained in the bones has been made the subject of special investigation by Stark:<sup>1</sup> it cannot generally be determined with much accuracy, but Stark's observations show that the flat bones contain more water than the cylindrical (probably from the former being the more vascular).

Although the female skeleton is on an average far lighter than that of man, the comparative analyses of the same bones of both sexes show very trifling, and, as it would appear, altogether unessential differences. If we may be allowed to assume (with physicians) the existence of a certain predisposition, we would say that it would appear from the various recorded analyses of morbid bones, that the female bones more readily undergo a loss of earthy constituents than male bones, or to speak more correctly, that processes which contribute to the absorption

<sup>1</sup> Edin. Med. and Surg. Journ. vol. 163, pp. 308-325.



of bone-earth are more frequently developed in the female than in the male organism.

It has been found that in man as well as in the other mammalia, and in birds, the bones in youth, especially in the human race, contain less earthy constituents than those of adults, but that in advanced age, the bones are universally richer in earthy or mineral matters (Thilenius, Davy, Schreyer, Frerichs,<sup>1</sup> von Bibra). We cannot decide from the facts in our possession whether the diminution of the earthy matters, which has been often observed in the bones of aged persons, is dependent on physiological or pathological causes. Different observers have arrived at very different conclusions regarding the ratio of the carbonate to the phosphate of lime at various periods of life. It has been already stated (vol. i. p. 379) that I found far more carbonate of lime in proportion to the phosphate in the bones of a new-born child, than in those of an adult and of an old man, while von Bibra found on an average far less carbonate of lime in the bones of young animals. Moreover, von Bibra found rather more phosphate of magnesia in the bones of several very young animals than in the corresponding bones of those that were older. The period of life exerts, according to Bibra, no essential influence on the amount of fat in the bones.

It can hardly be doubted that the food must exercise some influence on the constitution of the bones—a view which seems proved, not merely by the experiments of Chossat and von Bibra<sup>2</sup> (referred to in vol. i. p. 374), but also more especially by the investigations of the latter observer on the bones of different classes of animals.

It appears from the numerous investigations of von Bibra and Stark on the effects of different kinds of food on the bones of the *mammalia*, that the amount of cartilage remained unaffected, but that essential differences were induced in the composition of the inorganic constituents. The bones of the herbivora contain on an average rather more carbonate of lime than those of the carnivora; the bones of the pachydermata and cetacea were found to be especially rich in this salt by von Bibra (who always used the femur in these comparative analyses). There seems to be no perceptible difference in the amount of fat in the bones of the carnivora and herbivora; von Bibra, however, found that the bones of horses contained very much more fat than those of other animals. The bones of fat animals usually contain more oily matter than those of lean ones, and hence the bones of hibernating animals contain considerably more fat before than after their winter-sleep. According to Stark, human bones are richer in water than those of any other mammal.

Von Bibra almost invariably found more bone-earth in the bones of *birds* than in those of mammals. The rases were the richest in mineral substances (the mean being 75.8%; in *Columba Turtur* the earthy matter rose to 84.3%). The bones of carnivorous birds are generally only slightly richer in earthy salts than those of mammals. The ratio of the carbonate of lime to the phosphate is generally greater in the bones of birds than in those of mammals. There is, on an average, rather more fat in the bones of birds than of mammals, and the granivorous, and especially the aquatic birds, in this respect exceed those living

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 43, S. 251.

<sup>2</sup> Op. cit. p. 47.



on flesh. According to Stark, the bones of birds contain more water than those of mammals. Moreover, the bones of granivorous birds contain rather more silica than other bones.

Stark has also instituted comparisons between the organic and inorganic substances in the bones of mammals and birds, but his results are not in accordance with those of von Bibra. In all probability, the osseous substance had not been perfectly dried in most of Stark's comparative analyses.

Our knowledge of the composition of the bones of the *amphibia* is almost entirely due to the labors of von Bibra. These bones contain an average less inorganic matter than those of mammals and birds (those of the *Salamandrida*, for instance, only 55%, and those of the frog 63%); moreover, the ratio of the carbonate of lime to the earthy constituents generally, is less in the bones of the *amphibia* than in those of the preceding classes. As has been already stated in vol. i. p. 398, von Bibra found a considerable quantity of sulphate of soda<sup>1</sup> in these bones.

The bones of *fishes* are poorer in mineral constituents than those of any of the preceding classes (the earthy matters varying from 21 to 57%). Although, with regard to the earthy salts, the carbonate of lime appears to a certain extent to rise and fall with the phosphate, no definite proportion can be detected as existing between them. As in the case of the *amphibia*, von Bibra found that these bones contained more sulphates and fat than those of mammals or birds. According to Stark, the bones of fishes contain more water than those of any other animals.

Notwithstanding the enormous number of analyses of *morbid bones* which have been made by different chemists, very few results with any claim to certainty have been obtained regarding the composition of the bones in definite diseases. To this unfortunate circumstance we must in a great measure ascribe the difficulties which present themselves in diagnosing diseases of the bones during life, and often even after death, if we regard the diseased bone merely as an isolated pathologico-anatomical specimen. We need only refer to the osteomalacia of children (rachitis) and of adults, to the different kinds of osteoporosis, to primitive and consecutive sclerosis, to the various osteophytes and ivory-like exostoses, &c. It appears to be often difficult, without a previous knowledge of the mode in which the bone-disease was developed, to give a decided opinion on its nature, even when it is brought before us as a piece of morbid anatomy. We are, moreover, inclined to believe, without in any way criticising the anatomical observations hitherto made in connection with diseases of the bones, that the whole subject requires further development in a pathologico-anatomical point of view. The chemist must therefore be pardoned if (as has more than once happened) he should mistake osteoporosis for osteomalacia, if he should regard an osteopsathyrosis as softening of the bones, and not as a subdivision of osteoporosis; in short, if in many cases he should confound osteoporosis with osteomalacia, and rachitis with caries. It is no wonder, then, if in

<sup>1</sup>[The editor regrets to find that a rather important *erratum* escaped his notice in correcting the page referred to in the text. In line 10 from the top of page 398, read "sulphate of soda" in place of "soda."]



the analysis of osteoporotic bones we rarely or never ascertain whether the rarefaction of the osseous tissue depends upon a simple syphilitic, arthritic, or tuberculous ostitis, or on an excessive growth of medulla, or on simple atrophy of the bony tissue; that is to say, upon the disappearance of the above-mentioned concentric osseous lamellæ from the Haversian canals. Nor need we wonder that we are yet so comparatively ignorant regarding the chemical constitution of the osteoscleroses; for excepting the analyses of Ragsky,<sup>1</sup> von Bibra,<sup>2</sup> Schlossberger,<sup>3</sup> Gerster,<sup>4</sup> Gruber and Baumert,<sup>5</sup> C. Schmidt,<sup>6</sup> and C. O. Weber,<sup>7</sup> we find very few chemical investigations accompanied with a history of the disease under which the patient labored. In the absence, therefore, of an accurate history of the case, we can ascertain very little from our numerous analyses of morbid bones, seeing that in the great majority of cases only very unimportant differences are apparent in the composition of very differently named morbid bones. Moreover, such different methods have been employed in preparing the bones for analysis, and in conducting the examination, that the results that are obtained do not admit of comparison.

On entering upon the special examination of the results of these numerous investigations, we have, first of all, to notice the general proposition enunciated by von Bibra, that in almost all morbid processes implicating the bones, the mineral substances are abstracted from the tissue earlier and in larger quantity than the organic matter; and that in almost all diseased bones a relative increase of the cartilage is observed. The bone-earth is not only earliest separated from already formed bones during morbid conditions, but it is also last deposited in the bones after the cessation of disease, as, for instance, is seen in the composition of the scleroses; for a bone, or a part of a bone, often exhibits the most decided physical characters of sclerosis when the earthy constituents are far below the normal average. It is an error to suppose that in sclerotic bones there is more earthy matter and less cartilage than in normal bones. This much only is true, that in consecutive sclerosis, that is to say, after osteoporosis or osteomalacia, the bone gradually recovers its earthy constituents, although not always to such a degree as to reach the normal proportion between the inorganic and organic matters. At all events, the analyses of Ragsky and Baumert do not prove more than this.

The *cartilage* is very rarely affected in morbid bones. Most observers have obtained the ordinary gluten from the cartilage of diseased bones. (In some cases of very decided rachitic bones both Marchand and I have failed to obtain any true gluten.)

The amount of *fat* in the bones has only been accurately determined in a few cases; but von Bibra's analyses lead to the inference, that generally when, in consequence of disease, a bone has suffered a loss of earthy matter, and still more of its cartilage, the quantity of its fat is increased.

<sup>1</sup> Rokitansky's Handb. d. Pathol. Anat. Bd. 2, S. 201-205 [or English translation, Vol. 3, pp. 180-182].

<sup>2</sup> Arch. f. phys. Heilk. Bd. 6, S. 287-299.

<sup>3</sup> Ibid. Vol. 8, pp. 69-87.

<sup>4</sup> Ibid. Vol. 6, pp. 142-146.

<sup>5</sup> Beiträge z. Anat. Physiol. u. s. w. 2 Abth. Prag. 1847.

<sup>6</sup> Ann. d. Ch. u. Pharm. Bd. 61, S. 329.

<sup>7</sup> Commentatio præmio ornata. Bonnæ, 1851.



A very important question forces itself upon our notice in considering the diseases of the bones, namely, whether there are constant changes in the *relative proportions of the mineral constituents*, and especially whether, when there is resorption of the bone-earth, the strongly basic phosphate of lime is replaced by a less basic salt. Unfortunately most of our analyses of morbid bones are not of such a nature as to enable us to elicit from them even a probable answer to this question. How seldom, after the bones have been properly prepared for analysis, has it been attempted to ascertain the quantity of carbonate of lime in the fresh bone, or in the earthy constituents, by the direct determination of the carbonic acid! Indeed, in most analyses, the older method of Berzelius for the determination of the phosphate of lime has been employed, according to which we could never be certain whether we were weighing  $8\text{CaO} \cdot 3\text{PO}_5$  or  $3\text{CaO} \cdot \text{PO}_5$ . We shall presently notice the reasons why this and similar questions are not so easy to answer as might at first sight be supposed. It appears, from the analyses in our possession, as if the carbonate of lime first diminished and subsequently again increased in a corresponding proportion with the phosphate, in diseases of the bones; it is only in osteophytes and new formations of bone that we frequently find the carbonate of lime exceeding the normal standard.

After the preceding observations, it would scarcely seem necessary to consider the composition of the bones in reference to the ordinary nosological classifications; we must, however, attempt this course, partly to show how deficient our knowledge on this subject is, when we cease to be contented with abstract diagnoses or mere nominal designations, and attempt a more scientific mode of consideration, and partly also to demonstrate that unless we implicitly follow the leading maxims afforded to us by pathology, little real advance can be made in this department.

If we follow the method of inquiry at present pursued in pathology, which refers almost all anatomical changes of the tissues and organs to a so-called inflammatory process, we must begin by studying the chemical changes which are coincident with the textural alterations of the bones that are induced by an ostitis, a periostitis, disease of the medulla, &c. But when we see the results of an ostitis exhibiting themselves in various ways, according as it depends on purely local causes or on specific or general diseases, or as it attacks this or that group of bones, we may at all events conclude, *à priori*, that even where the textural changes are nearly the same, the chemical constitution of the altered bones need not be similar or even analogous. Thus it is easy to form a conception of osteoporoses whose origin might be dependent on such different morbid affections that according to the different diseased condition from which they arose, they must have a thoroughly different chemical composition, although morphologically they might be extremely similar. This is shown in a certain degree by the analyses which we at present possess of osteoporotic bones, although these investigations are far from being altogether satisfactory; and seems most decidedly established in the case of caries. Adopting the view held by morbid anatomists, that inflammation of the bones terminates in hypertrophy, we have three kinds of hyperostoses to consider, which morphologically, and in part also chemically, differ from one another, namely, primary sclerosis, osteophyte, and exostosis.



We possess two analyses, made by Ragsky, of *primary sclerosis*, whose occurrence is generally supposed to depend upon the gradual conversion into cartilage, and finally into bone, of an exudation within the medullary cavities and the Haversian canals (by which the osseous tissue becomes condensed and almost ivory-like); they do not, however, at all indicate an augmentation of the mineral constituents of the bones. Even in true sclerosis there is never an excess of earthy matter in proportion to the organic substance deposited in a bone, and hence, we cannot suppose that in primary sclerosis such an augmentation of the mineral substances should occur. When the exudation is transformed into osseous substance, this newly formed structure must at first contain less mineral matter than true bone, and on this account, as indeed is completely in accordance with the analyses, it happens that we often find a relative diminution of the earthy matters in sclerotic bones as compared with normal osseous tissue. All that we can deduce from our analyses of such bones is, that on the one hand their organic basis differs in no respect from the ordinary gelatigenous cartilage, and that on the other, there is a considerable augmentation of the carbonate of lime in proportion to the phosphate.

As *osteophyte* is a new formation of osseous substance on the surface of bone, its composition must naturally vary very considerably with the length of its existence, that is to say, with the stage of development into which it has entered from the period of the original formation of the exudation. In the majority of cases both of puerperal and other osteophytes, it has been found both by Kühn and myself, that there has been an excess of organic substance and of carbonate of lime above the normal mean. As in callus (according to Valentin), so also in osteophyte, there is more carbonate of lime than in those products which are more similar to osseous tissue. No attempt has been made to ascertain whether in the early stage the cartilage yields chondrin on boiling, as is the case in callus and bones previous to ossification; but gelatigenous cartilage is contained in perfectly ossified osteophytes.

The analyses of *exostoses* lead to the same conclusions as those of osteophytes (Lassaigne).

*Osteoporosis*, which is a dilatation of the medullary cells, and of the Haversian canals, may also be the result of inflammation of the bones, since the exudation that is deposited induces a resorption of the lamellæ, and consequently a rarefaction of the tissue. But, according to Rokitsky, osteoporosis may also result from excessive development of the medulla, which then penetrates the canals, dilates the cavities, and thus increases the volume of the affected bone. Finally, osteoporosis may arise in consequence of old age or of certain *dyscrasiæ* (arthritis, syphilis, &c.), through simple atrophy with resorption of the lamellæ surrounding the canals, and it then yields an extremely brittle product (osteopsathyrosis). In the chemical investigation of bones that have undergone rarefaction (or expansion) these three conditions must not be overlooked; in all previous investigations, however, little or no attention has unfortunately been paid to these differences. Analyses of porous bones have shown nothing beyond the fact that in general the resorption of the mineral matters of the bones, even in osteoporosis, proceeds more abundantly than that of



the cartilage, and that the cavities which have been produced are filled sooner or later with fluid fat. It has been inferred from these analyses, that the carbonate of lime is resorbed in relatively larger quantities than the phosphate; but it is only in a few analyses that this relation is perceptible, and in these, the nature of the osteoporosis affecting the bone is doubtful. Glutin has been found in the cases in which the cartilage of such bones was examined for gelatin, and consequently the chemical constitution of the organic substance remained unchanged.

In a chemical point of view, *osteomalacia* has been more investigated than osteoporosis; but here we must distinguish between the osteomalacia of childhood, that is to say, rachitis, and the softening of the bones in adult life. Yet, notwithstanding the analyses of Marchand,<sup>1</sup> von Bibra,<sup>2</sup> Davy, and Ragsky, to which I may add my own,<sup>3</sup> we are still in ignorance of the pathological process and the morbid product of true rachitis. Our analyses are only so far accordant, that all agree in assuming that rachitis induces a considerable diminution of the mineral constituents of the bones, although it still remains to be decided whether this diminution may not be in part a relative one, depending merely upon an increase of cartilage. The assumption of many pathological anatomists, that the rachitic process is connected with true hypertrophy of the bone-cartilage, must at the present day be regarded as, to say the least, very improbable; for when rachitic bones, which have been only moderately macerated and deprived of their fat, are examined in thin sections under the microscope, the Haversian canals and *lacunæ* (bone-corpuscles) are not found to be filled with organic matter, but are either empty or dilated. If we calculate the analysis of an imperfectly macerated bone, containing all its fat (and the gelatinous substance effused into the medullary canals) for 100 parts, we shall indeed obtain an absolute excess for the organic constituents, and a relative deficiency for the inorganic matters; but these relations do not prove the existence of hypertrophy of the cartilage. Such a condition can only be microscopically and chemically shown in those rachitic bones which exhibit a tendency to healing through sclerosis; an absolute augmentation of the cartilage can be detected only in these cases, and not in the highest stage of the special rachitic process. Hypertrophy of the cartilage constitutes the basis, not of softening of the bones, but of osteosclerosis, more especially when it occurs after rachitis, or after osteoporosis. The nature of the cartilage generally remains altogether unchanged in rachitis; but Marchand and I have observed cases of highly developed rachitis, in which no glutin could be extracted from the bones, although after prolonged boiling I obtained a slightly gelatinizing substance which yielded some of the reactions of chondrin. An exact determination of the relations of the earthy constituents of rachitic bones is the more important from the light which they appear to throw on other processes, and on the nature of rachitis itself. The carbonate of lime appears from several analyses to diminish proportionally to the earthy phosphates, but other analyses (as for instance those made by Marchand and myself) yield a higher amount for the carbonate of lime than the normal proportion. Although

<sup>1</sup> Journ. f. prakt. Chem. Bd. 27, S. 92.

<sup>2</sup> Op. cit. p. 291.

<sup>3</sup> Schmidt's Jahrb. der. ges. Med. Bd. 38, S. 280.



the phosphate of lime is often much diminished, the rachitic process cannot be conditional upon the occurrence of free acid, as has been assumed from a single observation by Marchand. The assumption that carbonate of lime is removed from the bones, is controverted not merely by the result of analyses, but also by the indifferent behavior of decidedly rachitic bones towards blue litmus. The ash of these bones occasionally yields more carbonate of lime than we calculate from the direct determination of the carbonic acid in the fresh bones (after being merely deprived of their fat); a portion of their lime must therefore have been combined with some organic acid, which, however, need not necessarily be lactic acid, since a fatty acid or some other substance may have been combined with this base. The frequent occurrence of free uric acid, lactic acid, and oxalate of lime, in the urine of rachitic children, cannot be regarded as affording evidence of the existence of a so-called lactic acid diathesis or dyscrasia; we shall indeed have occasion to show that the osteomalacia of adults presents more grounds for the establishment of such an hypothesis. Whether the basic phosphate of lime found in the bones of rachitic patients is converted into the  $\frac{3}{4}$  basic salt, is a question which must be decided by more exact and direct investigations than any hitherto made.

The *Craniotabes* (of Elsässer) is probably nothing but a form of rachitis which affects the occipital and parietal bones during the period of suckling, and we should, therefore, make no special reference to it, were it not for the purpose of drawing attention to the admirable investigations made by Schlossberger<sup>1</sup> on this subject, which may, indeed, serve as a model for all similar inquiries. He ascertained that the 63% of mineral substances, which he found to occur in the normal occipital bones of healthy children during the first year of their age, diminished to 51% in the simply attenuated parts of the bone, and to 40 or even to 28% in the thickened and spongy softened parts; he found that the carbonate of lime was present either in a normal quantity, or only slightly diminished, and that the cartilage was so far sound that it yielded ordinary glutin on boiling, whilst the fat, when compared with that in the rachitic bones of children of more advanced age, was not at all or very slightly increased.

The *osteomalacia of adults*, which undoubtedly depends upon osteoporosis accompanied with diminution of volume and a deposition of fluid fat in the dilated and newly formed cavities, would appear to be more referable than rachitis to the excessive formation of acid in the organism; but a thorough investigation of the nature of this remarkable disease and its products (such as that by Schlossberger on *craniotabes*, to which we have already referred) is still wanting. Bostock,<sup>2</sup> Prösch,<sup>3</sup> Bogner,<sup>4</sup> myself,<sup>5</sup> von Bibra, Ragsky, Gerster,<sup>6</sup> C. Schmidt,<sup>7</sup> and Weber,<sup>8</sup> have submitted these bones to examination. The earthy constituents of the bones are more diminished here than in any of the other bone-diseases

<sup>1</sup> Arch. f. phys. Heilk. Bd. 8, S. 69-87.

<sup>2</sup> Medico-Chirurgical Transactions. Vol. 4, p. 38.

<sup>3</sup> Comment. inaug. de osteom. adult. Heidelb, 1835.

<sup>4</sup> Valentin's Repert. 1842, S. 294.

<sup>5</sup> Arch. f. phys. Heilk. Bd. 7, S. 142-146.

<sup>7</sup> Ann. d. Ch. u. Pharm. Bd. 61, S. 281.

<sup>5</sup> Op. cit.

<sup>8</sup> Op. cit.



we have considered; but the physical examination shows that a large portion of the cartilage is also destroyed, whilst the almost brittle network of residual bony matter floats in thin fluid fat, which amounts in some cases to 20 or 30%. The osseous substance which is obtained from these bones occasionally yields gluten on boiling; but when the bones are very thoroughly affected by the disease, the organic matter yields no gelatinizing substance like gluten or chondrin. I could not discover that the fat of these bones contained phosphorus, as Nasse<sup>1</sup> found was the case with ordinary bones. C. Schmidt proved in the most unequivocal manner that free lactic acid was present in the fluid of the cylindrical bones. The fluid occurring in these bones exhibits very often, although not invariably, an acid reaction; and although the excessive quantity of fat may in some cases impede the action on litmus paper, I have known cases in which some of the bones of a patient affected with osteomalacia exhibited an acid reaction (as the femur and tibia), whilst others (as the ribs and pelvic bones) showed no trace of the presence of acid, even where there was a smaller accumulation of fat. We cannot, therefore, refer the resorption of the bones to the occurrence of free lactic or fatty acids, unless in direct opposition to well-attested facts. The occurrence of the lactic acid may perhaps be owing to the development of a chemical process in the broken-down fragments of the bones, which gives rise to the formation of an acid, as Gerster, Schmidt, and Weber observed in the case of perfectly disintegrated bones. The anatomical investigation, as well as the analysis of the individual morbid process, renders it more than probable that the occurrence of the fat in the bones does not exert a primary influence on their disintegration, but acts only in a secondary manner within the spongy parts. The mineral substances decrease very considerably when compared with the cartilage in this form of osteomalacia, as will be readily seen if we exclude the fat in the calculation of the analysis. It is remarkable that notwithstanding the acid reaction of the juice permeating the bone, carbonate, as well as phosphate of lime, is found in the macerated bones from which the fat has been removed, and that the former even appears to be less decreased than the latter. Weber is the only one who has investigated the composition of the phosphate of lime contained in these bones; he found, in addition to carbonate of lime,  $\frac{3}{8}$  basic phosphate of lime, and believes that the phosphate of normal bone ( $3\text{CaO}.\text{PO}_5$ ) is converted by means of the free acid into this less basic salt. If this interesting fact should be confirmed by future investigations, it must still appear very striking that so much carbonate of lime could be present in fresh bone, together with the free acid. The affections which we comprehend under the term osteomalacia may, therefore, possibly admit of being subdivided into two different processes. It will in like manner depend upon future and more carefully conducted investigations to determine whether, as we are induced from various reasons to believe, the arthritic process actually corresponds with that of osteomalacia.

Carious bones, the products of ulcerous osteitis, have been very carefully examined by Valentin<sup>2</sup> and von Bibra.<sup>3</sup> The ulceration so gradually destroys the bone, that the mineral constituents disappear to a

<sup>1</sup> Journ. für prakt. Chemie. Bd. 27, S. 274

<sup>2</sup> Valentin's Repert. 1838.

<sup>3</sup> Pogg. Ann. Bd. 57, S. 356-372.



greater extent even than the cartilage before the entire destruction of the osseous tissue, and that the cavities formed in the bones by caries become filled with fat in the same manner as in osteomalacia; hence we always find a larger quantity of organic matter in carious than in normal bones: the residual cartilage does not differ from the ordinary bone-cartilage, or at all events the decoction exhibits the usual reactions of gluten. It appears from most analyses that the carbonate of lime diminishes in direct proportion with the phosphate. Bibra endeavored to ascertain whether the phosphate of lime exhibited any difference in the proportions of its proximate constituents in caries; he found  $\frac{3}{8}$  basic phosphate of lime, but further investigation was required to determine this question decisively.

The chemical investigation of portions of *necrosed* bone has not yet led to any important results; nor can we wonder at this, when we consider the conditions under which separate bones, or portions of bones, are necrosed: that is to say, how they are deprived of nutriment by the intervention of healthy parts. Our analyses yield, therefore, very nearly the same composition for necrosed as for healthy bones; the organic matter sometimes appears to be rather augmented, although it is occasionally slightly diminished; they commonly present the same characters as strongly macerated bones.

*Fossil bones* have also been made the subject of numerous investigations.<sup>1</sup> The locality from which they have been removed should always be considered in these inquiries, for to this we must obviously refer many of the modifications presented by their composition; thus, for instance, the mass in which they are imbedded frequently exerts a chemical action upon them by decomposing or metamorphosing the organic matter of the phosphate of lime, whilst it also readily becomes infiltrated (especially its carbonate and sulphate of lime) into the bone-canals.

The quantity of organic matter contained in fossil bones varies very considerably; thus, for instance, in some cases the organic matter contained in them has been found to be scarcely diminished when compared with that of fresh bones, whilst on the other hand many of these bones exhibit no remaining trace of organic matter. We have already referred to the observation made by Bibra, that the cartilage of fossil bones is generally converted into a substance which at once yields gluten, after the mineral matters have been thoroughly removed. It seems *a priori* more than probable that the composition of the phosphate of lime might undergo a change in fossil bones; but still this salt has almost always been found to consist of  $8 \text{ CaO} \cdot 3 \text{ PO}_5$ , which is the same composition as that occurring in fresh bones. It is therefore very questionable whether the occurrence of small crystals of apatite,  $3 \text{ CaO} \cdot \text{PO}_5$ , in fossil bones, or in bones which have lain for a long period of time in the earth (Girardin and Preisser),<sup>2</sup> can depend upon a metamorphosis of the chemical constitution, or (as seems less improbable) on an arrangement of the minute particles of phosphate of lime into crystals. Carbonate of lime generally occurs in far larger quantities in fossil than in recent bones, although this increase is frequently only relative, in consequence of the

<sup>1</sup> On the literature of this subject, see vol. i. p. 383.

<sup>2</sup> Ann. de Chim. et de Phys. 3 Sér. T. 9, p. 370-382.



organic substance having disappeared from the bone; more commonly, however, this carbonate of lime is absolutely augmented either by infiltration from without, or in certain soils, from a portion of the phosphate of lime being decomposed by carbonic acid or carbonates. Magnesia often occurs in larger quantities in the fossil remains of vertebrated animals than in the fresh bones of the present animal world. The greater abundance of fluoride of calcium which some of our best analysts have found to occur in fossil bones has excited considerable attention, more especially since Liebig<sup>1</sup> has shown that even the cranial bones excavated at Pompeii exhibit a larger proportion of fluoride of calcium than the bones of the present generation (see vol. i. p. 383). On the other hand, Girardin and Preisser have found that the fluoride of calcium had greatly diminished in human bones which had lain long in the earth, and in some cases had even wholly disappeared. There is thus sufficient proof that it may increase as well as diminish in a perfectly normal manner in the bones, although this increase or decrease cannot always be referred to definite causal relations. Alumina, oxide of iron, and silica, are substances which are very frequently found in fossil bones, although we must undoubtedly regard their presence as due merely to infiltration.

We shall consider the bones and cartilages of the invertebrate animals in a subsequent portion of the work.

The *analysis of bones* is undoubtedly one of the simplest operations of zoochemical research, but so many different methods have been attempted that, notwithstanding the great number of analyses, we have arrived at no conclusive results; we see, for example, that the chemical composition of the phosphate of lime contained in the bones is still doubtful, even at the present time. Thus, too, a number of questions present themselves to our notice on entering upon the consideration of the constitution of pathological bones, which have either been wholly unanswered or very imperfectly solved by the analyses in our possession. A more exact knowledge of the specific gravity of the bones must have thrown considerable light upon their physiological and pathological conditions; but whilst in many cases, as for instance, in the examination of urine, the density of the fluid to be analyzed is in general more or less accurately determined, the determination of this property has been almost entirely neglected in the case of the bones, excepting in the analyses made by Ragsky. Independently of the fact that the *density* is an important physical property, deserving special attention in the consideration of the numerous modifications to which the bones are subject in a healthy and morbid condition, we might expect, by a careful study of the subject, to ascertain the existence of a definite law indicating a relation between the density and the proportions of organic and inorganic matters contained in the bone, which is obviously a point of the highest importance. As, however, the proportions both of water and of fat contained in the bone exert a great influence on its physical properties, and these must necessarily be most intimately connected with its specific gravity, it should be one of the first points in the investigation of this subject to institute a comparison between the specific gravities

<sup>1</sup> Die. org. Ch. in Anwendg. auf Agric. u. Physiol. S. 140 [or English Translation, 1840, p. 156].



of different bones after being dried in the air, after the removal of their fat, and in a perfectly anhydrous condition. The determination of the absolute weight has been almost as much neglected as that of the specific gravity, in comparing together normal and diseased bones, although it is only from this determination and from a comparison with the specific gravity, that we can form a judgment of the metamorphosis of matter going on in the bone during any physiological or pathological process (and not from the proportional numbers of a single chemical analysis). Although we must presume that our readers are acquainted with the methods, cautions, and modes of correction required for the determination of the specific gravity, we would simply draw attention to the fact, that the pulverized bone (in all conditions under which it may be submitted to examination, whether it have been dried in the air, deprived of its fat, or have been wholly freed from water) should be kept for several hours in a vacuum after it has been well shaken and impregnated with distilled water, such a precaution being necessary for the thorough removal of all particles of air.

Few observers, with the exception of Nasse and Stark, have satisfactorily investigated the *quantity of water* contained in the bones. Nasse was indeed induced to believe, from his observations, that the water contained in bones exerted no influence on their hardness, but we cannot deny its influence in morbid bones on this and other physical properties. As bone is very hygroscopic, we ought to notice the state of the thermometer and hygrometer in comparing the quantity of water present in different bones which have been dried in air, before the pulverized bone is thoroughly deprived of its water in an oil or air-bath.

The determination of the quantity of fat contained in the bones is more uncertain than that of most of the other constituents. The fat, as we have already observed, is limited for the most part to the medulla of the bones, extending only slightly into the Haversian (or so-called medullary) canals. The fat which is not contained in the cavities and interstices of the bones, but adheres to the true osseous tissue, is very inconsiderable in quantity, and is, at all events, only mechanically mixed with it; it should, therefore, we think, be always merely compared with the quantity contained in other bones, and not be included in the percentage representation of the chemical analysis as a constituent of bone. The influence exerted by the fat of the true osseous tissue on its physical properties has not as yet been accurately ascertained. We have already spoken (in vol. i. p. 220) of the rules which should be observed in the determination of the fats.

In order to study the composition of the true osseous tissue (and this has been the object of most of the analyses hitherto made), the bones should in the first place be minutely pulverized, carefully washed with water, and then deprived of their fat by the action of ether; for the analysis can yield no clear representation of the composition of true bone until the fatty constituents, and the substances soluble in water, and derived from the blood and the bone-plasma, have been carefully removed. The presence of these substances not only increases the difficulty of the technical performance of the analysis, but the analysis itself naturally gives only a very imperfect result in relation to the osseous tissue in various physiological or pathological conditions.



It was formerly customary to calculate the quantity of *carbonate of lime* contained in bone by the quantity of lime in the fluid from which the phosphate of lime had been precipitated (according to Berzelius's method) by ammonia free from its carbonate; but this method has been shown by many analysts to be exceedingly uncertain. The quantity of carbonic acid in the bones should therefore always be determined by Fresenius's apparatus. It is very useful to compare the quantity of carbonic acid contained in the bones after they have been well washed and deprived of their fat, with that present in the ash. We usually find rather more carbonic acid in well-prepared ash than in fresh bone; this excess, which is slight in healthy bones, rises in some cases very considerably in morbid bones. This is indeed the only method which admits of our estimating how much lime is combined, not with carbonic acid, but with organic matter.

The method employed in preparing the bone-ash is not devoid of importance; for the determination of the earths, we must first wash the pulverized bone and thoroughly remove the fat by ether, and then after it is completely dried, submit it to the process of combustion. Erdmann's muffle affords the most rapid and complete means of incinerating bones; burning them in a platinum crucible over Berzelius's lamp is a much less rapid method of proceeding; in either case it is advisable that the bone-ash should be moistened with carbonate of ammonia and again heated before it is weighed. There is almost always a more or less considerable quantity of caustic lime formed during incineration. When the above precaution is neglected, the ash is often found to yield less carbonic acid than the fresh bone, a result which may, however, depend upon other circumstances.

With regard to the individual determinations of the *phosphoric acid*, *magnesia*, *fluorine*, and traces of *sulphuric acid*, we presume that our readers are acquainted with the different methods employed in analytical chemistry; we would, however, especially recommend the mode of procedure devised by W. Heintz.<sup>1</sup>

We have only very unsatisfactory data for the determination of the *quantitative relations* existing between the bony skeleton and the whole weight of the animal organism in different classes of animals, and during different diseases; and in many cases we have no data of any kind.

At the age of 21 years, the weight of the skeleton is to that of the whole body in the ratio of 10·5 : 100 in man, and in that of 8·5 : 100 in woman (the weight of the body being about 125 or 130 lbs.)

The special consideration of the parts which stand in a close relation to the bones, such as the periosteum, the marrow, and the cartilaginous investments, does not fall within the limits of our inquiry, since they are organic parts composed of several simple tissues, and cannot, consequently, be made the subject of a rational chemical investigation.

Although numerous histological observations have been made on the development of the bones from cartilage, the subject has been very imperfectly considered in a chemical point of view. In reference to the development of individual bones, we scarcely know more at the present day than what was known long since, independently altogether of chemi-

<sup>1</sup> Monatsber. der Akad. der Wiss. z. Berlin. 1849, S. 50-53.



cal investigations; namely, that the bone, as long as it continues in a state of cartilage, contains a substance yielding chondrin, which becomes converted into a body yielding glutin during the progress of ossification, when the earths are simultaneously deposited in the bone in large quantities. Boussingault made some interesting experiments on pigs in connection with the absorption of mineral substances during the development of the skeleton. It would appear from these observations, that the skeleton of a pig increases on an average about 11.7 grammes in weight daily during the first eight months after birth; that is to say, that about 6.2 grammes of cartilage are daily formed, and 5.5 grammes of earths (including 2.4 grammes of phosphoric acid) are taken up by the bones. At a subsequent period, as, for instance, till the eleventh month, the skeleton increases on an average about 6 grammes daily, that is to say, there are only about 2.6 grammes of earths (including 1.4 grammes of phosphoric acid) deposited daily in the bones.

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## THE TEETH.

The teeth have commonly been considered, in a chemical point of view, as organs possessing very great analogy with the bones, and they have been regarded as purely mechanically acting parts, rich in mineral substances, and analogous to the products of inorganic nature—in short, to minerals; but this mode of investigating the subject cannot satisfy the requirements of the histologist or the physiologist. Independently of their mode of development, the structure of the teeth differs so entirely from that of the bones, and is moreover so complicated, that it would be wholly irrational to regard the teeth as formed of homogeneous simple tissues, and to submit them directly to chemical analysis.

When we analyze an entire tooth, we are guilty of the same error as the chemists of an earlier age who triturated complicated organisms in a mortar, and then attempted to analyze the chaotic mass. Even in a *chemical* investigation of the teeth, we should remember that every tooth consists of three morphologically different parts, namely, the dentine or tooth-substance, the enamel, and the cement.

The predominant part of the tooth, and that on which its form depends, is the dentine (*substantia tubulosa*), a fusiform or wedge-like body, provided with a club-shaped hollow extremity for the reception of the nerves and nutrient vessels. Histological investigation has shown that dentine is not a homogeneous body, but that it consists of a perfectly structureless<sup>1</sup> mass, resembling the matrix of bone, and perforated by a very large number of minute ramifying canals. These canals have comparatively thick distinct walls, and proceed from the cavities, diverging towards the external surface of the dentine, in the vicinity of

<sup>1</sup> [In the previous edition Lehmann says "not perfectly structureless." According to Kölliker, the matrix of the dentine in the recent tooth is quite homogeneous. After the extraction of the calcareous salts from the dentine, it, however, exhibits a great tendency to break up into fibres.—G. E. D.]



which they are still more minutely ramified. We do not observe bone-corpuscles, or other structures peculiar to bone in the dentine; but in their place we have the *interglobular spaces* of Czermak,<sup>1</sup> which resemble the holes made by bullets. We must, therefore, take into account the contents of these tubes (probably the nutrient fluid of the tooth), and of the above-named cavities, in the chemical investigation of the fresh teeth. It is clearly shown by microscopico-mechanical examination, that here also the salts of lime are not deposited in the canals or cavities.

Hoppe<sup>2</sup> exposed to the prolonged action of boiling water thin sections of the molar teeth of the pig, the salts having been previously extracted with hydrochloric acid, and the cartilage of the cement having been removed with water. The external part swelled up, became transparent, and dissolved, with the exception of a few flakes; while, on the other hand, the interior became white and transparent, crumbled down, and was scarcely at all soluble. The solution only contained gluten. The undissolved residue, when examined under the microscope, presented the dentinal canals in a perfectly isolated state, and aggregations of dark globules, with distinct nuclei: these globules perfectly corresponded with the above-mentioned interglobular spaces. Acetic acid dissolved neither the canals nor the globules. Hence, according to Hoppe, the canals, like the bone-corpuscles, possess independent walls which do not consist of a gelatigenous substance; Hoppe considers the globules to be cells.

Slight as is the resemblance between dentine and osseous tissue in a morphological point of view, there is still less similarity between the vitreous investment of the crown of the tooth (or the enamel) and bone. The enamel is a very hard and rather brittle compact mass, not permeated by canals or pores, and composed of fibres resembling 4 or 6-sided prisms, diverging from the crown of the tooth: whether these fibres (the so-called enamel prisms) are agglutinated together by a special intermediate substance, is not yet decided: a more accurate chemical investigation may probably enable us to determine this point.

According to Hoppe,<sup>3</sup> the enamel, after the extraction of its salts by means of hydrochloric acid leaves structures which present the characters of epithelium: the remains of the prisms readily fall asunder, and do not dissolve on boiling, but break in pieces.

While the crown of the tooth is covered by enamel, the neck and root are invested with a layer of cement of varying thickness. The cement is a substance presenting the greatest resemblance to bone, and exhibiting the bone-corpuscles or bone-cavities with their prolongations; it differs, however, from dense bone in the absence of true Haversian canals.

Histologists have not hitherto succeeded in throwing any great amount of light on the chemical composition of these tissues composing the teeth, although Berzelius<sup>4</sup> and Lassaigne have certainly drawn attention to the essential differences existing in the composition of the dentine and the enamel, and von Bibra<sup>5</sup> has devoted much attention to the same

<sup>1</sup> Zeitsch. f. wiss. Zool. Bd. 2, S. 295-322.

<sup>2</sup> Arch. f. pathol. Anat. Bd. 5, S. 170-188.

<sup>4</sup> Lehrb. der Chem. Bd. 9, S. 553. (4 Aufl.)

<sup>3</sup> Op. cit.

<sup>5</sup> Op. cit. p. 276.



subject. All that is known regarding the chemical constitution of the teeth and their individual histological parts, we owe almost entirely to these observers.

The *chemical composition of dentine* is very similar to that of bone; the organic matter consists of gelatigenous cartilage, whilst the mineral parts are precisely the same as those occurring in the bones. The quantitative ratio between the organic and inorganic matters in dentine is somewhat varying, approximating very closely in some cases to that occurring in the dense bones; but in the majority of the small number of cases recorded, the organic substance amounts to about 28%. A little fat is always found to be present with the cartilage. The mineral constituents of dentine are identical with those of the dense bones, and occur in nearly the same relative quantities. The quantity of carbonate of lime appears, however, to be more variable here than in the bones; from 3 to 8% of carbonate of lime have been found with from 65 to 67% of phosphate of lime. Berzelius demonstrated that fluoride of calcium and phosphate of magnesia are also present in the dentine.

The *enamel* differs in a chemical point of view from dentine, for no cartilage can be obtained from it, whilst the amount of the whole organic matter, which, after being treated with acids, appears like a membranous tissue, does not exceed 2.0 or at most 6.6% of the dried mass. From 81 to 88% of phosphate of lime, with about 7 or 8% of carbonate, are found in the enamel. We have already spoken of the abundance of fluoride of calcium present in the enamel. (See vol. i. p. 383.) The chemical investigations of this substance have left it undecided whether the phosphoric acid and lime enter into a different combination in the enamel and dentine from that occurring in the bones.

Although the *cement* of the teeth has been most imperfectly examined, yet von Bibra, Lassaigne, and Marchand concur in regarding this substance as more analogous in its composition to bone than dentine was found to be; it differs from the latter in containing a little more organic matter.

Lassaigne and von Bibra found on an average a rather larger quantity of mineral substances in the molars than in the incisors.

It would appear from observations made by Lassaigne, that the organic matter diminishes with age in the teeth as well as in the bones.

The comparative experiments of Lassaigne and von Bibra on the teeth of different animals have yielded very few results which would justify the establishment of general propositions; the last named of these observers could not even discover any definite difference in the composition of the teeth of carnivorous and herbivorous animals. Bibra's observations show that there is a striking relative excess of organic matter in the grinders of the elephant and the wild boar, and that the teeth of these pachydermata contain a very considerable quantity of phosphate of magnesia (as much, according to him, as from 6 to 12%).

*Carious* teeth do not very readily admit of chemical investigation; but it may be observed that, according to Marchand, the tendency of the teeth to this mode of destruction may be referred to their containing an excess of carbonate of lime.

The remarks already made concerning the *analysis* of the bones



refer equally to that of the teeth; excepting only that it is more difficult to prepare the materials for examination in the latter case, more especially in exhibiting pure enamel or cement; the best method of obtaining the former of these substances is by heating the tooth to a few degrees above  $100^{\circ}$ , when one portion of the enamel becomes spontaneously detached, and the removal of adjacent pieces by mechanical means can be then readily effected. These detached portions require, however, still further cleaning to remove the tissue of the dentine which may be attached to them. In consequence of the difficulty in drying the enamel thoroughly when in masses, von Bibra's method should be adopted, which consists in pulverizing the purified enamel, and then drying it.

## CARTILAGE.

Cartilage belongs to that class of tissues which, although they appear to act for the most part mechanically, and to possess a small amount of vital activity, nevertheless exhibit a tolerably composite and very varied structure.

Histological investigations show that cartilage must be classed under at least two heads, depending upon structural differences: namely, true cartilage and fibro-cartilage.

Amongst the *true cartilages* of the human body we must include those of the ribs, the ensiform cartilage, the cartilages of the nose, of the larynx and trachea, and the cartilaginous masses investing the articular heads of bone. This true cartilage is so far identical in character in these parts of the organism, that it exhibits in all cases more or less numerous cavities occurring in a tolerably homogeneous mass, and containing one or more cells with a simple nucleus. This matrix is by no means perfectly amorphous; in most cases it is finely granulated, but frequently it is fibrous.

The *fibro-cartilage* composing the intervertebral ligaments, the *symphysis pubis*, the claviculo-scapular ligaments, the Eustachian tube, &c., contains, in addition to cells, a thoroughly fibrous matrix; these fibres are either parallel to, or intersect one another in various directions, present sharp dark outlines, and exhibit no trace of nuclei.

These differences, which the microscope reveals in cartilage, admit equally of recognition by means of chemical investigation. Müller's<sup>1</sup> observations, which were the earliest prosecuted in relation to this subject, have been followed in more recent times by those of Donders and Mulder.<sup>2</sup>

When we examine this tolerably homogeneous matrix of true cartilage in a chemical point of view, we find, on carefully treating the triturated cartilage with boiling water, that it is this substance, and not the cartilage-cells, which yields the chondrin described in vol. i. p. 362. Thus, for instance, if we boil the cartilage of the ribs from 12 to 48 hours in

<sup>1</sup> Pogg. Ann. Bd. 38, S. 295.

<sup>2</sup> Versuch einer phys. Chem. S. 658 [or English Translation, pp. 545-559].



the open air (Mulder), or from three-quarters of an hour to an hour in a Papin's digester (Hoppe),<sup>1</sup> the matrix will be dissolved, leaving only the other morphological elements of the cartilaginous tissue, namely, the cartilage-cells and their nuclei, which remain undissolved, together with vessels and the coagulated protein-bodies of the blood-plasma. Before the solution of chondrin is perfectly gelatinized, a small deposit is generally formed, and in this these morphological elements may be readily and distinctly recognized by the microscope. But there is a slight opalescence observable even in the clearest solution of chondrin, which is owing to the suspension of these cells and their fragments. The chondrin which has been examined by chemists, must therefore always contain a larger or smaller quantity of morphological elements, which cannot be perfectly removed, even by Hoppe's very admirable mode of procedure. We cannot, therefore, regard the elementary analyses of chondrin as more trustworthy than those of cartilage itself, since we have to deal in both cases with a mixture of obviously different bodies, and not with a simple chemical combination. It is alike remarkable and worthy of regret that the elementary analyses of these substances should have yielded such identical results; several of our most distinguished and skilful analysts having found that the composition of cartilage, which abounds in cells, and of chondrin, which contains only few cells, although not entirely devoid of them, is almost entirely identical. Setting aside the cells altogether, there would appear grounds for concluding that the conversion of the cartilage into chondrin depends only upon a deposition of atoms, and not upon chemical decomposition due to the assimilation or elimination of certain elements.

According to the micro-chemical investigations of Donders and Mulder, the matrix of cartilage has far less power of resisting the stronger chemical reagents, such as concentrated sulphuric acid or a strong solution of potash, than the cells contained within it. Its behavior towards concentrated sulphuric acid shows, however, that even this matrix is not a perfectly pure chemical body. Thus, for instance, on the application of concentrated, and afterwards of diluted sulphuric acid, the granules of the granulated cartilage are less rapidly dissolved than the matrix itself, whilst the fibres of the fibrous mass yield still later to this action. It appears, therefore, probable that the matrix may contain three different, although very nearly allied, substances. The question whether the difference existing in these three substances depends upon a different aggregation of the very minute mechanical particles, or whether it is of a chemical nature, is one which even the latest observations, made on the chondrin obtained from the decoction of the matrix, have failed in deciding. The inquiry is rendered the more difficult by the circumstance, that the chondrin itself becomes partially changed during the process taken to obtain it; chondrin being converted, like gluten, by boiling into a substance which does not gelatinize, and is soluble in cold water.

The products of the decomposition of chondrin have also failed in affording us any important results; we merely know from Hoppe's observations, that chondrin, when decomposed by concentrated sulphuric

<sup>1</sup> De cartilagineum structura et chondrino, diss. inaug. Berol. 1850.



acid, yields (in addition to extractive matters) leucine only, and no glycine, but when treated with a concentrated solution of potash, glycine only, and no leucine, besides extractive matters.

The fibrous matrix of fibro-cartilage must have a totally different composition from that of true cartilage, as we see from the micro-chemical investigations of Donders and Mulder. After exposing cartilage of this kind (as, for instance, one of the intervertebral bodies) for a moderate time to the action of a concentrated solution of potash, or of sulphuric acid, the fibrous character of the matrix, when observed under the microscope, is found gradually to disappear, but these agents fail equally with concentrated acetic acid in actually dissolving it; for a close examination shows that the individual fibres merely swell and assume a gelatinous appearance, and consequently become less perceptible to the eye. Donders further observed that, in addition to the cartilage-cells, there were fibres situated between these gelatinous bundles, which remained almost wholly unchanged in the sulphuric acid, and bore some resemblance to nuclear fibres, and besides these there were some fibres of connective tissue. The fibro-cartilages dissolve for the most part on boiling, and leave only a deposit of granular nuclei and a few cells. The gelatinizing fluid obtained from these cartilages exhibits nearly the same reactions as the chondrin extracted from the intercellular substance of true cartilage. According to Donders, this solution yields only a slight precipitate with tannic acid, but on the addition of alum yields, like chondrin, a compact deposit, which, however, does not disappear in an excess of the solution. Bichloride of platinum produces a considerable precipitate, which is insoluble in an excess of the test.

The semilunar cartilages of the knee-joint have commonly been reckoned amongst the fibro-cartilages, but J. Müller showed long since (in the case of the sheep), that they yield no chondrin, but gluten only, on boiling. Donders, Kölliker, and other histologists, agree in considering that these cartilages, like the interarticular cartilages of the lower jaw, of the sterno-clavicular articulation, and of the wrist-joint, consist of true but very solid fibrous connective tissue, enclosing true cartilage cells, in addition to a few nuclear fibres. We cannot wonder, therefore, that (as connective tissue always yields gluten) these cartilages should, on boiling, yield ordinary gluten or bone-gelatin, notwithstanding the presence of cartilage-cells.

Donders distinguishes a third kind of fibro-cartilage, which he terms *elastic*; to this class belong the cartilages of the larynx, and the external ear, and the cartilage investing the condyle of the lower jaw. These structures consist of a dense tissue of fine elastic fibres, in which isolated cells are enclosed. These fibres are not altered by the action of a concentrated solution of potash, but the cells disappear after four or five hours; even after the application of sulphuric acid, the elastic fibres remain almost unchanged, while the cells are found to have disappeared after six or eight hours' action, and on the repeated addition of water.

On boiling these cartilages in water, Donders obtained only a little chondrin, and as elastic tissue generally is not gelatinous, he referred this chondrin to the metamorphosis of the cells, the more especially because he found that after these cartilages had been boiled for five or



more hours no cells could be any longer discovered by the microscope. Hoppe, on the other hand, considers that during the process of boiling, the cartilage-cells in part escape from the elastic tissue, while the residual tissue so completely surrounds the cells that are retained, that they can only be recognized by the aid of a compressor. He is further of opinion that, possibly, Donders might not have sought in the fluid for unchanged cartilage-cells, and that he could not see them in the contracted tissue without using a compressor.

The present does not appear a fitting place to enter into a consideration of the different forms and groupings of the *cartilage-cells* or *cavities*, of their scattered occurrence or arrangement in rows, of the endogenous formations of parent and secondary cells of the first and second generations, &c.; although all these relations could obviously not exist without simultaneous differences in the chemical substrata. Our chemical knowledge is, however, still too defective to admit of our hazarding any conjecture in reference to the methods by means of which we may hope to ascertain the controlling chemical relations.

Mulder and Donders saw the morphological elements of true cartilage disappear into very fine granules when exposed under the microscope to the action of a solution of potash, sulphuric acid and water; the granular or slightly fibrous intercellular substance first disappeared, next the margin or investing membrane of the original parent-cells (which also disappears after prolonged exposure to the action of acetic acid), then the membranes of the cells, and finally their nuclei. If from this it would seem a probable conclusion that the cell-walls and the nuclei did not essentially differ in their chemical constituents from the intercellular substance, the more especially as by continuous boiling with water the cells appear to be expelled and converted into chondrin, yet Mulder and Donders were led, from the relations of elastic fibro-cartilage, to the view that the morphological elements of cartilage closely resemble, in a chemical point of view, the intercellular substance, and that the observed differences are only dependent on a varying degree of cohesion of the deposited materials. The elastic fibro-cartilages, for instance, yield chondrin on boiling, while, with the exception of the cartilage-cells, they appear to contain no chondrin-yielding substance; while, on the other hand, the semilunar cartilages of the knee, notwithstanding their containing an abundance of cartilage-cells, yield only gluten, and not a trace of chondrin. It was this last-named circumstance that induced Hoppe<sup>1</sup> to take up the rigid investigation of fibro-cartilage and its relations, and he came to the conclusion that the cartilage-corpuscles are imbedded in a chondrin-yielding substance within the elastic tissue. He found, namely, that after elastic fibro-cartilage had been boiled for three hours, a certain amount of chondrin was formed, but that the cartilage-cells (for the most part perfectly unaffected) might be observed in the fluid as well as in the residual, strongly contracted elastic tissue. (The compressor was requisite to see them in the latter.) Hence Hoppe concluded that cartilage-cells cannot consist of gelatigenous substance, and was led to the axiom that cell-membranes and cell-contents never consist of such a substance, and further, that a cell-membrane can never be meta-

<sup>1</sup> Arch. f. pathol. Anat. Bd. 5, S. 170-188.



morphosed into gelatigenous tissue. Donders has, moreover, essentially modified his former view regarding the chemical constitution of the walls of the cartilage-cells, and both these experimentalists may be regarded as perfectly coinciding in these general statements and results. (See "Elastic Tissue.")

Mulder first proved that chondrin contains a small quantity of *sulphur*; but the amount of this substance in the tissue of true cartilage, and whether the sulphur exists in all, or only in some of the morphological constituents of the cartilage, are questions still to be answered.

*Fat* has been found in the cartilages to the amount of from 2% to 5% of the dry substance; it occurs principally in the cells, but is also found in solitary globules and in the intercellular substance of true cartilage. Small fat-globules may be discovered in almost all cartilage-cells in addition to the simple or multiple nucleus, and occasionally the nucleus is rendered perfectly invisible by being completely enveloped in fat. No very essential difference has been found to exist between this fat and the fat of other organs.

The *amount of water* present in the cartilage, and which must obviously exert considerable influence on its physical properties, varies in different cartilages, fluctuating between 54% and 70%. No definite series of experiments, conducted on a given system, have been made in relation to the quantity of water contained in different cartilages, or as regards the specific gravity of these tissues.

From 3% to 6% of *mineral substances* have been found in the cartilages, but the experiment was limited to the cartilages of the ribs, and even these have not been examined with sufficient accuracy. Phosphates of lime and of magnesia, chloride of sodium, carbonate of soda, and (what is more remarkable) a large quantity of sulphates, were found; but it can hardly be doubted that the latter are in part due to the sulphur of the organic substance of the cartilage. The occurrence of alkaline carbonates indicates, as Berzelius<sup>1</sup> has shown, that the cartilaginous substance must be partly combined chemically with lime or soda; but whilst Fromherz and Gugert found upwards of 18% of carbonate of lime in the ash of cartilage, von Bibra<sup>2</sup> found at most only traces of alkaline carbonates in the costal cartilages of the human subject at different ages, as well as in those of animals. The very variable quantity of chloride of sodium found in the ash of cartilage (from 1% to 8%) would seem to indicate that it does not exist in chemical combination in the cartilage, but that it originates in the special juice which permeates that tissue, and which, unfortunately, has not yet been investigated.

The methods to be adopted in *the analysis of cartilaginous tissue* are sufficiently obvious from the remarks in the preceding pages.

[Much information on bone, the teeth, and cartilage, will be found in Schlossberger's "First Attempt at a General and Comparative Animal Chemistry,"<sup>3</sup> now in the course of publication.—G. E. D.]

<sup>1</sup> Lehrb. d. Chem. Bd. 9, S. 563.

<sup>2</sup> Op. cit. pp. 412-417.

<sup>3</sup> Erster Versuch einer allgemeinen und vergleichenden Thierchemie. Von Julius Eugen Schlossberger. Erste Lieferung. Stuttgart, 1854.



## CONNECTIVE TISSUE.

The term *connective* or *areolar* is applied to a tissue which is chemically allied to cartilage, although of a simpler character, and is understood by histologists to comprise not merely that porous, soft, cellular tissue, characterized by the readiness with which it may be filled with air, which connects together the organs and various tissues of the animal organism, and was formerly termed *cellular tissue*, but also those morphological elements which constitute the solid basis or the main constituent of no inconsiderable number of animal membranes and ligaments. This tissue, uniting the organs with one another, which forms a network of variously sized meshes, composed of long slender fibres, for the most part combined in bundles, has been named *amorphous* connective tissue, but it very gradually passes into the *formed*<sup>1</sup> variety; the serous membranes and muscular fasciæ contain a dense network of rather large meshes; when the bundles of fibres follow a more definite direction, and approximate more closely to one another, forming dense striated masses, tendons and ligaments will be the tissues developed from them. The connective tissue may also, to a certain extent, impart their form to the bursæ mucosæ, to the matrix of the mucous membranes, to some of the above-mentioned interarticular cartilages, to the submucous areolar tissue of the intestine (the *Tunica nervea*), to the dartos, to the longitudinal and annular fibrous coats of the veins, &c.

Unfortunately, however, a careful microscopico-mechanical examination shows that the tissue we are investigating is not a simple one. All its parts contain, without exception, heterogeneous matters, differing both mechanically and chemically from the substance of the true connective tissue; and hence chemists have hitherto been unable to make an analysis of this tissue in a perfectly unmixed condition. In addition to vessels, nerves, fat-cells, and similar structures, the connective tissue constantly exhibits *elastic fibres* (*nuclear fibres*), and very frequently also *smooth muscular fibres*. As these intermixed parts do not admit of being mechanically separated from true connective tissue, such tissues only have been selected for chemical analysis as present the fewest of these morphological elements. On this account the tendons, for instance, have been chosen for analysis. But when so accurate an analyst as J. Scherer<sup>2</sup> has found that the chemical elements are in the same numerical relations in tendon, notwithstanding this admixture, as in the gluten produced from connective tissue, we cannot wholly reject the assumption that the connective tissue possesses the same elementary composition as gluten. Much weight cannot, however, be attached to conclusions drawn from the best elementary analyses of these substances with high atomic weights; for even the fact that the tendinous tissue intersected with elastic fibres was found to present the same ultimate composition as the gluten produced only from the fibres of connective

<sup>1</sup> [The terms *amorphous* and *formed* connective tissue were introduced by Henle; they correspond to the *loose* and *solid* connective tissues of Kölliker.—G. E. D.]

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 40, S. 1-45.



tissue in the tendons, sufficiently proves that our analytical methods are not very sensitive in detecting slight admixtures of even very different substances. We should, however, be guilty of rashness, if we regarded it as an established fact, that the connective tissue is isomeric with glutin; for the constitution of the latter has not been determined with certainty.

On placing connective tissue in boiling water, it usually at first contracts, but soon swells up, assumes a gelatinous form, and dissolves after prolonged boiling (the length of time depending upon the density of the tissue, or the minuteness of its previous division). It contracts also in a slight degree, and thus loses the tendency to putrefaction, when treated with bichloride of mercury, alum, basic sulphate of iron, and tannic acid. If the connective tissue is treated for a prolonged time with dilute acids or alkalis at the boiling-point, it is found to be much more rapidly metamorphosed into glutin than when it is boiled in mere water.

The connective tissue swells in concentrated acetic acid and becomes transparent, or at all events this is the case with the tendons, ligaments, &c., which are chiefly formed of this tissue; but this gelatinous mass is only thoroughly dissolved on the addition of water and the application of heat, and neither red nor yellow prussiate of potash produces any precipitate from this acetic-acid solution. The true fibres of the connective tissue are found by micro-chemical investigation to swell on the addition of dilute acetic acid, and to become transparent, till they finally altogether disappear; but they are not actually dissolved even after many hours' exposure to this action, for on washing with pure water, or on neutralizing the acid with ammonia, they may be rendered perfectly visible in their original form. As most of the other textural elements which are intermixed with the connective tissue are not similarly affected and rendered invisible by acetic acid, they are brought more distinctly in view by its application; and hence this agent becomes a valuable aid to the histologist in his study of the tissues.

The fibres of connective tissue also swell and assume a gelatinous form in alkalis, but after the prolonged action of the alkali they cannot be again brought to view by the addition of water, being completely dissolved.

We thus close our remarks on these three groups of tissues, which were all indicated as gelatigenous, even by the older histologists, and in which the most recent investigations have recognized a very surprising analogy. The labors of Virchow,<sup>1</sup> Donders,<sup>2</sup> and Kölliker,<sup>3</sup> have thrown much light upon this subject. Donders and Virchow especially coincide in this point, that the gelatigenous intercellular substance of these tissues does not originate from cells, but is directly separated from a plastic fluid, while the other elements in these cases (as for instance, in bones, the bone-corpuscles with their prolongations; in cartilage, the cartilage-cells; and in connective tissue, the nuclear or elastic fibres with their nuclei) are primarily formed from cells. Kölliker is also convinced that the nuclear fibres are undoubtedly not formed from the nuclei of the

<sup>1</sup> Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 2, S. 150 u. 314.

<sup>2</sup> Zeitsch. f. wiss. Zool. Bd. 3, S. 348.

<sup>3</sup> Verhandl. d. phys.-med. Ges. zu Würzburg. Bd. 3, S. 1.



cells of embryonic connective tissue, but from the cell-walls, but he denies that the fibrillæ of connective tissue are a direct deposition from the cytoblastema.

We must not here overlook the fact, which is remarkable in a chemical point of view, that the embryonic connective tissue, according to Scherer, contains no gelatin, but consists, in addition to fusiform cells, of a peculiar intercellular substance, which on digestion with water yields not only albumen, but a gelatinous or mucous substance. Virchow has proposed the term "mucous tissue" for this class of structures, of which the gelatinous substance of Wharton (in the umbilical cord) affords the best example.

### ELASTIC TISSUE.

The elementary fibres of this tissue are somewhat extensively distributed in the animal organism, although they seldom occur in sufficiently large quantities to form special organs; they occur, for instance, in the yellow elastic ligaments (the ligamenta flava of the vertebral column, the inferior vocal cords, the ligamentum nuchæ of mammals, the elastic ligaments of the claws of animals of the Felidæ, and the hinge-ligament of bivalves). We meet with larger groups of elastic fibres connected into membrane-like sheaths in the fascia lata, and in the middle coat of the arteries and veins. Smaller accumulations of elastic fibres also occur in many other parts, as for instance, in the corium, and under the mucous membrane, more especially in the pharynx, the pylorus, the cæcum, &c. We need only observe here that the elementary fibres of this kind are met with under different forms of grouping, either in wide-meshed or very intricately formed nets having hook-like indentations; as fenestrated membranes exhibiting tolerably large intervals, and resembling an anastomosing vascular network; or lastly, only as bundles or fibres twining around other tissues in a spiral manner. It is at the present day assumed by most histologists, that these true elastic fibres, which occur in the form of flat, rather broad, somewhat brittle, and much ramifying bands, are perfectly identical with those far narrower, spirally coiled *nuclear fibres*, which are often studded with nuclei, and are invariably present in connective tissue; and they have arrived at this conclusion, partly from watching the development of these tissues, and partly because the slightest transition from one form to the other admits of recognition; moreover, the chemical reactions of the two forms do not indicate any difference between them.

The elastic fibres never occur independently of other histological elements, however much they may predominate; most commonly they are found intermixed with the fibres of connective tissue, very frequently also with smooth muscular fibres (Kölliker's fibre-cells),<sup>1</sup> as in the middle coat of the arteries. Close to the fenestrated coat, the elastic fibres, intermingling in part with nuclear fibres, merge into the so-called con-

<sup>1</sup> Zeitschr. f. wiss. Zool. Bd. 1, S. 78-82.



tractile tissue, which is principally formed of these smooth fibres, to which they undoubtedly owe the property of contracting under the action of cold (Schwann)<sup>1</sup> or magnetic electricity (E. H. and E. Weber<sup>2</sup>). The elastic fibres themselves are wholly deficient in animal contractility, and are only distinguished for their extraordinary elasticity, a property which is not destroyed by spirit, or by boiling (J. Müller).

The *chemical* investigations of elastic tissue which have been hitherto made, have unfortunately not led us to any clear knowledge of its constitution and general chemical relations. J. Müller<sup>3</sup> and Eulenberg<sup>4</sup> obtained by the prolonged boiling of elastic tissues, a non-gelatinizing fluid, which yielded some reactions similar to those afforded by long-boiled chondrin. Mulder and Donders<sup>5</sup> failed, on the other hand, in obtaining any gelatinous substance, after forty hours' boiling, from well-purified elastic tissue, which had been freed from all admixture of connective tissue and fibre-cells, by means of acetic acid and a solution of potash; and they also found on making a micro-chemical examination, that the fibres were entirely unchanged.

M. S. Schultze<sup>6</sup> has arrived at the conclusion, that the purified elastic fibre of the arterial coats is but slightly, or not at all changed, even after it has been boiled for sixty hours with water; whilst on the other hand, it becomes converted into a brownish, non-gelatinizing fluid, which has an odor of gelatin, after thirty hours' boiling at the temperature of 160° in a Papin's digester. This fluid was precipitated by tannic, picric, and kinic acids, tincture of iodine, and corrosive sublimate, but not by other reagents which commonly precipitate chondrin. We cannot conclude with Schultze, from these reactions, that the elastic tissue yields gelatin; for it would, in our opinion, be attaching too wide a significance to the idea of gelatin, were we to apply this name to substances which do not gelatinize, and merely yield precipitates with tannic acid and similar substances, which precipitate a great number of organic matters, and in other respects, exhibit only negative properties. In that case we should be compelled to include Mulder's tritoxide of protein under the head of gelatin, and to denominate as gelatigenous numerous other matters, such even as albumen, since when boiled in water under high pressure and at a high temperature, they yield substances which are soluble in water, although they do not gelatinize.

According to the investigations of Donders and Mulder, elastic fibre is entirely insoluble in cold concentrated *acetic acid*. It is only after continuous boiling for some days in this acid that it gradually dissolves.

When heated with moderately diluted *hydrochloric acid*, it dissolves with a brown color; the dissolved substance is soluble in water and in alcohol.

Xanthoproteic acid is formed by the action of *nitric acid*.

According to Zollikofer,<sup>7</sup> when pure elastic fibre is digested in *sul-*

<sup>1</sup> Müller's Handb. der Physiologie. Bd. 1, S. 170, u. Bd. 2, S. 20 [or English Translation, Vol. 1, 2d edition, p. 218, and Vol. 2, p. 876].

<sup>2</sup> Berichte der k. sächs. Gessellsch. d. Wiss. 1849, S. 91.

<sup>3</sup> Pogg. Ann. Bd. 28, S. 311-313.

<sup>4</sup> De tela elastica; diss. inaug. Berol. 1836.

<sup>5</sup> Mulder's Vers. einer phys. Chem. S. 594 [or English Translation, p. 543].

<sup>6</sup> Ann. der Ch. u. Pharm. Bd. 71, S. 277-295.

<sup>7</sup> Ibid. Bd. 82, S. 168-180.



*phuric acid*, diluted with  $1\frac{1}{2}$  times its weight of water, it yields leucine only, and no glycine.

[We may here remark, that Zollikofer recommends the following as the best method of preparing leucine. Take elastic tissue (for instance, the ligamentum nuchæ of the ox), purify it by extraction with boiling acetic acid and with water, and afterwards boil it for forty-eight hours with sulphuric acid of the above-mentioned strength, then neutralize with milk of lime, boil the pulpy mass that is now formed, and filter. During the evaporation of the filtered fluid on the sand-bath, the lime-salts that become deposited must be as far as possible removed. On further evaporation in the water-bath, the fluid readily yields crystals of leucine. No glycine (as is remarked above) is formed, and the leucine may be purified without animal charcoal by mere recrystallization in spirit and alcohol.—G. E. D.]

Elastic tissue remains unchanged for a long time, at an ordinary temperature, in a moderately concentrated *solution of potash*, and it is only after it has been heated for some days that it becomes converted into a gelatinous mass.

Pure elastic fibre cannot be obtained by mechanical means, but must be procured, as we have already observed, by removing the fibrillæ of cellular tissue and the fibre-cells by boiling with acetic acid, and then adding a dilute solution of potash.

Tilanus found in the elastic substance of the ligamentum nuchæ, after it had been purified in the above-described manner, 55.75% of carbon, 7.41% of hydrogen, and 17.74% of nitrogen. We do not think that any reliable formula can be obtained from this analysis, even by the help of the analysis of the chlorine compound.

Donders<sup>1</sup> has recently come to the view, that all *cell-membranes* consist of a substance identical with, or at all events, very similar to elastic tissue. This opinion is specially based on histological grounds, and rests, on the one hand, on the development of elastic tissue and especially of nuclear fibres from the walls of cells, and on the other hand, on the circumstance that certain membranes and textural elements, which in their physical and chemical properties closely approximate to elastic tissue (as for instance, the sheaths of the nerves), may be found to be formed from cell-membranes. According to Donders, the walls of all true cells, whether occurring in the neurolemma, the capsule of the lens, &c., have the following physical and chemical properties in common with one another and with the elastic tissue obtained from them. The physical properties are their structureless, glossy character, their transparency, elasticity, strong refractive power, and a specific gravity higher than that of water. The chemical properties are their insolubility in water, alcohol, and ether (all the physical properties remaining unaffected by the application of these reagents)—their insolubility in acetic and other vegetable acids—their difficult solubility in dilute sulphuric, hydrochloric, and nitric acids—their insolubility in ammonia, and their slight solubility even in concentrated solutions of soda and potash—their swelling in acids and alkalies, and their alkaline solutions gelatinizing—their difficult solubility in boiling water, and the absence

<sup>1</sup> Zeitsch. f. wiss. Zool. Bd. 3, S. 348–358, and Bd. 4, S. 242–251.



of gelatinization in the solution. The animal cellulose is rendered yellow by nitric acid, then after the addition of ammonia, orange; the color is scarcely affected by hydrochloric acid, or by a mixture of sugar and sulphuric acid; it is turned red on the application of Millon's test. Acetic acid throws down from the alkaline solution a substance which is insoluble in an excess of the reagent, and possesses the main characters of animal cellulose; it does not readily become decomposed, even in morbid processes, if we except fatty degeneration.

However important such generalizations of the facts in our possession may be for histology—however such general views may throw light on the further progress of this science, and may open out future paths of inquiry, it would be by no means expedient, in the present state of our knowledge, to regard all cell-membranes as perfectly identical with the substance of elastic tissue; for independently of the circumstance that the above-mentioned properties are not found in every cell-membrane and in every elastic membrane, we know how differently reagents often act on cells and tissues, according to their age or the state of their development. Further, it can scarcely be questioned that the walls of very young cells, as for instance, blood-corpuscles, pus-corpuscles, the deepest epidermic and epithelial cells, and the cells of the glandular follicles (Köl liker), are composed of a protein-body, that is to say, a substance far more nearly allied to albumen and fibrin than to the matrix of elastic tissue, seeing that they are readily soluble in acetic acid, and in very dilute alkalies.

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### HORNY TISSUE.

In former times the tissues belonging to this class were regarded as amongst the simplest in the animal organism, and considered merely as different forms of one and the same matrix, which certain chemists were ready enough to discover, and to designate by the term *Keratin*. The zealous labors of recent histologists have, however, shown us that even these apparently homogeneous tissues have a complicated, and in many respects, a variable structure. There exists the same correspondence between the structure of the epidermis, the nails (claws and hoofs), the horns, and whalebone, as that which we observe in the chemical constitution of these tissues, all of which are so far analogous to one another that they proceed from cells or nucleated vesicles, which are not morphologically developed like the cells of other organs, but to a certain extent dry up, and are only agglutinated together by an intercellular substance, which often does not very readily admit of detection. They also exhibit great resemblance in a chemical point of view, for when compared with other tissues they all contain a large quantity of sulphur in combination with a substance, or with atomic groups, whose origin from, or affinity with the so-called protein-bodies cannot be denied when we consider their behavior towards certain reagents, and their percentage composition. Although we are still far removed from a correct know-



ledge of the chemical constitution of these tissues, or rather of their elements, chemistry has, nevertheless, very largely contributed to place the question of the histological conformation of these tissues on a level with the present state of science; in confirmation of which we need only indicate the admirable labors of Donders<sup>1</sup> and Mulder, of Paulsen,<sup>2</sup> Kölliker,<sup>3</sup> and several other observers.

The questions to which the present condition of histological inquiry leads the chemist in his examination of the horny tissues, are briefly these: Is there a substance which holds together the cells of these tissues, agglutinating them to a certain extent, and, if so, what are the chemical properties and the composition of this substance? What is the chemical character of the morphological constituents of these dried cells or vesicles of the horny tissue? What is the nature of the cell-membrane, and of the nuclei which exist in almost all of the cells, and finally, of what do the generally dried contents of these cells consist? Are the morphological elements identical in different kinds of horny tissue, or do they often differ essentially from one another, as various reactions would seem to indicate? What is the constitution of these morphological elements in the newly forming or just formed cells in the vicinity of the *rete mucosum* of the skin or the mucous layer of the nails? What metamorphoses do analogous elements undergo during the gradual drying and the alterations in form of the originally filled spherical or oval cells?

It unfortunately happens that the chemical investigations hitherto instituted on this subject have contributed rather to the suggesting than to the answering of these questions; for although chemical reagents have enabled us duly to examine the morphological elements of the horny tissue, chemistry is still wholly incompetent to indicate the position which, from its form, each structure ought to occupy in the series of organic atomic groups. We should consider it a great step in advance, if we knew how to isolate any one of the morphological constituents of the horny tissue, in the same manner as we can isolate elastic fibre by chemical means from the yellow ligaments or the middle coat of the arteries. The different horny tissues have hitherto been regarded by chemists simply as homogeneous bodies, and analyzed as such, after they had been freed by indifferent solvents from fat, salts, and the so-called extractive matters. Although these kinds of analysis have most frequently been conducted under Mulder's superintendence, no one is more thoroughly convinced than Mulder himself of their insufficiency in respect both to the histological and chemical knowledge of these tissues.

We abstain from entering more minutely into the consideration of the internal structure of the different horny tissues, as the observations already made on this subject will sufficiently explain the state of our chemical knowledge of these structures. The micro-chemical reagents to which we are now about to refer, afford, as we have already observed, a closer insight into the histological than the chemical constituents of the horny tissues.

<sup>1</sup> Holländische Beiträge. Bd. 1, S. 39 u. 126, and Mulder's Vers. ein. physiol. Chem. S. 542-579 [or English Translation, pp. 493-530].

<sup>2</sup> Observationes mikrochemicæ; diss. inaug. Dorpati Liv. 1848.

<sup>3</sup> Mikrosk. Anat. Bd. 2, S. 58-62, u. 85-88.



The horny tissues become gradually loosened when treated with cold or warm *water*. The epidermis is rendered so soft after prolonged soaking, as to admit of being easily broken down, and separated into individual cells, or smaller accumulations of them. The cells themselves are rendered more distinct; the extremely thin, irregularly formed epidermic plates appear somewhat swollen and faintly granulated. The nucleus, if one be present, becomes more distinct. The cylindrical or round cells of the *rete mucosum*, which contain a nucleus, and resemble vesicles expanded with fluid contents, are but slightly altered by the action of water.

The nails are on the whole very similar to the epidermis; however they only swell in water and become softer, without admitting of being triturated.

Horns and hoofs soften in water, especially on the application of heat, and then commonly develop a little sulphuretted hydrogen. The cellular structure cannot easily be recognized under the microscope, even after the tissue has lain for a long period in water; scarcely anything beyond fibres, which often appear to be torn, can be detected.

Water produces no visible alteration on whalebone or tortoise-shell, whether it be applied hot or cold, and however long it may be suffered to act upon either.

The best reagents for exhibiting the cellular structure of all these tissues are highly concentrated solutions of the *caustic alkalies*; in many cases *caustic soda*, as recommended by Kölliker, is preferable to *caustic potash*. A dilute solution of potash or soda, especially on the application of heat, acts, however, more rapidly upon the epidermis, and exhibits its cellular structure far better than the concentrated solutions. The concentrated solutions render the epidermic plates roundish, pale, and smaller; and it is only after a prolonged action that they swell, and distinctly exhibit their cellular form. Dilute alkalies convert the epidermic plates, in a short time, into oval or spherical clear vesicles, without a nucleus or granular contents. The cells of the *rete mucosum* show still more distinctly that the nuclei of the epidermic cells are sooner and more rapidly dissolved than their cell-membranes; for if the epidermic cells are exposed to the prolonged action of hot solutions of caustic alkalies, the cell-walls become dissolved, so that there only remains a small gritty and partially granular mass.

A solution of potash acts upon the substance of the nails in the same manner as upon the epidermis, converting it into a mass of colorless non-nucleated vesicles; but, according to Kölliker, a dilute solution of caustic soda brings into view the most beautiful polygonal or oval cells, with distinct nuclei.

The fibrous structure of cows' horn disappears under the prolonged action of a concentrated solution of potash, but no cells (especially nucleated ones) become distinctly visible until water has been poured over the object. After repeated neutralization with sulphuric, or even acetic acid, the cells generally appear in the form of oval or spherical vesicles without contents; the nuclei have consequently disappeared.

Whalebone consists, according to Mulder and Donders, who have subjected it to a very exact histo-chemical examination, of thin lamellæ,



which lie parallel to the outer surface, and to the tubular system which resembles the medullary canals. Each of the lamellæ consists of a number of compressed cells, which are brought into view by the action of water after they have been treated with concentrated caustic potash. In this case, also, the cell-wall resists the action of the reagents for a much longer period than the nucleus and the other contents.

The same observers were also the first who accurately examined tortoise-shell; they found that this tissue also breaks up into polygonal and oval cells on the application of caustic alkalies, although a much more prolonged action of the potash is necessary here than in the case of the above-described horny tissues. The cells are not very readily isolated, and it is only on the addition of water that they appear individually; they are without nuclei, but always contain a slight amount of granular substance. Moreover, independently of the cells, granular matter is always perceptible on the addition of water.

*Acetic acid*, even when concentrated, scarcely produces any action on epidermis, even after it has been softened by water; but by prolonged boiling with concentrated acetic acid, the scales become isolated, and swell into extremely pale, distended, but still somewhat flattened vesicles, entirely devoid of granules or nuclei. According to Kölliker, the walls of the epidermic cells do not dissolve, but only those of the cells of the *rete mucosum*.

Acetic acid acts upon the substance of the nails in the same manner as upon the epidermis, only with less rapidity; it generally causes the nuclei of the cells to come beautifully and prominently into view.

Cows' horn is very little affected by the action of concentrated acetic acid, even after prolonged boiling; and the microscope detects even still less alteration in whalebone or tortoise-shell that has been acted upon by this acid, although the former is converted into a gelatinous substance when boiled with the concentrated acid.

The epidermis very rapidly swells in concentrated *sulphuric acid*, exhibiting vesicular cells which become even more distended on the addition of water. The cells of the *rete mucosum* remain unchanged in cold sulphuric acid, but when boiled they are completely dissolved.

Concentrated sulphuric acid acts very slowly on the substance of the nails, but on the application of heat it brings into view, in the course of a few minutes, flat, polygonal cells, some of which are provided with nuclei.

It is only after the prolonged action of concentrated sulphuric acid for many hours that cows' horn gradually resolves itself into cells.

Whalebone is gradually converted, by this acid, into a mucous mass, in which the cell-membranes may be distinctly recognized.

Sulphuric acid exerts an equally inefficient action on tortoise-shell, and it is only after prolonged soaking or boiling with concentrated acid that cells can be detected in the gelatinous swollen mass; but even these are not isolated.

Concentrated *nitric acid* imparts a yellow color to most horny tissues, and isolates the cells of some, without, however, bringing them distinctly into view.

These tissues have, as we already observed, been subjected to ele-



mentary analyses, after having been previously treated with alcohol and ether. In order to exhibit the analogy of their composition, we subjoin the empirical results obtained from the analyses of Scherer,<sup>1</sup> Mulder, Tilanus,<sup>2</sup> and van Kerckhoff.<sup>3</sup>

	Epidermis.	Nails.	Horses' hoofs.	Cows' horn.	Whalebone.	Tortoise-shell.
Carbon,	50.28	51.09	51.41	51.03	51.86	54.89
Hydrogen,	6.76	6.82	6.96	6.80	6.87	6.56
Nitrogen,	17.21	16.90	17.46	16.24	15.70	16.77
Oxygen,	25.01	22.39	19.94	22.51	21.97	19.56
Sulphur,	0.74	2.80	4.23	3.42	3.60	2.22

These tissues differ also in the quantity of inorganic matter which they contain, but this difference does not vary much beyond 1%.

On boiling these tissues with a solution of potash, they generally, as we have already seen, become dissolved, with the exception of a comparatively very small residue: a large quantity of ammonia is developed, and the fluid contains much sulphide of potassium, the presence of which may be detected immediately after the first application of the alkaline fluid. When the alkaline solutions are saturated with acetic, hydrochloric, or other acids, precipitates are formed, which, according to Mulder, differ in the character of their composition. These deposits exhibit the property of adhering together, and forming almost resin-like masses on being heated in water. Mulder includes them amongst his protein-oxides.

It will scarcely be necessary, after this notice of the reactions exhibited by these tissues, to remark that our knowledge of their chemical history is still too deficient, in a histological point of view, to afford any satisfactory reply to the questions already propounded. For although Mulder,<sup>4</sup> in his most recent communications, has calculated formulæ from his experiments, and has been consequently led to regard all these tissues as *combinations of protein or protein-oxides with sulphamide*, this hypothesis must certainly be limited to one of the main constituents of the horny tissue only, and cannot refer to the whole mass. Every horny tissue contains at least three different kinds of substances: namely, the substance of the cell-membranes, which is so difficult of solution in alkalies; the cell-contents, including the nucleus, which dissolve more readily in alkalies; and the granular matters, consisting by no means of fat solely, which remain after the complete solution of some of these tissues, and are wholly insoluble in alkalies. These three chemically-demonstrable matters can hardly be regarded as isomeric or polymeric, and could not, even in that case, be brought forward in support of the sulphamide hypothesis.

The principal portion of every horny tissue is formed, as we have already observed, by the cell-membranes; their contents and the nucleus being so subordinate to these that the elementary analysis of such a tissue must be regarded as giving an average expression for the compo-

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 40, S. 1-45.

<sup>2</sup> Scheik. Onderz. D. 3.

<sup>3</sup> Ibid.

<sup>4</sup> Untersuch. übers. v. Völcker. II. 2, S. 272.



sition of these cell-membranes. They do not behave, however, as if they consisted of a sulphamide compound, for micro-chemical examination shows that the ammonia and sulphuretted hydrogen which we see developed on the macro-chemical treatment of these tissues with even very dilute alkalies, are not derived from the main substance—that is to say, the cell-membranes—but must originate in the cell-contents, or what is still more probable, in the connecting medium. If therefore a sulphamide of protein actually exists, it must be sought for in the tissue connecting the cells of the horny tissue, or, at all events, in their contents.

Although this connecting medium or true intercellular substance of the horny tissue can certainly not be detected by the microscope, it cannot possibly be wholly wanting; for independently of the fact that some of the above-described micro-chemical reactions testify to its existence, it would not be easy to understand how the cells formed in the mucous layer—the true matrix of this horny tissue—and driven forward, and gradually drying during the growth of the tissue, could entirely divest themselves of the adhering plasma. The cell-contents and the intercellular substance, the cell-wall and the nucleus, must stand in the active living cell, not only in a physical, but also in a chemical antagonism; and cannot possibly so far lose this diversity of character in the dried, atrophied, or disintegrated cell, as to form a chemically homogeneous substance, a simple sulphamide compound.

These remarks are, by no means, intended as an attack on Mulder, whose labors, even on this subject, are very valuable.

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## THE HAIR.

If we are scarcely able to arrive at a clear or distinct view of the chemical relations of the morphological elements of the comparatively simple horny tissues, we are still less able to do so in reference to the far more complicated tissue of the hair. On examining a hair, we find that there are at least three morphologically different substances brought under our notice; namely, the cuticle, the cortex, and the medullary substance.

The cuticle of the hair consists of plates arranged in the manner of tiles, one above the other; these are rendered more visible, according to Donders and Kölliker, by the use of those reagents which cause the cortical substance of the hair to swell, as, for instance, sulphuric acid, or caustic potash or soda. This scaly covering of the hair is not itself affected by such reagents, but by friction, individual scales may be isolated, which then appear extremely transparent and quadrangular, and are devoid of nucleus or other contents, although they are generated from perfectly normal cells, as is seen by examining the root of the hair. Kölliker<sup>1</sup> draws attention to the fact, that these epithelial scales

<sup>1</sup> Mikrosk. Anat. Bd. 2, S. 122.



on the hair differ from the other elements of the hair, and from all the constituents of other horny tissues, by their perfect insolubility in alkalies and concentrated sulphuric acid. We do not, however, agree with the supposition of Donders,<sup>1</sup> based on this mechanical relation, that these scales consist of a protein-compound.

The cortical or fibrous substance, constitutes, as is well known, the principal part of the hair. By the use of the reagents above referred to, namely, concentrated and gently heated *sulphuric acid*, this substance separates into flat, long fibres, which again divide into long, very narrow plates, having a dark, elongated nucleus. After prolonged digestion with a dilute *solution of potash*, the cortical substance dissolves, with the exception of these long, spindle-shaped nuclei. Even if these plates did not so plainly bear the stamp of cell-formation, they would readily be recognized as cells by examining the corresponding part of the root of the hair. These plates gradually shorten, and the elongated nuclei become thicker towards the root of the hair, and at length, in the lower part of the root, we find oval or roundish cells with oval nuclei.

Kölliker's observations show, that here also the chemical metamorphosis corresponds with the change of form, and that the cells of the cortical substance in the lower part of the root of the hair are not merely more easily affected by alkalies and concentrated sulphuric acid, than the fibre-cells of the same substance, but that they become swollen, and are in part dissolved even by acetic acid, which produces no effect on the other cells. According to Kölliker, there are within the fibrous substance certain cavities filled with air, and also accumulations of pigment-granules, the quantity of which varies with the color of the hair.

The inner portion of the hair is composed of the medullary substance, the nature of which cannot be recognized distinctly until the cortex has been rendered transparent by the action of alkalies. It consists of closely arranged rows of quadrangular, or more rarely, round cells, which, after the above-mentioned treatment with potash, are seen to contain dark fat-like granules, in addition to a clear roundish or oval speck (the rudiment of a nucleus). Many of these roundish gray granules are observed between these cells in fresh hair, that has not been treated with potash. Kölliker<sup>2</sup> has shown by several admirable experiments, that the dark granules which occur in colored as well as in white hair, are, for the most part, mere cavities filled with air occurring between and in the dried medullary cells.

Such are the most important histological grounds on which a rational chemical examination of the tissue of the hair must be based. Unfortunately, however, chemists have hitherto been unable to analyze the hair when considered from this point of view. We have some admirable observations on this subject by Scherer<sup>3</sup> and Van Laër,<sup>4</sup> who, although they have not investigated the chemical constitution of these parts in accordance with histological requirements, have yet exhibited the great analogy subsisting between the substance of the hair and other horny tissues, and have, moreover, successfully elucidated several important points involved in the inquiry.

<sup>1</sup> Vers. einer physiol. Chem. S. 572 [or English Transl. p. 523].

<sup>2</sup> Op. cit. p. 115.

<sup>3</sup> Ann. d. Ch. u. Pharm. Bd. 40, S. 58-63.

<sup>4</sup> Ibid. Vol. 45, pp. 147-183.



Scherer's elementary analyses of the hair correspond with those of Laër, excepting that there is a slight difference in the amount of hydrogen:

Carbon,	.	.	.	.	.	.	.	50.65
Hydrogen,	.	.	.	.	.	.	.	6.36
Nitrogen,	.	.	.	.	.	.	.	17.14
Oxygen,	.	.	.	.	.	.	.	20.85
Sulphur,	.	.	.	.	.	.	.	5.00

Like most other horny tissues, the hair dissolves, with the exception of a few fine molecules, on prolonged digestion in a solution of potash, there being at the same time a development of ammonia. The solution yields, on the addition of acetic acid, a slight deposit, which is a less oxidized protein compound than the far more considerable precipitate produced by the addition of a larger quantity of acetic acid; the latter, which is Mulder's deutoxide of protein, contains sulphur, and entirely agrees in its reactions with the substance which is obtained by the precipitation of the alkaline solution of other horny tissues on the action of acids. Mulder also regards the substance of the hair as a sulphamide compound. No conclusions can be drawn from any analyses hitherto made in reference to the nature of the individual constituents of the hair, as, for instance, its connective tissue, cell-contents, &c.

Notwithstanding the closest search, Laër was unable to discover any special pigment in the hair, although the microscopical examination of the cortical substance of differently colored hairs—that is to say, the existence of certain colored molecules—indicates the presence of a definite pigment. It is, however, well known that white hair is especially rich in air, and that to this circumstance it mainly owes its glistening color. Laër has further shown by numerous experiments on differently colored hair that the iron which is present, and to which Vauquelin had drawn attention, exerts no influence whatever on its color.

Laër found nothing but margarin, margaric acid, and olein in the fat extracted from hair; this fat had an odor of hair, or rather of sweat.

The amount of ash in the hair differs very much, although it does not bear any relation to the color, or any other property of the hair. Laër found from 0.54 to 1.85% of ash in the hair, and from 0.058 to 0.390% of peroxide of iron, but he could not detect manganese; he found, however, some silica with phosphate of lime. Von Gorup-Besanez,<sup>1</sup> who has made a very elaborate examination of the quantity of silica in the hair, found that the hair of animals contained, on an average, a much larger amount of this substance than human hair (the latter containing only from 0.11 to 0.22%, whilst the former contained from 0.12 to 0.57%).

Wool and bristles do not differ essentially in their composition from hair: the chemical constitution of feathers has, however, been found by Scherer to differ very considerably from horny tissues generally, and from hair especially. He found as the mean of two analyses of the beard and the quill, 52.448% of carbon, 7.161% of hydrogen, and 17.787% of nitrogen. Gorup-Besanez found considerable quantities of silica in feathers. He has treated, in a most careful and complete monograph, of the influence of the most varied physiological relations, such as sex, age, mode of life, species, &c., on the quantity of silica in the feathers.

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 66, S. 321-342.



## CONTRACTILE FIBRE-CELLS.

We are especially indebted to the recent investigations of Kölliker<sup>1</sup> for a more accurate knowledge of those histological elements which have hitherto been included in their aggregation in the animal body under the name of *organic* or *smooth muscular fibres*. These cells commonly appear in the form of long fusiform narrow fibres, with finely attenuated extremities, frequently also in that of elongated, quadrangular, or club-shaped plates, whose margins are occasionally fringed. The majority exhibit, especially when acted upon by acetic acid, a prominent nucleus, which is either cylindrical or baton-like. The nucleus appears to be perfectly homogeneous, a nucleolus being scarcely ever found in it. The substance of the cell occasionally exhibits pale or dark granules, which are partially arranged in rows corresponding to the axis of the fibres, but in other respects this is also homogeneous. It cannot be decided with certainty whether it is surrounded by any special cell-membrane. These fibre-cells form by the lateral juxtaposition of their extremities the bundles of smooth muscle which are visible to the naked eye, and occur, amongst other places, in the intestinal canal. Kölliker divides the smooth muscle into the *pure* and *mixed* variety, according as the cells are arranged in larger quantities so as to form bundles and membranes, or are merely interspersed amongst other simple tissues; to the former class belong those which have been long known, and in which Henle<sup>2</sup> first recognized the presence of true fibre-cells, namely, the muscular coat of the lower half of the œsophagus, of the stomach and intestinal canal, the nipple, the bladder, the prostate gland and vagina. The coarser bundles of these muscles are likewise held together by connective tissue, but they are not so thoroughly intersected by it, and divided into separate fibrillæ, or smaller bundles of fibrillæ, as the mixed smooth muscles. The latter, which often appear as if they were scattered over connected tissue, embedded, as it were, in the elastic and nuclear fibres, were first shown by Kölliker<sup>3</sup> to occur principally in the trabecular tissue of the spleen. They have since been discovered in many other compound tissues, which had been known as contractile and had been carefully examined with reference to their histological elements, without our recognizing these cellular parts as identical with organic muscular fibres; especially in the tunica dartos, in the middle coat of the arteries, in the choroid coat of the eye, in the veins and lymphatics, in the corpora cavernosa, the prostate gland, the Fallopian tubes, the uterus and urethra; also in many mucous membranes, and especially around the intestinal villi (Brücke). In the trachea, the bronchi, the ureters and vasa deferentia, as well as in the internal muscular tunic of the testicle, they approximate more closely to the pure smooth muscles. Finally, the smooth muscles are never enclosed by a true sarcolemma.

These histological structures do not serve the animal organism by their physical properties like the elastic fibres, in conjunction with which they

<sup>1</sup> Zeitsch. f. wiss. Zool. Bd. 4, S. 48-87.

<sup>2</sup> Allg. Anat. S. 576.

<sup>3</sup> Mittheilungen der Zürich. naturf. Gessellschafft, 1847.



so frequently occur; but it is to them that those tissues, in which they were formerly either only imperfectly, or not at all recognized, owe their contractility *under the influence of the nervous system*. The admirable labors of Ed. Weber<sup>1</sup> have yielded us the most valuable information in reference to this subject, and have clearly elucidated the essential differences existing between the action of the contractile organs and that of the animal muscles. Weber has shown that in the case of almost all the organs which are provided with these cell-fibres, a mechanical or chemical irritant, such, for instance, as the employment of a galvanic current, generated by the rotatory apparatus, induced only a gradual, and, at first, a very limited contraction, which, however, became diffused, after a time, over a larger portion of the part in question. Neither the bundles touched by the pole, nor the parts depending upon the excited nerves, contracted in any very appreciable period after the application and interruption of the galvanic current, but the adjacent bundles became successively affected, and a movement was thus induced which did not finally disappear for a long time. Ed. Weber succeeded, both independently and in conjunction with E. H. Weber,<sup>2</sup> in detecting the contractions in veins and arteries of medium and small calibre in nearly the same forms as they occur in other organs. Kölliker<sup>3</sup> also has recently observed them in the bloodvessels and lymphatics of man.

Ecker<sup>4</sup> and Kölliker<sup>5</sup> have, however, fully shown, by comparative demonstrations of the elements of motion in the lower animals, that this contractility, or property of contracting on the application of stimuli to the nerves, is not connected in the animal organism solely and exclusively with the fibre-cells of the smooth muscles, but appertains to other histological forms, such as amorphous membranes, tubes, vesicles, filaments, &c.

Our interest is naturally increased, as we here find ourselves dealing, for the first time, with a form of animal tissue which exhibits vital activity, or, in other words, moves through the influence of the nerves; and we find, moreover, that the chemical relations are here wholly different from those which we have hitherto noticed in those tissues of the animal organism which act solely by their physical properties.

The following remarks embody all that is known from my own observations, and those of Donders,<sup>6</sup> Schultze,<sup>7</sup> Paulsen,<sup>8</sup> and others, in reference to the *micro-chemical reactions* of these fibre-cells.

The most generally known of these is the action of *acetic acid*, which, when employed in a more or less diluted state, causes the substance of the fibre to swell, whilst it increases its transparency; the nucleus, which was pale and scarcely visible, now stands out more prominently, and commonly presents the appearance of a sharply outlined, baton-shaped, often somewhat bent and even twisted dark body, in which no nucleolus can be seen. According to Kölliker, acetic acid frequently causes the nuclei to contract in a slight degree; not unfrequently, it induces an

<sup>1</sup> Handwörterbuch der Physiologie. Bd. 3, Abth. 2, S. 1-122.

<sup>2</sup> Berichte der k. sächs. Gess. d. Wiss. 1849. S. 91-96.

<sup>3</sup> Zeitsch. f. wiss. Zool. Bd. 1, S. 257-260.

<sup>4</sup> Op. cit. pp. 213-217.

<sup>5</sup> Op. cit.

<sup>7</sup> Op. cit.

<sup>4</sup> Ibid. pp. 218-245.

<sup>3</sup> Op. cit.



augmentation in their breadth, rendering the nuclei paler instead of darker.

Concentrated acetic acid completely dissolves the fibre, until even the nuclei are gradually rendered indistinct. Fat-globules and molecular granules are then the only things to be discovered between the hyaline fibres of connective tissue.

*Extremely dilute hydrochloric acid* (1 part of anhydrous acid in 3,000 parts of water) behaves in almost the same way as dilute acetic acid, although, according to my experience, in a more decisive manner. The nuclei appear more distinct and dark, the substance of the cell becomes very pellucid, but at the same time assumes a curled or wave-like appearance; the nuclei lying in a curve of the fibre present, collectively, a crescentic appearance, and their extremities are in some cases twisted in opposite directions. By the prolonged action of the acid the substance of the cell is dissolved, leaving, in addition to amorphous granules, nothing but nuclei, which now, for the most part, assume somewhat the form of cucumber-seeds. The fibres of connective tissue, which are occasionally present, appear as very transparent, broadened, perfectly homogeneous bands. I was much surprised to find, on examining organic muscles which had been frequently washed in water, and macerated for a long time, that no nuclei could be rendered visible either by the dilute acetic or hydrochloric acid. Henle<sup>1</sup> was led to infer, from the result of his experiments, that the superficial layer always soonest undergoes decomposition, and hence its nuclei are first destroyed.

The fibres shrivel up very readily in *concentrated hydrochloric acid*, but the nuclei are not rendered more transparent. After a prolonged exposure to the action of the acid, entire, finely striated bundles are brought into view. Water causes the fibres to swell, and form thick, sharply outlined strings, in which state they resemble the representations (or rather the diagrams) formerly made by histologists of normal organic muscular fibres.

*Concentrated sulphuric acid* renders the bundles of fibres more transparent and gelatinous; after the repeated addition of water the bundles contract, and again appear distinctly fibrous (Donders). No nuclei can be distinctly recognized, but I have frequently observed in preparations which had been treated with concentrated sulphuric acid, and after the repeated addition of water, the existence of coarse granules of an oval or irregularly rounded shape and isolated fat-globules, whilst the other histological elements had wholly disappeared.

The fibre-cells become somewhat contracted in *concentrated cold nitric acid*, and exhibit a curled appearance. The smaller bundles are divided into isolated fibrils of a pale-yellow color; no nuclei can be detected with certainty; the fibres of connective tissue remain smooth and narrow, and are not colored yellow. The yellow color appears in a remarkably beautiful manner in the fibre-cells on applying caustic ammonia to the object after it has been treated with nitric acid. The fibre-cells are perfectly dissolved in boiling concentrated nitric acid, whilst nothing appears in the fluid beyond a few scattered fat-globules.

<sup>1</sup> Jahresber. der ges. Med. 1851, S. 44.



A concentrated *solution of chromic acid* renders the bundles of smooth muscle so perfectly soft that they break up on the slightest pressure into greenish-yellow, somewhat curled rods, which nowhere exhibit, with certainty, even a trace of a nucleus.

The prolonged action of a *dilute solution of soda* loosens, softens, and finally dissolves the bundles of fibres, leaving only fine long threads, which belong to the nuclear fibres. At the same time a number of coarse granules of a very irregular form are brought into view, whose chemical nature could not be closely investigated. There were no nuclei to be detected.

A *concentrated solution of potash*, after prolonged action, causes the almost total disappearance of the individual fibres, there remaining only rows of granules. On the addition of water, everything is dissolved excepting some minute filaments (in the same manner as by the action of dilute soda).

The fibre-cells undergo no visible alteration in a solution of moderately concentrated *carbonate of potash*.

On digesting a carefully prepared and well-washed portion of the muscular coat of the stomach of a pig for a prolonged period (from 18 hours to 3 days) in a solution of 6 parts of *nitrate of potash* in 100 parts of water, at a temperature of 30° or 40°, no essential change will be observed in the individual smooth muscular fibres; as in the case of carbonate of potash, they simply swell, and become somewhat more translucent. No nuclei can be discovered in either case. The muscular substance itself becomes somewhat harder.

*Millon's reagent* (see vol. i. p. 291) colors the whole mass of the bundles intensely red, but when seen under the microscope the individual fibre-cells do not appear very highly colored.

An *aqueous solution of iodine* causes the fibre-cells to shrivel up, renders the nuclei less distinct, and imparts a yellow color to the whole mass. The nuclei cannot be brought into view even by the repeated application of a dilute acid.

The bundles of fibrils become gelatinous in *concentrated phosphoric acid*. Under the microscope, fibrillation is still perceptible, which, however, becomes more distinct on the addition of water to the object. Here, too, we have a granular matter which does not, however, appear to contain a nucleus. The granules precisely resemble those which are brought into view on the addition of water, after the fibres have been treated with concentrated hydrochloric acid or a potash solution.

If the middle coat of the arteries, or the muscular coat of the stomach or intestinal canal, be treated with concentrated acetic acid, after having been cut in shreds and carefully rinsed, and afterwards boiled for a considerable time in water in order to remove the gelatigenous connective tissue, a substance is dissolved which is precipitable both by yellow and red prussiate of potash. This may be again precipitated by neutralizing the acetic acid; it contains a considerable quantity of sulphur.

The substance of the fibres of smooth muscle behaves towards very dilute hydrochloric acid (1 p. m.) in the same manner as Liebig showed was the case with the striated fibres. (See note to vol. i. p. 320, on

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 73, S. 125-129.



*Syntonin*, in the Appendix.) Thus, for instance, if the muscular coat of the stomach (of the pig), after being cut in shreds and thoroughly rinsed with water, be treated with hydrochloric acid of this dilution, the fibres of the smooth muscles become dissolved; on neutralization of the acid, the solution behaves in precisely the same manner as the hydrochloric-acid solution of syntonin from striped muscle: the flakes, which gradually separate, dissolve very readily in an excess of an alkaline solution, and likewise in lime-water; this solution coagulates on boiling, like albumen; if, however, too much lime-water be added, the solution merely becomes opalescent, and it is not till it is neutralized with acetic acid that we have a copious curd-like precipitate. The original hydrochloric-acid solution of the fibrils is strongly precipitated by concentrated solutions of the neutral salts of the alkalies and alkaline earths; as, for instance, chloride of potassium, sulphate of soda, hydrochlorate of ammonia, chloride of calcium, and sulphate of magnesia.

I obtained precisely the same reactions on treating the well-washed middle arterial coat of the ox, the bladder of the pig, and the tunica dartos of the bull in a similar manner with dilute hydrochloric acid.

No sarcolemma can be chemically demonstrated in the organic muscles. Kölliker thought he could sometimes perceive indications of a cell-membrane in individual fibre-cells, but I have been unable to demonstrate its presence by any chemical reagents. The nature of the nucleus, which is insoluble in acetic and dilute mineral acids, has not yet been closely examined.

C. Schmidt<sup>1</sup> attempted some years ago to make an elementary analysis of smooth muscle (the large thoracic muscles of the Cockchafer and the adductor muscles of *Anodonta cygnea*), for the purpose of comparing its composition with that of striped muscular fibre. He found that both kinds of muscle were perfectly identical in composition (52·3% of carbon, 7·2% of hydrogen, and 15·3% of nitrogen). We think that this coincidence scarcely proves anything more than the insufficiency of our elementary analyses; for supposing that the fibre-cells of smooth muscle were identical with the fibrils of striped muscle, it appears singular that the presence of sarcolemma and of tracheal ramification in the one tissue, and of fibres of connective tissue in the other (that is to say, of foreign substances, which cannot be removed by the most careful preparation), should not induce any difference in the results of the analyses. We do not, therefore, think that we are justified in drawing a conclusion in favor of the identity of composition of the organic elements of motion from these analyses, although they were undoubtedly conducted in accordance with the best chemical methods.

If, as it would appear, smaller quantities of carbon and nitrogen have been found to be present in the tissues which have been analyzed than in fibrin and albumen, it is more probable that the difference is rather owing to the amount of connective tissue and of chitin, than to a different composition of the contractile elements themselves.

We have, therefore, regarded it as more in accordance with the induc-

<sup>1</sup> Zur vergleichenden Physiologie der wirbellosen Thiere. Braunschweig, 1845, S. 32-69 [or Taylor's Scientific Memoirs, vol. 5, pp. 14-28].



tive method to institute, for the purpose of comparison, various elementary analyses of this substance, which is extractible from every contractile tissue by dilute hydrochloric acid, first precipitating it by a dilute solution of soda, and then extracting it with alcohol and ether. Although we have not so far deceived ourselves as to regard as perfectly pure this matter, which, at all events, is mainly derived from the substance of the contractile fibre-cells (such a supposition being controverted on chemical as well as histological grounds), we yet believe that the analyses of this matter, obtained from different compound contractile tissues, are better adapted for comparison, and lead to more reliable results, than the analyses of the complex tissues themselves. And in point of fact, this cell-substance, which is soluble in water containing hydrochloric acid, invariably presented the same composition, whether it had been obtained from the muscular coat of the stomach of the pig, or the middle arterial coat of the ox, or the tunica dartos, or the bladder. It also appeared that this substance, which is derived from smooth muscular fibres, has the same composition as the analogous substance derived from striped muscular fibres, which was first obtained by Liebig and analyzed by Strecker. As we shall have to consider more fully in another portion of this work these analyses of my own, I will here limit myself to an enumeration of the mean results, merely for the purpose of comparison with the fibrin of the blood and that of the animal muscles; there were found on an average 53.84% of carbon, 7.30% of hydrogen, 15.81% of nitrogen, and 1.09% of sulphur.

This substance further corresponds with the protein-body extracted from striped muscle in being perfectly insoluble in nitre-water (containing 6% of  $\text{KO.NO}_3$ ), as well as in carbonate of potash. Although the above-mentioned micro-chemical reactions demonstrated this point with tolerable certainty, the following experiments were additionally made. The muscular coat of the stomach was reduced to fine shreds and rinsed in water as long as any coagulable substance continued to dissolve; a portion of the rinsed mass was then digested for an hour in a solution of 1 part of carbonate of potash in 10 parts of water; the filtered fluid showed only traces of a dissolved protein-body. Another portion of the muscular coat, which had been freed from albumen, was digested for two days in the above-mentioned nitre-water at a temperature of  $37^\circ$ ; at the end of that period there was not a trace of any substance coagulable by heat or acetic acid.

As this substance appears, according to the present state of our knowledge, to be altogether peculiar to contractile fibre, as it differs essentially from the fibrin of the blood, and lastly, as it does not merely occur in the true muscles, we have thought that it would be desirable to distinguish it from ordinary fibrin by some peculiar designation, and we have suggested as appropriate the name of *syntonin* (from  $\sigma\upsilon\nu\tau\epsilon\acute{\iota}\nu\epsilon\iota\nu$ ).

It is probably a very significant fact, that the more active organs of the animal body are bathed in a fluid which differs very essentially from an ordinary transudation from the blood, or from the blood-plasma itself. Berzelius long since directed attention to the muscular fluid, and Liebig's admirable investigation of this subject is well known. According to



Liebig's discoveries, a fluid differing in every respect from the plasma of the blood surrounds the fibres of the striped muscles; and the same is the case with the fibre-cells of the smooth muscles. M. S. Schultze<sup>1</sup> found, on examining the middle coat of the arteries, that it was permeated by a fluid very rich in casein. He found in 100 parts of the well-dried annular coat of the thoracic aorta from 17.4 to 23.1% of soluble constituents, amongst which there were 7.24 parts of casein. He also found in the middle coat of the carotid, which, as is well known, contains a smaller quantity of elastic fibre, but far more contractile fibre-cells than the aorta, 39% of soluble constituents, of which 21 parts were casein. Moreover Schultze found that this interstitial fluid had a faintly alkaline reaction, and contained in addition to the casein and salts, small quantities of two substances, one of which was coagulable, and the other non-coagulable by heat.

My own observations on the juice permeating the contractile tissues have shown that the fluid obtained from the muscular coat of the stomach of the pig has a distinctly acid reaction, although not in so intense a degree as that derived from the striped muscle; the analogous fluid of the middle coat of the arteries (the ascending and descending aorta, and the carotid of the ox) reddened litmus paper slightly, but quite decidedly. The fluid from the tunica dartos exerted no reaction on vegetable colors. Schultze found that the juice of the middle coat of the arteries was alkaline, which may be owing either to the admixture of the alkaline fluid of the cellular tissue, or to the occurrence of incipient decomposition. The middle coat of the arteries and the tunica dartos yield more casein and less albumen than the muscular coat of the stomach of the pig; the latter is as rich in albumen as is the juice of the animal muscles.

Creatine occurs in much smaller quantity here than in the juice of the striped muscles; but as the inadequate amount of this substance precluded the possibility of making any elementary analysis, the crystallo-metric determination constituted the only evidence of its presence. Besides a small quantity of lactic acid, we find acetic and butyric acids. The ratio of the potash to the soda was as 38 : 62 in the juice of the smooth muscles of the stomach, and as 42 : 58 in that of the middle coat of the arteries. The soluble phosphates were to the insoluble as 82 : 18 in the muscular fluid of the stomach, and as 79 : 21 in the fluid of the middle coat of the arteries.

Siegmund<sup>2</sup> has recently found creatine, acetic acid, and formic acid in the juice of a pregnant uterus; and Walther<sup>3</sup> has, under my superintendence, extended the above-mentioned micro-chemical investigations regarding the fibre-cells, and the chemical analysis of the juice by which they are moistened.

All these relations, which are at the present time undergoing a more accurate investigation, show that there exists, at all events, a very great analogy between the juice of the striped muscles and that of the fibre-cells. If we concur in the doubts expressed by some of the most dis-

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 71, S. 277-293.

<sup>2</sup> Verh. der phys.-med. Ges. zu Würzburg. Bd. 3, S. 50.

<sup>3</sup> Diss. inaug. med. Lips. 1851.



tinguished histologists regarding the existence of these fibre-cells in the middle coat of the arteries, in which Kölliker believes he has found them, it would, at all events, seem to be proved, in regard to the chemical view of the case, that the fibrils of the striped muscles, like the smooth muscles and the contractile tissues, not only contain a solid substance which is chemically identical in all, but that this textural element is invariably surrounded by a juice which differs essentially from all other animal juices by its acid reaction, the abundance of its potash-salts and phosphates, and by its containing creatine, &c. It remains for a more exact investigation to establish with greater precision the differences which the provisional analyses indicate between the constitution of these juices in the different contractile tissues.

Although we have already sufficiently indicated the course to be pursued in the investigation of contractile tissue, we will briefly review the mode of proceeding. If we are once assured that the object which we are examining is a tissue composed of various histological elements, which, moreover, is permeated by a fluid differing in all respects from the blood-serum,—whether such contractile tissue be obtained from the middle arterial coat, the muscular layer of the intestine, the urinary bladder, the tunica dartos or the uterus,—our first endeavors should of course be directed to the removal of the unimportant constituents from the fibres of the smooth muscle. Unfortunately, we are quite unable to obtain perfectly pure fibre-cells free from nerves, connective tissue, and nuclear and elastic fibres; we are therefore compelled to have recourse to various indirect means of obtaining a knowledge of the chemical nature of this histological element. When the tissue has been carefully reduced to minute shreds, and rinsed in lukewarm water until no trace of organic matter is longer visible in the fluid that is poured over it, two methods present themselves for our choice in preparing the substance of the fibre-cells for chemical examination. We may dissolve either the connective tissue or the fibre-cells; either method, however, is open to serious objections. No other solvent than boiling water should be used for dissolving the connective tissue when an albuminous tissue is present; and, even then, we only attain our object in a most imperfect manner; for, in the first place, the fibrinous substratum of the cells is reduced to a state of coagulation, which precludes the possibility of separating this substance from the nuclei of the fibre-cells; secondly, the fibre-cells themselves are attacked by the prolonged boiling which is necessary for the purpose of effecting as completely as possible the solution of the connective tissue (a substance corresponding to Mulder's tritoxide of protein, dissolving with the gelatin, as Schultze formerly remarked); thirdly and lastly, notwithstanding all boiling, the nuclear fibres of the connective tissue remain undissolved (as has been often already mentioned), and even when no true elastic fibres are interspersed amongst the contractile tissue, constitute a residual mass which cannot be regarded as a chemically pure body. The coagulated substance of the smooth muscles does not dissolve readily in alkalies, and cannot, therefore, be very perfectly separated from the substance of the nuclear fibres, as this also partially dissolves in alkalies, more especially on the application of heat. The quantity of sulphur contained in the con-



tractile fibre-cells cannot therefore be determined with certainty by this method, nor is the method of dissolving the substance in alkalies, and precipitating it by acids, to be unconditionally recommended; if, however, we would analyze for its sulphur the substance after being only boiled in water, without having been previously dissolved in alkalies, we should in every case find too small a quantity of sulphur; for the nuclear fibres augment the matter which is free from sulphur, and some of the sulphur of the substance also escapes on boiling it in the air.

It is better, therefore, for these reasons to endeavor to dissolve the substance of the fibre-cells, and we may employ as a solvent dilute alkaline solutions, moderately dilute acetic acid, or water containing hydrochloric acid. I have found that the most efficacious of these three solvents is the very dilute hydrochloric acid (containing from 0.1 to 0.5% of the acid). A dilute solution of soda renders the connective tissue too gelatinous, and very probably also dissolves some of the nuclear substance of the contractile fibre-cells, and makes the determination of the sulphur uncertain. Acetic acid is better, but the first of the objections advanced against the use of the soda solution exists also in the case of this acid. The hydrochloric-acid solution must be regarded as a tolerably pure solution of the substance of the cells of the contractile tissue, as the connective tissue, the nuclear fibres, and the nuclei of the fibre-cells themselves remain undissolved. The substance of the fibre-cells is thrown down from this solution by careful neutralization in the form of a soft gelatinous mass, which is perfectly adapted for the determination of the sulphur and for the elementary analysis generally, after it has been extracted with alcohol and ether. The substance composing the nuclei of the fibre-cells cannot be obtained in an equally pure state, since its best solvent is a dilute solution of soda, which always dissolves some of the connective tissue, or at all events, occasions the gelatinous parts to pass through the filter.

We abstain from making any remarks on the method of examining the parenchymatous fluid, partly because we have already frequently spoken of the mode of determining the individual constituents of the animal fluids, and partly because we shall have occasion to revert to this subject under the head of the Striped Fibres.

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## TRANSVERSELY STRIPED MUSCULAR FIBRES.

These textural elements, which have also been termed *animal* (Breschet), or *articulated* (Treviranus) muscular fibres, or *bundles of contractile fibrils* (Kölliker), are peculiar to those organs of motion which, at least to a certain extent, are *subject to the will*.

If we examine any muscle (as, for instance, one of the abdominal muscles) in both longitudinal and transverse sections, we perceive, even with the naked eye, that it consists of a more or less considerable number of parallel, longitudinally striped bundles (the secondary muscular bundles), which are surrounded by connective tissue (*perimysium*



*internum*), serving to unite them together. In this connective tissue we may trace, on a careful examination, a few bloodvessels and nerves; but when we examine these striped bundles under the microscope, we perceive that the longitudinal stripes are dependent on yet finer bundles, which may be recognized under higher magnifying powers as roundish, irregularly flattened cylinders or strings, whose transverse section occasionally appears hexagonal, and which exhibit distinct transverse striation. A more careful examination of these very fine, transversely striped bundles (primitive muscular bundles) shows that they consist of closely approximating, necklace-like filaments, which are closely surrounded by a homogeneous smooth investment (*sarcolemma*). This investing membrane of the different primitive bundles is held together by filaments of connective tissue; between the sarcolemma of the different bundles we find the well-known vascular network of the muscles, with its generally rectangular meshes, and the tortuous windings of the nerves. It is not a settled point whether the sarcolemma in the developed muscle contains nuclei; that is to say, whether the nuclei, which are apparently perceptible in it, appertain to it, or whether they lie under it, and belong to the muscular fibrils of the primitive bundles, and therefore to the contents of the sheaths of sarcolemma; at all events, we may perceive in the sarcolemma roundish nuclei, frequently resembling drops of oil, or, more rarely, having a spindle-like form, of which some at all events, according to Schwann and Kölliker, are situated between the sarcolemma and the muscular fibrils, but are not intimately connected with any of these parts. We find, as has been already observed, that the substance enclosed in the sarcolemma always presents a strongly marked transverse striation, and generally a less distinct longitudinal marking; so that the primitive bundles might just as readily be supposed to consist of superimposed disks (Bowman) as of long, transversely striated fibrils. In muscles, however, which have been submitted to chemical treatment (whether simple boiling or the action of reagents), we very frequently see a separation or disintegration of the contents of the sarcolemma into constricted filaments, which has led most histologists to regard these contents as composed of fibrils. It is very generally believed that the constrictions of the transversely striated primitive fibrils stand in the closest relation to the function of the muscles; on making a microscopical examination of the muscles of just killed or still living caterpillars, we perceive the dark stripes approach one another, and again separate. In paralyzed muscles (which have not yet undergone fatty degeneration) these stripes are observed to be more widely separated from one another than in healthy muscles, &c.

Although several very admirable investigators will not admit that these observations afford sufficient evidence of the essential part which these constrictions of the elementary fibrils take in muscular contraction, the constrictions, or, perhaps more correctly speaking, varicose dilations, which are so constantly observed in this group of animal fibres, cannot be wholly purposeless or accidental, for, granting that our theory of the contraction of the fibrils is very complicated, the want of homogeneity in the fibres must exert some influence on their contraction. The elementary fibres are assuredly not formed of an entirely homogeneous



substance; for in the first place, we occasionally see the muscular fibre break up transversely into discs (Bowman<sup>1</sup>) or into parallelopipeds, and each separate fibril into smaller linear sections, and, finally, into serially arranged granules (see vol. i. p. 520). The continuity of the elementary fibres is therefore readily destroyed in the direction of the contractions. On the other hand, the muscular fibrils, as I perceived long before I was acquainted with Bowman's observations on the subject, undergo certain alterations of form by which they are either shortened or lengthened, when subjected to the action of water and other substances. I treated the muscular fibres of the extremities of tolerably developed embryos of the common mouse (*mus domesticus*) with different chemical reagents; I found that the addition of water had the effect (as Bowman has very often observed) of rendering the striation more indistinct, and sometimes even causing it wholly to disappear; but when very saturated solutions of neutral salts, such as chloride of calcium, sulphate of soda, hydrochlorate of ammonia, or of sugar, &c., were added, the transverse striæ which were originally at a relatively great distance from one another, came nearer together, the shortening being readily appreciable by the micrometer. The transverse striæ themselves appeared to be sharper and more distinct, but separated again more widely from one another when the saline solution was washed out as much as possible by water; and although their outlines grew fainter, they could not again be made wholly to disappear. This observation, which was frequently repeated, proves, at all events, that the muscular fibrils have a different capacity for imbibition at their varicosities and constrictions, depending upon a difference in the aggregation of their smallest mechanical, if not chemical, particles. The elementary fibre of the animal muscles cannot therefore be considered as homogeneous; nor can we regard the phenomena which are produced on the application of saline solutions, as the effect of simple contortions of the fibres, such as Henle observed in connective tissue.

If the physical examination of the muscular fibrils shows that they are not simple, homogeneous, partially folded strands, this is still more distinctly proved by a chemical investigation, as it destroys the fibres; for whatever may be the reagent employed, the fibrils are always unequally dissolved. First of all, there are formed small filaments resembling vibriones, which, together with fat-globules, resolve themselves into a number of molecular, often serially arranged granules. If we regard the primitive fibres as not homogeneous, this must be still more the case with the primitive bundles. We have already referred to the nuclei on the surface of the muscular fibres; the elementary fibrils themselves, however nearly they approximate to one another, or however closely they are invested by the sarcolemma, are yet connected by an intermediate substance, which is itself of a double nature; for, in the first place, certain distinguished microscopists have observed, on transversely cutting through a muscular fibre, that there is a granular and molecular substance lying between the extremities of the individual fibrils; and secondly, we can scarcely seek for the juice, which has been so admirably investigated by Liebig, elsewhere than within the sarcolemma of the primitive bundles, which it appears to permeate.

<sup>1</sup> Philosophical Transactions for 1840, p. 457.



We must, therefore, separate our chemical investigation of the animal muscles into several sections; of these, passing over the ever-present connective tissue of the perimysium as not at present concerning us, the numerous ramifications of bloodvessels, the nervous twigs, and the sparingly scattered lymphatics, the micro-chemical investigation of the sarcolemma and of the cylindrical bundles of fibrils within it demands our special attention; from this we will pass to the macro-chemical reactions, which can be exhibited with muscular tissue, terminating our inquiries with the examination of the parenchymatous juice.

Very dilute *acetic acid* (1 part of acetic acid in 5000 parts of water) causes the primitive bundles of the muscles to swell very rapidly, and to assume an extremely pale color; after a prolonged action of two or three or even four days, we observe that the bundles are much swollen, that the transverse striæ are very distinct, and approximate more closely to one another, and that the nuclei parallel to the long axis of each bundle are very narrow, elongated, granular, and not sharply defined; many of them are constricted at four or five points, whilst others protrude with the muscular substance from the sarcolemma, and are scattered about transversely and obliquely in relation to the axis of the muscular bundles. There is never any appearance of longitudinal striæ (indicating the existence of primitive fibrils) in the muscular substance itself; on the other hand, a transverse striation may often be distinctly perceived.

Fig. 27.



Striated muscular fibre (from the abductor muscles of the rabbit), treated with acetic acid.

At the cut extremities of several primitive bundles we may frequently recognize portions of muscular substance, corresponding to an individual transverse striation, and which, without having any distinct form, such as Bowman has delineated, clearly show the division of the muscular fibre in the direction of the individual transverse striæ; under favorable illumination, and by the help of the diaphragm, the flat sections are seen to present a net-like appearance, resembling lines which intersect one another at acute angles, and are somewhat swollen at the points of intersection. The transverse separation of the muscular fibres may often be recognized by the fact, that the half only of a disk corresponding to the



transverse cleavage is torn off, whilst in some cases one of the transverse disks of a muscular fibre is loosened and coiled back on itself; or again, a muscular fibre is somewhat bent and torn up at its convexity into separate transverse disks, causing them to diverge like the leaves of a badly bound open book.

Concentrated acetic acid produces the same effect after from 5 to 10 hours' action, as the dilute acid does in a much longer period.

The *sarcolemma* is not altered either by dilute or concentrated acetic acid; at the parts where it has been deprived of its contents, it presents the appearance of a structureless membrane without nuclei, but interspersed at different points with fat-globules.

Very *dilute hydrochloric acid* (1 part of acid in 12,560 parts of water) produces nearly the same effect on the muscular bundles as acetic acid, rendering them paler, whilst the nuclei come prominently forward; the muscular fibres do not, however, swell to so great an extent as when dilute or concentrated acetic acid is used; the transverse striations are sharply marked, but a transverse cleavage of the fibres is not so frequent; there is no appearance of longitudinal striations (primitive fibrils). The mode of action of a less dilute hydrochloric acid will be considered at a subsequent page.

Donders<sup>1</sup> maintains that by prolonged digestion in dilute hydrochloric acid, the *sarcolemma* (at all events, in the primitive bundles of the heart) is rendered very distinct.

*Concentrated hydrochloric acid* converts moderately sized pieces of muscle, after a short time (8 hours), into a viscid mass, which can be easily stirred in the fluid surrounding it. We discover under the microscope, that the fluid contains rather short parallelopipeds, having a very distinct and often sharply defined transverse striation. Although longitudinal striæ may be detected here and there in the fibres, the primitive bundles are only torn or cleft in a transverse direction; but whilst the transverse striæ always follow a tolerably parallel course, they frequently exhibit several interstices or cavities which do not extend through the whole bundle, but give it the appearance of being strongly marked at intervals by black lines. The transverse striæ in many of these parallelopipeds are only indicated by the presence of fine granules arranged in a more or less decidedly parallel direction. Some of these strongly granulated fibres appear as if they had been eroded on their longer sides; but there is never any appearance of the bundle being divided longitudinally. The substance of the fibres is rendered intensely yellow by an aqueous solution of iodine, and the addition of water causes it to swell to a trifling extent only. Nuclei and *sarcolemma* can only be recognized at occasional spots, and for the most part after the addition of iodine.

In *concentrated nitric acid* the primitive bundles dissolve into yellowish parallelopipeds with a sharply defined transverse striation, after an interval of time varying from one to ten hours. The bundles are cleft only in a transverse direction, exhibiting larger or smaller openings between the striæ, in the same manner as when they are exposed to the action of concentrated hydrochloric acid; that is to say, two adjacent

<sup>1</sup> Nederlandsch Lancet. 3 S. 1 J. S. 559.



transverse disks are more separated from one another at one point than at another, and are only partly in contact. At some of the smaller sections of the bundles, all the transverse disks diverge from one side in a brush or tuft-like manner. There is never any trace of longitudinal striation.

Very dilute nitric acid exerts the same action as dilute hydrochloric acid.

In concentrated sulphuric acid, the muscular fibres, after from ten to thirty hours' action, are resolved into a reddish-purple viscid fluid, in which, at a first glance through the microscope, we can only perceive longer or shorter filaments; a more accurate examination, however, shows that they are very thin hone-shaped or fusiform plates. The red color disappears on the addition of water, when a grayish-yellow coagulum is deposited, which appears perfectly amorphous, as seen under the microscope, exhibiting merely granular patches, in the same manner as we commonly observe with the coagulated protein-bodies.

Sulphuric acid, when somewhat diluted, exerts precisely the same action as concentrated hydrochloric acid, bringing the transverse striæ very distinctly into view. The longitudinal striæ which Mulder and Donders saw in these cases, I could scarcely recognize with any degree of distinctness even after the prolonged action of this acid.

Very dilute sulphuric acid acts in the same manner as acetic acid, or extremely dilute hydrochloric acid.

A concentrated solution of chromic acid causes the muscular fibres to be resolved, after prolonged action, into parallelopipeds of an intense yellow color, some of which exhibit a sharply defined longitudinal striation without any perceptible transverse striæ, whilst others are characterized by the most beautiful and delicate transverse striation. Both in the longitudinally and transversely striated portions we frequently find four, five, or even more transverse rents and clefts, but never any cleavage in the longitudinal direction. Many of the fibres are broken up into irregular flakes; but the muscular fibres do not in any case appear to resolve themselves into definitely formed morphological elements. The sarcolemma is gelatinous and finely granulated.

When a muscular fibre has been exposed to the prolonged action of a saturated solution of bichromate of potash, the transverse striæ stand sharply out, whilst the fibre corresponding to them is torn at different spots, or exfoliated in the individual transverse striæ.

When small carefully prepared portions of muscle are digested for a long time at a temperature of from 30° to 40°, in a solution of six parts of nitrate of potash in 100 parts of water, no solution of one or other of the elementary parts of the muscular tissue can be observed. The transverse striation is generally visible in the primitive bundles, while the longitudinal striæ are rendered far more conspicuous. I know of no menstruum which so clearly exhibits the longitudinal cleavage of the muscular bundle projecting from the sarcolemma. This projecting portion splits in the form of a tuft into diverging, primitive longitudinal fibres, which individually exhibit distinct transverse striæ. These, however, do not exhibit the form of varicose dilatations of the fibrils, but present the appearance of clear and light spots, which succeed one another



in a very regular manner, and have the same transverse diameter. The fibres appear as if composed of linearly arranged parallelopipeds of translucent but not transparent substance.

Fig. 28.



Striated muscular fibre (from the abductor muscles of the rabbit), digested for fourteen days, with a solution of nitrate of potassa of 10 per cent.

Pieces of muscle, when exposed for a prolonged period to the action of *sub-nitrate of mercury* (with the nitrite), are converted into a violet-colored, hard, brittle mass, which admits of being reduced to a nearly purple-colored powder. When examined under the microscope, the muscular bundles appear in the form of pale bluish-red parallelopipeds, which exhibit the most delicate and sharply defined transverse striation. In thin sections, cut somewhat obliquely to the axis of the muscular bundle, we remark detached lamellæ arranged upon one another in such a manner that the muscular cylinder or bundle appears to consist of plates or disks superimposed on one another. The sarcolemma, which we can often distinctly recognize here, remains as free from color as the interspersed connective tissue.

A moderately dilute solution of *carbonate of potash* renders the muscles hard and rigid, as was especially shown by Virchow. On making a microscopical examination of muscle that has been hardened in this manner, the bundles are observed to be somewhat swollen, presenting no appearance of longitudinal striæ; the transverse striæ are fine and sharply defined; the cut surfaces of the bundles are generally very distinct; but wherever the preparation has been torn or pressed in its adaptation for microscopical purposes, the extremities exhibit exfoliated and partly somewhat recurved lamellæ; but I have never succeeded in obtaining the round laminæ in the isolated state in which Bowman has obtained his disks (as, at least, would appear from his diagrams). Pieces frequently presented themselves resembling sections of concentrically arranged circles; the lamellæ were in some cases only faintly granulated on their broad surfaces, in others sharply punctated. The sarcolemma was indistinct; no nuclei were visible.

After the prolonged action (varying from eight to seventy-two hours) of an extremely dilute *solution of soda* (consisting of one part of the



alkali in 8500 parts of water), the muscle was reduced to a thoroughly gelatinous mass; the primitive bundles were for the most part dissolved, and those which were not thoroughly dissolved exhibited a faint longitudinal striation, caused by the regular deposition of granules in rows, so that the whole resembled tuberculous, stringy, bronchial mucus, which, on the addition of water, frequently exhibits a similar appearance of granules, arranged so as to imitate fibres. There was not a trace of nuclei, or of transverse or longitudinal striation. Here and there were remarked empty portions of sarcolemma, which appeared either perfectly hyaline or faintly granulated, and bore a close resemblance to the hyaline cylinders in the urine in Bright's disease, which correspond to the *membrana propria* of the tubes of Bellini. It is worthy of notice that these cylinders of sarcolemma have generally a much smaller diameter than the original primitive bundles, which furnishes a proof of the great elasticity of the sarcolemma, and of its close approximation in its normal state to the cylindrical bundles of fibrils. The elements of the perimysium admit, moreover, of being most admirably brought into view by the action of a dilute solution of soda.

A concentrated solution of potash causes the primitive bundles to swell and become transparent, rendering the transverse striation less distinct. Its prolonged action causes the disintegration of the bundles into parallelipeds, and renders the transverse striæ less distinct, and only to be detected by the appearance of parallel rows of granules; here and there longitudinal striæ may be seen, which, in conjunction with the granules of the transverse striæ, form necklace-like filaments, such as Mulder and Donders have already noticed. Nuclei are not always to be observed or in every kind of flesh; but wherever they occur, they are observed to be much swollen, rather oval than fusiform, and granulated. On the addition of water everything is dissolved, with the exception of portions of the sarcolemma, which are reduced in their transverse diameter, and the nuclear fibres.

When a very dilute solution of potash or soda is allowed to flow over a fresh preparation under the microscope, the muscular bundles become much swollen, the transverse striation disappears, a partly filamentous and partly granular mass projects from the sarcolemma, whilst, as Kölliker observed, the nuclei are simultaneously brought into view. The nuclei commonly swell very considerably, become roundish, gradually lose their clear outline, and finally altogether disappear.

An aqueous solution of iodine imparts an intense yellow color to the primitive bundles, and more frequently causes the longitudinal striæ to appear than any other reagent; it does not, however, cause the transverse striæ wholly to disappear, but often renders them somewhat less distinct.

Fragments of muscle which have been repeatedly washed with distilled water, and exposed to strong pressure, either entirely lose their transverse striation, or show only faint indications of it, whilst the longitudinal striation is peculiarly visible. If these muscular bundles, after being rinsed with water, are treated with a very concentrated solution of chloride of calcium, the transverse striæ are often brought very prominently into view; the primitive bundles increase transversely; the terminal



surfaces of the torn primitive bundles are very irregular, and do not correspond either with the transverse or the longitudinal striations; most of them have a digital form with convex ends, as if the soft mass of the fibrils had been compressed by the swelling of the sarcolemma, and had somewhat protruded from it. The sarcolemma and nuclei can seldom be clearly distinguished. A saturated solution of *carbonate of potash* acts upon the macerated muscles very much in the same manner as chloride of calcium; the individual bundles have a very sharply defined outline, and are enlarged transversely; the longitudinal striation almost wholly disappears, and leaves the transverse striation so sharply defined as to make the dark striæ appear much thicker than the lighter ones. *Concentrated nitric acid* certainly causes the transverse striæ in the macerated primitive bundles to reappear; the dimensions of the latter are considerably diminished transversely.

*Dilute hydrochloric acid*, such as that employed by Liebig,<sup>1</sup> for the extraction of muscle-fibrin (1 p.m. H Cl), causes the sarcolemma to come prominently into view. Pieces of muscle which have been thus treated show an amount of connective tissue, and more especially of nuclear fibres, far exceeding what one would expect to meet with, judging from the ordinary modes of examining muscular tissue. As has already been observed, the individual portions of sarcolemma bear a strong resemblance to the cylinders in the urine in Bright's disease; they have a much smaller diameter than the primitive bundles which they surround. The smaller portions of sarcolemma are entirely empty, and are simply interspersed here and there with granules of various sizes. In the longer pieces of sarcolemma the nuclei appear irregularly disposed, near and amongst one another, and, in addition to the nuclei and granules, there appear at intervals bodies similar to masses of fat, sometimes resembling the pulp which protrudes from the nervous fibres, or at other times appearing as very small granular cells. The true membrane of the sarcolemma is extremely hyaline, and can generally be only clearly made out by the aid of very good illumination and simultaneous shading with the diaphragm. When these preparations are acted upon by a saturated solution of *carbonate of soda*, the nuclei and a portion of the granules disappear, and the sarcolemma becomes almost more hyaline. *Concentrated nitric acid* also causes the nuclei to disappear, but colors the sarcolemma yellow, whilst the connective tissue remains uncolored. This difference of color is rendered very conspicuous on saturating the acid with potash. *Chromic acid* also imparts to the sarcolemma a very beautiful yellow color, whilst, at the same time, it contracts it to so great a degree that the diameter is scarcely one-third or one-fourth of that of the original primitive bundle; the nuclei disappear entirely. On adding a very *dilute solution of soda* to the fibres which have been treated with dilute hydrochloric acid, the nuclei swell in the sarcolemma from which the fibrils have been thus removed, and very rapidly disappear; the very hyaline sarcolemma continues to exhibit a faintly granulated appearance.

These micro-chemical investigations show that the three morphological elements which we distinguish in the primitive bundles of muscle differ

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 73, S. 125-129.



chemically from one another, constituting respectively the true substance of the fibrils, the substance of the nucleus, and the sarcolemma.

The chemical properties of the substance of the fibrils (syntonin) have been already glanced at in p. 225 [and will be further considered in the Appendix to this volume]. The micro-chemical investigations already made on the substance which may be extracted from the muscles with dilute hydrochloric acid, leads us to concur in Liebig's view of this being the matrix of true muscular fibre. We have already observed that the primitive bundles of muscle, even when they have been digested for a prolonged period in a solution of nitre at a temperature of 30° or 40°, do not exhibit any change under the microscope which can justify us in believing that there is the slightest partial solution of the finest muscular fibrils.

As, however, these experiments were mostly made with the flesh of oxen and calves, and as the fibrin of the blood of oxen is, as is well known, nearly insoluble in a solution of nitre, whilst that of other animals is dissolved very readily after a short digestion (see vol. i. p. 313), the precaution was taken to select swine's flesh, which was freed as far as possible of its fat (the blood-fibrin of the pig being very readily soluble in a solution of nitre), and, after cutting it into very fine pieces, to rinse it with distilled water until the fluid that was pressed out of it exhibited no traces of albumen. After this mass had been freed as far as possible from soluble protein-bodies, it was digested for two or three days in a solution of nitre, of the strength already specified; but there was no trace of any dissolved protein substance which was either coagulable by heat, or precipitable by acetic acid or any other reagent. The syntonin contained naturally in the muscular fibrils is, therefore, quite as insoluble in a solution of nitre as that which is artificially obtained from the muscles by means of hydrochloric acid, &c.

We are led to conclude from the micro-chemical reagents already indicated, that the *substance of the nuclei* enclosed in the sarcolemma does not differ very much from syntonin. It is dissolved with nearly equal rapidity by dilute alkalies; it swells in concentrated alkalies, dissolving very rapidly when water is added. It behaves in precisely the same manner as the substance of the fibrils towards concentrated acids, as, for instance, nitric acid. A difference is observed in the case of acetic acid, and of the mineral acids, when extremely diluted; for, although these reagents render the nuclei more distinct, they exert a certain amount of solvent action upon them; the nuclei wholly disappearing after a prolonged digestion in dilute acids, leaving only some fine molecules, which probably consist, for the most part, of fat.

We may readily convince ourselves that the clots or granules visible in the sarcolemma which has been emptied by acids or alkalies, consist for the most part of fat, either by repeatedly shaking with ether the remains of muscular fibres that have been treated with a dilute solution of soda, or, better still, by repeatedly boiling them in alcohol; for we can not only recognize the presence of fat in the ether or alcohol, but fewer clots and granules can be detected under the microscope in the less granulated sarcolemma.

Kölliker<sup>1</sup> and Scherer have demonstrated that the *sarcolemma* does not

<sup>1</sup> Mikrosk. Anat. Bd. 2, S. 250.



consist of connective tissue, and that it yields gelatin on boiling; and this view is confirmed by the above-mentioned micro-chemical reactions, which show most obviously that its chemical substratum has no affinity whatever to protein-bodies. If we bear in mind that neither acids nor alkalies cause the sarcolemma to lose its elasticity, which, as in the case of elastic tissue, resists alike the action of alcohol and boiling, we shall be led to concur in Kölliker's opinion, that the sarcolemma contains a substratum analogous to the elastic tissue; but it is by no means easy to determine whether, like elastic tissue, it acquires a yellow color from the action of concentrated nitric acid. Kölliker was unable to produce any yellow color in the sarcolemma of the Axolotl by means of nitric acid. As may be inferred from the above-described micro-chemical relations of nitric acid towards the muscular fibre, the sarcolemma cannot be isolated and distinguished in the flesh of the higher animals; but the yellow color produced in the elastic tissue by nitric acid is not so distinctly visible on a microscopical examination as in the protein-like tissues, and on that account the microscope can afford no reliable information in reference to this point; when it occurs on a large scale, the elastic tissue is certainly colored yellow by nitric acid (especially on the addition of potash), and this is also the case in the empty sheaths which remain after the repeated treatment of muscular fibre with a dilute solution of soda, and a thorough rinsing with water; but we are yet without any conclusive proof that these tissues were wholly free from all protein-like substances when they were submitted to the action of the nitric acid, and it would be extremely difficult to prove that such was the case.

We have already frequently referred to Liebig's admirable investigation of the fluids contained in the flesh; these researches have not only tended materially to elucidate a very obscure subject of inquiry, but have also thrown considerable light on nearly all departments of physiological chemistry. We have now merely to consider generally the composition of the juice extracted from the striped muscles, and to enlarge somewhat more fully upon certain points of discussion which had before been only incidentally touched upon.

The freshly expressed *muscular juice* is generally of a whitish color, and turbid or opalescent from the presence of suspended fat; it reddens litmus paper very strongly, and forms on boiling a considerable coagulum; acetic acid, moreover, gives rise to a turbidity, which depends upon the presence of casein in the fluid, as I have satisfied myself by the application of rennet, &c. As the true muscular juice cannot of course be obtained without the admixture of the transudation entering into the connective tissue, and of the blood contained in the vessels of the muscular substance, a very great part of the albumen may be derived from this source; but the amount present is too large to be referable to this only, more especially as we have met with it in considerable abundance in comparatively non-vascular tissues provided with smooth muscles, as, for instance, in the middle coat of the arteries. The casein must, however, be derived solely from the true muscular juice, since, as we have already shown in vol. i. p. 338, its presence cannot be demonstrated with certainty in the blood. We have already spoken at length, in vol. i. pp. 86, 128, 131, and 200, of the occurrence of *creatine*, *creatinine*, *inosic acid*, and *lactic acid*, in the muscular juice.



Scherer<sup>1</sup> has discovered a special substance in the decoction of the flesh of the heart of the ox, to which he has applied the term *inosite*. [See note to vol. i. p. 249 (on *inosite*) and p. 264.—G. E. D.]

Scherer<sup>2</sup> has also described several volatile acids, belonging to the group  $C_nH_{n-1}O_3 + HO$ , which he found in the muscular juice; amongst these, acetic and formic acids were conspicuous.

It has generally been assumed that the muscles derived their color from the quantity of the blood contained in them; but we incline rather to Kölliker's<sup>3</sup> view, that there is a special coloring matter in the muscles. This pigment is very similar to that of the blood. It assumes a brighter red tint in the air, and is rendered darker by sulphuretted hydrogen; it may be extracted by water, and coagulates with the albumen of the muscular juice. These properties might dispose the chemist to regard the pigment of the muscle as identical with the coloring matter of the blood; but certain physiological grounds indicate that this pigment is not contained in vessels and blood-corpuscles, but adheres in a free state to the fibrils; the muscles retain their color during vital contraction; colorless muscles are frequently as rich in bloodvessels as those which are strongly colored; and a yellow color may sometimes even be distinctly detected under the microscope in particular bundles.

The inorganic constituents are of considerable importance in the muscular juice, as well as in every other fluid; and we are indebted to Liebig<sup>4</sup> for the light which he has thrown on this subject by his carefully conducted observations. The inorganic, like the organic substances, must be regarded as something beyond mere incidental constituents of the muscular juice. This fluid, like most acid fluids, is rich in *potash salts* and *phosphates*, but poor in salts of soda and chlorides. It would appear, from numerous determinations of Liebig, that the relation of potash to soda in the blood of certain animals, on the one hand, and in the muscular juice of the same animals on the other, is about as follows: in the ash of both fluids there occur, for 100 parts of soda,

In the hen	40.8	of potash in the blood, and	381	in the muscular juice.
“ ox	5.9	“	279	“
“ horse,	9.5	“	285	“
“ fox,	—	“	214	“
“ pike,	—	“	497	“

It must be borne in mind that the muscular juice can never be obtained free from blood and transudations, and that, consequently, the proportion of soda in the muscular juice would be even smaller if we could in any way exclude the admixture of blood.

A similar consideration presents itself to our notice when we proceed to estimate the quantity of *phosphoric acid* in the muscular juice. R. Weber<sup>5</sup> found from 45 to 47% of phosphoric acid in the ash of horses' flesh, and about 2% in that of the serum of the blood of the same animal. The phosphoric acid in the muscular juice is principally combined with potash, and only slightly with lime and magnesia. Chevreul

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 73, S. 328-334.

<sup>2</sup> Ibid. Bd. 69, S. 196-201.

<sup>3</sup> Mikrosk. Anat. Bd. 2, S. 248.

<sup>4</sup> Researches on the Chemistry of Food. Edited by William Gregory, M.D., Professor of Chemistry in the University of Edinburgh. London, 1847.

<sup>5</sup> Pogg. Ann. Bd. 74, S. 91-115.



found that the ash, yielded by a decoction of flesh, contained 81% of salts soluble in water, and R. Weber has more recently estimated their amount at from 79 to 80%. Liebig found in the ash of the muscular juice of oxen, horses, foxes, and deer, bibasic and tribasic alkaline phosphates, and in that of hens, a small quantity of monobasic alkaline phosphate, in addition to the bibasic. The ash contains, therefore, in every case, more phosphoric acid than is required for the formation of the neutral phosphates of the alkalies. The conclusion to which we are led, that the muscular juice, when fresh, contains acid phosphates of the alkalies, gains confirmation from the fact that a large quantity of free lactic acid is contained in the fresh juice. We shall consider more fully, under the head of the "Metamorphoses of Animal Matter," the interesting views advanced by Liebig in connection with these relations.

R. Weber never found more than 7% of *chloride of sodium* in the ash of the muscular juice of the horse, but nearly as much as 73% in that of the blood-serum of the same animal.

The *alkaline sulphates* occur only in mere traces in the muscular fluid, and Liebig refers these salts to the admixture of blood.

Whilst the *phosphate of lime* is present in the blood in far larger quantities than the *phosphate of magnesia*, the reverse holds good in the muscular juice; in the muscular juice of the hen, for instance, according to Liebig, the ratio between these salts of lime and magnesia is as 10 : 39.2; and R. Weber found a similar ratio in the ash of horses' flesh.

Schlossberger<sup>1</sup> and Von Bibra,<sup>2</sup> who have made comparative analyses of the flesh of different animals, have obtained the same results as Berzelius and Liebig for the amount of *muscular fibre* in the flesh of mammals and birds, viz., from 15.8 to 16.7%; in the case of young animals, the numbers were somewhat less; in the flesh of reptiles and fishes, they were from 9.4 to 13.2%.

The substance of the vessels and nerves, as well as the nuclear fibres of the connective tissue and the sarcolemma, are naturally mixed with the muscular fibre in these determinations.

The question here arises whether we may, or may not, regard the protein-substance extracted from the flesh by means of water containing hydrochloric acid, as true muscular fibre; that is to say, as the cylindrical muscular bundles which are enclosed in the sarcolemma. According to Liebig,<sup>3</sup> this solvent extracts very different quantities of this protein-substance from the flesh of different animals; thus, for instance, the muscular fibres of the ox and the hen are almost entirely dissolved; a greater amount of substance remains from the flesh of sheep, and far more than half in the case of calves' flesh. We have already seen that by treating the flesh with acidified water the sarcolemma is perfectly emptied, with the exception of nuclei and granules, and a few small clots; hence, as Liebig's experiments are perfectly correct (as any one may ascertain by repeating them), it follows that calves' flesh contains relatively less fibre-substance (syntonin), and relatively more connective tissue, than the other kinds of flesh which were examined; as, for instance, that of oxen. This observation is further corroborated by a

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 72, S. 116-120.

<sup>2</sup> Arch. f. phys. Heilk. Bd. 4, S. 536-577. <sup>3</sup> Ann. d. Ch. u. Pharm. Bd. 75, S. 126.



simple microscopical comparison of the primitive bundles of muscle in the ox and the calf. Donders<sup>1</sup> noticed the striking difference of diameter in the primitive bundles of the cow and the calf, and he is of opinion that the number of the bundles remains the same during the growth of the calf; in which case, the fibre-substance (syntonin) would alone increase during the growth of the animal, whilst the sarcolemma and connective tissue remained the same. It may be assumed that the diameter of the primitive bundles of the calf is from  $\frac{1}{4}$  to  $\frac{3}{8}$  smaller than that of the primitive bundles of the full-grown ox. If the number of the bundles remains the same, and if the sarcolemma and connective tissue do not increase with the growth of the muscle, it becomes a mathematical necessity that less muscle-fibrin (syntonin) admits of being extracted from the flesh of calves than from that of oxen. There can be no doubt, from the micro-chemical reactions already indicated, that the protein-substance which can be extracted by dilute hydrochloric acid constitutes the essential part of the muscular fibrils, and is perfectly identical with the substance of the smooth muscular fibres of other contractile tissues.

The ratio which the sarcolemma bears to the enclosed cylinder of muscular fibre has never been even approximately determined. The usual method of determining the connective tissue contained in the muscles is by ascertaining the quantity of gelatin yielded by boiling the previously rinsed muscle, but this can only be regarded as a very rough mode of determination. Liebig gives 5.6% as the mean quantity of gelatigenous substance in flesh; Von Bibra found about 2% in the majority of the different kinds of flesh which he examined.

If we take the gelatin that is formed as a measure of the quantity of connective tissue contained in the muscles, we must bear in mind that, on boiling with water, the nuclear fibres (which, it would appear from micro-chemical investigations, are present in considerable quantities in the Muscles) remain undissolved, whilst the protein-substance, in quantities varying according to the duration of the boiling, becomes dissolved with the gelatin (Mulder's tritoxide of protein).

Liebig estimates the *constituents* of ox-flesh which are *soluble* in water at 6%, of which 2.96% are *albumen*. This result agrees with the analyses of Berzelius, Braconnot, Schütz, Schlossberger, and von Bibra. In the flesh of birds the quantity of soluble substances amounts to as much as 8%, as is shown by the analyses of Schlossberger and von Bibra.

*Fat* is always to be found in flesh, notwithstanding the most careful preparation of the muscle, being derived not only from fat-cells, but from the blood, the nerves, and even from the muscular substance itself, in the fibrils of which we frequently observe fat-globules amongst the nuclei. Liebig always found 2% in the flesh of the ox, von Bibra found even as much as 4.24% in that of a man aged fifty-nine years, but only about 2% in that of other mammals, whilst he could not discover more than about from 0.54 to 1.11% in the muscle of fishes.

The quantity of *water* in the muscles, when in a fresh state, was estimated by Berzelius<sup>2</sup> at 77.17%, by Schlossberger<sup>3</sup> at 77.5%, and by Schütz<sup>4</sup>

<sup>1</sup> Mulder's *Vers. einer physiol. Chem.* S. 630, Anm. [or English Transl. p. 578, note.]

<sup>2</sup> *Lehrb. de Chem.* Bd. 9, S. 588.

<sup>3</sup> *Untersuch. über d. Fleisch verschiedner Thiere.*

<sup>4</sup> *Vergleichende chem. Untersuchungen des Fleisches verschiedner Thiere.* 1841.



at 77·6%, in the ox; von Bibra found from 72·56 to 74·45% in human muscles. These and similar determinations, which have been instituted as to the muscles of different animals, are not devoid of significance; but as they vary even in the same species of animals, they cannot attain any high degree of importance until they can be compared with the quantity of water contained in the blood, or, better still, with that in the blood-serum. Thus, for instance, it would be highly important in reference to the mechanical metamorphoses of matter, to ascertain the proportions existing between the water contained in the muscles and that in the blood under different physiological and pathological conditions. A course of experiments, bearing on this subject, has lately been instituted by one of my pupils. It was found that, on an average, there are 9·9% less of water in the muscle than in the serum of the blood, and that this proportion continues nearly the same whether the blood was in a concentrated state or contained an excess of water. This proposition, which is precisely what might have been anticipated, was found to be fully confirmed in comparative analyses of the blood and muscle of persons who have died from cholera, as well as in so-called hydræmic conditions. We may, unquestionably, expect the most important results regarding the mechanical metamorphosis of animal matter from investigations into the proportions existing between the quantity of water contained in the blood and the other juices, tissues, and organs of the animal body, under different conditions.

It will be readily understood that the determination of the quantity of water contained in the muscles should be conducted with the utmost care, as pieces of muscle very rapidly lose a certain quantity of water when exposed to the air, and thus afford only a very inexact result. Great care must be taken to avoid any evaporation from the portion of muscle which is to be weighed. Another circumstance which calls for attention is, that while the surface of the piece of muscle, when placed in an air-bath or in a vacuum, dries very rapidly, the interior obstinately retains its water. It should moreover, be borne in mind, that it is not always easy to obtain a portion of muscle alike poor in connective tissue and vessels, and that the amount of connective tissue essentially influences the quantity of water. In examining the muscular substance of the human subject, the observation is rendered very much more difficult, from the circumstance that dissection must necessarily be postponed till eight or even fifteen hours after death, when endosmotic currents may have been already established in the muscular substance as well as in the blood, which do not affect the distribution of the water in the living body.

The serum of the blood obtained from the dead body was not found by these observations to differ in its amount of water from the blood drawn by venesection during life; but, on an average, a larger amount of water than that given by any former observers was found in the muscles (upwards of 80% in the bodies of healthy persons who had committed suicide); it must remain undecided for the present whether this excess of water depends upon an absorption of the fluid by the muscles after death, or whether a more careful mode of determining its amount may have yielded a higher number for the water, and thus afforded a more correct result.

Both for the purpose of giving a general view of the subject, and in



order to furnish certain definite points of support for the establishment of future observations on the metamorphoses of animal matter, we here subjoin a list of the mean results of former determinations of the individual constituents of the muscular substance; we limit ourselves more especially to the flesh of oxen :

	Per cent.	Per cent.
Water, . . . . .	74.0	to 80.0
Solid constituents, . . . . .	26.0	" 20.0
	100.0	100.0
Muscular fibre, . . . . .	15.4	" 17.7
Gelatinogenous substance, . . . . .	0.6	" 1.9
Albumen, . . . . .	2.2	" 3.0
Creatine, . . . . .	0.07	" 0.14
Creatinine, undetermined.		
Inosic acid, do.		
Fat, . . . . .	1.5	" 2.30
Lactic acid ( $C_6H_5O_5.HO$ ), . . . . .	0.60	" 0.68
Phosphoric acid, . . . . .	0.66	" 0.70
Potash, . . . . .	0.50	" 0.54
Soda, . . . . .	0.07	" 0.09
Chloride of Sodium, . . . . .	0.04	" 0.09
Lime, . . . . .	0.02	" 0.03
Magnesia, . . . . .	0.04	" 0.05

It would scarcely appear necessary to enter more particularly into the consideration of the methods to be employed in the *chemical investigation* of the animal muscles, as the remarks already made in reference to the analysis of the organic muscles apply equally to the animal muscles; we must, however, offer a few remarks on certain points to which we have not been previously able to allude. We refer especially to the examination of the fluid contained in the sarcolemma, and permeating the muscular bundles. We are, unfortunately, unable to procure this fluid free from the *liquor sanguinis*, and hence we know of no better method to recommend than that adopted by Liebig. It is self-evident that the muscle selected for examination should be fresh, and freed, as far as possible, by means of the scalpel from fat, tendon, membranes, cellular tissue, vessels, and nerves; it should then be finely minced, chopped, or shredded, taking care that no splinters of wood or other extraneous substances are mixed with the object. According to Liebig's directions, half of the chopped flesh should be put into an equal weight of water, and after being duly kneaded into a pulpy mass, should be exposed to pressure in a linen strainer. The residue, after pressure, must be again twice kneaded with water and pressed, so that we obtain three extracts from the first half of the flesh. The fluid of the second pressing of this first half is employed for the first extraction of the second half of the reserved chopped flesh; whilst the fluid of the third pressing is used for a second extraction of the second portion, which is then again extracted with pure water. The flesh of fishes and certain amphibia cannot be submitted to pressure in a finely chopped state, as it swells in water into a thick gelatinous mass, which clogs up the pores of the linen. According to Liebig, we must here have recourse to the process of displacement. The muscular substance of frogs differs from that of fishes; it admits very readily of being pressed, and is, therefore, peculiarly well adapted for experiments of this nature.



The expressed acid fluid, which is either turbid, or at all events opalescent from the presence of fat, must be treated in the water-bath until all the coagulable matters separate from the solution. The expressed fluid, after the removal of the coagula by filtration, is either of a faint reddish hue, or nearly colorless. The evaporation requires to be conducted with extreme caution, and Liebig has drawn attention to the circumstance that the fluid is disposed to assume a brownish color during the process of evaporation, in consequence of the presence of the free acid. On this account Liebig recommends the addition of baryta water, so long as any precipitate is deposited, not only for the purpose of neutralizing the fluid, but also that the phosphates may be removed as far as possible. The next step is to crystallize the greater part of the creatine contained in the fluid, according to the method indicated in vol. i. p. 127, and this being done, the inosic acid must be separated in the manner described in vol. i. p. 200, viz.:—by adding alcohol to the mother-liquid of the creatine. About 5 times the volume of spirit should then be added to the mother-liquid of the inosates of potash and baryta, on which the fluid separates into two layers, the upper one of which contains lactate, acetate, and butyrate of potash and creatinine. In order to separate the latter substance, we treat this lighter fluid with ether, on which it again separates into two layers, the upper one of which contains nearly pure creatinine, which crystallizes on the evaporation of the ether. The lactic acid and the above-described volatile acids of the heavier layer are separated according to the usual methods. In the heavier stratum of the mother-liquid of the inosates which is formed by the action of the spirit, the main contents, in addition to the extractive matters, are inosite and chloride of potassium. It is easy to obtain evidence of the presence of creatinine in fresh muscular juice by Liebig's method or boiling the solid residue of the mother-liquid of the inosates in spirit of wine, and adding chloride of zinc to the spirituous fluid, which causes the compound of chloride of zinc and creatine to separate in a crystalline form.

The examination of the parts which are insoluble in water does not call for any additional remarks, as it has been already noticed in detail in the preceding pages; in general, however, the mode of investigation corresponds with that which has been described for the organic muscles.

If we inquire whether the chemical investigations of the muscular substance which have been hitherto made, throw any light on the nature of its functions, we find that very little information has been gained which can either afford support to any of the existing hypotheses, or can suggest new ones. By proceeding with the greatest caution by the method of induction, we arrive at the following conclusion:

The protein-substance, which can be extracted from the muscular fibrils by extremely dilute hydrochloric acid, is the most essential element of animal motion; it is one and the same in the striped muscular fibres, in the smooth muscles, and in the tissues which were formerly termed contractile. It is, however, peculiar to those organs whose movements are dependent on the nervous system. We are unable to explain on chemical grounds the manner in which this substance alters its physical properties during the contractions of the tissues.



The voluntary and involuntary muscles contain moreover a fluid surrounding and permeating the above-described matrix of the contractile fibres, which is distinguished by its acidity, and differs entirely from the plasma of the blood. Liebig has calculated that the voluntary muscles alone contain more than sufficient free acid completely to destroy the alkalinity of the blood. We have already seen that wherever contractile fibres or fibre-cells are present, the potash-salts and phosphates predominate in this fluid, whilst the blood-plasma, on the contrary, is poor in these salts, but rich in alkaline chlorides and soda-salts. The difference thus observable in the intercellular fluid of the blood-cells and that of the contractile fibres cannot be merely accidental; and Liebig has suggested that it very probably either occasions, or is occasioned by an electrical current. We know, however, that Du Bois Reymond<sup>1</sup> has subsequently arrived at many novel views, and obtained some brilliant results relating to the electrical phenomena of muscular contraction, in repeating the observations of Matteucci. The existence of an intimate connection between the development of electricity accompanying muscular contractions and the acid of the muscular juice on the one hand, and the alkali of the blood on the other, and the importance of the chemical constitution of the muscular juice on the function of the organ, are corroborated by the striking and well-known fact, that all muscles, whether voluntary or involuntary (both the striped and the smooth) lose their contractility very rapidly in water. (Lukewarm water at  $+37^{\circ}$  scarcely acts less rapidly on this property of muscles than cold water.) The experiment of the younger Liebig<sup>2</sup> seems opposed to this observation, which may be tested by any one who watches by means of a rotatory apparatus the contraction of the transversely striated muscles of a recently killed animal, or its stomach, intestinal canal, bladder, &c. This observer found that muscles, which had been freed as thoroughly as possible from blood by the injection of water into the vessels, retained their contractile property as long as those muscles which still contained blood. These two observations do not, however, involve a contradiction; for if the muscles do not lose their contractility in the absence of blood, but do so on the addition of water, it simply shows that the muscle loses its capacity for contraction by the dilution of the muscular juice. If, therefore, we connect the development of electricity during muscular contraction with chemical forces, we shall find that the causes of the phenomena of polarity depend less upon the antagonism of alkali and acid than on that of the solid muscular fibrils (syntonin) and the muscular juice.

Although we purpose at a future page reverting to the interesting observations of the younger Liebig, we cannot abstain from making a few remarks in relation to them in the present place. It would appear from these experiments that muscle is dependent on oxygen to enable it to contract; for Liebig found that frogs' muscles retained their contractility much longer in an atmosphere of oxygen than in air which did not contain oxygen, as, for instance, in carbonic acid, nitrogen, or hydrogen. It was further shown by two carefully conducted experiments that,

<sup>1</sup> Unters. üb. thier. Elektrizität. Berl. 1848 u. 1849.

<sup>2</sup> Ber. der Akad. d. Wissensch. zu Berlin, 1850, S. 339-347.



whilst the muscle is in a state of contraction, oxygen is absorbed, and a corresponding quantity of carbonic acid is exhaled,—facts which confirm the previously advanced proposition, that a large portion of the carbonic acid formed in the animal body is generated not in the capillaries, but in the parenchyma of the organs, and is especially produced by muscular action. We need scarcely remark that the results of these observations are of the highest importance in relation to the theory of metamorphosis of matter, whilst they afford powerful support to the purely physical hypothesis of the elder Liebig in relation to this subject.

## NERVES AND BRAIN.

The nervous system and the brain contain nerve-fibres and nerve-cells as their special and peculiar morphological constituents.

The *nerve-fibres* or tubes which are distributed throughout the peripheral nerves, the spinal cord, the brain, and the ganglia, do not all present the same appearance, when seen under the microscope; hence the nerve-fibres have been divided into two kinds, namely, the thicker (animal, cerebro-spinal), and the more delicate (sympathetic, vegetative, organic); there is no ramification observable in either of these classes of fibres, except at their extreme terminations.

Fig. 29.



Nervous fibres from sciatic nerves of a recently killed rabbit; treated with water.

The thicker nerve-fibres form cylindrical filaments, varying from 0.004 to 0.010''' in diameter; they occur especially in the nerves springing from the spinal cord, but they are also met with in other parts of the nervous system. When these nerve-fibres are examined under the microscope in a perfectly fresh state, especially after the addition of a little albumen, they appear entirely homogeneous and transparent, exhibiting a sharply defined contour. But after lying for some time or having come in contact with water, they exhibit a double contour, re-



sembling broad dark bands, with a clear stripe running down the middle. This peculiarity, together with the size of their diameter, especially distinguishes them from the so-called sympathetic fibres. Distinct morphological elements may be recognized in each of these fibres; and, in the first place, we must distinguish between the coat or sheath and the contents.

The coat or limitary membrane of the nerve-tubes can scarcely be recognized in very recent nerves, for this membrane is an entirely structureless, transparent, somewhat elastic membrane, which can only be rendered visible by the application of certain chemical reagents which we shall presently mention.

The substance contained in the nerve-tubes (the nerve-medulla or pulp) appears at first, as we have already observed, to be perfectly homogeneous, whence it has been assumed by many observers to be an entirely homogeneous, closely mixed matter. It is quite immaterial to our purpose, whether we admit the correctness of this view, or adopt the opinion held by others, that the subsequently visible separation of the medulla into a cortical substance and a cylindrical axis-fibre, exists preformed in fresh nerves; but, judging from a chemical point of view, we are compelled to assume the most decided morphological separation. Thus, the application of cold, or the addition of water, or of certain chemical agents, gives rise to a kind of coagulation in the medulla, causing the outermost layer of the contents of the nerve-tubes to become darker, somewhat grumous, or even granular; whilst in the interior, that is to say, in the long axis of the nerve-fibre, there remains a clear, somewhat sharply defined filiform stripe—the central or axis-fibre, or axis-cylinder. The actual medullary substance, or nerve-pulp, assumes very different forms when subjected to rough pressure, appearing in different cases in nodular, cylindrical, or clavate shapes as it protrudes from the sheath. Within the tubes the substance is frequently accumulated in an irregular manner, distending the sheath unequally at different points, which gives rise to those varicose nerve-fibres which we so frequently meet with in examining the brain.

The finer or sympathetic nerve-fibres have a diameter varying between 0.00212 and 0.00300'''. These fibres bear less resemblance to tubes than to solid cylinders, and have generally no trace of any contents. They occur principally in the sympathetic, forming bundles of a somewhat bluish-gray color, whilst the cerebro-spinal fibres appear white and of a silvery lustre. They are, however, found interspersed in various quantities in all other nerves, more especially in those of the involuntary muscles, the skin, and the mucous membranes (Bidder and Volkmann),<sup>1</sup> and lastly in the posterior roots of the spinal nerves and in those of the sensitive cranial nerves (Kölliker).<sup>2</sup> It is only in the peripheral extremities of the cerebro-spinal nerves that the animal fibres become so attenuated that they resemble in their diameter and general appearance the above-described sympathetic fibres. These nerve-fibres are also enclosed in a sheath, which cannot always be distinctly recognized, even after the

<sup>1</sup> Die Selbstständigkeit des sympathischen Nervensystems. Leipzig, 1842.

<sup>2</sup> Selbstständigkeit und Abhängigkeit des sympathischen Nervensystems. Zürich, 1844.



application of chemical reagents; on the other hand, the axis-cylinder may be very easily brought into view in these nerves by chemical means, which we shall notice more particularly in a future page.

Nerve-fibres containing no medulla have been detected by R. Wagner, Remak, Bowman, Kölliker, and other histologists, in the pale fibres of the Pacinian corpuscles, in the extremities of the olfactory nerves, in the nerves of the cornea, in the electrical organ of the Torpedo and Ray (where there is an actual ramification of the fibres), and in the extremities of the nerves of the skin of the mouse. These fibres appear from the observations hitherto made in relation to this subject, to consist only of a sheath and an axis-cylinder.

Another class of nervous fibres has been assumed to exist, namely, Remak's fibres, in which nuclei may be detected, more especially after the addition of acetic acid; but it has not yet been decided whether these elements which have been observed in the ganglia of the sympathetic, &c., are true nerve-fibres, or merely a peculiar form of connective tissue.

Larger or smaller bundles of nerve-fibres are surrounded by a fibrous, strongly glistening, white, dense membrane, called the neurolemma. It appears on a closer examination to consist of different forms of connective tissue, with which are interspersed numerous elastic fibres.

The Pacinian bodies form a very singular appendage to the nerve-fibres. These bodies, which are present in very large numbers in the hands and feet of man and many carnivorous animals, and in the mesentery of the cat, are oval, consist (somewhat like onions) of nearly concentric membranes, measure from 0.5 to 2.0''' , and a nerve-fibre terminates in each of them. These concentric membranes are composed of connective tissue, and between the coats there is a serous fluid, which collects in larger quantities in the narrow, long, central space of these Pacinian bodies. Each of these corpuscles is attached to the nerve to which it belongs by means of a short pedicle, which is formed by layers of the connective tissue of the bodies, and by the neurolemma; through this pedicle an animal nerve-fibre proceeds from the nerve, and extending to the central cavity of the corpuscle, diminishes rapidly until it resembles the axis-cylinder. It traverses the narrow central space, and, after splitting into two or three parts, terminates opposite its point of entrance in fine nodules.

In the nervous system, and more especially in the central organs, as the brain, the spinal cord, and the ganglia of the spinal nerves and of the sympathetic, there occur, in addition to the fibres, peculiar cells, termed the nerve-cells (accessory corpuscles, or ganglionic globules). These bodies are true cells, consisting of an investing membrane, a nucleus with one or more nucleoli, and soft contents interspersed with molecular granules. The size of these nerve-cells is as various as the diameter of the nerve-tubes, and they may be divided into large and small, as we divide the nerve-tubes into thick and thin. The smaller nerve-cells occur principally in the ganglia of the sympathetic, and the larger ones in company with the double-outlined fibres of the cerebro-spinal nervous system; but this rule is not without many exceptions. The diameter of the larger nerve-cells is about 0.05 or 0.06''' , whilst



that of the smaller cells is frequently not more than 0.002 or 0.003''' (Kölliker).

These cells vary in form no less than in size. Large, almost spherical or oval cells occur principally in the gray substance of the brain and spinal cord. Fusiform, trapezoidal, irregularly triangular nerve-cells, provided with numerous, and often ramifying processes, abound in the gray substance of the central organs. We find in the ganglia of the sympathetic scarcely any cells which have not one or two pale processes. Many of the nerve-fibres take their origin from these cells, and we often see one, and not unfrequently two fibres proceeding from a single cell.

The nerve-cells are covered externally by a structureless membrane, which is in some cases extremely thin and scarcely visible, and in others somewhat thicker and easy of recognition. The cells which have thin walls occur more especially in the central organs, whilst those having thicker walls are almost limited to the ganglia. The investing membrane of the latter is very elastic, so that the cells, without being lacerated, admit of being compressed and expanded, resuming their former shape when the pressure is removed. The processes, like the axis-fibres, are remarkable for their elasticity (R. Wagner, Kölliker).

The nuclei, which generally occupy the centre of the cells, are for the most part spherical or oval, have sharply defined outlines, and contain clear fat-like matters, amongst which one, or even two roundish or elongated nucleoli may in general be distinguished. The size of the nuclei varies from 0.0015 to 0.008''', whilst the nucleoli measure from 0.0005 to 0.0003''' (Kölliker).

In addition to the nuclei the nerve-cells contain a tough, semi-fluid mass, which is either colorless, or of a faint yellow hue, and holds in suspension finer or coarser granules. In some cases, and more especially in the stellate<sup>1</sup> cells of the spinal cord, this dark granular mass is collected into various groups or masses, whilst other portions of the cells appear to be less granular.

We see from this short description of the morphological constituents of the nervous system, that we have to take into consideration in the chemical investigation of the nervous mass numerous substances, whose difference is made apparent by their variety of form. We will now consider somewhat more minutely the alterations effected on the above-described morphological elements by the action of various chemical reagents, and then endeavor to give a more general representation of the chemical constitution of nervous matter.

We have already observed that pure *water* effects a change on fresh nerves which have been removed from animals immediately after they had been killed. The contents of the nerve-tubes pass into a state resembling that of coagulation, which causes the double contour of the cerebro-spinal nerves to appear more distinct, and a coarsely granular mass to separate itself from the periphery towards the centre, whilst in the centre itself there remains an irregularly twisted intestine-like stripe of a light or pale reddish color. The nerve-cells are scarcely altered by

<sup>1</sup> [The terms *caudate* and *stellate* have been applied to these cells, according as they have one or several of the processes or prolongations.—G. E. D.]



the action of water, or, at all events, no alteration can be definitely recognized in any part of the cell.

Cold *alcohol*, since it abstracts water from the nervous and cerebral matter, renders these parts harder and almost brittle, but it gives rise to very few visible alterations in the microscopical characters of the nervous substance. Hot, or more correctly speaking, boiling alcohol behaves differently; for, as we might assume *à priori*, it coagulates the coagulable parts of the nerves, and dissolves the fat and the salts of the fatty acids. When the nerve-fibres are boiled in alcohol the nerve-sheath exhibits a sharper outline, appearing at different points as a special membrane, distinct from the granular contents. The contents have the appearance of less dark and less well-defined granules, and are generally translucent and somewhat faintly defined. The axis-cylinder often stands out very well in some fibres, although a careful preparation and some minutes' boiling are necessary to exhibit this clearly. The nerve-cells are but slightly altered by boiling with alcohol, the change they undergo being for the most part limited to an appearance of slighter granulation. The alcohol in which the nervous matter has been boiled exhibits on cooling white flakes, which appear, when seen under the microscope, to be neither crystalline nor of the nodular form common to the fat of the nerves, but to consist of a confused mass of fine molecular granules.

Cold and hot *ether* behave towards the nervous elements in much the same manner as alcohol, and like the latter, render large pieces of nervous substance somewhat harder. When examined under the microscope the double contour of the cerebro-spinal nerves is found to disappear under the prolonged action of ether, whilst the sheath appears more distinct at certain points, and studded, as it were, with granules in many parts. The granular contents are rendered considerably paler, whilst here and there the axis-cylinder is seen paler, and like a twisted thread. The action of ether on the nerve-cells is as slight as that of alcohol. The ether in which the nerve-fibres have been digested deposits on evaporation white granules, which appear, when seen under the microscope, to consist of crystals of margaric acid and nodular masses of brain fat.

Dilute *acetic acid* produces no marked alteration in the morphological character of the nerve-tubes, but when this acid is used in a highly concentrated state, the nerve-fibres after its prolonged action acquire a sharply defined outline. Although the inner contour becomes somewhat distorted after boiling, the sheath becomes distinctly visible at certain points on the cut surfaces of the nerve-fibres; between the inner contours there remains a coiled, often pale reddish stripe; thin, very pale threads frequently project from the extremities of the torn nerve-fibres; they can often be traced for some distance along the uninjured nerve-tube, and are unquestionably axis-cylinders. Kölliker has noticed the difficulty and slowness with which these filaments dissolve even on being boiled with concentrated acetic acid. When concentrated acetic acid is added to a nerve-fibre whilst under the microscope, the nerve is seen to retract instantaneously, whilst the granular nerve-pulp and very pale fibres, which are evidently the axis-cylinder, project from the cut ends



(Kölliker). The fine nerve-fibres of the sympathetic system also swell in acetic acid, their contents become grumous, whilst at different spots an axis-cylinder becomes visible under favorable circumstances. Besides these fibres we may frequently discover the pale nucleated fibres of Remak; we must, however, be careful not to confound them with the fibres of connective tissue, which also exhibit many narrow nuclei in the cerebro-spinal nerves on the addition of acetic acid.

It will be found that the behavior of the nerve-cells towards acetic acid precisely accords with the account given by Kölliker. The individual parts of the cell generally become somewhat more visible in dilute acid; the cell-membrane exhibits a more distinct contour, the contents of the cells become more granular and often more turbid, but notwithstanding this the nucleus not unfrequently appears distinctly visible. Concentrated acetic acid, after prolonged action or on the application of heat, causes the cell-membranes to swell till at length they become wholly invisible. The granular contents are dissolved, with the exception of the darker granules, which occur in some of the cells; and even the nuclei, which at first come more distinctly into view, finally disappear.

Very dilute *hydrochloric acid* (1 part in 12,560 parts of water) causes the nerve-fibre to swell, and renders the contents far more transparent. The separate fibres exhibit beautiful, sharply defined double contours; between which there remains in the middle a perfectly transparent, tolerably broad space, which appears almost empty. Neither nerve-sheath nor axis-cylinder can anywhere be distinctly recognized. The delicate fibres of the sympathetic are not visibly altered in this very dilute solution of the acid, but the nuclei of Remak's fibres, as well as those of the connective tissue, are brought more prominently to view.

There is very little alteration perceptible in the nerve-cells, even after a very prolonged action of this solution of the acid; at most the membrane is rendered somewhat more hyaline and the contents rather more grumous.

Concentrated hydrochloric acid does not bring into view the individual morphological elements either in the fibres or the cells; but converts the whole into a pultaceous mass of smaller or larger strongly granulated dark clots, which, although most commonly roundish, may assume the most varied and capricious forms. If any remains of nerve-fibres are present, they are found to be very much thickened; the dark clots are perfectly isolated and arranged only in one direction, and no trace of a nerve-sheath is perceptible. When a freshly prepared microscopical preparation is treated with concentrated hydrochloric acid, the individual nerve-fibres diminish in length, but increase to an extraordinary degree in breadth; the nerve-pulp becomes coarsely granular and dark, whilst from the cut extremities nodular or coarsely granular masses protrude, and most distinctly bring into view the coiled roundish threads or axis-cylinders. In this way more frequently than by any other method of exhibiting the axis-cylinder, I have been able to see the sheath and nerve-pulp dissolve in the middle of a fibre, leaving only the axis-cylinder, which at these points might be traced in both directions through the comparatively uninjured nerve-fibre. The peculiar



property of concentrated hydrochloric acid in simultaneously thickening and shortening the nerve-fibre is beautifully illustrated in small bundles of nervous fibres, which are surrounded by the neurolemma. The latter varies in expansibility according to the amount of connective or elastic fibres which it contains. When, therefore, the nerve-tubes which it encloses are much swollen, several protuberant dilatations and corresponding constrictions appear in one and the same bundle. The fibres projecting from the neurolemma at the extremities of the bundles diverge in a brush-like form, whilst the nerve-pulp protrudes from the cut extremities of the fibres, giving to the whole a bouquet-like appearance.

When fresh nerve-fibres are allowed to remain for some time immersed in concentrated *nitric acid*, the whole mass becomes intensely yellow and very friable or soft. On observing under the microscope the direct action of nitric acid, we find that the individual fibres are thickened and shortened as in the case of concentrated hydrochloric acid, although in a less degree. The double contours cease to be recognizable in fibres which have been treated for a longer period with nitric acid; the whole contents of the nerves appear coarsely granulated, and we can perceive no light interspace, or bright central stripe: the nerve-tubes are generally found to have become thinner rather than thicker, and the nerve-sheath can scarcely be recognized with certainty. It is seldom, however, that a microscopical preparation of this kind is thoroughly examined without our detecting some nerve-fibres with the axis-cylinder most distinctly projecting from one extremity like the wick from a taper. Frequently, indeed, six or more of these taper-like nerve-tubes may be seen, the projecting axis-cylinders of which exhibit a distinct yellow color; these have frequently an undulating outline when they project to any great distance, and in some rarer cases have an intestine-like coiled appearance. If fibres, which have been treated with nitric acid, are boiled with absolute alcohol, they become very hyaline, and their outlines grow less distinct, although the yellow transparent nerve-sheath may still be detected at different spots, whilst the interior exhibits a faint granulation, the color of which cannot, however, be determined with certainty. The axis-cylinders are often thus seen more distinctly than by the mere application of nitric acid.

If we boil teased (or unravelled) nerves with alcohol and ether, and after the removal of these fluids allow them to remain for some time in concentrated nitric acid, the nerve-sheath, as Kölliker has already observed, is brought into view, exhibiting faint granules and very beautiful, often detached axis-cylinders. Under favorable conditions there is scarcely any means by which the sheath and axis-cylinder can be more beautifully exhibited.

The first effect of concentrated nitric acid upon the nerve-cells is to render the cell-walls more distinct, and the contents more granular; the cell-membrane, however, soon disappears, and we can perceive only the nucleus in addition to a confluent granular pulpy mass. When the gray substance of the brain has been immersed for any length of time in concentrated nitric acid, nothing can be recognized in addition to the elements of the fibres, excepting nuclei and nucleoli, which are the sole remnants of the nerve-cells.



Concentrated *sulphuric acid* (the third hydrate) forms a fine purplish-red or violet fluid, after remaining for some time in contact with the nerve-fibres. The color resembles that which appears in Pettenkofer's bile-test. The addition of sugar is not necessary for the production of this color. The separate nerve-fibres exhibit a very beautiful violet tint when seen under the microscope; the nerve-sheath, which is found to swell in a gelatinous manner when sulphuric acid is added to a fresh preparation, is rendered entirely invisible in this case. The nerve-pulp is converted into an uncommonly fine granular indistinct body, and it is only in rare cases, although then with extreme distinctness, that the axis-cylinders can be recognized in the individual fragments of nerves. The fluid containing granules and viscid globules, and surrounding the partially undestroyed nerves, is likewise of a violet color.

*Chromic acid*, or a saturated solution of the bichromate of potash, when decomposed with a little sulphuric acid, contracts the transverse diameter of the nerve-fibres, and imparts to them an intense yellow color. After the nerve-fibres have been immersed for a considerable time in this fluid, they appear somewhat narrower, but sharply defined (the double contours of the animal nerve-fibres are, however, no longer visible); the nerve-pulp becomes more coarsely granular and renders the fibres opaque, so that the axis-cylinder can no longer be seen within them. The contracting action of this reagent on the sheath is very beautifully and distinctly shown; we observe at different spots irregular, nodular, but most commonly roundish drops of nerve-fat protruding from it. When the action of the chromic acid is not too strong, the sheath exhibits rents, from which the viscid nerve-pulp exudes, and this appearance is so clearly defined that it is impossible to refer it to any deception. The sheath is completely burst or destroyed at different points, and the nerve-pulp diffused through the fluid, so that nothing but the pale-colored, sharply-outlined filiform axis-cylinder remains visible, whilst in other nerve-tubes the transition of the cylinder into slightly altered fibres may be distinctly traced. With the exception of the following reagent, there is nothing which exhibits the morphological constituents of the nerve-tubes more distinctly than chromic acid.

This acid causes the nerve-cells in some degree to contract, and generally renders their outlines more distinct. The contents are scarcely rendered more grumous than they previously were, whilst there is no important difference to be perceived either in the nucleus or the nucleolus. The cerebral and the ganglionic masses are moreover hardened by the action of chromic acid.

An *aqueous solution of iodine* (or what is better), iodine in a solution of hydriodic acid, colors the nerves yellow, and leaves the fibres tolerably coherent, so that they may be very easily prepared for microscopical investigation, and traced into the individual filaments. After the prolonged action of the above-named fluid, each individual nerve-tube acquires a pale yellow appearance, and becomes broader, showing a tolerably distinct contour (the animal fibres without double contours); the sheath can be readily recognized at individual points; the grumous, but very finely granular pulp appears to fill the whole cylinder, although by a proper mode of arrangement the axis-cylinder may be traced with



the greatest distinctness within the nerve-fibre, following a straight rather than a coiled direction. If the preparation has been very thoroughly unravelled, the axis-cylinder may often be seen protruding from  $\frac{1}{10}$ th to  $\frac{1}{5}$ th of a line beyond one of the uninjured nerve-fibres, being generally straight or slightly bent, rounded, and of a faint yellow color; but occasionally presenting a somewhat coiled appearance.

The aqueous solution of iodine acts upon the nerve-cells in nearly the same manner as upon the fibres.

*Millon's reagent* (subnitrate of mercury with nitrous acid) renders portions of nerve hard and tough, and gives them an intense purple color. The individual bundles do not admit readily of being separated into fibres. Under the microscope the nerve-sheath exhibits a sharp outline; the pulp is not so coarsely granular as after the application of chromic acid, nor so delicate as after the action of hydriodic acid. The granules render the whole nerve-tube very dark, and prevent the recognition of the axis-cylinder. In preparations obtained by unravelling or teasing, we see, however, a number of axis-cylinders either isolated or projecting in a very twisted form from a portion of undestroyed nerve-fibre. The microscope scarcely shows any trace of color in the individual nerve-fibres, or, at most exhibits only a yellowish, and not a violet color.

A solution of *corrosive sublimate*, which is especially recommended by Purkinje for the exhibition of the axis-cylinder, acts independently of the coloration in very nearly the same manner as subnitrate of mercury; but the use of this reagent scarcely facilitates the detection of the axis-cylinder within the uninjured nerve-tube more than the preceding fluid.

The gray cerebral substance, and the sympathetic ganglia harden when immersed in solutions of these two metallic salts. The nerve-cells slightly shrivel, and the cell-membrane is rather more distinct: the contents become more grumous and untransparent, so that the nuclei cannot easily be detected, and the nucleoli only with great difficulty.

A very concentrated solution of *chloride of calcium* renders small nerve-bundles somewhat transparent, but at the same time extremely tough and elastic, so that it is only with great care that we can obtain even a moderately good preparation, in consequence of the extreme difficulty of separating the fibres. When viewed under the microscope the isolated nerve-fibres appear coiled in an intestine-like manner and somewhat distended, the sheath cannot readily be distinguished, and the pulp is converted into a somewhat coarsely granular matter, showing no distinct central fibres; it is only at particular points that a portion of the axis-cylinder may be seen projecting from the extremity of a fibre like the wick from the end of a candle.

When immersed in a concentrated solution of *carbonate of potash*, the nerve-tubes swell somewhat up, and seem partially twisted, the nerve-sheath being unequally extended, so that the tube resembles the colon in form. The individual dilatations are not sharply separated from each other, but on the whole the contents are rather clear and translucent than granular; the axis-cylinder and sheath cannot be recognized. Some light roundish filaments may be seen at the extremities of individual



nerve-fibres which bear an extraordinary resemblance to axis-cylinders, although it is not very certain that they may not be due to the connective tissue, which frequently gives rise to precisely similar filaments. In our description of the above experiments we have therefore only designated these filaments as axis-cylinders in those cases in which their form and position showed they could be nothing else. Objective certainty was unattainable in regard to these filaments, although it seems in the highest degree probable that the axis-cylinder remains uninjured in carbonate of potash.

Virchow<sup>1</sup> first noticed that the substance of the nerves becomes hardened in solutions of carbonate of potash; the fact, observed by my friend Ed. Weber, is especially worthy of notice, that the course of the fibres may be traced in an extremely beautiful manner in the brain and spinal cord, when they have been previously treated with a solution of this salt.

The nerve-cells are also but slightly altered in form in solutions of carbonate of potash.

If prepared nerves are suffered to be immersed for any length of time in a *dilute solution of soda*, the separate fibres appear to become more faintly granulated, somewhat contracted in their diameter, and no axis-cylinder can be detected; the double contours of the cerebro-spinal fibres are also no longer visible. But when a dilute solution of soda is added to a fresh preparation whilst under the microscope, the sheath contracts, as was observed by Kölliker; while the nerve-pulp protrudes either at the extremities of the torn fibres, or through the sheath, which bursts at the point of contraction, in the form of vesicles and granules and more or less sharply defined light or dark globules. It is only in rare instances that the gelatinous swelling and final disappearance of the axis-cylinder can be distinctly traced.

When nerve-preparations which have previously been boiled with *alcohol* or *ether* are suffered to remain for a considerable time in a *dilute solution of soda*, the nerve-tubes appear to be considerably contracted, and to become almost perfectly pale; there is very little indication of any granulation in them, and the appearance presented to us is that of contracted nerve-sheaths from which the contents were entirely removed.

The nerve-cells swell in a dilute solution of soda and become paler; in the meanwhile the cell-membrane is frequently rendered more distinct (Kölliker), but after a time the nucleus wholly disappears. When the gray substance of the brain, or any other nervous substance rich in cells, is exposed to the action of a dilute solution of soda, the cells, that is to say, both the walls and the nuclei, wholly disappear, leaving only a more or less finely granular substance.

When the nerve-fibres have lain for a prolonged time in a *concentrated solution of potash*, the whole mass becomes converted, on being well shaken, into a white emulsive fluid; under the microscope, in addition to simple and double outlined, light or dark vesicles, there appear the most complicated forms of this fat-like matter. Although baton-like bodies

<sup>1</sup> Zeitsch. f. rat. Med. Bd. 4, S. 276.



having double contours, or long filaments varicosely swollen at individual points, become visible, these cannot be regarded by any one who observes them attentively, as the remains of nerve-fibres, for both the sheaths and the axis-cylinders are completely dissolved on prolonged digestion. But when a concentrated solution of potash is added to a fresh preparation of animal or vegetative nerve-fibres, the contents of the individual tubes become granular, the double contours of the animal fibres disappear, and no trace of the axis-cylinder remains. If the preparation is suffered to remain in the air for a prolonged time (until it absorbs water), or if water be added, the outlines disappear gradually, but completely, leaving only serially arranged granules which indicate the former position of the fibres.

When fresh preparations are treated with a concentrated solution of potash, the nerve-cells become slightly contracted, their contents exhibit a more granular appearance, and neither nucleus nor nucleolus is visible; on the addition of water they are observed to swell up, and the contours gradually to disappear in the fluid; the nuclei do not appear, and at length nothing remains visible but a little granular matter.

When preparations of nerves which have been immersed in *concentrated nitric acid* for any length of time are brought in contact with a dilute *solution of potash*, the granular contents exude in the form of pale drops or globules from the yellow-colored portions of fibre, leaving only the empty sheaths, which appear to be of an extremely pale yellow color. This method, which was first suggested by Kölliker, is, perhaps, the best adapted for bringing to view the sheaths of the individual nerve-fibres.

When nerve-fibres, which have been immersed for a considerable time in *concentrated acetic acid*, are treated with boiling ether or alcohol, their appearance is found to differ according as these agents have acted more on small bundles or on individual portions of fibres. The longer portions, or the nerve-fibres that have been separated by the method described in the preceding paragraph, appear to be somewhat contracted when compared with the thick coarsely granular fibres which have been treated with acetic acid only; the pale contours, corresponding to the sheath-membrane, become distinctly visible at certain points; invested in this membrane we see short portions of a granular substance, which are separated from one another by light intermediate spaces; there is usually no axis-cylinder to be recognized in these fibres. If the acetic acid has not exerted its action for too long a time, and especially if it has not been warmed, the axis-cylinder may be very distinctly seen in the torn fragments of a nerve-fibre after it has been treated with alcohol or ether, and its projecting end may be traced for a considerable distance within the tube. Very short portions of nerve-tubes seem, however, to be perfectly empty, appearing like tolerably regular, very faintly granular, extremely transparent cylinders, bearing some resemblance to the urinary cylinders in Bright's disease, which are composed of the *membrana propria* of the tubes of Bellini, only they are far narrower and at least equally hyaline.

If we now proceed to consider the conclusions which may be deduced from the above-described micro-chemical reactions, and from others on



a larger scale, we find that the following is the *chemical constitution of the separate morphological constituents* of the nerve-fibres and cells.

*The sheath of the nerve-fibres* consists, according to the above observations, of a structureless, somewhat elastic membrane, which does not swell in a gelatinous-like manner in acetic acid, is not dissolved either by boiling or by treatment with dilute alkalies, and cannot, therefore, at all events, consist of pure connective tissue. It dissolves completely in concentrated acetic acid, as well as in solutions of potash and soda after prolonged digestion or boiling, and likewise in concentrated sulphuric acid, but does not dissolve in concentrated nitric acid, which appears to impart a yellow color to the empty sheaths, although it cannot be distinctly determined by the microscope whether this pale yellow color proceeds from the sheath itself or from the small quantity of albuminous matter remaining in the partially emptied nerve-fibre. We are thus led to the hypothesis advanced by Mulder<sup>1</sup> and Kölliker,<sup>2</sup> that the sheath of the nerve-fibre consists of a substance not unlike elastic tissue, from which it, however, differs by its solubility in boiling acetic acid, and by its greater solubility in a solution of potash. It is very analogous to the substance of the sheath of the primitive bundles of muscles, but resembles a true protein-substance much more nearly than does the elastic tissue.

*The axis-cylinder* consists, according to all the above-mentioned reactions, of a protein-substance which presents many resemblances to the substance of the muscular fibrils (syntonin), although it is certainly not identical with it. The substratum of the axis-cylinder shows itself to be a protein-substance by its behavior towards acetic acid and very dilute hydrochloric acid, towards dilute and concentrated alkaline solutions, towards concentrated nitric acid and potash, as well as towards concentrated sulphuric acid. This substance differs from ordinary blood-fibrin by the difficulty with which it dissolves in acetic acid, and by its perfect insolubility in carbonate of potash, as well as in a solution of nitre after a prolonged digestion at a temperature of 30°; and it is distinguished from muscle-fibrin (syntonin) by its insolubility in dilute hydrochloric acid, and by the difficulty with which it dissolves in acetic acid. It is scarcely possible to confound it with the substratum of any other elementary tissue. The substratum of elastic tissue is perfectly insoluble in dilute alkalies and in acetic acid. Moreover, the substance of the axis-cylinder cannot be composed of gelatigenous connective tissue; for, independently of the above-described behavior towards acids and alkalies, it undergoes no change whatever when boiled with water. Least of all could we have expected that any one should regard the axis-cylinder as composed of fat, or at all events, of a very fatty substance, as Mulder and Donders have actually done. The constantly recurring cylindrical form which is observed on the application of the very different reagents which have been mentioned, the great coherence, the elasticity and sharp outline of the axis-cylinder, its complete insolubility in boiling alcohol and ether, its continuous visibility on the application of reagents which expel and dissolve the fat from the nerve-tubes, and, lastly, the entire absence of experimental evidence that a fat can under any circumstances be converted

<sup>1</sup> Vers. einer physiol. Chemie, S. 655 [or English Translation, p. 602].

<sup>2</sup> Mikrosk. Anat. Bd. 2, S. 397.



into a consistent and resistant filament, incline us to believe that Mulder's assertion must be ascribed either to a simple error of memory or to a *lapsus calami*; for, although we may not be able to prove definitively that the axis-cylinder is wholly free from fat, the above reactions appear to show beyond a doubt that it consists essentially of a protein-like body, and that the fat which is so abundant in the nerves is principally, and in all probability, entirely accumulated in the nerve pulp. Kölliker has been led to advocate this view from his investigations regarding the axis-cylinder.

The *medulla* or *nerve-pulp* appears, as we have already seen, to be perfectly homogeneous in recent preparations of the nerves, and moreover so perfectly transparent, that we can scarcely conceive it to be anything more than a viscid emulsive fluid, although the above-indicated micro-chemical reactions, and the behavior of the nerve pulp in water, and on exposure to cold, show, that in addition to an abundant supply of fat, it also encloses a protein-substance, permeated by aqueous moisture. I can hardly compare this protein-substance to coagulated albumen, as some other observers have done, for albumen in a state of coagulation would easily admit of being distinguished under the microscope from fat, by the molecular form which it presents in this condition. It may very probably be regarded as corresponding with soluble albumen or casein, for when chemists engaged in analyses of the cerebral substance speak of coagulated albumen, they do not refer to the albumen of the true nerve-pulp, but to the fibrin-like matter of the axis-cylinder. The albuminous substance of the nerve-pulp is, however, entirely different from the matter forming the axis-cylinders. This substance is soluble in, or rather it may be extracted from, the nerve-pulp by a dilute solution of soda, and by acetic acid when not too much diluted; so that after repeated treatment with boiling alcohol or ether, the nerves appear to be perfectly empty, with the exception of the axis-cylinder. When nerve-fibres have been treated with alcohol or ether, after having been exposed to the action of concentrated nitric acid, or conversely when they have first been treated with nitric acid, and subsequently with a fat-solvent, they still exhibit finely granular yellow-colored contents, which can be nothing else than this protein-substance, which is now in a coagulated state. I have frequently been at great pains to ascertain the presence of a protein-substance coagulable by boiling or by acetic acid in cerebral matter which had been extracted with water; but from various causes, amongst which may be mentioned the emulsive form which the fluid constantly presented, the blood-serum which it always contained, and the power exerted by acetic acid in decomposing the fatty matters, I was prevented from obtaining any undoubted result. Although it is very difficult to obtain direct proof from microscopical observations, or rather to form a judgment from them, the descriptions of the alterations experienced by the nerve-pulp on the addition of different reagents (in becoming coarsely or finely granular or crystalline) seem to indicate that the nerve-pulp contains a soluble protein-substance in the closest admixture with a fat dissolved by easily decomposable soaps, and that the visibility of the pulp is owing less to the coagulation of this albuminous body than to the separation of the fat from the decomposing soaps and



the albuminous substance. It might, indeed, be assumed from the alteration which is gradually perceptible in the pulp of fresh nerves, on exposing them to the action of the air, water, or cold, that a substance similar to the fibrin of the blood was in solution in the fresh nerve, and subsequently coagulated like blood-fibrin; but repeated microscopico-mechanical investigations of the nerve-fibre do not especially favor this hypothesis, for the substance which is separated has always more or less the character of fat, but not that of fibres (like coagulating blood-fibrin), or that of the finest molecular granules (like other protein-bodies in coagulating). For even if we assume such a spontaneous coagulation of the albuminous substance of the nerve-pulp, the undoubted separation of the fat would still remain unexplained, and we should be compelled to have recourse to the preceding conjecture, regarding the separation of the fat from the solution of the salts of the fatty acids. It seems to us, however, that Henle's<sup>1</sup> view, that the nerve-pulp is not an emulsion, but an actual solution or mixture, leaves no doubt in relation to this question.

It may be observed that Bence Jones<sup>2</sup> has made an elementary analysis of the residuum which is left after boiling the brain in alcohol, ether, and water, and found that its composition was the same as that of albumen. It is scarcely necessary to remark that in the present state of our knowledge, no conclusions can be deduced from such analyses as these.

The *fats* of the nervous substance can more readily be submitted on a large scale to accurate chemical investigation than any other constituents of the nerve-fibres, but this very circumstance has thrown extraordinary difficulties in the way of inquirers, which have been increased from the fact that the chemical investigation was not simultaneously associated with a careful microscopical examination of the matters that were being chemically treated. Whilst so distinguished a chemist as Couerbe<sup>3</sup> has distinguished a number of indistinctly characterized fats, as a *cephalot*, *cerebrot*, *stearoconnot*, *eleëncephol*, &c., a no less distinguished chemist, Fremy,<sup>4</sup> arrived at very opposite results, which, although they threw considerable light on this question, did not by any means exhaust the subject in a chemical point of view. Gobley,<sup>5</sup> as we have already observed in vol. i. p. 218, separated phosphate of glycerine from the brain-fat. The following facts are almost the only ones possessing any certainty which have been obtained from the investigations hitherto made in relation to these fats (which were nearly all extracted from the brain). According to Fremy, boiled alcohol will extract from triturated cerebral matter olein and oleic and margaric acids, and fats which are combined in part with soda, potash, or lime; on then digesting the residue with hot ether, cholesterin and cerebrie and oleophosphoric acids are obtained in solution. The separation of these two groups is not, however, so perfect as might have been supposed from the above remarks; for a considerable

<sup>1</sup> Allg. Anat. S. 624.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 40, S. 68 ff.

<sup>3</sup> Ann. de Chim. et de Phys. 2 Sér. T. 56, p. 164-180.

<sup>4</sup> Journ. de Pharm. T. 26, p. 769-794, and Ann. de Chim. et de Phys., 3 Sér. T. 2, p. 463-488.

<sup>5</sup> Journ. de Chim. et de Phys. 3 Sér. T. 11, p. 409-417, et T. 12, p. 5-13.



amount of cerebrie acid and cholesterin passes into the alcoholic solution, whilst oleic and margaric acids are found in the ethereal solution.

Fremy obtained the *cerebrie acid* tolerably pure, by again stirring the ethereal extract of the brain with cold ether, from which a white mass separated, which soon assumed a waxy character after decantation of the ether on exposure to the air. The fatty acid was combined here with soda and lime; this soap was next dissolved in boiling anhydrous alcohol, and decomposed with a few drops of sulphuric acid. After the sulphates (which contained a little coagulated albumen mixed with them) had been removed by filtration, the hot solution was allowed to cool; from this the cerebrie acid separated itself, mixed with a little oleophosphoric acid, which latter substance was removed by means of cold ether, and the cerebrie acid once more crystallized in hot ether.

This substance, which Goble thinks he has also found in the fat of the yolk of egg, forms a glistening white powder, which is insoluble in cold alcohol and ether, but dissolves in both upon boiling. The white granules swell in water. This acid combines with most bases and forms salts, which are perfectly insoluble in water. Fremy found in the dried baryta salt 7.8% of baryta; in 100 parts of the acid, according to separate determinations, 66.7% of carbon, 10.6% of hydrogen, 2.3% of nitrogen, and finally 0.9% of phosphorus. The quantity of oxygen must, therefore, have amounted to about 19.5%, whilst the saturating capacity was about 0.884.

Fremy's *oleophosphoric acid* has been examined even less accurately than cerebrie acid. He obtained it by treating the ether-extract of the brain, from which the cerebrie acid had been deposited, with cold ether. It remained combined with soda after the ether had been removed by distillation, and presented the appearance of a viscid mass. It appears to be separable from the base by washing with a dilute acid. When isolated, it forms a yellowish viscid mass, which is inflammable, and leaves a bulky carbonaceous residue, from which phosphoric acid may be extracted by water; it is insoluble in water and cold alcohol; but dissolves in hot alcohol as well as in cold and hot ether. If this acid is boiled with alcoholic solutions of mineral acids or alkalis it is decomposed, according to Fremy, into olein, and oleic and phosphoric acids. Although Chevreul conjectured that the brain-fat might be a combination of olein and phosphoric acid, such a decomposition of oleophosphoric acid is somewhat remarkable, considering our present views of the decomposition of the fats; and indeed, Goble believes that he has found that oleophosphoric acid yields only oleic acid and phosphate of glycerine, and not olein, during the decomposition which it undergoes during the putrefaction of the brain. This question does not, however, admit of a ready solution, since it is very difficult altogether to free the substance which Fremy terms oleophosphoric acid from the olein and cerebrie acid adhering to it. We may, however, readily convince ourselves that Fremy was mistaken in believing free phosphoric acid to be formed, the substance being, as Goble has found, phosphate of glycerine. I succeeded on one occasion in most unquestionably demonstrating the presence of phosphate of glycerine in the mass obtained from a very diffused yellow softening of the brain, which, as Rokitansky has shown, contains a free acid. Moreover while Fremy found from 1.9 to 2.0% of phosphoric acid in his oleophosphoric acid, Goble, on decomposing the



same acid by acids and alkalies, always obtained margaric acid in addition to oleic acid,—a proof of the obscurity which still envelopes the whole subject. It seems indeed to be proved, from the observations hitherto made in relation to this question, that the elements of these two kinds of cerebral fats are very unstable, that is to say, that they are extremely prone to numerous decompositions, and that they are mere admixtures of substances of which the one may have served the other as a medium of solution or distribution. The presence of nitrogen in the cerebrie acid, and Fremy's assertion that albumen passes into the ethereal solution, are questions which, singularly enough, have hitherto failed to excite observers to any more exact investigations, although they are at variance with pre-existing observations, and may very probably be of great significance in reference to the function of the nervous system, which is so immutably combined with its chemistry.

The *cholesterin* which occurs in the fat of the brain is partly taken up by the alcoholic extracts, and partly dissolved by ether, together with the cerebrie and oleophosphoric acids, which it accompanies in all their solvents.

The analyses of so careful an observer as Fremy preclude the possibility of doubting that pure olein is contained in brain-fat, although we cannot consider it as demonstrated that this olein is derived from the (so-called) oleophosphoric acid.

The quantity of oleic and margaric acids obtained by Fremy on extracting the brain-fat with alcohol containing ammonia, is very small. When, as is often the case, these fatty acids are found in considerable quantity in the brain, their presence may in reality be owing to the facility with which the brain and its fats are decomposed.

We know but little of the chemical composition of the morphological elements of the nerve-cells, for the micro-chemical reactions already given lead us to a very few conclusions on this point. From these observations it appears that the investing membrane of these cells does not easily dissolve in acetic acid and in alkalies, although it certainly cannot be regarded as entirely insoluble in them. It may, indeed, bear some resemblance to syntonin, for the cell-membrane is insoluble in carbonate of potash, and, as we have already stated, the nerves harden in a solution of this salt. It is worthy of notice in reference to this subject, that the gray, highly cellular substance of the central organs becomes more hardened than the white.

The nuclei of the nerve-cells, like those of most other cells, are rendered more distinctly visible by acids, whilst they disappear in alkalies, without, however, enabling us to form any exact idea of their chemical nature.

It appears from the micro-chemical reactions, which have been previously described, that the semi-fluid granular contents of the nerve-cells are much poorer in fat than the pulp of the nerve-tubes; for after the application of acetic or hydrochloric acid, or other reagents, we perceive a far smaller quantity of coarse granular fatty matter in them than in the nerve-pulp. This observation would appear to acquire corroboration from the smaller quantity of fat in the gray than the white substance of the brain, provided, indeed, that any definite conclusions can be drawn from



analyses of entire portions of the brain. All analysts have found only very little fat in the gray substance, which is so rich in cells, whilst in the fibrous medullary substance there is at least four times as much fat present. As, moreover, the contents of the nerve-cells are not rendered much paler by the application of alcohol or ether, their granular appearance must be owing less to fat than to other molecular matters. These granules must not, however, be confounded with those very dark granules which are insoluble in caustic alkalies, and which we chiefly see in the nerve-cells which are either stellate or provided with long processes or prolongations. These consist of a substance which is still chemically unknown to us, but which is not very dissimilar to pigment-granules. It would appear, therefore, highly probable from the above observations, that the principal part of the contents of the nerve-cells consists of a partly dissolved, and partly only swollen protein-substance.

If we now take a glance at the little that is known regarding the composition of the cerebral and nervous masses generally, the following points present themselves to our notice; we must, however, bear in mind that the cerebral mass contains a large number of bloodvessels, and, consequently, a quantity of blood, which must not be included in the analysis.

We were not in possession of any very carefully conducted investigations respecting the amount of *water* and *fat* present in different parts of the brain, until the subject was recently undertaken under Schlossberger's superintendence by Hauff and Walther,<sup>1</sup> and by von Bibra.<sup>2</sup> These investigations have led to results which are on the whole of a very conclusive and accordant character. It is perfectly established that the white substance of the brain is much poorer in water and richer in fat than the gray matter. With reference to individual portions of the brain, the quantity of water seems to stand in an inverse ratio to that of the fat. In the cortical substance of the hemispheres Hauff and Walther found from 85 to 86% of water, and only from 4.8 to 4.9% of fat; and von Bibra from 84 to 88% of water, and from 5.5 to 6.5% of fat; whilst the former of these observers found 70.2% of water, and from 14.5 to 15.5% of fat in the white substance of the corpus callosum, the latter obtained from 63.5 to 69.2% of water, and from 20 to 21% of fat. On comparing the quantity of fat and water found by these analysts in the different parts of the brain, we find that it may be predetermined with tolerable accuracy according to the relative amount of the white and gray substances. The same relation was found to exist not only in man, but in all animals in which the brain is sufficiently large to admit of the analysis of the separated gray and white matter for fat or water. Moreover Lassaigne<sup>3</sup> had previously found that the gray substance was richer in water than the white, the former yielding 85.2%, and the latter only 73.0% of water.

Von Bibra found that in man, as in most animals, the greatest quantity of fat was deposited in the medulla oblongata.

Vauquelin, as well as Fremy, found that the whole brain (gray and white substance mixed) yielded with tolerable uniformity 80% of water and 5% of fat, whilst Dennis found only about 78 or 76% of water, but

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 85, S. 42-55.

<sup>2</sup> Ibid. p. 201-224.

<sup>3</sup> Compt. rend. T. 9, p. 703, et T. 11, p. 763.



as much as 12 or 13% of fat; von Bibra found on an average 75.54% of water and 14.43% of fat. In animals the quantities of water and fat were found to differ considerably.

Bibra found from 1.5 to 1.9% of *phosphorus* in the brain-fat.

Fremy found 7% of *albuminous matter* in the brain; and Lassaigne 7.5 in the gray cerebral substance, and 9.9% in the white substance.

Lassaigne, singularly enough, found only from 2.2 to 2.3% of salts in the brain of an insane patient, whilst, according to Vauquelin and Fremy, 6% is the smallest normal quantity.

Schlossberger<sup>1</sup> has recently made the remarkable observation on the brain of a child which died at birth, that, in the first place, the corpus callosum in new-born infants is as rich in water as the gray substance; further, that the quantity of fat is nearly the same at this age in the gray and white substance; and, finally, that the brain of new-born infants is generally much richer in water and poorer in fat than the brain of adults.

Schlossberger found that the quantity of water in the brain of the child referred to, varied only in different parts from 87.4 to 89.6%, whilst the fat fluctuated between 4.5 and 3.8%.

When we pause to inquire whether any important conclusions can be deduced from the chemical investigations hitherto instituted in reference to the nervous mass, as to any special function of the nervous system, we are obliged to admit the complete insufficiency of our chemical knowledge. But, however forcibly we may be compelled to admit the incapacity of chemical assistance to explain the actions of the nervous system, chemists will not suffer themselves on that account to be deterred from further investigations; for they must be well aware that, without a careful examination of the chemical phenomena presenting themselves in the nervous system, they can never succeed in tracing nervous action to definite physical laws. The very great significance of the axis-cylinder discovered by Remak, and termed by him "the primitive band," the important discoveries of Dubois regarding electric currents in the nerves, and the minute and ingenious physiological experiments on the different functions of the individual systems of nerve-fibres and cells, will not afford us any deeper scientific insight into the general functions of this most delicate of animal matters, or justify us in establishing definite laws, and not merely individual propositions or rules, until we shall succeed in forming for ourselves a mental representation of the reciprocal actions of the chemical substrata when the nerves are in a state of activity. If observers should ever succeed in detecting the presence in the nerves of a peculiar agent, active only in living animals, or if the propagation of nerve-force, and the corresponding phenomena of reflex action, irradiation, &c., should be found to depend upon electrical currents passing through cylinders endowed with more or less thoroughly isolating walls, chemistry must still be called to our aid if we wish to obtain an exact physical explanation of such phenomena. Chemistry is too intimately associated with all the most important questions concerning the theory of the nerves to be excluded from its just participation in the study of that most noble of all animal matters in

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 86, S. 119-125.



which are concentrated the highest vital functions. The share taken by chemistry in the explanation of the functions of the nervous system is now so thoroughly and fully admitted that it is unnecessary to enlarge upon this point. In correspondence with the physical and physiological phenomena of the nerves, we find a substance accumulated in them which exhibits such mobility in reference to its proximate constituents as is not to be met with in any other organ of the animal body; the chemical phenomena very probably, therefore, stand also here in the closest relation to the physical and physiological. Scarcely any one can entertain the idea that the nerves which (as Ludwig<sup>1</sup> has shown in his admirable Memoir on the influence of the nerves upon the salivary secretion) co-operate directly in the elaboration of certain secretions from the blood, and influence their accelerated or modified separation, can control such functions without undergoing chemical change. The chemical substrata of the nerves are conformable to their functions; for, as in all other organs, the physiological importance of the chemical constitution, and the relations of affinity between the chemical substrata, must accord with one another. (See vol. i. p. 36.)

The *analysis* of the nervous tissue is obviously still very imperfect, as must be seen from the above remarks.

The most suitable object for an investigation of this kind is probably the white matter of the hemispheres of the cerebrum, if we have reference only to the facility with which considerable quantities of it may be obtained. The white matter is far preferable to the gray, as it contains fewer bloodvessels, no nerve-cells and scarcely anything but nerve-fibres.

In making the determination of the quantity of water, the same precautions are required as in the case of every other organ, and especially of the muscles. We have already shown the importance of such precautions in our observations on the latter organs.

In determining the mineral constituents of the cerebral matter, it must be borne in mind that the ash exhibits an acid reaction from the presence of free phosphoric acid, and that it, on that account, generally encloses a considerable amount of carbon. As is well known, phosphorus is given off in a volatile form when carbon is heated with phosphoric acid or with acid phosphates, and any metallic chlorides or phosphates which may be present, are simultaneously decomposed; hence, it is absolutely necessary to triturate the dried cerebral mass before its incineration with a little carbonate of baryta—a precaution which will prevent any kind of loss.

The most rational method of separating the organic, and especially the morphological elements, and the one which accords most closely with the micro-chemical reactions, is to treat the triturated cerebral mass with a dilute solution of carbonate of potash, as this solution does not attack the axis-cylinder or the nerve-sheath, and alters the nerve-pulp less than any other reagents, inasmuch as it simply dissolves the albuminous substance and the greater part of medullary fat; the filtered fluid certainly passes in a turbid state through the filter, just as when pure water is used in place of the above reagent, but here a much smaller quantity of

<sup>1</sup> Mitt. d. Zürch. naturf. Gesellschaft. No. 50, 1851.



fat is held in suspension, and a much larger amount actually dissolved. Mere traces of only histological elements, and often not even these, penetrate through the filter, and after repeated rinsings with the solution of carbonate of potash there remains on the filter only a very little fat (principally a little cerebrie acid) with the other organic matters. The albuminous substance of the nerve-pulp may easily be detected in the solution by means of the ordinary reagents after the fluid has been saturated with acetic acid, the precipitate separated by filtration, and the suspended fat removed by ether.

The residue of the cerebral mass, which is insoluble in carbonate of potash, and, besides a part of the cerebrie acid, contains only the axis-cylinders and the nerve-sheaths, must be heated in a dilute solution of potash or soda for the purpose of dissolving the acid; from this solution the albuminous substance of the axis-cylinders, together with a little cerebrie acid, is precipitated by acids, with the development of a little sulphuretted hydrogen.

The residue of the cerebral matter, which is insoluble in dilute solutions of the caustic alkalies and their carbonates, contains scarcely anything but the nerve-sheaths and a little cerebrate of lime, the latter of which may be removed by boiling this residue first with dilute acetic acid, and subsequently with ether. We cannot, however, unfortunately consider this residue as a chemically pure substratum of the nerve-sheaths, as the walls of the capillaries are intermixed with it.

The methods of investigation which we have described do not, however, as we stated, suffice to separate the cerebral fats in any rational manner from one another; nor can we hope to see good methods employed for quantitative separation until the chemical constituents of the cerebral and nervous matter shall have been determined with much greater exactness.

[I have just received a copy of a Memoir by von Bibra, entitled "Comparative Investigations of the Brain of Man and the Mammalia;"<sup>1</sup> his principal conclusions are here given. Much interesting matter upon the subjects discussed in this section will also be found in Schlossberger's Memoir on the Nervous System in his "First Attempt at a General and Comparative Animal Chemistry,"<sup>2</sup> which is now in the course of publication.

Von Bibra's Memoir is divided into nine sections, which treat respectively of:

- I. The relative proportions of water, fat, and solid constituents in the brain of man and animals.
- II. The fats of the brain.
- III. The water-extract of the brain.
- IV. The inorganic constituents of the brain.
- V. The amount of phosphorus in the brain.
- VI. The gray and white substance of the brain.
- VII. The brain in insane patients.

<sup>1</sup> Vergleichende Untersuchungen über das Gehirn des Menschen und der Wirbelthiere. Von Dr. Freiherrn Ernst von Bibra. Mannheim, 1854.

<sup>2</sup> Erster Versuch einer allgemeinen und vergleichenden Thier chemie. Von Julius Eugen Schlossberger. Erste Lieferung. Stuttgart, 1854.



VIII. The brain in the embryo and in extremely young animals.

IX. The weight of the brain as compared to that of the body.

I. From a very large number of analyses (he determined the amount of fats, water, and solid constituents in more than 100 cases in the human brain, in 138 other mammals, in 75 birds, and in 13 amphibians and fishes) he draws the following conclusions.

1. Within certain limits the quantity of fat is constant in the brain of man, as also in that of other animals.

2. Diseases of the general system, and even such as induce a diminution or disappearance of the fat in other parts, do not occasion a diminution in the amount of the brain-fat.

3. Fattening an animal appears to exert no special influence on the amount of fat in the brain.

4. The brain in other mammals contains less fat than the human brain. Where the opposite is the case, it appears to be induced by the ratio of the weight of the brain to that of the body, that is to say, the smaller quantity of cerebral substance is compensated for by a larger quantity of fat.

5. The brain in birds contains less fat than the brain in mammals.

6. The brain in amphibians and fishes contains a trace less fat than that of birds.

7. In man, other mammals, and birds, the medulla oblongata contains the largest amount of fat.

8. The quantity of fat in the hemispheres is both relatively and absolutely greater in man than in the other mammals, and in the latter than in birds.

9. The whole quantity of brain-fat in old men is a little less than that in adults in the prime of life.

10. The water and solid constituents (the fat not being included) fall and rise in their amount in all classes of animals with the augmentation or diminution of the fat, the albuminous matters being liable to the greatest variations.

11. It is not definitely established that the brain in mammals contains a larger mean quantity of water than the human brain; it would appear as if in this class of animals the smaller quantity of fat is compensated for by the albuminous substance rather than by water.

12. In birds, on the contrary, the amount of water in the brain is unquestionably larger than man or other mammals.

Von Bibra believes that the analyses, from which the preceding conclusions are drawn, establish beyond all question the importance of the fat in relation to the functions of the brain.

II. The brain-fats seem to have been submitted by him to a very careful investigation. The following are his chief conclusions. The brain-fats consist of cerebrie acid and cholesterin, and of a series of fatty acids which possess very different properties and very diverse fusing points. These fatty acids are not the same in different brains even of one and the same species; and it would seem probable that in the living



organism they are undergoing perpetual decomposition, passing into one another, and taking a share in the cerebral functions. They contain no nitrogen or sulphur, and those which solidify below  $-12.5^{\circ}\text{C.}$ , contain no phosphorus.

His cerebrie acid agrees very well with the acid described by Fremy: von Bibra however finds as a mean of five analyses only 0.52% of phosphorus (the extremes being 0.49 and 0.55%), whereas Fremy fixed this constituent at 0.9%. He found that in adult men the brain-fat contains 20 or 21% of cerebrie acid, and from 30 to 33% of cholesterin, while the remainder is made up of the above-noticed fatty acids and their salts.

The cerebrie acid is rather more abundant in the brain of man than in that of the other large mammals.

The gray substance of the brain contains the least cerebrie acid, a mean quantity of cholesterin, and an excess of the other salts.

The white substance contains more cerebrie acid and cholesterin than the gray, and consequently less of the other fats.

Although all these constituents of the brain-fat are found in the smaller mammals as well as in birds, amphibians, and fishes, and likewise in young infants and in the embryo, yet the quantity of cerebrie acid seems to diminish as we descend the animal scale, and to be smaller in the infant and foetus than in the adult.

III. His examination of the water-extract was not very satisfactory. He found

1. That the water-extract of the brain both of man and other mammals was entirely devoid of all those crystallizable bodies which have as yet been found in other parts of the organism.

2. That lactic acid was certainly present, and probably also another non-volatile acid, in addition to volatile acids.

3. That, besides albumen coagulable by heat, there were present various modifications of albuminous substances which were not precipitated from their solutions by boiling; and that at least two nitrogenous substances were present, one of which was soluble in water alone, the other in water and alcohol.

IV. From a large number of analyses of the mineral constituents of the brain he deduces the following conclusions:

1. The inorganic constituents of the cerebral substance are the same as we meet with in other organs and in the formative fluids.

2. This qualitative condition holds good in all the classes of the vertebrata.

3. The ratio of the potash to the soda is nearly intermediate between the ratios occurring in the ashes of flesh and blood respectively.

4. Sulphates are almost entirely absent, and the quantity of the chlorine is very variable.

5. In man and other mammals the medulla oblongata contains more earthy phosphates than the other parts of the brain.

6. The amount of inorganic constituents is greater in the brain of birds than in that of man or other mammals.

7. The brains of amphibians and fishes contain more inorganic constituents than those of the other classes of animals.



8. The amount of earthy phosphates is moreover greater in the brains of amphibians and fishes than in the other classes of animals.

V. We quote the following determinations of the amount of phosphorus in human brain-fat.

MAN AGED FIFTY-NINE YEARS. BRIGHT'S DISEASE.

	Phosphorus.
100 parts of fat from	
The medulla oblongata, contained, . . . . .	1.65
The cerebellum and Pons Varolii, contained, . . . . .	1.83
The crura cerebri, contained, . . . . .	1.76
The hemispheres, " . . . . .	1.83
The corpora striata, " . . . . .	1.65
The optic thalami, " . . . . .	1.54
The corpus callosum, " . . . . .	1.54
The mean for all the parts being, . . . . .	1.68

In a girl aged 19 years, the mean quantity was 2.53; in a man aged 65 years, who died from marasmus senilis, 1.72; in a man aged 80 years, who died from old age, 1.93; and in a man aged 25 years, 1.89.

In three cases of insanity, the patients being men of the respective ages of 36, 38, and 52 years, the percentage of phosphorus in the brain-fat was 1.75, 1.93, and 1.87.

Von Bibra draws the following conclusions from his numerous analyses:

1. The amount of phosphorus in the brain-fat is very nearly the same in man, in other mammals, and in birds. With the exception of a single case, that of the chamois, in which it amounted to 3.40, it never exceeded 3.0%, and it never sunk below 1.0%, except in *Falco nisus*, in which it was as low as 0.72%.

2. The phosphorus in the brain-fat of insane persons does not exceed the mean amount; nor does extreme old age modify the quantity.

3. The brain in very young persons, and in the embryo, presents no peculiarity in this respect.

4. The fat of the gray matter contains rather more phosphorus than that of the white substance of the brain.

Von Bibra believes that the phosphorus of the brain belongs to one of the brain-fats, and in part, unquestionably to the cerebrie acid, and that consequently its amount varies in different brains with the amount of fat: there is, however, no reason to believe that there is any special connection between the intelligence and the amount of phosphorus.

VI. The gray and white matter of the human brain were separately analyzed by von Bibra. We quote his analysis in the case of a man aged 30 years, who died from pulmonary phthisis.

	a. Gray substance of the hemi- spheres.	b. White substance of the corpus callosum.	c. White substance of the medulla oblongata.
Fat, . . . . .	6.43	20.43	14.67
Water, . . . . .	83.57	69.19	71.55
Solid constituents (ex- clusive of fat), . . . .	10.00	10.38	13.78



This brain-fat was again analyzed, and found to be composed as follows:

	a.	b.	c.
Cerebric acid, . . .	2.64	20.72	24.70
Cholesterin, . . .	34.74	37.07	47.06
Other fats, . . .	62.62	42.21	28.24

Hence it follows that the gray substance contains less fat than the white, and that the fat is here replaced by water: and further, that the cerebric acid, and to a certain extent the cholesterin, preponderate in the white substance.

VII. In the analyses of various parts of the brain of three insane persons he was unable to detect any striking chemical peculiarity.

VIII. We give his analyses of the brain of the human embryo at different stages, and of that of a child aged 6 months.

	At 10 weeks.	At 12 weeks.	At 14 weeks.	At 18 weeks.	At 20 weeks.	At 21 weeks.	At 37 weeks.	Child.
Fat, . . . . .	1.26	0.99	1.53	1.06	1.07	1.23	8.06	6.99
Water, . . . . .	85.10	86.71	86.24	86.90	86.03	85.93	87.90	82.96
Solid constituents (exclusive of fat),	13.64	12.30	12.23	12.04	12.60	12.84	9.04	10.04

From these and similar observations on the lower animals (dogs, cats, pigs, horses, goats, and cows), it appears that the amount of fat in the brain of the foetus is far less than in that of the adult individuals, the difference being made up by an excess of water. The great and sudden augmentation of fat towards the end of foetal existence, and shortly after birth, is a fact of much physiological interest.

The last section of von Bibra's Memoir pertains rather to Anatomy than to Chemistry, and therefore requires no notice in the present place. —G. E. D.]

## EXUDATIONS AND PATHOLOGICAL FORMATIONS.

We have often had occasion to comment upon the inefficiency and imperfection of our chemical knowledge, when compared with the great expectations which have been entertained in respect to its applications to physiology and pathology; yet there is scarcely any subject which more thoroughly calls for a confession of our weakness and incapacity than the one we are now about to consider. The exudations constitute the most important object of zoo-chemical investigation in reference to pathology, and the whole scope of pathological anatomy may be said to consist in the study of these structures and their different metamorphoses. But whilst pathological morphology may be said to have already reached a very high degree of development, the chemistry of morbid structures is still very obscure. The history of the development



of pathological forms has contributed very little to clear up these difficulties, notwithstanding the great advance which this branch of science has made in recent times; and it is an undeniable fact that in the case of many pathological forms we are wholly ignorant whether we have before us the beginning or the end of the process, the first formation, or the last stage of disintegration. The science of pathological histology, which alone can guide the chemist, is so full of uncertainties, subjective conceptions, and varying conjectures, notwithstanding some signal advances, that it scarcely ever presents any starting-point for chemical investigation. Few attempts have been made to institute a micro-chemical analysis even of the simplest pathological forms, and how can the chemist, if he have no certain point to start from, arrive at correct conclusions amidst opposing opinions, and the most variable forms and the apparently similar products of the most widely differing processes? Let the chemist once obtain a fixed basis on which to found his inquiries, and he will not fail to resolve purely physical processes into tangible phenomena.

It must be admitted, however, that the causes which prevent the chemist from responding to the demands of the theoretical physician do not depend solely upon deficiencies of physical proofs and pathological observations, but upon an obscurity in the corresponding departments of chemistry. We have endeavored (see vol. i. p. 31) to explain the causes which prevent chemistry from participating in the investigation of pathological matters, and we would indicate some points which may serve to justify the mode of treatment we have adopted in this chapter, and to explain the inefficiency of chemistry to solve pathological inquiries.

We referred, in the introduction to histo-chemistry, to our very deficient knowledge of the protein-bodies as the principal cause of our inability to comprehend the elaboration of the tissues; yet the metamorphoses of the protein-bodies of the blood play the principal part in the pathological exudations, cells, and tissues. It therefore appertains to the chemist to follow the individual metamorphic stages in each of these bodies, as the histologist endeavors to trace the gradual formation of morphological elements in their metamorphosis into cells and tissues. But whilst the parent substances, and their relations to one another, are so imperfectly known that we cannot, with any certainty, attempt to establish for them a chemically rational formula, we have but little prospect of being able to elucidate their proximate derivatives and the relations of affinity they bear to one another. The prospect would be less discouraging if we were as well acquainted with the first stages of metamorphosis as with the protein-bodies themselves. It should be remembered how difficult it is to distinguish albumen and casein when they are associated in the yolk of egg and elsewhere; that casein itself appears to be a mixture of several substances; and lastly, that it is a matter of extreme difficulty, indeed almost an impracticable operation, to extract chemically demonstrable substances from pathological products—whether recent or older exudations. Even in those cases in which the chemist succeeds in extracting one or other of these substances, he seldom obtains satisfactory evidence of their chemical purity, without



which they are wholly inapplicable for a true chemical investigation. A chemist cannot be satisfied that he knows a substance until he has submitted it to an elementary analysis, and can attain, at all events, an approximate determination of its atomic weight; in fact, a body which has been submitted by the chemist to a few reactions only, however striking they may be, but for which he is unable to establish a formula based upon elementary analysis, may be almost considered as unknown to him. In this sense (and in exact investigations we can only take this view) all substances which manifest themselves as transition-stages from the protein-bodies of a plastic exudation are wholly unknown to us, and must remain equally unexplained until we are able to elucidate the mystery of protein.

Although there may be an established conviction that the chemist is still unable to trace the metamorphoses of plastic matter in the exudations, and to note the processes by means of which one or other form is produced, we may be disposed to inquire what qualitative alterations, what heterogeneous constituents, and what special substances are to be perceived in the inflammatory, or the so-called specific exudations.

Like others, we have undertaken numerous investigations of this subject in obedience to the requirements of physicians, and we have succeeded in proving the presence of true biliary substances both in plastic and non-plastic exudations under many different relations, which scarcely admit at all times of being fully demonstrated, and have exhibited taurocholate of soda as well as beautiful crystals of glycocholate of soda. Urea, sugar, certain extractive matters, &c., may be shown to exist in nearly all exudations. However interesting such observations may be in many respects, the presence of these substances can scarcely, as far as we are at present able to judge, have any important influence on the metamorphosis of the fluid exudation, or any special signification in respect to the formation of this or that form of tissue. What additional point have we ascertained if even we succeed in showing that cystine forms the principal constituent in tuberculous masses, succinic acid possibly in cancerous growths, or some other unusual substance in other diseased matters, if no connection can be traced between the presence of such a substance and the other circumstances of the case? The qualitative examination of pathological products is, moreover, essentially obstructed by numerous relations. Every pathologist knows how rare it is to meet with very recent exudations in the dead body; how difficult it generally is to determine the age of an exudation, even with any degree of accuracy; how insufficient, even under the most favorable circumstances, is the quantity of the material in which we have to seek for special constituents; and how rapidly decomposition sets in after death, even while the body is yet warm.

We would here touch upon only one of these impediments. We have already often had occasion to notice in this work the admirable contributions made by Liebig to our knowledge of the metamorphosis of animal matter by his investigation of the muscular fluid; these experiments were, however, conducted under very favorable circumstances; for independently of his genius and dexterity, we need only refer to the mass of the material which he employed, and to the fact that perfectly



fresh materials and analogous objects could be easily procured for comparison. It was reserved for Liebig and Schlossberger to rediscover creatine, to which Chevreul had long before drawn attention, whilst to them also belongs the merit of making us more intimately acquainted with its nature. Notwithstanding the favorable circumstances already indicated, Liebig himself was only able to indicate a few substances, as inosic acid, &c. Moreover, Scherer's inosite can only be exhibited when we have large quantities of material at command; and it seems, as it were, to evade the experimenter, by becoming converted into butyric acid, if the fresh material and the separate extracts are not carefully guarded from the risk of decomposition. In a word, whilst even the qualitative investigation of objects derived from healthy animals has to contend with such difficulties that very few animal juices admit of being very accurately examined, the qualitative analysis of pathological products is opposed by insurmountable obstacles. We must, therefore, wait till the physiological juices and their metamorphoses in the animal body have been more attentively studied, before we venture to submit the solid or fluid pathological products, the more or less remote allies of the blood and of its protein-bodies, to a truly scientific qualitative investigation.

If we have, therefore, very slight prospect of being able to trace pathological processes by a qualitative examination of exudations, or of attaining any scientific aim by such a mode of procedure, we are led to inquire, with some hesitation, whether the quantitative analysis of these products would be attended by any better result. On closely considering the question, we certainly find that the quantitative investigation of the exudations justifies us in entertaining far higher hopes, and that it opens to us a rich and varied field of inquiry, while at the same time it affords but little encouragement to the present tendency of physicians towards humoral pathology. We must here rather abide by physical laws, which will afford us the best and securest support in our endeavors to give a more general character to the results of such inquiries. But here we have first to determine the points of view from which such quantitative investigations of pathological products should be considered, as long as our knowledge of qualitative analysis is so deficient.

We endeavored, under the head of Animal Juices (p. 38), to distinguish excessive transudations from exudations, although we did not believe that any very strictly defined line of demarcation could be drawn in individual cases between these two kinds of fluids, which are both exuded from the blood. If we exclude from our consideration the transitional forms, those differences to which we have referred (see above), and which have been more than sufficiently described by pathologists and histologists in the distinctions between plastic and non-plastic exudations, are rendered sufficiently prominent. We have endeavored to show, from our own experiments and those of others, that the formation and constitution of transudations depended upon certain physical relations. We think we shall scarcely be in error if we assume that definite numerically reducible relations will be discovered for the exudations, by which their composition and subsequent metamorphosis may be established. In short, no one who is not dazzled by the fantastic forces, which have been



supposed, during the last few years, to play so prominent a part in the animal body, can doubt that these exudations are subjected to definite, physically determinable laws. Although the nervous influence may act in a tolerably direct manner upon the chemical relations of the exudation, the quantitative relations must solely depend here, as in all similar processes of the animal body, upon alterations in the mechanical relations. When, therefore, we have investigated the quantitative relations of the products, we shall undoubtedly find enough certain results to give us some insight into the mechanical conditions. It will of course be understood that we do not, in the least, underrate the great theoretical difficulties which present themselves in this inquiry; the task we propose to ourselves is the simple one of solving the question of the connection between the quantitative relations of the exudations and the mechanical conditions necessary for their formation.

Perfect as in many respects the phenomenology of the exudative process may be already considered, obvious as are the mechanical conditions which give rise to exudation as well as to transudation, and great as have been the advances made in our endeavors to trace the laws by which the most minute fluid particles distribute themselves through membranes or through other fluids, and strive reciprocally to establish themselves in a certain equilibrium, we can yet never expect to obtain an inductive proof for our mechanical hypotheses until we can succeed in making the quantitative composition of the products of these processes harmonize with the laws or provisional hypotheses which we have elsewhere endeavored to establish. The labors of some of the most distinguished physiologists have afforded us considerable insight into the knowledge of the phenomena which exhibit themselves both around and within the capillaries during the existence of the inflammatory process which precedes the exudation. The disturbances of the circulation, whose hydraulic laws have been traced even in the smallest of these tubes, have not yet been followed to their individual controlling causes, and much difference of opinion still prevails in relation to this subject; but there is no lack of elements having a physical basis which may serve to explain these phenomena. In close connection with changes in the modulus of elasticity of the capillary walls there are a number of phenomena which we may very frequently show, with almost mathematical exactness, to be mechanically necessary consequences of these changes. We would here merely indicate, amongst the most recent investigations relating to physiological mechanics, the able inquiries of Jolly<sup>1</sup> and Ludwig<sup>2</sup> on endosmosis and endosmotic equivalents, C. Schmidt's<sup>3</sup> experiments on the relation between the coefficients of density and equivalents of diffusion of saline solutions, and Graham's<sup>4</sup> remarkable discoveries in relation to the diffusion of dissolved substances. If to these we add the recent classical investigations of Volkmann,<sup>5</sup> and E. H. Weber<sup>6</sup> on hæmatodynamics and the well-known investigations of Du Bois Reymond,<sup>7</sup> we shall have sufficient

<sup>1</sup> Zeitsch. f. rat. Med. Bd. 7, S. 83-148.

<sup>2</sup> Ibid. Vol. 8, pp. 1-52.

<sup>3</sup> Charakteristik der Cholera. S. 22-28.

<sup>4</sup> Ann. d. Ch. u. Pharm. Bd. 8 77, S. 56-89, u. 129-160 [or Phil. Trans. for 1850, p. 1].

<sup>5</sup> Die Hæmodynamik nach Versuchen. Leipzig, 1850.

<sup>6</sup> Ber. der k. sächs. Ges. d. Wiss. 1850, S. 164-204.

<sup>7</sup> Unters. über thierische Elektrizität. Berl. 1848-49.



materials at our command for tracing the abnormal as well as the normal circulation of matter in the animal body to purely mechanical conditions. But all these new discoveries, and the observations of earlier inquirers, only yield us a number of hypotheses regarding the mechanical metamorphosis of matter; but the inductive proof of their accuracy can only be obtained by means of a series of systematically conducted quantitative analyses of the animal fluids.

If we would investigate the alterations which occur in exudations, and the laws by which these changes are regulated and controlled, it is obvious that we must direct our attention not only to the exudations themselves, but also to the mother-fluid from which the exudations are derived, namely, the blood. It is obvious that it is only by the juxtaposition of the analysis of the exudation and of the corresponding blood, that any value can be attached to the results of the former. The analyses of such exudations should, however, be capable of comparison with one another, and not conducted at hazard merely when the physician may happen to meet with some interesting case.

It may appear superfluous to those who know that the result of an experiment nearly always depends upon the method employed in the inquiry, if we venture to suggest that an accurate investigation of the exudations demands a strictly systematic mode of treatment, or, in other words, an elaboration of the subject from definite points of view, requiring the most careful consideration of all the conditions involved, with a constant regard to the length of time the exudations have existed, the nature of the products exuded, the morphological metamorphoses exhibited by the latter, and many other similar relations. If any apology be necessary for these remarks, we would only observe that, to our knowledge, no one has ever attempted to conduct the examination of the exudations in the above-described rational manner.

We may be permitted to ask, with some show of reason, whether the quantitative analyses of the animal juices are at present conducted in so perfect a manner as to satisfy the requirements for which they are instituted.

We have already considered at length, in different parts of this work, the results which may be yielded by quantitative zoo-chemical analyses, while we have shown, in no very favorable colors, the fruits which they have actually afforded us; but although they fall far short of our expectations, they are yet fully sufficient to answer some of the most pressing questions; for the most important substances are precisely those which are conspicuous by the quantity in which they present themselves for observation; thus, for instance, the insoluble and coagulable protein-bodies, the fats, the collective mass of organic substances soluble only in water, or soluble both in water and alcohol, certain organic acids, and the mineral constituents generally, are perfectly accessible to exact quantitative determinations, as has been recently shown by von Gorup-Besanez<sup>1</sup> in his admirable treatise on zoo-chemical analysis. As the mineral constituents certainly seem to present a field of the greatest promise, they should be first and especially investigated. We know from

<sup>1</sup> *Anleitung zur zoochemischen Analyse*. Erlangen, 1850 [or Second Edition, enlarged, 1854].



the study of the transudations and the animal fluids generally, that the distribution of the potash and soda salts on the one hand, and that of the phosphates and metallic chlorides on the other, is very far from uniform in the different animal juices, and we are almost constrained to follow out this subject more at length, since Graham's investigations have directed our attention to the great inequality in the diffusibility of these substances, and Schmidt's determinations have indicated the difference of these coefficients of condensation of saline solutions when compared with this inequality. The determinations of the organic matters, as for instance, the soluble protein-bodies (accompanied by acids or alkalies) and the fats, will yield far more important results than one might at first sight be inclined to anticipate. If, therefore, the chemist freely confesses his incapacity for the prosecution of qualitative analyses of pathological products, and would gladly abstain from attempting them, he has, on the other hand, before him a vast field of noble, although less arduous labors, with the certain prospect of being able to enrich physiology and pathology with the most brilliant results.

If the difficulties we have indicated in the qualitative investigation of the exudations deter the chemist from prosecuting such inquiries, he will not fail to perceive the great number of difficulties which obstruct his progress when he enters upon the determination of the quantitative relations of the blood, and its more or less abnormal derivatives. Independently of those difficulties, which from the nature of the case appertain to the scientific means employed, external relations necessarily present numerous obstacles in the way of such an inquiry. Although large hospitals and extensive pathological materials are by no means always requisite for the prosecution of investigations which may be productive of great results to pathology, if an experimentalist were desirous of analyzing exudations in accordance with the points of view we have been considering, he would of course feel the want of the necessary material in the neighborhood of merely a small hospital; for in every case the investigation should begin with the most recent exudations, and it is precisely these which are the most rarely met with. In addition to the age of the exudation, other points have also to be observed; for the exudative matters yielded by similar cavities and tissues, ought to be compared together, which it would not be easy to do in small establishments, whilst the accompanying morbid processes, to which the physician attaches the greatest weight, ought to be noted, together with the stages of the exudation and the cavities or organs in which the effusion occurs; but for these purposes we require a larger amount of materials than can often be obtained. If, moreover, the chemist should have the misfortune to be associated with physicians who have a prejudice against venesection, however much theory and practice may favor its adoption, he will be compelled to relinquish the examination of the exudations, for unless he has obtained a previous blood-analysis, such an investigation will be of no value. One of the greatest difficulties which present themselves in the way of obtaining materials necessary for these observations is the circumstance that either from regulations connected with medical jurisprudence, feelings of humanity, or other considerations, examinations are not undertaken until twenty-four hours, or even a longer interval after



death, a period within which various processes of decomposition may have set in, and the alterations produced by death may have attained a very high degree of intensity by diffusion and endosmosis. Many of these impediments might be obviated by conducting such experiments as we have described in the neighborhood of large veterinary institutions, and indeed the advantages of employing diseased animals for such investigations are so obvious that it seems wholly superfluous to refer more fully to them in the present place. Unfortunately, however, very few pathologico-chemical investigations have been prosecuted in institutions of this kind; we must hope, however, that they may speedily be made to contribute towards the establishment of a rational pathological chemistry, since institutions of this class afford much more abundant available materials than hospitals even, for the analyses of the blood. Some of the principal difficulties which we have enumerated present themselves even when we have an abundance of diseased animals at our disposal, for all exudations taken indiscriminately are not equally suitable for a rational investigation, since anatomico-physical relations often render it perfectly impossible to exhibit the object in a pure state.

When we consider the difficulties which present themselves at the very outset of all attempts at quantitative examinations of the exudations, we can hardly wonder that many chemists should shrink from the prosecution of such unsatisfactory labors, more especially when we bear in mind that pathology offers for our consideration numerous questions, the solution of which promises more abundant results, and should, as is obvious to reason, precede the analysis of the exudations. It is to be hoped, that physicians will acquire sufficient insight into chemical and physiological science to avoid propounding questions which without admitting of any exact solution, only bring to light the ignorance of those with whom they have originated, whilst it is equally to be desired that chemists, whether they be expert or not, will avoid placing themselves as mere tools in the hands of their pathological brethren, and increasing the mass of crippled facts and perverted deductions with which pathological chemistry is already overburdened.

From this somewhat prolix introduction to the mode of investigating exudations from a physiologico-chemical point of view, it will be clearly seen, that our positive knowledge in this department of science is extremely small, whilst the majority of the few materials collected in reference to these subjects of inquiry (as, for instance, some wholly irrelevant analyses of cancerous tumors, pleuritic exudations, tuberculous masses, peritoneal exudations of doubtful character, &c., &c.) must be rejected as entirely worthless. We can, therefore, only give a very fragmentary sketch of the subject, and we think we shall scarcely be in error if we wholly omit, or at most only glance at, the ordinary descriptions of the histological conformation, or the microscopical characters of the pathological objects referred to, under the heads of the respective physiological tissues; without such a precaution we fear we might incur the risk of giving a mere outline of pathological histology which would wholly mask the pathologico-chemical nature of the objects under examination. As there is often but little to be said in reference to the chemistry, we shall frequently be compelled to give a histological introduction without



being able to describe the chemical composition. If any chemist should be disposed to direct his attention and energies to this intricate department of science, he will nowhere find a better guide than in Henle's recent and masterly exposition of this subject,<sup>1</sup> where the accumulated stores of histological materials have been carefully sifted, the objects clearly delineated, and the various points of the inquiry ably treated.

Since the exudations manifest every variety of difference, partly in reference to their morphological characters, partly in the metamorphoses which they undergo, and partly from their different modes of origin, and since we are still far from comprehending their differences from a chemical point of view, the only principle to be adopted in making a division of the whole subject is to choose a plan of arrangement based upon direct observation of the characteristic differences which exist in the physical properties of the objects. Great as has been the labor expended in the attempts to describe and classify the exudations in accordance with their external characteristics, we think the chemist can find no safer guide than that most accurate pathologist Rokitansky.<sup>2</sup> For although the description which Rokitansky gives of the differences of the exudations may be interwoven with designations and the indications of a theory of crases which the chemist does not recognize, we nevertheless meet with the most minute observations which are perfectly true to nature, and which alone ought to form the basis of a more extended physico-chemical investigation. We therefore purpose following Rokitansky's mode of arrangement in giving the few known chemical relations; and shall consider the exudations 1, as fibrinous, which are again subdivided into simple plastic and croupous; 2, as albuminous; and 3, as purulent, under which head are included ichorous and hæmorrhagic exudations.

The attacks which have been made by many of our chemical physicians against Rokitansky's mode of considering and classifying the exudations, apply less to his own views than to those of some of his pupils and followers who have distorted his facts by the most wild and paradoxical hypotheses. In reference, however, to any objections which may be advanced against the mode of expression adopted by the founder of pathological anatomy, it should be observed that the expressions *albuminous* or *serous* exudations are intended simply to designate a physically and definitely characterized form of exudation; but that Rokitansky had no idea of employing them to designate the internal composition of these objects. A mineralogist might in a similar manner accuse Rokitansky of want of scientific accuracy in applying the term hard to certain new formations, although they are actually softer than the least hard substance in the mineralogical scale of hardness. We do not, however, wish to enter the field against those who are entitled from personal acquaintance with pathology and pathological anatomy, and from independent research, to pass judgment on Rokitansky's systematic arrangement and the craseology on which it is based; but we certainly are of opinion that a system cannot be established without the aid of hypothetical modes of conception, and on this account we have adhered to the mode of representation adopted by this experienced and careful observer.

<sup>1</sup> Handb. d. rationellen Pathologie. Braunsch. Bd. 2, S. 667-832.

<sup>2</sup> Handb. d. allgem. pathol. Anatomie. Bd. 1, S. 194-224, and in other places.



The *fibrinous plastic exudation* is the only one which can be easily obtained in a perfectly fresh and tolerably pure state. Fresh wounds afford the best means of obtaining it after the hemorrhage has been arrested, that is to say, when thrombi have formed in the smaller vessels. It can be obtained, however, in larger quantities from animals after portions of muscle have been cut away under the skin, and, consequently, from wounds with a loss of substance. A perfectly fresh exudation of this kind exhibits all the physical and chemical characters of the intercellular substance of the blood. The fluid is faintly opalescent, of a sickly taste, alkaline, and in a short time there is a separation of a colorless, trembling, gelatinous mass. Provided the exudation has been obtained perfectly free from blood, which is not always easily accomplished, no morphological elements can be discovered in it besides the fibrin, which coagulates as in fresh blood. If the fluid obtained from the subcutaneous wounds (with loss of substance) is not perfectly fresh, we perceive in about half an hour or an hour granules and nuclei, which constitute the beginning of the suppurative process. These secretions from wounds are therefore obtained in the greatest purity from animals which are little or not at all prone to suppuration, as, for instance, from birds. Frogs cannot be used for such experiments in consequence of the large quantity of lymph which is poured into the secretion in these animals from the subcutaneous lymphatics.

The constituents of these perfectly fresh exudations do not differ in *quality* from those of the liquor sanguinis. The same substances which impede the rapid coagulation of the fibrin of the blood either retard or prevent the coagulation of the fibrin of the exudations (see vol. i. p. 311). The spontaneously coagulated fibrin becomes perfectly dissolved after digestion for some time at a temperature of  $30^{\circ}$  in a solution of nitre, being converted into a coagulable fluid. In water containing hydrochloric acid the exudation swells up in a gelatinous form, but does not dissolve, in which respect, as in all other reactions, it perfectly coincides with the blood-fibrin. Precisely the similar remark applies to the albumen; and the mineral constituents, in as far as we can determine them from the small quantities of these exudations generally at our command, differ in no essential respect from those occurring in the liquor sanguinis.

No detailed *quantitative analysis* can be made with very recent exudations owing to the small quantities in which they are obtained. I have, however, constantly found more water in them than in the liquor sanguinis, which is the more striking, seeing that in collecting these fluids the evaporation of the water cannot be so readily prevented as when the blood is drawn from the opened vein. In five experiments on rabbits and in three on geese, I found from 1.94 to 4.28% more water in the secretion from the wound than in the plasma of the mixed blood, that is to say, of the mixture of arterial and venous blood, which was obtained from the carotid and jugular vein. I could not determine with any degree of certainty whether the amount of *fibrin* in the exudation was greater or less than that in the liquor sanguinis; but the quantity of *albumen* was decidedly somewhat smaller than in the blood-serum, the difference being greater than could be accounted for by the relative increase of water in the exudation. In geese there was always rather more *fat*



in the exudation than in the corresponding liquor sanguinis; but here it was difficult to determine whether the fat from the subcutaneous cellular tissue was not in part mixed with the secretion from the wound. No difference could be detected in the quantity of salts contained in both fluids. Strict determinations in the case of the *phosphates* and *metallic chlorides* on the one hand, or of the *soda* and *potash salts* on the other, were impracticable; but I endeavored in six cases to determine the average proportions of these substances in the secretion from the wound and in the corresponding blood-serum, and I think that I am scarcely in error in stating that the secretion from the wound contains relatively more of the phosphates and potash salts, and that the serum contains an excess of soda salts and chlorides.

The very recent exudations obtained in rare cases from the serous sacs of human subjects present very different relations, not being homogeneous, but already separated into a coagulum and a fluid.

The *coagulum* varies very much in form and color according to the relations under which it separated, and the quantity of blood which it contains. The microscopical characters are generally, or indeed principally, the same as those of spontaneously coagulated fibrin, but in addition to the somewhat swollen, almost spherical blood-corpuscles, there occur certain other morphological structures, as, for instance, granules, clots, nuclear structures, and occasionally also cytoïd corpuscles. The coagulum swells in water containing hydrochloric acid as well as in dilute acetic acid, but it does not form a gelatinous mass of such perfect translucence as the fibrin of the blood, or as that of the secretion from a wound. If the coagulum, after having been comminuted and carefully washed, be digested with a dilute solution of nitre, we certainly obtain a fluid coagulable by heat, although some portion of it always remains undissolved in the menstruum in the form of dirty grayish flakes.

The fluid portion of the more recent plastic exudations is generally clear and transparent; it only becomes opalescent and turbid after the exudation has remained for some time in the cavity. The reaction is commonly less strongly alkaline than that of the blood-serum; it, however, coagulates on boiling, not into minute flakes, but generally into curd-like clots, or into a milky or whitish gelatinous mass. The fluid occurring above the curd-like flakes is strongly opalescent, and even whitish; it passes with difficulty through the filter, which it very quickly obstructs; it forms, on evaporation, the so-called casein-membranes. Acetic acid does not enable us to detect any casein, and the originally limpid fluid is rendered only slightly turbid on careful neutralization with acetic acid; but this turbidity disappears instantly on the addition of a little more dilute acetic acid. The application of rennet only affords negative evidence regarding the presence of casein. The salts and extractive matters differ in no respect from those occurring in the blood-serum.

The *quantitative composition* of these exudations, when compared with that of the corresponding blood, is far more unstable than that of fresh wound-secretions obtained from animals. The quantity of the *fibrin* does not even admit of being determined approximately, for independently of the fact that such fibrin (that is to say, the coagulated



portion of the exudation) contains insoluble morphological constituents, which cannot be washed out by water, and which cannot possibly be regarded as fibrin, the exudation cannot generally be obtained as an entire mass, that is to say, all the solidified as well as the still fluid parts cannot be removed from the cavity into which they have been effused. In the meanwhile it would appear, from approximate determinations, that the relation between the solidified and fluid matters varies very considerably, a circumstance which confirms the well-known experience derived from personal observation that a large proportion of the exudative fluid is soon resorbed. According to our experience, there is no definite relation between the part of the exudation which remains fluid and the serum of the corresponding blood; but in most cases, here as well as in the secretions from wounds, the solid residue of the exudation-fluid is inconsiderable, and consequently the amount of *water* is greater. I found this difference between the fluids the greatest, namely, about 3.47% in a very fresh peritoneal exudation. In some cases, however, the quantity of the solid constituents in the exudations exceeded that in the corresponding blood-serum. There was usually less of the *coagulable protein-substances* in the exudative fluid than in the corresponding blood-serum; an apparent excess of these substances occurred only in one-seventh of the cases observed, but then the fluid had become turbid, and had not been thoroughly cleared by previous filtration. These fluids differed less in respect to the *extractive matters* which they contained; indeed, if the latter were considered in reference to the quantity of water in both fluids, the difference was in most cases so inconsiderable that it could scarcely be said to exceed the amount of such errors as are unavoidable in observations of this nature. But on comparing them in their relation to the solid residue, we commonly find that there is a small excess for the extractive matters of the exudations. The sum of the *salts* is generally somewhat higher in the exudations than in the blood-serum of the same individuals. On comparing together the different salts we find, without exception, relatively and absolutely more of the *phosphates* and *potash-salts* in all these exudations than in the blood-serum.

However much one might be disposed, from these results of my analyses, to find a confirmation of the view that has already been advanced elsewhere, that the phosphates, and with them probably also the potash-salts, contribute very essentially towards the plasticity of the exudations, we cannot regard the point as definitively settled, for it is not easy to determine to what extent the quantity of blood-cells in the exudations contributes to this result. I have met with no single plastic exudation (I refer to those only which I examined under the microscope) which did not exhibit a larger or smaller amount of strongly tinged, unaltered, or pale, rounded blood-corpuscles. As, moreover, the blood-corpuscles never continue to be developed in a plastic exudation, but, on the contrary, seem rather to disappear, the proximate cause of this excess of phosphates and potash-salts might therefore be sought in the disintegration of the blood-cells contained in the exudation; for we know that it is the blood-cells principally which contain the phosphates and potash-salts (see vol. i. p. 569). In point of fact, a comparison between my different analyses will show that the exudations which contained a large amount of



blood-cells exhibited a greater proportion of these salts than those which were poorer in blood-cells. The observation made by different physiologists on the relations between the capillaries and the blood contained in them during the inflammatory process lead us to expect that blood-corpuscles will always be present in exudations. Although the constant occurrence of blood-corpuscles in the true plastic exudations, as noticed in the bodies of men or animals after death, would seem to favor the conclusion that the plasticity of the exudations depends principally on the quantity of blood-corpuscles which they contain, such a view is controverted by the fact that exudations which are very rich in blood are not in general the most plastic; and that, as we have already seen, when considering the secretions from wounds, an exudation may be plastic without containing blood-cells. If, therefore, we cannot assert that the blood-cells, as such, together with the fibrin, are the direct cause of the plasticity of the exudations, they at all events appear, from the above-mentioned positive observations, to stand in some indirect relation to the plasticity. For where are we to seek for the source of the excess of potash-salts and phosphates which is constantly present in the plastic exudations, if not in the blood-corpuscles? Even in those wound-secretions, in which we can find no blood-cells, we must refer these salts to blood-corpuscles which have passed into a condition of stasis and solution in the capillaries surrounding the focus of exudation. The phosphates and potash-salts originating from the remains of the blood-cells must therefore penetrate through the walls of the inflamed capillaries, and thus contribute towards the plasticity of an exudation containing no blood-corpuscles. This at the same time explains the cause why the transudations, even when they contain fibrin and some blood-corpuscles, are not plastic, for the separation of the transudations is not preceded or accompanied by a true inflammatory process with complete stasis and with the entire destruction of the blood-cells in the capillaries, as is always the case in the exudations.

We do not, however, think that it has been satisfactorily proved that the plasticity of the exudation is necessarily dependent upon the presence of these salts, but it is a characteristic of the human mind to catch at the slightest facts for support in the arduous paths of inquiry. Some aid might perhaps be afforded towards the establishment of inductive proof by the results of a series of experiments which I instituted on the blood of horses, comparing the blood of different vessels with the arterial blood. The results of the comparative analyses of eighteen samples of blood from different veins showed that in those capillaries which supply the muscles (organs peculiarly rich in potash-salts and phosphates) the largest number of blood-cells were destroyed; and that in the venous blood, which flowed from the corresponding parts (from the cephalic, external abdominal, digital, and median veins) there were far fewer blood-cells and a much smaller quantity of the phosphates and potash-salts than in the corresponding arterial blood or in the blood of other veins, which return the blood from other organs. These differences are so considerable, that in the venous blood of the muscles there are on an average from one-fourth to one-third fewer blood-cells than in the arterial blood, whilst in the blood of other veins the difference is either far



smaller or there are relatively more cells (that is to say, absolutely less intercellular fluid).

We have already spoken (in vol. i. p. 323, and in this volume, p. 40) of the doubt which still exists regarding the influence exerted by the presence of the fibrin on the plasticity of the exudations.

The present would be a fitting place to consider more attentively the more persistent exudations, and to investigate somewhat more circumstantially the chemical metamorphoses which run parallel with the morphological formations, but unfortunately this is a point on which we know little or nothing. As the solidifying parts of the exudation are far less accessible to chemical investigation than the fluid, our attention must of necessity be limited almost exclusively to the latter. I have made some attempts to ascertain the differences in the composition of the fluid which occurs in association with the solidified exudation, in so far as they are dependent on the metamorphoses which the original exudation has undergone. We know that these metamorphoses may be of three different kinds; in the first case, the exudation is gradually resolved, and the coagulated fibrin slowly dissolved in the originally only slightly modified exudative fluid, or in a serous fluid which is afterwards separated; in the second case, the solid part of the exudation hardens, ceases to swell in acetic acid, and becomes converted into a horn-like mass; and thirdly, the exudation is converted into true tissue, namely, connective tissue. One might suppose that the fluids remaining in these older exudations, or permeating the newly-formed tissues, would exhibit differences which would readily admit of being chemically distinguished; but although these fluids certainly exhibit differences of composition on analysis, my observations at all events have failed to detect any definite constitution for any one special alteration of the exudation. We are still deficient in any more careful investigations for showing the character and composition of those forms of exudation, which tend towards the formation or regeneration of specific tissues (such as cartilaginous substance, osseous substance, &c.)

*Croupous exudations.*—It is only in rare cases that we can succeed in subjecting to a chemical examination exudations of this kind whilst still in a perfectly fresh state, that is to say before they have been changed either by different metamorphoses which they have experienced during life, or by decomposition in the dead body. It may be shown with tolerable certainty that these exudations on their first separation are as fluid, and as similar to the blood-plasma as all other exudations; but they present this peculiarity, that when the fibrin has been coagulated, the fluid portion of the exudation is resorbed with such extreme rapidity that almost every effort to obtain it fails. It almost appears in the case of many of these exudations, as if only a kind of fibrinous juice had permeated the walls of the vessels, and had been deposited in a gelatinous form upon mucous or serous membranes. There is often scarcely a trace of blood-corpuscles to be detected in fibrin of this kind, and on rinsing the exudation with water, we obtain only a very small quantity of coagulable matter, and thus lose all hope of being able to ascertain the original composition of the exudation from the fluid enclosed in the coagulum. Then, moreover, it must be observed, that



these coagula, or solid exudations, are in general formed gradually, and thus deposited in distinct strata, some of which experience greater alterations than others. However important it would be to ascertain the composition of these exudations immediately after their separation, the chemist is compelled to admit his entire inability to solve any of the questions which suggest themselves in connection with this point, and must direct his attention almost exclusively to the solid parts of the exudations, which are always more or less altered.

Rokitansky, who would naturally judge of the nature of the depositions solely from their physical character, has arranged croupous exudations in three subdivisions, a mode of division which has been much objected to, but which is undoubtedly recommended by experience, if we simply compare together facts under the most widely differing forms which they can assume, and exclude all those which merge into one another, as must be done in every artificial mode of division. A simple microscopical examination of these croupous exudations shows that the object which we are here considering is not pure fibrin, for even in the most recent formations the microscope reveals in addition to a fibrous substance not very unlike freshly coagulated fibrin, a great number of molecular granules and flake-like laminæ, which at certain spots appear to be jagged. After they have existed for a longer time, we observe in them nuclei and cytoïd corpuscles; indeed the occurrence of the latter is often so sudden (or in other words the metamorphosis of the solid exudation into pus-corpuscles is so rapid) that many observers have altogether doubted the previous separation of fibrin. The questions which have been propounded to chemists since Rokitansky's original subdivision of the various kinds of fibrin, are in part solved by microscopical investigation. The substances to which Rokitansky applied the term croupous or aphthous fibrin, or which he regarded as the primary matrix differing from ordinary fibrin, is now in a great measure found not to be fibrin at all; and he himself has noticed the absence of that network of fibres which is peculiar to coagulated fibrin both in the aphthous coagulum and in the croupous exudation  $\beta$ . These granular solid exudations are no longer fibrin, having undergone various chemical as well as morphological metamorphoses before they come under our notice. One might, indeed, here assume, as has been done, the existence of a dimorphism, such as has been shown in recent times to exist in the case of many mineral substances; but independently of the fact, that true heteromorphism is far less frequent in organic chemistry, and that its existence in respect to fibrin still remains undetermined, the qualitative chemical investigation of these exudations shows us that the granular matter which they contain is by no means chemically identical with the unaltered fibrin which is often still contained in these deposits.

In those exudations, which Rokitansky names *aphthous*, we find after careful washing, no material which, after the exudation has been digested for a short time in a dilute solution of nitre, becomes dissolved and is coagulable or precipitable by acetic acid. (The washing is, however, by no means easy, and frequently entirely fails, since the turbid fluid passing through the filter very soon closes its pores.) This insoluble residue swells up in a gelatinous form in very dilute hydrochloric acid; but some



portion is actually dissolved, without, however, yielding the reactions of ordinary muscle-fibrin. A microscopical examination shows that the constituents of the very numerous cells contained in aphthous exudations are dissolved by water containing hydrochloric acid. Rokitansky's croupous exudation  $\alpha$ , or fibrin  $\beta$ , contains true fibrin, in addition to the granular matter and the first stages of cell-formations; but although it is not very rich in blood-corpuscles, it is never entirely free from them. After an exudation of this kind has been comminuted and carefully washed with distilled water, and then immersed in a solution of nitre of the previously named concentration, at a temperature of  $30^{\circ}$  or  $40^{\circ}$ , a great portion of it is always dissolved, whilst the fluid is also found to contain a protein-substance, which is precipitable by heat at the boiling-point, as well as by acetic acid; and here I must not omit to mention, that with the exception of two cases, I never found the so-called arterial fibrin (which is perfectly insoluble after digestion in a dilute solution of nitre), even in those exudations which according to microscopical examination appeared to contain true fibrin. The croupous exudation  $\alpha$ , after being previously well washed in water, swells in dilute acetic acid; but a very small amount of the protein-substances, especially such as are recognizable by chromate of potash, are dissolved. Rokitansky drew attention to the large amount of *fat* contained in these exudations, and the fact may be readily confirmed by careful chemical analysis. The fat does not differ essentially from that of fibrin; but the fat containing phosphorus or rather the phosphate of glycerine appears to be present in rather larger quantities in the croupous exudation  $\alpha$  than in exudation  $\beta$ , or in the aphthous kind; but it must be admitted that there exists considerable uncertainty as to the quantitative determination of these substances. This observation seems to be confirmed by the fact, that these exudations on an average leave more *earthy phosphates*, and in general more acid phosphates, on the incineration of the constituents insoluble in water, than the ordinary blood-fibrin. I never found less than 2%, and often more than 4% of phosphates in the insoluble residue of the exudation.

Notwithstanding my conviction of the insufficiency of elementary analyses for the examination of such substances, I have very frequently instituted analyses of this kind with the residue (insoluble in water, alcohol, and ether) of the croupous exudation of the first order ( $\alpha$ ); but the results were so variable, that it was impossible to compare them with the composition of the blood-fibrin. According to most of the analyses, the fibrin of the exudation contained somewhat less nitrogen than the fibrin of the blood of the same individual; and it was only once in seven cases that the nitrogen equalled the quantity found in the blood-fibrin. The quantity of carbon was equally variable, for in some cases I found rather more, sometimes from 1 to 2% less, than in the blood-fibrin.

The croupous exudation of the second order ( $\beta$  Rokitansky) may be regarded as holding an intermediate place between that of the first and third order when considered in a chemical point of view. I have never found it to be perfectly free from pus-corpuscles.

Rokitansky distinguishes yet a third form of fibrinous exudation, namely, the *tuberculous*. Although in a purely physiological or even logi-



cal point of view, we can scarcely admit the assumption of such an exudation as a special form, its recognition is advantageous in a practical point of view. We entirely set aside the idea of an entirely specific process, and simply adhere to that which for ages has been attached to the term tubercles. In characterizing this exudation, Rokitansky has here, as in other cases, not studied the original fresh product of the exudation, but only the peculiar form in which it most commonly comes under our notice. Persistence in a very low stage of development has in general been adduced as the most characteristic property of tuberculous exudations, and indeed we seldom meet with more than molecular granules, minute aggregations which have been regarded as of a special nature (tubercle-corpuscles), and, at most, faint indications of cellular structures. The absence of plasticity in these exudations has commonly been referred to the too rapid resorption of the fluid parts, and either to the actual absence of blood in the smaller vessels, or to other causes preventing these parts from being readily permeated with moisture. Where such a permeation as this takes place, we less commonly observe a formation of cells than of cytoïd corpuscles, which then give rise to what is termed softening of the tubercles. Tubercles have been divided, as is well known, in accordance with their form and mode of deposition, into miliary and infiltrated, and further subdivisions have been suggested, based upon their consistence and age (as for instance, gelatinously infiltrated, cretified, &c.) On microscopic investigation, most of them are found to consist of fat-globules and molecular granules.

Notwithstanding the rapidity with which the tuberculous exudations are separated, and the circumstance that they are frequently secreted to the last moment of life in tuberculous patients, no attempts have as yet succeeded in obtaining for examination a perfectly fresh, still fluid exudation, of which one might presume with tolerable certainty that it would have been "tuberculized" had the life of the sufferer been prolonged. Even should these attempts succeed, it would still remain questionable whether the chemical investigation of these exudations would afford any further information regarding the so-called tuberculous process than has already been obtained from the analyses of the blood of tuberculous patients.

There is no exudation which, when once formed, admits more readily than the tuberculous of being studied with reference to the length of time which it has existed, and the various metamorphoses which it has undergone; thus we find on examining the lungs of persons who have died from chronic tuberculosis, that the most recent deposits are in the lower lobe, and the older formations in the upper one; but still the most careful and numerous micro-chemical and even microscopical investigations scarcely yield any reliable results, and the various micro-chemical analyses which I have made, in part conjointly with my friend Hasse, of the most varied pulmonary tubercles, have not yielded the slightest amount of scientific information. It would, therefore, be absurd to enter circumstantially into the details of these series of experiments, which are so frequently at variance with one another, although at the period when these analyses were made, many slight differences may have been passed over, which, in the present advanced state of animal chemistry, might



perhaps have thrown some light on the subject; but still the results are so different, and even frequently so contradictory for entirely analogous objects, that no support can be obtained for even the most general mode of classification. We therefore withhold these details, trusting to future investigations for more satisfactory results.

The scattered facts yielded by works devoted to the subject may be limited to the following points. The tuberculous mass, when of recent date, contains, in addition to one of the protein-bodies, which is soluble with more or less facility in acetic acid and alkalies, a large quantity of fat, partly in very fine granules and partly in vesicles. In tubercles of longer existence the fat appears in much diminished quantities. The obsolete or cretified tubercles consist chiefly of cholesterin, which may be recognized by the microscope, together with carbonate of lime, and a little phosphate of lime. The tubercles are generally deficient in salts, although the statements of authors on this point are as variable as the results which I obtained from my analyses of the different forms of these exudations. There is on an average more carbonate of lime in the ash of tubercles than in that of any other substance of the animal body which is rich in protein. The recent observation, that xantho-cystine occurs in old tubercles, is very remarkable, but I have not hitherto had any opportunity of verifying the correctness of this assertion. (See vol. i. p. 158.)

We must confess our inability to form a perfectly clear idea of Rokitsky's *albuminous exudations*, although we do not by any means believe that they can be classed under the same head as the purulent, or any other form of exudation. We have found that they presented very considerable chemical differences; and the turbidity which occasionally gives them a milk-white appearance is probably the simultaneous result of many different relations. The microscope shows that, in addition to the cellular elements, which occasionally become developed into spindle-shaped or caudate cells, there occur also a number of molecular granules, fat-globules, and a viscid filamentous substance, forming under the microscope hyaline stripes, and here and there probably also flakes of true fibrin. The turbidity arises in different cases from different microscopical elements.

This *filamentous matter* cannot, however, be regarded as true coagulated fibrin; for, independently of the circumstance that it cannot microscopically be confounded with ordinary fibrin (since, like bronchial mucus, it acquires its filamentous appearance solely from the pushing or turning of the thin glass plate covering it, or from other mechanical conditions), it differs completely from fibrin in the following chemical reactions. It commonly dissolves with considerable facility in solutions of neutral alkaline salts, when not too highly concentrated, without requiring any prolonged digestion or exposure to heat. Besides this, it frequently acquires a certain degree of opacity or milky turbidity, and is rendered less tough when exposed to the action of dilute acetic acid, dissolving only in an excess of this acid, or when it is concentrated; and (excepting in two cases), it has been found to dissolve easily in very dilute hydrochloric acid. The molecular granules occasionally consist of fat only, but they may frequently be made to disappear by means of alkalies



and alkaline salts, on which account we may probably include them amongst the protein-bodies. We shall speak more fully at a future page of the micro-chemical relations of the other cellular structures which may occur in exudations of this kind. These fluids exhibit very different reactions; they are frequently so strongly alkaline and ammoniacal that one is disposed to refer their filamentous character to the strongly basic albuminate. The presence of the latter seems to be confirmed by the small quantity of coagulum which the fluid yields on the application of heat, while on evaporation a membrane is formed on the surface (see vol. i. p. 298). Dilute acetic acid frequently gives rise to a strong turbidity in such fluids, and occasionally to the separation of white flakes.

I have been unable to convince myself of the presence of true *casein* in such fluids either by the application of rennet or by other means; the viscid character, and the reactions which these exudations exhibit are, therefore, probably owing to the presence of strongly basic albuminates. I have only on two occasions observed an acid reaction in these kinds of exudation (and this was after puerperal pyæmia), and here, also, acetic acid occasioned great turbidity in the filtered, opalescent fluid; the albumen coagulated into flakes when this exudation was boiled. The latter substance occurs, however, also in some cases when the fluid exhibits a faintly alkaline, or an almost neutral reaction (see above). In those cases in which the exudation has an acid or neutral reaction, the surface of the fluid, after the removal of the coagulated albumen, becomes covered on evaporation with a membrane, without, however, exhibiting the presence of true cases.

Notwithstanding the thick fluid character of these exudations, they seldom contain any large quantities of *non-volatile matters*, from 4 to 6% being the highest amount that I have found in these fluids. The amount of *fat* is not inconsiderable, although it frequently does not exceed the amount present in the normal, fibrinous, plastic exudations. The non-volatile *salts* are generally present in larger quantities than in the blood, but on comparing them with the salts of the plastic exudations, taking the solid residue as the unit, the number representing the salts is often higher in the fibrinous than in the albuminous exudations. Although it was found from a comparison of the salts as given by several analyses, that there was a relatively smaller amount of the phosphates in the albuminous than in the fibrinous exudations, this observation requires to be further corroborated; the more so, because I found in two cases (in puerperal fever with pyæmia) considerably more phosphates than one usually meets with in the salts of the exudations. The occurrence of large quantities of bile pigment and biliary acids, urea, sugar, &c., in certain albuminous exudations must be regarded as purely accidental, and as admitting of an easy explanation in individual cases.

Rokitansky's *serous dropsical exudations* coincide perfectly with the *transudations* which we treated of in pp. 38-56 but we think we have sufficiently explained, both there and in the introduction to the present section, the reasons which compel us to separate the transudations from the exudations. No one can deny that in some cases an exudation may become associated with a transudation, or, conversely, a transudation may associate itself with an exudation, but the two pro-



cesses must in principle be widely distinguished, as, in fact, they do occur distinct from each other in most cases, leaving no grounds for confounding one with the other. The erroneous idea that the plasticity of an exudation depends only upon the quantity of fibrin which it contains, has led many persons to doubt the propriety of separating exudations from transudations, as we meet with plastic exudations without fibrin, and non-plastic ones which contain fibrin; but we think we have satisfactorily shown from our own direct investigations, that the plasticity of the exudation is constantly associated with the presence of a certain amount of soluble phosphates, which occur either in very small quantities or are even wholly wanting in the transudations. As the phosphates and potash-salts can originate only in the blood-cells, they cannot occur in large quantities in the exudations, or render the transuded liquor sanguinis plastic, unless there is true stasis and destruction of the blood-corpuscles, when the contents of the latter transude through the lacerated or uninjured walls of the capillaries. The formation of transudations poor in phosphates and potash-salts, is solely dependent on a retarding of the blood-current in the capillaries and on other mechanical relations, and in no case depends upon a complete stasis or destruction of the blood-corpuscles,—in other words, it never depends upon true inflammation.

We do not, however, by any means, incline to the view, that the plasticity of an exudation is solely owing to the presence of phosphates (although their influence on the formation of the tissues in the case of animals, has been almost demonstrated by direct observation); it is, on the other hand, very probable that other substances may constitute essential requirements for producing plasticity, although these, like the former, would appear from the results of our investigations to derive their original source from the blood-corpuscles. To assert that the plasticity of an exudation depends solely upon the presence of the phosphates, would be no less unsuitable or uncalled for, than to assume that transudations owe their origin exclusively to a larger amount of water in the blood. We have already shown, under the head of "Transudations," the untenable nature of such a view, and we would here only remark that the blood of tuberculous, chlorotic, and hysterical patients is often found to be far more watery, without, however, transudations having taken place, than the blood of patients having dropsical accumulations in different cavities. We have already instanced amongst the conditions which favor the formation of a transudation, the amount of the lateral pressure exerted by the blood on the walls of the capillaries, the rapidity of the blood-current, the coefficient of elasticity of the walls, and many chemical relations. We cannot, however, venture here, any more than in the involved phenomena of vital processes generally, to refer an important process to one single, perhaps accidentally induced condition; for, in adopting such an unsatisfactory mode of evading a difficulty, we should run the risk of falling into the error which is too common amongst physicians of the present day, of referring the most complicated pathological processes to the merest chimeras, and endeavoring to explain the *modus operandi* of certain powerful or inefficient remedial agents by clumsy mechanical or chemical hypotheses.



The *purulent* and *ichorous exudations* show in special cases the same amount of affinity with the albuminous, and in part even with croupous exudations, as do the other exudative processes. In its purest state the purulent exudation generally, however, forms a yellowish, thick fluid, which differs from every other exudation by the considerable amount of corpuscles which are distributed through it with tolerable regularity.

These corpuscles, which, however, also occur in other places and in other fluids, as, for instance, in the lymph (as lymph-corpuscles), in the blood (as colorless blood-cells), in the mucus of the mucous membranes (as mucus-corpuscles), &c., are, as is well known, vesicles consisting of a cell-membrane, which often appears granular, of viscid hyaline contents, and of a nucleus which adheres to the cell-membrane. These corpuscles may or may not be included under the head of cells, according to the idea entertained of the physiological cell; and on this account it would be desirable, perhaps, to avoid the numerous designations which have been applied to these bodies, and to adopt the name of *cytoïd corpuscles* proposed by Henle.

We do not purpose entering more deeply into the morphology of pus, its mode of formation, &c., as this would be leading us too far from the main subject of our inquiries, and involving us in a labyrinth of unanswered or unanswerable questions and the vaguest conjectures, as the chemical investigations hitherto made in this department of inquiry have contributed very little towards the elucidation of pus and purulent exudations. Although we found ourselves compelled on a previous occasion, when investigating the micro-chemical characters of pus and suppuration,<sup>1</sup> to hazard various hypotheses on the morphological as well as the chemical nature of purulent formations, we are nevertheless of opinion that where chemistry is not sufficient in itself to solve the difficulties falling within its own scope of inquiry, it ought not to assume the semblance of being able to lay the foundation of a rational inquiry by the aid of unstable conjectures and mere assumptions—the imputation of which has, on too many occasions, clung to this science. We will not therefore, enter further into the genesis of pus-cells, or of the morphological elements allied to them, nor will we dwell on the physiological value of these cells, the different characters of laudable and malignant pus, &c., as almost every recent histological and pathological work abounds in the most comprehensive facts and opinions bearing upon these points. The sifting of the chemical facts before us will also be a matter of extreme facility, owing to the very small number of positive results yielded by the earlier chemical investigations.

The reason why a very subordinate degree of interest attaches itself to the earlier investigations made on this subject, many of which were conducted with great care, depends in a great degree upon the difficulty, or even impossibility, of separating the cytoïd corpuscles of the pus from the intercellular fluid (the so-called pus-serum), although such a separation is obviously necessary to afford such a view of the constitution of the pus, as may at once accord with nature and satisfy the requirements of physiology. A quantitative determination of the con-

<sup>1</sup> Arch. f. phys. Heilk. Bd. 1. S. 218–265 [a joint memoir by Lehmann and Messerschmidt].



stituents of the corpuscles, such as we have at all events approximately obtained for the blood, is scarcely possible as yet in the case of pus. Pus-corpuscles do not admit more readily than the blood-corpuscles of being separated by filtration from the intercellular fluid, and they also render indirect determination more difficult, in consequence of their possessing a far less sinking capacity than the blood-corpuscles; the cytoïd corpuscles of the blood remain, however, suspended like those of pus. After standing for some time, the pus-corpuscles begin gradually to sink; the pus is then, however, generally changed in character, and the cytoïd corpuscles exhibit more distinctly the nuclei which had previously been scarcely discernible. The serum of the pus has a less decided alkaline reaction than that of the blood; indeed sometimes it is acid, and when placed in a vacuum, this kind of pus commonly evolves sulphuretted hydrogen gas. We cannot, therefore, regard the serum of the pus, which is accessible to investigation, as a perfectly pure object. But although this condition of the pus-corpuscles must be regarded as the principal obstacle in the way of a rational investigation of this fluid, there are not wanting other causes which very frequently render the object unsuited for a conclusive analysis; amongst these we may especially enumerate the frequent occurrence of blood in pus, that is to say, particles of fibrin and blood-corpuscles, as well as the elements of newly formed, or recently destroyed tissues. Such fluids would, at all events, be unsuited for analyses, from which we might wish to draw conclusions regarding the special character of the pus, and of the purulent exudations generally. Another circumstance which calls for attention is, that to render an analysis of the pus thoroughly useful, it is essential to institute simultaneously an analysis of the blood; yet what physician would be so unconscionable as to prescribe venesection in the case of a patient in whom the purulent discharge was so copious as to afford the chemist sufficient materials for a proper analysis? We must, therefore, necessarily content ourselves with having recourse to the lower animals for this purpose. There is nothing of chemical pedantry in desiring parallel analyses of the blood, but yet the accuracy of a physico-scientific inquiry would not be invalidated by its omission. It is obvious that the constitution of the pus must in a great degree be dependent on that of the blood, and that an accurate examination of the former must embrace a notice of the character of the blood also; but one would hardly believe that this influence could extend so far as to manifest itself in the physical character of the corpuscles; yet it is by no means difficult, after some little practice, to determine from the form, size, granulation, &c., of the corpuscles, the nature of the source from which they have originated. Thus, for instance, the pus from accidental wounds or ulcerated parts in a phthisical patient presents under the microscope a totally different appearance from that of a typhous subject, whilst that of the latter would in its turn differ essentially from the appearance presented by the pus taken from a drunkard or from a patient exhibiting the cancerous dyscrasia; and this would be observable even in cases in which the suppurative fluids could not be regarded as the ordinary ichor of surgeons. In case these observations should excite a doubt in the minds of



those who have been accustomed to examine pus under the microscope, we would simply refer to the fact that the mere size of the linear diameter of a cytoïd corpuscle frequently furnishes a clue to the nature of the fluid from which it was obtained; thus, for instance, Henle<sup>1</sup> found that the cytoïd corpuscles in the pus measured on an average from 0·004 to 0·005'', that those in the saliva and mucus were somewhat larger, and those in the blood were, on an average, smaller. These differences he ascribes, undoubtedly with much truth, to the different densities of those fluids. When therefore we find that the mere density of the blood, on which depends that of almost all the other juices of the animal body, exerts so great an influence, we can scarcely suppose that the other qualities of the blood should exercise no action whatever on the chemical constitution of the pus. We can hardly therefore be accused of adopting any exaggerated or far-fetched view if we regard all analyses of pus, which are unaccompanied by simultaneous analyses of the blood, as devoid of all importance in interpreting a physiological process, or in promoting the recognition of the true constitution of normal pus. We have deemed it expedient to make these preliminary remarks, partly to free ourselves from the reproach of having neglected the laborious investigations of former inquirers in our representation of the chemical relations of pus, and partly to prevent, as far as lies in our power, the misapplication of efforts which would be lost to scientific pathology, by being expended on the chemical analysis of objects whose examination can in no way promote the advance of science.

We have already observed, in reference to the plasma or the germinal fluid of the pus, that it appears to be originally identical with the fresh plastic exudation which we examined from the secretion of a wound. We will here subjoin a few remarks in addition to the relations which we have already described. In one case the secretion was collected from wounds which had been inflicted upon eight rabbits in the manner already described: as soon as it began to flow free from blood-corpuscles, 100 parts of the solid residue contained (as was determined by direct incineration) 12·341 of mineral substances (the solid residue of the serum and of the fibrin yielding 9·971%); 100 parts of the salts of the secretion from the wounds yielded 41·145 parts of chlorine, 5·819 of phosphoric acid, and 6·941 of potash, whilst from that of the liquor sanguinis there were obtained 53·145% of chlorine, 2·014% of phosphoric acid, and 4·814% of potash. In the solid residue of the secretions from the wounds in three geese there were 15·148% of mineral substances (in that of the liquor sanguinis there were 11·155%); 100 parts of the salts of the wound-secretion contained 7·018 of phosphoric acid and 7·147 of potash, whilst in those of the corresponding liquor sanguinis there were 3·118 of phosphoric acid and 4·663 of potash. Several experiments of a similar nature conducted by my pupils, yielded analogous results. It has already been observed that the secretion from a wound does not long retain the character of a fresh exudation, but that it soon exhibits morphological elements, molecular granules, nuclei, and even cytoïd corpuscles, when the edges of the wound do not cohere, that is to say, when the wound does not heal *per primam intentionem*. It may therefore be assumed that the exudation, as soon as it has become pus, will exhibit a different

<sup>1</sup> Handb. der ration. Pathol. Bd. 2, S. 685.



composition from the fresh wound-secretion, which may be able to produce tissue, but cannot generate abortive cells (that is to say, pus-corpuscles). A similar mode of reasoning has led to the assumption that the first secretion from a wound which is free from blood may perhaps contain a sufficient quantity of phosphates and potash-salts to restore the integrity of the injured tissue, whilst the latter secretion very probably contains only enough salts to form cytoïd corpuscles, but not a supply adequate for the formation of perfect cells or fibres. It happens very frequently, however, that the idea we have been led to entertain of the plan adopted by nature does not coincide with actual observation. At all events, the limited experiments which I have been able to make, and which were restricted to rabbits, do not confirm such assumptions. The ash of pus always contains a larger amount of phosphates and potash-salts than the intercellular fluid of the corresponding blood, although when compared with that of the fresh secretion from a wound it exhibited a very variable amount of these salts. This relation, which requires to be confirmed by further observations, can scarcely excite surprise, for there is undoubtedly something more necessary than phosphates and potash salts to render an exudation truly plastic.

Without entering further into the consideration of the incidental morphological constituents of pus, we will at once proceed to its cytoïd corpuscles. On micro-chemical investigation they present the following reactions.

If fresh pus be very much diluted with distilled *water*, the corpuscles are seen to swell and become very pale; the granular character of their surfaces either wholly disappears or true granules become detached therefrom. The interior of the corpuscles occasionally exhibits a distinct nucleus, but more frequently only an aggregation of granular matter with no distinct outlines, whilst in addition to this, the corpuscles also exhibit in their interior fine granules, which are in a state of active molecular motion. Henle has especially called attention to the circumstance that, on the addition of water, some of the pus-corpuscles burst, and allow their viscid contents to escape, which then become dissolved in the dilute serum. The corpuscles then appear collapsed, are much darker, and still contain nuclei. The action of the water is best observed in the cytoïd corpuscles of the buccal mucous membrane; the lenticular nucleus, which may be here very readily recognized, is generally simple, that is to say, not cleft, and is then situated so close to the investing membrane of the corpuscle, that it frequently appears as if it were attached to this membrane on the outside of the cell. This nucleus is brought more prominently into view on the addition of water, which does not cause it to split.

Strong *alcohol* causes the serum of the pus to coagulate, and hence renders a microscopical examination of the corpuscle unavailing. But when spirit containing 23% of alcohol is employed, which induces no turbidity of the pus-serum, the corpuscles appear distorted, somewhat elongated, and, as it were, caudate or pointed.

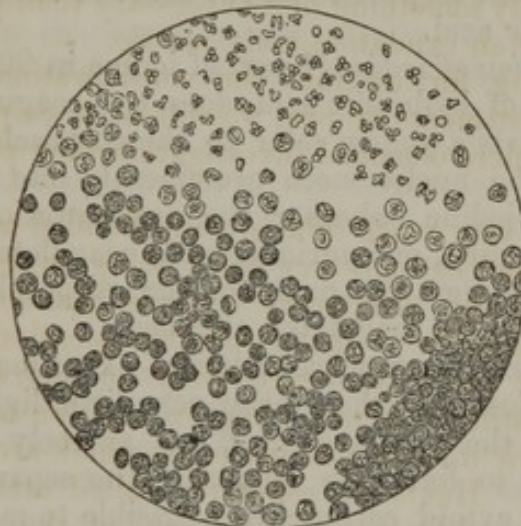
In *ether*, free from alcohol, the corpuscles are also distorted.

When fresh pus is treated with very *dilute mineral acids*, as hydrochloric acid (1 part in 2,800 parts of water), nitric acid (1 part of



anhydrous acid in 2,000 parts of water), phosphoric acid (1 part in 1,500 parts), or tolerably dilute *organic acids*, as acetic, lactic, oxalic, tartaric, racemic, or citric acids, no coagulation takes place, but the pus-corpuscles swell to so great a degree that they frequently attain double their original size. The granular appearance, which may very probably have been owing to plaits in the capsule, disappears; the latter, which appears to be extremely hyaline, very often bursts, when its torn and ragged fragments may be distinguished at different points, provided the light is good and the diaphragm be judiciously employed. Where the nucleus was originally visible, and of a simple, lenticular form, it retained this appearance after the action of these fluids; but in those cases in which it had originally been invisible, or where its appearance could only be detected by a darker spot in the corpuscle, the nucleus was generally tripartite and had a sharply defined outline. One or two dark granules may often be observed in or upon the nuclei, but we leave it to the physiologists to decide whether they should be regarded as nucleoli.

Fig. 30.



Pus, from an acute abscess. The lower half of the drawing shows the normal *pus-corpuscles*. The upper half shows the action of acetic acid upon the *pus-corpuscles*.

*Concentrated* mineral acids coagulate the protein-bodies, and hence the distorted corpuscles cannot be distinctly recognized amongst the separated granules of albumen. The organic acids act in the concentrated state in much the same way as when diluted, causing the variously cleft nuclei to appear perfectly distinct, although their different parts cohere together.

*The caustic alkalies*, if used in a moderate degree of solution, exert a rapidly destructive action on the cytoïd corpuscles; perfect solution never takes place, but after having continued for some time visible, the corpuscles disappear on the addition of water, leaving only a gelatinous-like residue, in which various lighter and darker points may be recognized. Dilute alkalies destroy the corpuscles even more rapidly than the concentrated solutions.

Aqueous solutions of *neutral alkaline salts* cause the sharp edges of the pus-corpuscles to disappear rapidly, contracting the latter until they



appear smaller, granular, and jagged,—an effect which is probably to be referred solely to endosmotic action; the fluid contents are discharged into the serum; the capsule then becomes plicated, and consequently assumes a granular appearance, which prevents the nucleus from being seen, although it may previously have been visible.

Solutions of *alkaline carbonates or borates* also contract and distort the corpuscles; their prolonged action produces the same results as caustic alkalies, for without having previously rendered the nucleus visible, they gradually dissolve the corpuscles, leaving only some few granules, which are held together by a tough hyaline substance.

If pus, in which the nuclei of the corpuscles have been rendered visible by *dilute acids*, be treated with solutions of *neutral alkaline salts*, the previously distended capsule contracts, and the nucleus becomes invisible, whilst the whole corpuscle is much distorted. But, conversely, if we add an extremely dilute mineral acid to pus which has been mixed with such a saline solution, it rarely happens that we can again render the nucleus visible. On this account we can rarely detect the presence of nuclei in the cytoïd corpuscles of the urine in catarrh of the bladder by means of a dilute acid.

An aqueous *solution of iodine* (1 part of iodine in 9000 parts of water), containing a trace of hydriodic acid, does not coagulate the serum of the pus, but it imparts a yellow color to the corpuscles, causes them to swell, and brings the nuclei more prominently into view. A concentrated solution of iodine (whether the concentration be effected by chloride of sodium, spirit, or hydriodic acid) coagulates the serum of the pus, and brings into view the nuclei of the corpuscles which are not entirely concealed by the coagulated albumen.

Whatever evidence these micro-chemical experiments may afford on the question of endosmosis, they throw very little light on the internal chemical nature of the pus-corpuscles, and scarcely even indicate the direction we ought to follow in rendering the separate morphological constituents of the cytoïd corpuscles accessible to more exact chemical inquiry. This much only seems clearly established, namely, that the investing membrane, the viscid contents, and the nuclei, are substances very closely allied to albumen; nearly all of them exhibiting the reactions peculiar to the protein-bodies. The *investing membrane* is a protein-body, which does not merely swell in a gelatinous manner in very dilute acids, but actually dissolves in these fluids. This property, which it exhibits in common with albumen and muscle-fibrin, distinguishes it very decidedly from blood-fibrin, which swells up, but does not dissolve in dilute hydrochloric acid. This membrane is wholly insoluble in alkaline salts, and does not dissolve readily even in the caustic alkalies. These properties very strongly exhibit the points which mainly distinguish it from neutral albumen which is poor in salts (such, for instance, as the albumen obtained from an alkaline solution by neutralization with acetic acid and by excessive dilution, or by the careful addition of dilute spirit), or from casein, which has been freed from salt and acid (according to Bopp's mode of exhibition), whilst its behavior towards the caustic alkalies and their carbonates and borates, makes it approximate more nearly to muscle-fibrin (syntonin). If the serum of the pus and the



viscid contents of the corpuscles admitted of being removed, the most practicable method would appear to be that of dissolving the cell-wall in water containing hydrochloric acid, and exhibiting the matrix in a similar manner as with muscle-fibrin; but this apparently practicable method of dilution with water and decantation, which, according to the above reactions, indicates no difficulties at the first glance, is found to fail most entirely on being tried, and we are still ignorant of any other method of removing the serum of the pus, without dissolving the investing membrane.

It may appear a very simple matter to isolate the *substance of the nuclei*, but even in this respect our expectations are not realized, for when we attempt to dissolve the cell-walls by means of dilute mineral acids or concentrated solutions of organic acids, we are scarcely ever able to succeed in completely dissolving the capsules of all the corpuscles, whilst, moreover, some portion of the viscid contents always remains undissolved in the form of fine molecules, which cannot altogether be regarded as fat, since they cannot be made to disappear when treated with ether. The great difficulty of obtaining the nuclei in a pure state consists, however, in the complete impossibility of separating the undissolved particles by filtration or decanting. When treated with concentrated nitric or sulphuric acid, or with chromic acid, the material of the nuclei exhibits reactions, which seem to place it in the group of the protein-bodies, whilst the difficulty of its solution in concentrated alkalis, and the facility with which it dissolves in dilute caustic alkalis even more rapidly than the cell-walls, seem rather to show that this substance possesses considerable affinity with the nuclei of the cells of the horny tissue.

We are unable to decide anything regarding the chemical nature of the nucleoli, for when the cytoïd corpuscles are digested with dilute alkalis till their distinctive character can no longer be recognized, there remain, as we have already observed, more or less deeply tinged molecules, among which the nucleoli may possibly be present. On treating these masses with ether, a portion of the punctated mass disappears, but individual granules are still visible. But we are unable to decide whether these are the remains of the granules which were previously visible, or whether they have been separated by the ether; and hence we do not know whether the original molecular granules consist entirely or only in part of fine fat-granules. If we treat the nuclei, which have been obtained from pus by digestion with acetic acid and subsequent decantation (as far as this is practicable), with a not too dilute solution of potash, we find that there is formed, on heating, a gelatinous mass almost insoluble in water. This substance, which was formerly believed to be the matrix of the nucleoli, and held to be a special material allied to horny substance (keratin), has been as yet found to present no differences from the strongly basic albuminates of potash, to one of which we have already referred in vol. i. p. 297. Other protein-bodies, moreover, besides albumen, enter into similar gelatinous combinations with potash, and, like them, do not very readily dissolve in water. A great number of the substances which have been pronounced to be *keratin*, are nothing more than compounds of strongly alkaline bases with protein-bodies.



In the experiments on pus made by Messerschmidt and myself, to which I have already referred, we were led from certain reactions to the erroneous conclusion, that we had been able to distinguish several varieties of fibrin in the capsule, nuclei, and nucleoli, an error which, unfortunately, met with more general approval than it deserved, considering the state of science at the time. We believe that we have now shown that there are not sufficient grounds for regarding any constituents of the pus-corpuscles as identical with fibrin, and we need scarcely repeat the remark we have so often made, that it is injurious to the cause of science to attempt to identify or name different substances without having had the power of closely investigating them. A deficiency in our knowledge is in such a case very far preferable to the mere accumulation of vague hypotheses.

We have already shown from direct observation (vol. i. p. 226) that *fat* is accumulated in the corpuscles of the pus.

We are, unfortunately, still deficient in observations which would enable us to judge of the quantity of *salts* contained in the pus-corpuscles when compared with the amount present in its serum.

We now proceed to consider the constituents of the *serum of the pus*. This fluid, when we can succeed in skimming it from the corpuscles, which only sink very slowly, is found to be entirely colorless, or of a faint yellow color, and perfectly clear; it rarely contains fat-globules; it has a faintly alkaline reaction, and, coagulates on being heated, most frequently into flakes, but sometimes in the form of a dense white mass. Acetic acid occasionally renders it strongly turbid.

The *albumen* of the intercellular fluid of the pus does not differ from that of the blood; at all events, all its reactions correspond perfectly with those of ordinary albumen. Moreover, the quantity of albumen in the serum of the pus is very variable, according to the source from whence it is derived; in the four analyses which I was alone able to make, I found from 1.2 to 3.7% of albumen in the serum of the pus of different persons.

*Mucin* is not present in pus, except the latter has been obtained from inflamed mucous membranes; it may in general be easily distinguished by a microscopical examination of the precipitate from other substances, which are precipitable by acetic acid. It presents an appearance of whitish striped flakes or membranes (see p. 87 of this volume).

*Pyin* is a substance which is in like manner precipitable by acetic acid, although it differs from mucin as much as from casein. This substance which was first shown by Güterbock<sup>1</sup> to be present in pus, is not of constant occurrence; it is certainly absent from the pus of wounds in healthy persons. Güterbock obtained it from the pus by coagulating the latter with alcohol, and extracting the residue with water; it is remarkable for being precipitable with acetic acid and a solution of alum, whilst it remains perfectly undissolved in both these fluids. Notwithstanding the frequent notices of this substance in works treating of pus and mucus, it has been very imperfectly investigated. Mistakes may, however, easily be made; thus, for instance, on coagulating the pus, the fluid becomes more strongly alkaline; the alkali dissolves a portion of

<sup>1</sup> De puris naturâ et formatione; diss. inaug. Berol. 1837.



the coagulated albumen, and this solution, when acted upon by acetic acid, deposits a considerable precipitate, but this latter does not dissolve in an excess of acetic acid as rapidly as one might have been led to expect from the assertions of most writers. A mistake may, therefore, easily occur even when the absence of mucus or casein can be demonstrated; the latter point is not very easy of proof, except in some special cases. Scherer<sup>1</sup> has submitted pyin-like bodies to elementary analysis, and in the course of these observations he found that what had been regarded as a simple substance, and supposed to be pyin, consists in fact of very various substances with the most different composition. Many persons have considered pyin to be an oxide of protein, indeed, as Mulder's trioxide of protein; but it will be found on a closer examination that the reactions of pyin do not correspond better with this substance than Scherer's elementary analyses of the latter do with Mulder's analysis of the trioxide. Many authors are of opinion that pyin may be a transition stage from fibrin to gelatigenous tissue, or a product of fibrin entering into a stage of suppuration; but these conjectures have not hitherto been confirmed by the positions in which this substance occurs, so far as they have yet been accurately observed, or by its chemical reactions.

Scherer has submitted to elementary analysis several specimens of pyin obtained from different exudations, and has found that their composition was almost precisely the same as that of protein; however, he also found other constituents of the exudations which appeared very similar to pyin, but differed very much from it in composition, being especially remarkable for their abundance of nitrogen (=22.37%).

*Casein* does not occur in normal pus, and its presence has not been proved with certainty even in abnormal forms of the secretion. The deficiency of our knowledge of the protein-bodies and their immediate derivatives is nowhere more forcibly shown than in the investigation of pathological products.

The quantity of *fat* in pus, the occurrence of which has been regarded as highly characteristic, differs extremely according to the source from whence it is derived; although, when compared with the amount contained in many other fluids, it is rather large. It is very considerable, and is always present in all abscesses of the *mammæ*; cancer of the breast, however, always exhibits a larger amount of fat than any other carcinomatous growth. In ordinary pus the quantity of fat varies, according to our observations, which agree with those of Güterbock, Valentin,<sup>2</sup> and von Bibra,<sup>3</sup> from 2 to 6%. The different fats seem to consist of olein and margarin, alkaline oleates and margarates, and variable quantities of cholesterin. We cannot entirely admit the correctness of Simon's view, who held that the fat-globules which appear on the addition of acetic acid to pus, consist principally of liberated fat derived from the corpuscles, since it may also be dependent on the decomposition of the *soaps* dissolved in the pus-serum; and, indeed, fat-globules are often perceived in pus-serum after it has been treated for some time with acetic acid, which were previously not to be perceived. Pus occasionally

<sup>1</sup> Untersuchungen zur Pathologie, S. 85-96.    <sup>2</sup> Valentin's Repert. 1838, S. 307.

<sup>3</sup> Chem. Untersuch. verschiedener Eiterarten u. s. w. Berlin, 1842.



contains a tolerably large amount of *cholesterin*, and Valentin found as much as 1% of this substance in pus which had been taken from an abscess in the thigh. On a careful examination of the masses of fat extracted with hot alcohol and ether from the residue of the pus, a little fat containing phosphorus may always be detected in the residue which is insoluble in cold ether.

Normal pus generally contains from 14 to 16% of *solid constituents*. The purulent exudations which occur in serous cavities and bad ichorous pus, often contain a smaller amount of solid constituents. These solid matters contain from 5 to 6% of mineral or inorganic substances in the pus of healthy persons, whilst the amount may rise to 10 or even 14% in bad pus and in watery transudations. The ratio of the insoluble to the soluble salts in healthy pus varies from 1 : 7 to 1 : 9, whilst in bad pus it often = 1 : 15 or even 23. It follows from these observations, that in bad pus a greater or smaller quantity of simple transudation must have become mixed with the true plasma of the pus.

The *insoluble salts* of pus are those which usually accompany the protein-bodies, namely, the phosphates of lime and magnesia, in addition to which there is always a variable amount of carbonate and sulphate of lime generated by the process of incineration. There is, moreover, always some oxide of iron to be detected in the ash of pus, even when no trace of blood-corpuscles is to be discovered in the fresh fluid.

*Chloride of sodium* constitutes the principal part of the *soluble salts* of pus. H. Nasse long since drew attention to the fact that the serum of the pus and its solid residue contains three times more of this substance than the blood-serum and its solid residue; and even when the quantity of the chloride of sodium of the whole pus is compared with that of the blood-serum, the former is always found to be the larger. A comparison between the chloride of sodium in the serum of the pus, and that which is present in pus rich in corpuscles, shows that here, as well as in the blood, the larger proportion of this salt is dissolved in the intercellular fluid, and that a very small quantity only is contained in the pus-corpuscles.

The ash of the pus does not contain a very large amount of *soluble phosphates*, but, as we have already stated, no approximate estimate or definite relation can be established between these and the other salts. The quantity of soluble phosphates in the ash of different kinds of pus varied between 3 and 10%. Moreover, the quantity of potash in the different kinds of pus did not admit of being definitely determined; this much only was constantly observed, that there was always more potash present than in the intercellular fluid of the blood. The experiments made on the pus of rabbits did not lead to any more definite results.

I succeeded by the same methods which I employed in the case of the blood and the transudations, to show the presence of *alkaline carbonates* and *free carbonic acid* in the pus.

In the pus, as in almost all other exudations, we meet with *bile-pigment*, the *biliary acids*, *urea*, and *sugar*, as incidental constituents.

Glycocholate and taurocholate of soda were found by one of my pupils in pus from a large abscess in the thigh of a patient with catarrhal



icterus; another pupil found sugar in the purulent discharge yielded by the blistered surface of a patient with diabetes.

We may conclude with the supplementary remark, that morphological elements which do not, strictly speaking, pertain to pus, are sometimes found in it; amongst these we must reckon the fibrinous coagula which are often met with in suppurative exudations when they liquefy into pus (pneumonic sputa). In the pus of old abscesses, and in the ichorous discharge from ulcers, we very often find crystals of phosphate of magnesia and ammonia, not unfrequently vibriones, and sometimes microscopical fungi and confervæ.

*Acid pus* is probably of very rare occurrence in the animal body; when pus has continued stagnant for a considerable time in the cavity of an abscess (in what are termed cold or congestive abscesses), it very generally undergoes alkaline fermentation; it then contains some *carbonate of ammonia* and triple phosphate, besides a large amount of *sulphide of ammonium*. I have only found the purulent exudations present in some few cases in empyema. Phthisical patients sometimes expectorate sputa having an acid reaction, although no acid substance had come in contact with the expectorated matters, either whilst they were passing through the mouth or after they were thrown up. The rare occurrence of acid pus is the more remarkable, as it very rapidly turns sour on being left in imperfectly closed vessels. When healthy pus is suffered to remain for several days in a corked bottle containing a certain amount of air, and exposed to a summer temperature, we find on examining it under the microscope, that the corpuscles have swelled and become more transparent, whilst the fissured nuclei are also speedily brought more distinctly into view; after a longer time the reaction is decidedly acid; numerous isolated nuclei without a trace of cell-walls, and some few perfect corpuscles are seen under the microscope, and interspersed amongst the corpuscles and the nuclei are innumerable molecular granules, whilst here and there we may detect tablets of cholesterin and a confused mass of threads of margarin. After pus has continued standing for several months, the different fats appear in the most beautiful forms, such as no artificial means are able to produce. Even with the naked eye we may detect white granules here and there in the pus; these granules consist partly of a confused mass of fine threads of margarin, but chiefly of ensiform, lily-leaf-shaped, variously contorted and intersecting bundles of crystals of margaric acid, in which are embedded separate groups of tablets of cholesterin.

The distinctions between pus and mucus, which so largely attracted the attention of the physicians of an earlier day, have lost all their supposed importance, since modern physiology has shown that the two fluids are separated only by the most gradual transitions, and that the mucus in inflammatory affections of the mucous membrane gradually presents large numbers of cytoïd corpuscles, together with albumen, and thus acquires great similarity, if not a perfect identity with pus, both in respect to its physical and chemical characters. Even the quantity of fat in the purulent fluid secreted by the mucous membrane in a state of inflammation, is very often fully equal to that of genuine pus, a fact to which Güterbock attached great diagnostic value. The pus of the mucous mem-



branes commonly retains the property possessed by mucus of gelatinizing on the addition of water or acetic acid.

Rokitansky's *ichorous exudations* constitute an ill-defined group, corresponding in many particulars with albuminous exudations. Their chemical properties differ as much as their physical characters; many are also entirely inaccessible to chemical investigation, which would, moreover be wholly useless, as they frequently are nothing more than simple products of putrefaction, and the detritus of the dead (gangrenous) tissue.

In like manner we cannot ascribe the acid reaction, which is more frequently observed in these than in other exudations, to an organico-vital process; nor do the scanty chemical investigations which we possess afford the slightest insight into the true source of the irritating character of many of these exudations, more especially of those which were originally coagulable, and deposited clots of fibrin. Rokitansky's *hæmorrhagic exudations* are even less amenable to chemical inquiry, and do not, therefore, fall within the scope of the present work, since they can only be considered from a purely anatomical point.

The hæmorrhagic exudations lead us to the consideration of the metamorphoses which the blood undergoes when it stagnates in vessels which have become occluded (in thrombus), or is effused in individual tissues (as in extravasations and apoplectic centres). Many of the most distinguished inquirers have made this question the subject of the most careful investigations; the morphological metamorphoses which occur in such sanguineous extravasations have been observed under the microscope, from their earliest origin to their persistent condition at a certain stage of development, or to their final disappearance; yet, notwithstanding all these researches, many of the points already observed remain obscure and wholly inexplicable, the different opinions of inquirers being here more entirely at variance with one another than in any other department in the history of development. The chemical history of these exudations is still more deficient, for here we have actually no observations. Histologists have endeavored by the aid of certain micro-chemical means to throw some light on this obscure subject; but these attempts have either been of no avail whatever, or have yielded very doubtful results, —an apparently similar structure behaving differently in different cases under the same reagents. A similar remark may be made in reference to the development of pathological exudations into those abnormal cellular masses which especially characterize cancerous structures, or into those fibrous tissues which we meet with in fibroid tumors. Many young physicists, despairing of the possibility of explaining these matters, and the processes on which they depend, by chemical means, have probably shared with us in the sanguine expectation that histology, which had already thrown so much light on the development of normal tissues, would aid our chemical researches; but in these expectations we have demanded more than chemistry is able to accomplish, whilst we have also probably underrated the extreme diversity of these highly complicated vital processes.



## ZOOCHEMICAL PROCESSES.

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AFTER having traversed the extensive domain of the organic substrata, which serve as the solid basis of the zoo-vital processes, and endeavored, in accordance with the principles of an enlightened physical inquiry, to form a correct estimate of the chemical and physiological value of the numerous members of those groups of atoms which serve the animal body both as materials for its structure, and as the means by which its movements are effected, we at length approach the special aim of our inquiries, namely, the study of the phenomena manifested during life in those parts of the animal organism which we have been considering, and the elucidation of the internal connection existing between such diversified phenomena and the causes on which they depend. We drew attention in the introduction to the present work (see vol. i. p. 26) to the maxims and principles which ought to guide us in our attempt to unravel the hidden processes of material life; we will not, therefore, enlarge upon our previous remarks, or expatiate any further upon a subject which has been treated with so much more ability by other writers, as, for instance, by Lotz<sup>1</sup> and John Stuart Mill.<sup>2</sup> Yet, when we take a survey of the collective mass of positive facts, we find a mere accumulation of disjointed fragments, the natural connection of which we are rarely able to discover, since we often lack the intervening links by which alone we should be enabled to follow the endless chain of vital phenomena. A careful study of the material substrata of animal life, as far as the present condition of science admits of such an investigation, cannot fail to show us how far removed we still are from obtaining a scientific basis for a true inductive treatment of the material processes of life; and, indeed, it would almost seem to require the marvellous powers of combination of a Liebig to collect together and combine into a connected whole the scattered threads which constitute the materials for the study of the metamorphoses of animal matter.

In proceeding to a minute investigation of the chemical processes in the animal or vegetable organism, we usually begin by considering such questions as—whether the masses acted upon by different forces in vital phenomena differ essentially from those in which we have studied mechanical or physical forces?—whether all those differences which force themselves upon our notice in no small number and in a very decisive

<sup>1</sup> Allgem. Physiologie des körperlichen Lebens. Leipz. 1851.

<sup>2</sup> A System of Logic, ratiocative and inductive London, 1843.



manner, on comparing together organic with inorganic, and organized with crystallized or amorphous bodies, are owing to essentially different causes, or arise simply from a multiplicity of intermerging forms, and only correspond to the more prominently marked points of limitation in the frequently intersecting series of qualities? This is not a question, however, which we purpose discussing at the present time; for, as we have already observed in our brief notice of it in the introduction to the theory of the Animal Substrata, it has been finally set at rest by pure chemistry. The belief which our predecessors cherished of an actual principle of vitality has passed away with them, and to attempt to attach even a semblance of reality to this exploded notion of a bygone period would be at once to condemn the most brilliant discoveries of the last few years, and indeed the whole labors of half a century, as the manifestations of mere delusive chimeras.

But whilst pure chemistry has shown us that the laws which control the cohesion of different atoms in stones and rocks are the same as those by which the persistence of the atomic composition of animal and vegetable substances is maintained, the theory of the animal substrata, juices, and tissues, affords a proof that the quality of the different particles of matter which serve as points of application for the active forces which exist in the animal body, invariably corresponds to the functions required for the performance of the purposes of life. When we pass in review the delicately linked series of chemical combinations taken by the animal body from that laboratory of all organic bodies—the vegetable kingdom—or generated anew within itself, the idea involuntarily presents itself to us, that the chemical quality of a substance for the most part corresponds to its physiological importance; thus we find that the more complex atoms, the chemical particles of which have a less stable equilibrium, occur especially wherever the higher functions of material life are manifested. Thus, too, we had occasion to notice, at the close of our description of animal matters, that even those more organized atoms which constitute the more simple substrata of the animal tissues are always formed in accordance with the functions which they control or the forces with which they are connected. However strikingly this observation seems to be confirmed, wherever the chemical movements of the animal body fall under our notice, it need not excite our surprise; for when we only observe the known laws of molecular motions, we perceive that their manifestations in these particles of matter must be different from those in inorganic nature. The manifestation of each force is connected with the nature of the mass which is to be acted upon, whilst the effects depend upon the circumstances under which the force is brought to bear upon the mass. If, therefore, we wholly disregard the question whether other forces than those with which the physicist is familiar may not act upon these masses, such forces appertaining exclusively to life, it follows *a priori* that the resulting action of these physical forces will be very different when exercised upon inorganic particles (which, although differently formed, present identical principles of structure), than when applied to the simpler forms of mineral substances. This proposition requires no further demonstration, but it indicates the direction we must follow if we would attempt to trace the internal connection of vital phenomena in their



individual phases, and thus investigate the various processes of animal life.

We have, in accordance with the plan of our work, passed in review the general mechanism of the animal organism, and considered the chemical nature of the individual parts; we proceeded next to investigate matter and its endless variety of forms, without however directing more than a cursory glance at the motions of the individual parts, or the various phenomena of physical life. We have now to enter into the phenomenology of the individual members of this vast series, postponing our investigation of the forces through the agency of which the phenomena are called forth, until we have gained a sufficient knowledge of the qualitative and quantitative relations of the individual phenomena. This is the simple and only practicable method of conducting every physical inquiry, and hence we ought not to neglect it in physiology. Nor can we enter into a causal investigation of the objects of our inquiry before we have considered the phenomena in the living organism from all points of view, and ascertained its relations of mass and weight. We shall have occasion to perceive, in our attempts to refer individual phenomena to their controlling causes, and to ascertain the inner connection of their reciprocal effects, that a great number of vital phenomena stand in the simplest relations of dependence to well-known, so-called physical laws, or more general propositions; and that it is to the special mode of arrangement of the individual elements of motion, and to a complication of numerous conditions, that we must, at all events to a great extent, refer the specific character which is impressed upon vital phenomena. We certainly very often fail in solving the mystery of the internal association of phenomena, or the connection of the laws or forces by which they are controlled. Even in the case of a purely mechanical or purely chemical effect, we very frequently fail in comprehending the complication of circumstances which has given rise to the peculiar results manifested. We must not, however, regard the various interruptions which present themselves to our notice in the consideration of vital processes as a proof of the development of forces pertaining exclusively to life.

Molecular forces themselves, and the manifold complications which they undergo in accordance with different circumstances and relations of mass, are not yet sufficiently elucidated to enable us to trace the causal connection of all the phenomena to which they give rise even in the inorganic world.

How numerous are the actions of affinity which we have hitherto failed in referring to any general rules, or even to the leading principles of chemistry! We do not even know whether chemical combination is the sole effect of chemical affinity. But the simplest effects of cohesion and adhesion manifest themselves under such numerous and various circumstances, that physicists have been unable to elucidate the conditions on which they depend. Who would have believed some years ago that the most strongly developed chemical affinity might occasionally be destroyed by simple diffusion? or who would have ventured even a few months back to plunge his hands into molten glass, or to immerse a living child in melted copper? When experiments of this nature were



attempted in former ages, mere vital force was regarded as too simple and inefficient to afford an explanation of this phenomenon; no power but the All-Highest being capable, according to the vulgar belief, of thus miraculously suspending the ordinary laws of life; yet this marvel, which still excites the wondering admiration of the ordinary spectator, admits of being reduced to very simple relations of cohesion. The effects of molecular forces have never been so thoroughly examined in all their bearings and modifications as to aid us in our consideration of the intricate mechanism of the innumerable results manifested in the animal organism. Even now a Graham is devoting his energies to the elucidation of the numerous effects of diffusion, and we scarcely yet possess any solid basis for our views of the phenomena which are termed endosmotic. Yet, notwithstanding this great deficiency in our knowledge, the few certain conclusions which we have drawn from our experiments on diffusion and endosmosis have already largely augmented our knowledge of many of the processes in animal life. Our insight into the movements of matter is daily being enlarged by numerous contributions from able physicists, who have elucidated many points which had previously been enveloped in obscurity, and which, without such elucidation, might with equal propriety have been referred to either a vital or to any physical force. Such labors are daily supplying us with the compass and the quadrants by which we may safely steer our course across the vast sea of vital phenomena, and learn the position and reciprocal bearing of each individual point. It will be better, therefore, to wait patiently for the advent of the new discoveries promised to us by these researches, instead of selecting as our guide the mysterious vital force which does not even interpret to our own satisfaction the phenomena we desire to elucidate, but merely plunges us lower into those conflicting depths of physical inquiry in which so many bold adventurers have been already lost. In plain words, it would be far more conducive to the advancement of science, were we to direct our efforts to the task of referring vital phenomena to mechanical conditions, instead of resigning ourselves to the fiction of a general principle, which will never satisfy that natural striving of the human mind which seeks to embrace all phenomena in one ideal connection.

The living body itself is not the place where we should seek to investigate the forces by which the movements of animal matter are controlled, and it is only when examined externally to the organism that we can make them subservient to the elucidation of the phenomena of life. This is the course which has been pursued by physiologists of recent times, to whose researches we owe a very considerable number of the most interesting conclusions regarding molecular motions. When the scalpel of the anatomist has brought to view the delicate structure of all organic parts, and the mode of arrangement and the mutual relations of different phenomena have been studied, the physiologist endeavors to trace the causal connection of facts to definite laws, and seeks to refer the course of phenomena to other forces besides those which appertain exclusively to the internal mechanism of the body. Whilst in former times physical laws were often not sufficiently taken into consideration in the explanation of vital phenomena, the tendency of latter times has rather



been to attach undue importance to them. All things which did not admit of being referred in a simple manner to known mechanical means, were ascribed to vital force, which, although as yet unknown, might, perhaps, serve as a guiding light to future generations in their advance on the paths of physical inquiry. But it was forgotten that there are very many phenomena in inanimate nature which must be explained by physical laws, and that we have very slight knowledge of the laws of molecular motion. The many cases, too, have been overlooked in which chemical phenomena are opposed to all the ordinary laws of affinity, whilst the theoretical deficiencies of our highly-vaunted science of chemistry have not been thoroughly admitted, notwithstanding the want of success which has attended all the attempts hitherto made to explain the highest chemical principles in simple mathematical symbols, and to calculate their results by simple formulæ.

When we consider the deficient state of our knowledge of many physical laws, and the varying circumstances by which their results are modified, we can hardly suppose that all the phenomena of animal matter can at present be referred to mechanical conditions, and we shall be compelled to admit that there are no grounds on which we can establish an exclusive vital principle by which the phenomena of life can be explained independently of purely physical forces. Physical inquiry demands that our investigations into the existence of a vital force should be preceded by a complete separation of all phenomena which can be referred to purely physical forces, from those which depend upon some force peculiar to life. Physical knowledge is, however, quite inadequate in its present state to afford proof of this nature, for which we must await a more perfect development of this branch of science. We are still ignorant of the relation borne by the obscure agency of the nerves to electricity; and, notwithstanding the attention that has been directed to the study of the phenomena of the nervous system, the physiologist would scarcely venture to determine whether these phenomena admit of being referred to certain physical relations, or whether we are compelled to assume the existence of some specific nervous agent peculiar to animal life. As, however, we are still unable to refer nervous actions and certain other phenomena of animal life to simple physical laws, we must leave the proof to those who, even in the present day, regard as undoubted the existence of a nervous agent or vital force. The correctness of the view which ascribes vital phenomena to mechanical conditions, cannot be fairly tested till the existence of this new force has been proved; but how can such proof be adduced in reference to a force the simplest effects of which are unknown to us, and which differs from other forces merely by its disregard of all restrictions, and of the limits prescribed by physicists to laws? It may be briefly asserted that the exclusion of physical agency affords no proof of a purely vital force; and yet there is no other means by which its existence can be established. The physicist who rigidly follows the leading maxims of his own science, must admit the possibility of a vital force, although he may regard any proof of its existence as at present impossible.

The time has passed when the assumption of different vital forces was supposed to afford sufficient explanation of all or any alterations occur-



ring in organized bodies, or when these same forces were fancifully represented as the architects of the organism, and the stewards of the vegetable and animal economy, providing all things, providently warding off all noxious matters, removing all that threatened evil, executing all useful things, and everywhere active, keeping a watchful guardianship over the whole organism. But physiologists still exist, who regard those phenomena in the vital economy, which we are as yet unable to explain on physical principles, as a proof of the existence of a specific vital force. Let us once more briefly consider the grounds which make such an assumption simply problematical.

If the proposition be established that no organized body can be formed from the fortuitous elements of inert matter, and if organized bodies must originate in organized structures only, and finally, if, without life, life could not be generated, the elaboration of organized bodies must depend upon that which is organized—upon life, or vital force. Such a sequence as this proves the impossibility of obtaining an insight, from a physical point of view, into the origin and development of organic matter. We must admit that in the physical sciences generally we meet with certain boundaries beyond which we are conscious that the human intellect never can or will pass. Thus astronomy, the most perfect of all the physical sciences, will never succeed in explaining how the planetary system, with its satellites, was first set in motion, or what gave the first impulse to the eccentric orbits of the comets which traverse our solar system. Notwithstanding Laplace's theory, we are ignorant of the primary cause of the formation of the earth; we are firmly convinced that, at a definite period of the earth's development, the seeds of all plants were simultaneously scattered over its surface; we know that for thousands of years an exuberant vegetation covered our globe, before the sun had matured the first germ of animal life; and we are equally convinced that it was only subsequently to the most recent revolutions on the earth's surface that the higher animals were created, and that, last of all, Man appeared. But here the physical science leads us to a boundary, which we distinctly recognize as such, and know that we can never pass, without leaving the domain of physical inquiry for the regions of metaphysics. But it does not follow that because we are unable to recognize the origin of certain natural phenomena, we may not be capable of comprehending their subsequent course. The human mind does not turn aside from the study of the movements of the heavenly bodies, because it does not, and never can hope to know the origin of their motion; and its efforts have been successful in attaining the most exact acquaintance with the laws of those motions, and the course of the motion when once imparted, and has even been able to predict what those motions will be at a future period; for the laws remain everlastingly unchanged, although the *primum movens* cannot be recognized after it has once imparted the motion which obeys the laws. Thus, too, in respect to the primary formation of organized bodies, either as seeds or ova, no investigation will ever show how the germ originated, or what regulated the first creation of ova and seeds; yet, notwithstanding this, we are as well able to investigate the laws of the organic motion that has been induced, as to study the regular movements of the heavenly bodies in



their orbits; for, as in the regions of space, the first moving force merely gave the impulse to motion and regularity, and did not again, by renewed influence, affect the motion imparted to the created body, so also when the force by which the germ was generated, had implanted in it the laws necessary to effect its development, and to control its further elaboration and assimilation, it ceased to interfere with the laws it had established; it gave to the living organism no guide or guardian by whose agency the sacred laws of its being were to be modified or miraculously suspended. The true miracle of nature is the unchangeable regularity of the course of all phenomena. Since, therefore, conformity to law has been implanted in organized bodies, we may hope, although perhaps at a later period, to examine the laws of organic nature as accurately as previous generations succeeded in elucidating the physical laws of cosmical phenomena.

Although in our study of the animal organism we frequently meet with phenomena which we cannot deduce from known chemical principles, and which indeed seem to be in direct opposition to them, we must not at once conclude that the laws of affinity are partially or wholly inefficient in these cases; nor should we suppose that there is any marvellous intervention of some force acting with a definite purpose. The chemical force is not destroyed, but the external relations, which control its activity, are altered. Force is obviously nothing more than the expression of the cause of natural laws; if, therefore, facts do not accord with our laws, we must either have formed a misconception of the ideas of these laws, or, at all events, we must have imperfectly investigated the different circumstances under which they are exhibited. The result of forces (which, in a physical sense, is only a short expression for the laws) must necessarily be different under different conditions.

Albinus<sup>1</sup> took no superficial view of the organic activity in nature when he established the axiom that the essence of vital force consisted in motion. Even if this expression be far too general for organic action, it cannot be denied that we assume life to exist wherever we perceive a constant alternation of phenomena and incessant changes, induced by the constant motion of the molecules of the organized body, as well as of the organs themselves. Although Albinus overlooked the fact that, on the one hand, something more than this is necessary to vital action (as we here for the most part consider the grounds and object of motion, often without comprehending its primary origin), and that on the other hand, we recognize a perpetual movement in the heavenly bodies without assuming that they are on that account possessed of life, this proposition is to a certain degree correct, when we limit it to the substrata of vital manifestations—to organic motion; for we find that wherever matter is endowed with life, its chemical molecules are endowed with incessant motion.

Metamorphoses are continually developed in the material substrata of the living body. Physical forces always strive to maintain themselves in equilibrium; the matter set in motion by them finds, or, at all events, may find, its centre of gravity—its point of rest. Physical forces con-

<sup>1</sup> De naturâ hominis, p. 39.



tinue to act upon matter after it has attained its position of equilibrium, for it is only by opposite actions that the equilibrium exists. A body which is moved by physical laws appears always to tend only towards a state of rest; inorganic chemistry continues active, and induces motion and metamorphosis until the closest affinities are satisfied.

The case is very different when physical forces act under organic conditions, or when motion occurs in organized bodies, for here we find a tendency to persistence; everything that is brought into the line of direction of these concurrent forces is impelled to similar motion, and although a temporarily preponderating force may be antagonized, equilibrium will not be induced; for equilibrium is rest, and in rest there is no life, and in equilibrium there is death.

If we may be permitted to bring prominently forward some few causes from the sum of the conditions under which physical forces act in the motion of living beings, there are three characteristic points which appear especially to challenge our attention. The question arises how this persistence of motion, which can only be maintained under purely mechanical conditions, can exist independently of vital stimuli. We are acquainted with a number of purely chemical motions or processes which require for their accomplishment a certain duration of time, or, in other words, a longer interval, to equalize all the conditions of affinity than is required for the usually instantaneous effects of chemical affinity. We need only refer to the solution of fibrin in nitre-water, to the decomposition of alcohol by caustic alkalies, to the formation of numerous compound ethers (Liebig<sup>1</sup>), and more especially to the processes of fermentation and putrefaction. In the meanwhile, notwithstanding the occasional constancy of all these chemical motions, they differ in a very marked manner from organico-chemical actions in living organisms. Thus in fermentation and putrefaction we observe that the chemical motion exhibits a tendency towards the simplification of the radical—a tendency to equilibrium; in these decompositions there are always produced more fixed combinations and more persistent bodies, until at length there are formed either undecomposable radicals or their most constant combinations, upon which equilibrium or rest follows. We perceive no tendency of this kind towards equilibrium in chemico-vital motion; for here one motion is produced only in order to call forth some other motion, the object of the metamorphosis being merely to effect a new change. The molecular motion itself is thus maintained by motion and gives occasion to new motion; a substance undergoing metamorphosis gives origin to a new substance, which in its turn becomes the source of new motion, that is to say, new substances are formed by chemical activity which are not characterized by their constancy, as in putrefaction and decay, but are distinguished by their marked tendency to generate new motion, new decomposition, and new metamorphosis. Hence we also observe that in processes of the highest vitality in the organs, the most decomposable substances, even self-decomposing bodies, are formed. Diastase, ptyalin, and pepsin, the most readily decomposable substances, are produced only during high organico-vital activity; but owing to the incessant metamorphoses which they undergo, even whilst they are being sub-

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 65, S. 350.



mitted to chemical investigation, they have been but imperfectly examined. It is not, therefore, the capacity for repose in inert matter, on which the persistence of motion, and, consequently life, depends; for the return of the molecules to a state of rest is prevented in the same manner as falling when a man is walking or running. The chemical molecules are not in a condition of stable equilibrium or of the strongest affinity; but the act of falling, the more constant union, the suspension of motion, is prevented by another simultaneous motion, the centre of gravity becoming unstable, and the manifestations of affinity being kept *au courant*. In consequence of the variety of substances which are brought into contact with one another during the metamorphosis of matter in plants and animals, one molecular mass is hindered by another, during the general motion and transposition, from attaining its natural centre of gravity, and is constantly drawn aside into new directions at the time it was striving to acquire equilibrium by the most powerful forces of affinity. Many poisons destroy life merely by suspending the action of some of the factors of organic motion; in the same manner as in fermentation and putrefaction, the special excitors of these processes induce chemical equilibrium.

Organico-chemical motion is the most complicated of all molecular changes; for besides the many new substances formed at one spot and at one time from other substances, there also occurs in an equal degree a disturbance and a new arrangement of the particles of the previously formed bodies. We may here instance the muscular tissue, in which the muscular fibre is formed, and where, after it has continued for some time to subserve the higher purposes of life, it undergoes a new metamorphosis in the muscle, simultaneously with the formation of new fibre. Thus we have here, at one and the same spot, the beginning or origin of a substance, its persistence or adaptation, and its termination or dissolution. Occasionally, one or other of the factors of motion becomes consolidated, without passing through the general course of the ordinary phenomena; an aggregation of molecules is here brought to a state of chemical equilibrium, and forms a more constant combination; individual groups are brought into rest, and become deposited; in this manner, for instance, fat and horn-cells are produced in the animal organism, and gum, resins, and oils in vegetable bodies.

If we consider life in the organic substrata from this point of view as an incessant movement of molecules and molecular aggregations, as an uninterrupted process in which beginning, progress, and termination of motions intersect one another at the same time, it will no longer excite our surprise that the chemist has hitherto been unable to trace physiologico-chemical processes in their various directions, to detect from amid a seeming chaos all the substrata which concur in effecting such a process, and to determine with exactness their different properties. Nor must the chemist flatter himself that he can at once, in the midst of the perpetual metamorphosis of matter, arrest the life and motion of the organic substrata, and thus examine the position of the chemical molecules at the moment of rest; and he would be equally in error were he to assume that the substances he has separated are entirely the same as they were when all the molecules in the organized body were in a state of vital



motion. It is impossible to arrest at will the machinery of molecular motion, to bring the moved parts at once to rest and render them rigid, to make them maintain the same unstable equilibrium, or to separate the individual parts of this chemico-vital mechanism. As we are not able to analyze ferments because it is by the very act of self-metamorphosis that they generate fermentation, so also does it defy the efforts of the chemist to investigate organized matter itself; for his solvents and reagents affect only the products of molecular motion in the living body, but not the act of motion itself. If the scalpel of the anatomist, which only reveals to us the often-mangled structures of life, has yielded such grand and brilliant results regarding material life as to form the basis of physiology, what may we not look forward to from the attainment of a more profound insight into the molecular movements? or need we wholly despair of being able, by physical investigations, to discover some magnitudes which will enable us to calculate the highest unknown magnitude?

Many persons have found it very difficult to understand how inorganic matter derived from the external world, can become subject to organic laws within the sphere of the living organism, and undergo the metamorphoses appertaining to that sphere without the co-operation of dynamical laws belonging exclusively to life. It was thought that the magic circle of the vital principle was sufficiently restricted if the mineral substances which we meet with in the organism were regarded as beyond the limits of vital force. Assimilation and reproduction, like growth, were regarded as inexplicable, according to physical laws. But although many individual points may defy all attempts at explanation, we cannot doubt that these phenomena must be susceptible of a general explanation; for if we limit ourselves to the known phenomena of motion, we shall find that there is not any indispensable necessity to assume that this kind of molecular motion requires the control of any such agent as vital force.

We meet with very many cases in which several bodies seem to induce in other bodies an action similar in force to the one they exhibit, although there is no appearance of a relation of affinity between the products of decomposition and those bodies which are still undecomposed. Organic chemistry is rich in cases of this kind, and similar instances are not wanting in inorganic chemistry; the most frequent and striking of these occur in the processes of fermentation; for we here find that a small quantity of a substance undergoing a definite metamorphosis, can induce a special form of decomposition or metamorphosis in an infinite quantity of some other substance. As the slightest contact with any individual point of matter in the molecules of iodide of mercury, arsenious acid, metallic iron, or fulminate of mercury, and in a hundred other similar substances, gives rise to an endless series of definite motions; so the smallest amount of a putrefying body is able to impart to the chemical molecules a definite motion, which is propagated in an uninterrupted sequence from atom to atom, and may thus call into existence new forms and new qualities. All these phenomena, which were formerly referred to a specific catalytic force, not amenable to any law, and which were first referred by Liebig to their true physical relations of causality, indicate the point of view from which we ought in a physical light to examine many of those vital phenomena which at an earlier period were ascribed solely to the *vis vitalis*.



The primary origin of all vital phenomena is as unfathomable a mystery as the first impulse by which suns with their planets and satellites were impelled in their orbits; but if we direct our attention to the motion once imparted to organic molecules, we shall be able to trace the co-operation of the laws of the impulse or propagation of motion in the development, growth, reproduction, and secretion observable in organized bodies. From our experience on these points we shall frequently see how it is possible that substances which appear in all chemical points to be opposed to one another, may present similarities. The germ in the egg and in the seed is surrounded by substances whose molecular arrangement may be disturbed by a slight impulse, and made to undergo metamorphosis. By a slight transposition of its atoms, or by the elimination or absorption of water, the starch of the cotyledons is very readily converted into bodies bearing very little resemblance to itself, but most extensively diffused through the vegetable kingdom, as, for instance, into gum, mucilaginous matter, cane and grape sugar, cellulose, &c. The white of egg is in like manner capable of undergoing the most various alterations without losing the most essential atoms of its constituents; albumen, the first and most important of animal substances, is a perfect *Proteus* in its metamorphoses, assuming the most singular forms both in animal and vegetable bodies; yet we everywhere meet with the same groups of atoms, although the molecular arrangement is constantly changing in order to invest them with different physical and even chemical qualities; and thus chemistry has hitherto failed in tracing the molecular motions of albumen in all its forms. Nature has surrounded the germ with variable substances such as these, whose molecular structure has so unstable a centre of gravity that whenever the slightest motion occurs in it, it readily extends to the other molecular masses; nature has, therefore, surrounded the mysterious source of life with substances which readily admit of being drawn into its current. Are we to believe that vital force resides in the germinating seed for the purpose of fabricating sugar from starch? or that the impulse of chemico-vital motion is propagated to the oscillating molecules, because we can communicate such an impulse to starch within a digesting flask as to change the grouping of the molecules, and alter the direction of their centre of gravity? The latter view, at any rate, furnishes some explanation of these processes, and is supported by numerous analogies, whilst the former is a mere ideal mystification of a simple fact obvious to the unaided senses. It would appear as if all the starch and all the albumen were drawn into the movement of germ-life before the stream of life had acquired sufficient force to increase its own mass by incorporating other molecular parts having a more stable centre of gravity. It is now only that the quantity of chemico-vital motion seems sufficiently great to impart to bodies having a more stable equilibrium a motion which is then regulated by physical and vital laws. The accession of new matter to the moved mass does not diminish the velocity of vital motion; the whole quantity of the motion is increased; for the destruction of the chemical masses which previously rested upon a solid basis gives occasion to a new impulse and to renewed motion; as, for instance, a single atom of oxalic acid is able to convert a hundred and more atoms of oxamide into oxalate of ammo-



nia, or as a single vesicle of air can produce fermentation in infinite quantities of vegetable juice, or as the avalanche which increases in mass as well as in velocity as it rushes down the snow-covered declivity of the mountain side. This kind of vital motion is at least not at variance with physical laws, whilst it presents analogies with purely mechanical motions. It is these analogies which the investigator of nature must endeavor to detect in vital motion, in order to deduce from the known factors the still unknown coefficients of this motion. The vital law cannot be discovered and elucidated until the chemical and physical laws by which these motions are regulated have been thoroughly investigated and distinctly recognized.

It appears strange, and scarcely reconcilable with physical laws, that the molecular motions in the living organism should so rarely deviate from their prescribed course, notwithstanding the innumerable causes which are constantly threatening to disturb them. Organic vital motion is neither straight nor uniform; all its manifestations exhibit an oscillating character, appearing invariably to incline first in one and then in another direction, although some compensating property seems to prevent excess beyond a certain limit. As the influence of heat is compensated in the animal body by the increased evaporation of the fluids, like the action of the same agent on the compensation pendulum; so also in organic motion, notwithstanding its extreme fluctuations, regularity is maintained by some one predominant force being spontaneously arrested, and by the simultaneous action of different particles in motion, which neutralize on the one side what might from the other side give rise to a disturbance in the regularity of the organic motion. The existence of this compensating capacity in organic motion meets with the fullest confirmation in its abnormal or pathological phenomena, which have consequently been regarded as affording the most convincing proofs of the reality of a wise and provident vital principle.

Although the dogma of the vital force cannot be wholly passed by in a text-book of physiological chemistry, we should not have treated it with the completeness with which we formerly<sup>1</sup> considered it, if there were not some cause of apprehension that there might occur a reaction in reference to this question, and that vital force, even if it did not regain its former position, might yet obtain a recognition injurious to scientific inquiry. The imperfect experiments which have been made with a view of deducing certain phenomena in the living organism from some simple physical law, or bringing them into harmony with some ordinary experimental fact, although these phenomena probably depend upon a sum of many individual forces acting under the most various modifications, simply afford evidence of the superficial and deficient physical and chemical attainments of those who instituted them, and have probably done more to support the belief in a vital force, than the fact that we have as yet no prospect of being able to refer the formation of cells and tissues, and the suitable conformation of all the individual parts of the animal organism to definite physical and chemical laws.

<sup>1</sup> In the first part of the original edition.



## ORIGIN OF ORGANIC MATTER IN THE VEGETABLE KINGDOM.

Before we proceed with our general review of zoochemical processes, we must consider the locality and the relations under which organic matter is mainly formed. Theoretical chemistry shows us that the composition and all the properties of those substances which are especially named organic, are not only not opposed, but actually afford the most brilliant confirmation of all the more general laws which refer to this department of chemistry. There seems, therefore, considerable probability that the formation of organic matter from inorganic substances may be due to the action of the more general laws of physics and chemistry. If affinity, like gravitation, be an integral property of matter, the first indications of the formation of organic matter must necessarily furnish the best point from which to investigate the chemical laws which control the generation of organic from inorganic substances. The relations on which such formations depend have not, however, been examined with sufficient exactness to admit of our representing the formation of organic matter by simple formulæ, based upon direct observations. Whilst an opinion prevailed in earlier times that plants, like animals, required for their well-being to appropriate to themselves at least some definite, but not inconsiderable, amount of organic matter in the form of humus, Ingenhouss held the opinion that plants derive their nutriment solely from inorganic nature; and this view has been most ably defended by Liebig, who has shown that the vegetable kingdom collectively, or at any rate the great majority of vegetable substances, is nourished solely by carbonic acid, water, and ammonia, and that, consequently, all organic bodies in the vegetable kingdom are generated solely from these three inorganic substances.

Priestley and Sennebier first made the observation that the leaves of plants, when exposed to solar light, *absorb carbonic acid and in its place exhale oxygen*. The admirable experiments of Saussure, and the later researches of Grischow, Boussingault, and others, have elucidated many points connected with this subject. We now know that it is not only direct solar light, but also ordinary refracted light, that produces this phenomena, which depends not upon the heating or the chemical rays of the spectrum, but mainly upon its yellow and green rays (Draper), and that, moreover, the green parts of the plant alone possess the faculty of exhaling oxygen after absorbing carbonic acid. Plants only exhale oxygen after the absorption of carbonic acid, which is probably taken up through the roots from water or through the leaves from the air. Boussingault has especially drawn attention to the extraordinary rapidity with which the leaves abstract carbonic acid from the air. The quantity of oxygen that is exhaled corresponds very nearly with the amount of carbonic acid which has been absorbed. These experiments were not, however, conducted with the exactness necessary to warrant us in drawing definite conclusions; for while the volume of exhaled air was perfectly equal to that of the absorbed air, there was always found in the



exhaled air a small quantity of nitrogen, the source of which could not be clearly ascertained. The experiments appear, at all events, to prove that there is always rather less oxygen developed than is contained in the carbonic acid, and consequently, that the entire volume of the oxygen is not returned to the air from the carbonic acid. Although a portion of this gas may pass into those organs of plants which absorb oxygen, although they are not green, certain chemical and other grounds render it more probable that a large amount of the exhaled oxygen may be derived from water, and that the carbonic acid cannot therefore be decomposed at once into carbon and oxygen. It would also appear, from the experiments of Saussure and others, that the amount of exhaled oxygen does not depend upon the mass so much as upon the extent of surface of the green parts of plants.

The undoubted fact that plants reverse this process during the night, by developing carbonic acid after they have absorbed oxygen, as is done during the day by those parts of a plant which are not green, led many physiologists to doubt whether the principal source of the carbon in plants was derived from the deoxidation of carbonic acid, which takes place in solar light; whilst, moreover, Saussure's experiments seemed to prove that at least one-twentieth of the carbon absorbed by the plants during this process could not be derived from the carbonic acid. It was believed that there must be some truth in the popular notion that the humus, that is to say, the decaying remains of vegetable and animal matter, serves the living plant as a highly carbonaceous nutrient substance, at least in respect to this one-twentieth. Although it cannot be denied that a certain number of plants, amongst which we may reckon many of the parasitical plants, and all plants which are not green, cannot draw all their carbon from the carbonic acid of the air and water, this no more proves the incorrectness of Liebig's view than the fact that oxygen is exhaled in solar light by certain green infusoria, as *Euglena* (which, moreover, contain a starch-like substance) refutes the view that the vital process in animals is constantly combined with an absorption of oxygen and an exhalation of carbonic acid. Although many plants may thrive better in a soil rich in humus than in one in which they merely obtain the necessary mineral nutriment, this beneficial effect may be owing to many other conditions besides the amount of carbon contained in the soil; for as the humus consists of substances undergoing decomposition, it must of itself supply an abundant source for the formation of carbonic acid.

Liebig refers this nocturnal development of carbonic acid to a purely mechanical cause. It is well known that plants absorb indiscriminately all substances held in solution in water, but that they give off, either by their roots or through other parts, all matters which may injure their vital activity; and that all terrestrial as well as atmospheric water contains larger or smaller quantities of carbonic acid, which, according to Liebig,<sup>1</sup> is not assimilated during the night, but is again evaporated in an unchanged condition through the leaves with the water. But whilst

<sup>1</sup> Die Chemie in ihrer Anwendung auf Agricultur u. Physiologie, 6 Aufl. 1846, S. 3-253 [or English translation, London, 1840, pp. 1-215]; Chemische Briefe, 1851, S. 240 ff. u. 629 ff. [or Letters on Chemistry, 3d edition, 1851, pp. 176 and 506].



Liebig regards the development of carbonic acid as purely mechanical, he considers the nocturnal absorption of oxygen to be a purely chemical process, and shows that the variations in the quantity of the oxygen that is absorbed are entirely dependent on the chemical constituents of the leaves. Thus, for instance, leaves which are proportionally rich in substances poor in oxygen, as for example, resinous ethereal oils, which even in their isolated state readily become more highly oxidized when exposed to the action of the air, are also found to absorb a relatively larger quantity of oxygen in the dark.

A complete process of acidification during the night, as the effect of oxidation, is occasionally met with in the leaves of certain plants, as, for instance, the *Cacalia ficoïdes*, *Cotyledon calycina*, and others, which, after being tasteless at noon, have a bitter taste in the evening, but are sharply acid in the morning.

Pelouze has shown that tannic acid is converted into gallic and carbonic acids by the absorption of 8 atoms of oxygen ( $C_{18}H_8O_{12} + 8O = 4CO_2 + 2C_7H_3O_5 \cdot HO$ ). We cannot wonder at the fact observed by Saussure, that the leaves of the oak, which are so rich in tannic acid, should absorb 14 times their volume of oxygen during 24 hours when in the dark, whilst the tasteless and scentless leaves of the *Agave americana* can scarcely absorb 3-10ths of their volume in the same time. The leaves of the white poplar, which contain a very resinous or oxidizable oil, absorb as much as 21 times their volume of oxygen in 24 hours.

Without entering more fully into the question of the respective results of these two reciprocally suspended processes of the vegetable kingdom, we would simply observe that, notwithstanding the grounds on which Liebig supports his view of the purely chemical nature of the absorption of oxygen, this process and the separation of carbonic acid, appear, from numerous phyto-physiological experiments, to stand in a more direct relation to the whole life of the plant; and that, in the vegetable kingdom, processes of oxidation also occur in addition to the preponderating processes of deoxidation in the same manner as we find that, in the animal organism, where life is so thoroughly characterized by continuous oxidation, processes of deoxidation may yet also occur, as, for instance, in the formation of fat from sugar and amylaceous substances. This is, however, so decidedly a purely phyto-physiological question, that it scarcely falls within the scope of our inquiries. According to our view, Liebig has given the most striking and ingenious proofs that the vegetable kingdom derives its large supply of carbon from the atmosphere alone, and that plants alone possess the faculty of generating organic matter from inorganic substances.

When we consider that the atmospheric air contains only 1-1000th of its volume of carbonic acid, it might at first sight appear as if the atmosphere could not supply plants with all their carbon—an opinion which was once generally entertained; but certain simple calculations made by Liebig show that, instead of believing the carbonic acid in the atmosphere to be insufficient for the growth of plants, we might rather wonder how it is that, notwithstanding the vegetable kingdom, the quantity of carbonic acid in the atmosphere has not been considerably augmented in the course of ages. The atmosphere exerts a pressure of



2216·16 lbs. on every square foot, and if it were as thick in all parts as it is at the surface of the sea, it would extend 24,555 Paris feet in height, or, after excluding the aqueous vapor, 22,843 feet, or 1 German geographical mile [about 8,100 yards]. If the radius of the earth be assumed at 860 such German miles, the volume of the atmosphere (at the pressure of an atmosphere of mean temperature) must be equal to 9,307,500 such cubic miles, in which, in addition to 1,954,578 cubic miles of oxygen, there would be about 3,862·7 cubic miles, or about 28 billions of cwts. of carbonic acid—a quantity which must be more than sufficient for the wants of all the vegetables occurring on the land or in the water of our planet.

If, on the other hand, we consider that enormous masses of carbonic acid are continually being conveyed to the atmosphere from the earth's surface, we cannot help wondering that it should have experienced no sensible increase in the amount of the carbonic acid which it contains; at all events, there has been no change in it during the period that has elapsed since the destruction of Pompeii, in the year 79, A.D. (as is proved by the analyses of air which had been contained in funeral urns which had been excavated from that city): whilst, on the other hand, geological investigations have rendered it almost certain that at some definite period, ages since, and long before the higher forms of animal life had appeared upon the earth, the atmosphere was far richer in carbonic acid than it is now. A rough estimate of these relations yields the same numbers which Liebig has deduced from a more complicated calculation. Thus, for instance, if a man daily consumes 45,000 cubic inches of oxygen, which would give 9505·2 cubic feet for the year, 9 billions and 505,200 cubic feet of oxygen will be abstracted from the atmosphere by a thousand millions of men; and if, further, it be assumed that about double this amount of oxygen is lost by the respiration of animals, and by the processes of decomposition and combustion, it follows that all the oxygen of the atmosphere would be exhausted in 800,000 years. This constancy in the quantities of oxygen and carbonic acid during 1800 years would therefore be wholly inexplicable, if we did not perceive that the growth of plants furnishes the means of abstracting from the atmosphere the carbonic acid which has been conveyed to it, whilst the discovery of inexhaustible deposits of carbonaceous vegetable *débris* furnishes one of the most striking explanations of the diminution of carbonic acid since the pre-adamite age.

When plants are introduced into an atmosphere containing no oxygen, and care is taken that the oxygen which they exhale by daylight is absorbed by iron filings or other means, they wither as rapidly as they would in an atmosphere devoid of carbonic acid, or in the dark, where they could not decompose the carbonic acid. These and similar experiments certainly indicate that the oxygen stands in a definite relation to the whole life of the plant; and on this account, many of the most distinguished physiological botanists have held the view that oxygen gas is a true vital air to plants as well as to animals, with this difference only, that plants possess at the same time the power of generating for themselves the oxygen they require (H. Mohl).<sup>1</sup>

<sup>1</sup> Handwörterb. d. Physiologie. Bd. 4, S. 235-250 [or Henfrey's Translation of Mohl, On the Vegetable Cell. London, 1852, pp. 77-93].



Liebig has shown that the humus of the fertile soil is not one of the humus acids of chemists, and that it cannot serve directly for the nourishment of plants, but that as it is formed by the decomposition of organic substances, it is only by means of the products of its decomposition, and by the carbonic acid which is formed from it, that it can supply plants with nourishment; while, on the other hand, the manure promotes the growth and thriving of plants less by the quantity of nitrogen and carbon which it contains, than by the large amount of mineral substances, which are equally important to the development of plants as water and carbonic acid.

We very rarely meet with fossil roots, and the plants belonging to an earlier world usually appertain to genera which are distinguished by the smallness of their roots; the first plants whose seeds were scattered over the surface of the earth found no humus from which they could extract nourishment, but shot luxuriantly forth beneath a dense atmosphere, abundantly charged with carbonic acid, which yielded them copious supplies of carbon, although the sun's light, which was variously refracted through the denser strata of air did not fall directly upon them. Thus we find even now that the luxuriant plants of tropical climates have very small roots; consequently such plants can scarcely receive the adequate amount of nourishment from this part of the vegetable organism.

Everywhere on the earth's surface we find that the increase of the humus depends upon vegetation. Plants spring forth on the naked rock, which must derive their nourishment solely from the atmosphere, and afterwards dying and mouldering away, they serve as a support for other plants; if, however, these plants absorbed for their nourishment the carbon contained in the mouldering vegetable *débris*, vegetation would soon cease, and the naked rock would be again exposed to view. In the virgin forest the remains of numerous generations of plants are accumulated upon one another; each layer of plants serving in its turn to increase these vast accumulated strata of humus. A large quantity of carbon is generally abstracted year by year from cultivated woods and fields, yet this does not prevent grasses and trees from springing up unchanged and attaining their full growth without manure or any adventitious supplies of humus. How small a quantity of carbon is added to a cultivated farm by the annual amount of manure used on the land, and yet what immense masses of this substance are extracted each year in the form of fruits and straw, which are only again returned to the earth in the form of carbonic acid by the respiration of animals, and by the processes of combustion and decomposition!

It cannot be denied that small quantities of humus-like substances may pass into plants, in as far as the roots indiscriminately absorb the substances presented to them; but even if the above remarks show that the quantity thus taken up must not be regarded as inappreciably small, the fact that the humus acids form with bases insoluble salts, which consequently can scarcely enter into vegetable bodies, proves further that very little importance can be attached to this circumstance. Moreover, humus which is exposed to the natural action of the weather gives off a very small quantity of matter soluble either in water or lime-water.

The composition of most vegetable substances shows that *water* must



undergo decomposition in plants during the production of organic matter ; for, although we meet with certain substances in the vegetable kingdom in which oxygen and hydrogen occur under the same relations as they occur in water, we find many others in which the amount of oxygen falls far below that of hydrogen, as, for instance, the resins and fatty oils ; and there occur some combinations of carburetted hydrogen ; which are entirely free from oxygen, as, for instance, the ethereal oils and caoutchouc. A decomposition of water may also be more readily explained from a chemical point of view, than a reduction of the carbonic acid ; Alexander v. Humboldt has even observed a development of hydrogen during the vegetation of several fungi.

We possess very few reliable experiments from which we can ascertain the relations under which plants generate organic matter from water and carbonic acid during their exposure to the action of the sun's light. According to certain observations of Saussure, a plant of *Vinca minor* generated, under definite conditions, a quantity of organic matter, in which there were contained 40·87% of carbon. In two plants of *Mentha aquatica* there was organic matter produced which contained 50% of carbon.

The *origin of the nitrogen* in plants is a subject of far more difficulty ; for whilst carbonic acid and water are conveyed to plants from almost every direction and under all conditions, we are unable to detect the source from whence plants derive their nitrogen. Both Saussure and Boussingault<sup>1</sup> have shown by the most exact and ingenious experiments, that plants are unable to condense free nitrogen from the atmosphere, and to elaborate it into organic matter ; and they regard it as probable that nitrogen passes into plants only in the form of soluble nitrogenous products of decomposition of organic matter, and more especially in the form of ammonia. Here again it is to Liebig that we are indebted for the discovery of the hidden sources of this important element of vegetable nutrition. Liebig has shown that the origin of the nitrogen must be referred to the direct contact of ammoniacal salts with plants, seeing that he found considerable quantities of these salts in many vegetable juices. The juice of the maple, the red beet, the birch, fresh tobacco leaves, the tears of vines, and all blossoms and fruits, contained a certain amount of ammonia, without there being any indication that decomposition had set in. Exact calculations show that far more nitrogen is abstracted from well-cultivated fields than could have been conveyed to them by manure, or any other means. It has been seen from experiments on the solid excrements of animals, that ordinary solid animal dung, so far from containing much nitrogen, often contains mere traces of it, and that such manure is entirely inadequate to yield to plants the amount of nitrogen which is found in them. Whence, then, do forest trees derive their nitrogen, as they can never have been manured with animal dung ?

Until Liebig demonstrated the fact, it was not known that a constant quantity of ammonia was always present in the atmosphere, and that rain and snow contained determinable quantities of salts of ammonia. There can be no doubt, however, that nitrogen is supplied to plants as

<sup>1</sup> Ann. de Chim. et de Phys. T. 67, p. 5, et T. 69, p. 353.



food in the form of salts of ammonia; but, on the other hand, Liebig's view, that the atmosphere is the sole source from whence plants extract their salts of ammonia, has met with considerable opposition. Bous-singault and Liebig have endeavored to prove from a calculation of the quantities of ammonia present in rain-water, and of the annual amount of rain, that the ammonia extracted from the atmosphere by plants is quite sufficient to form those nitrogenous compounds which we discover in the products of our annual harvests; and they have also drawn attention to the fact, that there are at present in the humus, in dung—in short, in every fruitful soil—substances, which have the power, not only of fixing the ammonia of the water, but also of absorbing ammoniacal vapor directly from the atmosphere. Bouchardat's observation, that salts of ammonia exert a poisonous action upon plants, even when diluted 1000 or 1500 times, may perhaps depend upon their unsuitable form, and probably upon their insufficient degree of dilution; but it in no way refutes the general hypothesis that plants derive their nitrogen from ammonia; perhaps Mulder's<sup>1</sup> conjecture may also be correct, that the ammonia passes into plants in combination with organic acids, and that in this form it exerts no deleterious action on these organisms. It would appear from most of the experiments which have been made in reference to the absorption of ammonia by plants, that the roots are designed for the assimilation of salts of ammonia to the same extent at least as the green parts serve for the absorption of carbonic acid.

In the putrefaction of nitrogenous substances, there is a development of carbonate of ammonia from the beginning to the end of the process; its great volatility causes it speedily to be given off to the atmosphere, from whence it is again precipitated with the water in the form of rain and snow, and is thus returned to the vegetable kingdom. If we assume that every pound of rain-water contains only half a grain of ammonia, there must be a sufficient quantity of this substance in the atmosphere to supply all the plants existing on the earth's surface with the nitrogen requisite for their growth and perfect development. Ammonia has also been found in every kind of water occurring on the surface of the soil, in sea-water as well as in running springs, and has been extracted from the greatest depths of the earth; as, for instance, with boracic acid from Castel Nuovo, Cherchiago, and other volcanic districts.

Animals, when they have ceased growing, restore to the outer world nearly all the nitrogen which they take up with nitrogenous substances, and the very exact determinations of Boussingault and several other inquirers show that the quantity of nitrogen given off from the animal organism after the termination of growth equals that which is introduced, and that the amount of nitrogen present in full-grown animals varies only very slightly. Ammoniacal gas is given off directly during respiration; nitrogenous matters are also far more abundant in the fluid than the solid excrements, and they very readily become decomposed into ammoniacal combinations.

The reason of the beneficial effects of gypsum and of burnt clay as a manure has not hitherto been very clearly explained; but Liebig is certainly quite correct in referring it to the property possessed by these

<sup>1</sup> Versuch einer physiol. Chem. S. 715-752 [or English translation, pp. 651-691].



substances of fixing ammonia. The gypsum undergoes decomposition with the carbonate of ammonia in the atmosphere, forming sulphate of ammonia, which does not evaporate with the same rapidity as the carbonate. It has been long known that alumina and oxide of iron possess the property of absorbing ammonia. This same property of absorbing ammonia is observed in the case of powdered charcoal and decaying wood, the former of which condenses 98 volumes, and the latter 72 volumes of this substance. Mulder includes amongst the substances which fix the ammonia in a rich soil, the five acids which he discovered in the humus, namely, ulmic, humic, geic, crenic, and apocrenic acids. These acids, which are formed during the decay of animal as well as vegetable substances, decompose, according to Mulder's view, the carbonate of ammonia which is conveyed to the soil by rain, and having thus become soluble, are transferred, in the form of ammoniacal salts, to the roots of plants, where they are very rapidly decomposed (even in the extreme ends of the root-fibrils), and are converted into other bodies.

Fresenius<sup>1</sup> found on an average, 0.133 parts of ammonia in a million parts (by weight) of air. Now, if we adopt Marchand's estimate of 5,263,623,000,000,000 kilogrammes as the weight of the atmosphere, and if it contained in all regions equal quantities of ammonia, the amount of the latter would be 2,646,404 kilogrammes. Horsford<sup>2</sup> found a much larger amount of ammonia than this in the atmospheric air; the greatest quantity was observed in July, when there were 47.63 parts in one million parts (by weight) of air; the smallest quantity noted was in December, when there were only 1.2171 parts. It would appear from the observations of Horsford, that the quantity of ammonia in the atmosphere is at its maximum in the summer months, when the sources of ammonia are most abundant, and when it is not so frequently carried off by rain and snow as in winter, and it would seem to diminish in an almost constant ratio towards the winter.

Liebig calculates that if 1 lb. of rain-water contains only half a grain of ammonia, an area of 2,500 square metres will receive in the course of the year with the rain (which amounts to 2,500,000 lbs.) nearly 80 lbs. of ammonia, or 65 lbs. of pure nitrogen. This would be far more than is contained in the form of gluten and albumen in 2,650 lbs. of wood, or 2,800 lbs. of hay, or 200 cwt. of beet-root (this being the respective produce of an acre of wood, of meadow, and cultivated land).

Several nitrogenous substances which we constantly meet with in almost all plants, and more especially in their seeds, contain a certain amount of *sulphur*, and in addition to these there are the highly sulphurous ethereal oils, which may be extracted by distillation with water from several species of the Crucifers. As the air, rain, and ordinary spring-water, contain nothing beyond the merest traces of sulphuretted hydrogen, plants must obtain the necessary amount of sulphur from contact with alkaline sulphates, and especially the sulphate of ammonia. The sulphuric acid is then probably reduced by the same processes by which the deoxidation of the carbonic acid is effected. It is therefore obvious that the roots of plants are the organs through which sulphur is absorbed.

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 64, S. 101-106.

<sup>2</sup> Ibid. Bd. 74, p. 243.



Having briefly considered the nature of vegetable nutrient matters, and traced their various sources in inorganic nature, we have next to direct our attention to the mode in which this inorganic material is elaborated into organic matter in plants. We should, however, most assuredly arrive at very incorrect conclusions, were we to attempt to explain the formation of organic matter in plants without at the same time taking into consideration their mineral constituents. When we reflect that no plant can exist independently of certain *mineral constituents*, and that these occur only in certain definite quantities, and that some bases only, such as soda or potash, lime or magnesia, occur in plants,—and when, finally, we observe that these mineral substances are accumulated in very different proportions in the various organs of plants, and in accordance with the different periods of their development, although they present tolerably uniform relations under similar conditions and in identical organs,—we are necessarily led to the idea that these substances exert a definite influence upon the life of the whole plant, and upon the origin of its organic constituents from carbonic acid, water, and ammonia.

The bases we have enumerated are generally found in the ash combined with carbonic acid, although in the living plant they more commonly occur in combination with organic acids, as neutral or acid salts. Liebig, in his notice of these substances, has drawn attention to two much-disputed points of discussion: whether one base may be replaced by another in a plant, and whether the sum of the oxygen contained in the base is always one and the same for each species of plants. Although we must for the present regard these propositions as questions which still require a more special solution, it must be admitted that within certain limits they would appear to derive confirmation from several established facts; for although we find in the older experiments of Saussure, as well as in the more recent numerous analyses of vegetable ashes instituted by Emil Wolff,<sup>1</sup> by Wiegmann and Polstorff,<sup>2</sup> and by Staffel,<sup>3</sup> many facts which seem to be opposed to these general propositions, it must be remembered that even in vegetative life a number of relations present themselves to our notice, whose actions on these more general laws cannot be wholly overlooked. It may perhaps be maintained that these hypotheses of Liebig's have not been proved with sufficient precision; but, on the other hand, the few points in which they admit of dispute are not of sufficient importance to warrant us in regarding them as wholly controverted. We have still so imperfect a knowledge of the relations existing in the nutritive process of vegetable organisms, that it is much less easy to establish a convincing refutation than to adduce a strict proof.

In addition to alkaline carbonates, we likewise find alkaline sulphates, and especially alkaline phosphates, in the ashes of plants. These are not uniformly distributed throughout the entire plant, but are chiefly accumulated, as E. Wolff's experiments have shown, in the leaves, and still more abundantly in the seeds. As the careful observations made

<sup>1</sup> Journ. f. pr. Ch. Bd. 44, S. 385-488, u. Bd. 52, S. 37-122.

<sup>2</sup> Ueber die anorg. Bestandtheile d. Pflanzen. Braunschweig, 1842.

<sup>3</sup> Archiv. d. Pharm. 2 R. Bd. 64, S. 26-47.



in relation to their occurrence appear to prove that a plant can scarcely thrive without these salts,—for although it may bear scanty blossoms, it never arrives at fructification,—it can scarcely be doubted that they constitute an essential requirement of vegetable life and are true elements of nutrition.

We will here briefly notice some few facts which may serve as illustrations of the above remarks. Liebig was principally led to the establishment of these hypotheses by the following analyses of the ash of fir and pine wood, taken from trees which grew in various localities. Sausure found 1.187% of ash in the wood of pine trees growing on Mont Breve, and 1.128% in the same kind of wood from Mont La Salle. The following is the analysis of 100 parts of the ash of the pine wood of Mont Breve:

Carbonate of potash, . . .	3.60;	in the potash there were	0.415	of oxygen
“ lime, . . .	46.34;	“ lime, “	7.327	“
“ magnesia, . . .	6.77;	“ magnesia, “	1.264	“

Sum of the carbonates, . . . 56.71; Sum of the oxygen, . . . 9.007

A hundred parts of the ash of the pine wood from Mont La Salle yielded no magnesia, but gave the following result:

Carbonate of potash, . . .	7.36;	in the potash there were	0.85	of oxygen.
“ lime, . . .	51.19;	“ lime “	8.10	“

Sum of the carbonates, . . . 56.55; Sum of the oxygen, . . . 8.93

This relation is still more strongly manifested in two analyses of pine-ash made on French (Allevard) and Norway pine by Berthier, for here the difference between the soluble and insoluble salts in the two ashes is much more considerable than commonly occurs. In the ash of the French wood, Berthier found:

Potash and soda, . . .	16.8;	in which there were	3.57	parts of oxygen.
“ lime, . . .	29.6;	“	8.36	“
“ magnesia, . . .	3.3;	“	1.26	“

Sum of the bases, . . . 49.7; Sum of the oxygen, 13.19

The same observer found the following results in his examination of Norwegian pine:

Potash, . . .	14.1;	in which there were	2.4	parts oxygen.
Soda, . . .	20.7;	“	5.3	“
Lime, . . .	13.6;	“	3.82	“
Magnesia, . . .	43.5;	“	1.69	“

Sum of the bases, 52.75; Sum of the oxygen, 13.21

We must abstract from the oxygen of the bases in the first analysis 0.53 parts, and from that of the second analysis 0.79 parts, which belong to the bases which are combined with sulphuric and phosphoric acids; so that there would be 12.66 parts of oxygen for the first, and 12.42 for the second determination of oxygen.

The idea that these equal quantities of oxygen indicate that there are



equal quantities of acid to be saturated in the fresh plant, seems so obvious that its correctness might have been *à priori* suspected. At the same time, it was to be expected that this proposition would, under varying circumstances, be open to numerous exceptions, and that the direct results of the ash-analyses would rarely so accurately coincide as in the instances we have recorded. It is not, however, solely on account of their basic character that these alkalies and earths are necessary for certain plants; for we know, for instance, that in very many plants the potash at all events cannot be thoroughly replaced by soda; thus, for example, scarcely a trace of soda can be found in the ash of the horse-chestnut, even when a tree has grown in a soil in which this alkali abounds (E. Wolff, Staffel). The salts of soda are indeed absorbed in such cases, like other substances which are unsuited to the nutriment of the plant, but they are then speedily excreted, and principally by the roots.

We find in the ash of many plants, amongst others in that of the Cacti, that there is a much larger amount of carbonate of lime, and therefore a higher number for the oxygen of the bases, than corresponds to the true nutrient process of the plants. The carbonate of lime is here in part produced from the oxalate of lime, which is frequently deposited in the cells in a crystalline form, either as dead matter or as an excretion. Carbonate of lime is also deposited in a similar manner in many plants.

An exception to this rule, which may, however, be regarded as a proof of the correctness of the main proposition, is furnished by Liebig's discovery of the frequent occurrence of vegetable bases under relations in which the plant could not be supplied with any abundant amount of mineral constituents. Liebig draws attention to the fact that the quantities of the alkaloids found in cinchona bark, opium, and the potato plant, are always large in an inverse ratio to the small amount of mineral bases which they contain.

However restricted may be the sense in which we interpret many of Liebig's propositions, it is most clearly apparent, from all exact examinations of vegetable ashes, as well as from the careful observations of the influence of individual salts as manures, that the alkaline carbonates and their phosphates are of the highest importance in the different processes in the life of plants. It would carry us too far from the scope of our inquiries, were we to enumerate all the facts relating to this subject, with which we have been long acquainted; and we will therefore content ourselves with referring to some few of the results which have been obtained from E. Wolff's admirable investigation of the mineral constituents of the horse-chestnut. The carbonate of lime predominates in the bark and in the wood, whilst the fruit and leaves contain far more carbonate of potash than the bark and wood. Phosphoric acid is most abundant in the flower-stalks and kernels, whilst sulphuric acid and silica predominate in the leaves. In the horse-chestnut, very simple ratios exist between the quantities of oxygen in the bases combined with carbonic acid in the different parts of the plant (the carbonates being calculated for 100). The quantity of oxygen in 100 parts of the alkaline carbonate from the ash of the bark amounted to 27, that from the wood and leaves to 24, that from the leaf-stalks and brown husks of the ripe fruits to 21, and



that from all the other parts of the plant which were examined to 18, which corresponds with the simple arithmetical progression of 9 : 8 : 7 : 6. Wolff found that the ratio between the soluble and the insoluble constituents was very simple in all parts; thus, for instance, it was as 4 : 6 in the fluid circulating between the wood and the bark, and the same in the leaves, while on the other hand it was as 3 : 7 in the newly-formed wood, and as 6 : 4 in the leaf-stalks, while in the flower-stalks it was as 2 : 9, and in the interior of the kernels of the ripe fruit 2 : 7. Of all the mineral substances, sulphate of potash predominated in the leaves, and this was more especially the case in the spring, at the season of blossoming, whilst at the same period the juice of the bark and wood contained no trace of sulphuric acid. The ash of the leaves was very rich in insoluble phosphates, whilst that of the blossoms and fruit contained a larger amount of the soluble phosphates.

It is quite unnecessary to enter more fully into the question of the influence exerted by the alkaline and earthy carbonates, sulphates, and phosphates, upon the growth of plants as manure, for this is a point which has been sufficiently proved by innumerable experiments, conducted both on a large and a small scale.

Now that we have acquainted ourselves with the different substances which contribute toward the nutrition of plants, and have discovered that they consist of a few very simple combinations, derived from inorganic nature, the question almost irresistibly forces itself upon our notice, *how the vegetable organism is able*, from these few substances, to generate such an *endless diversity of organic bodies*? But this, unfortunately, is a subject which admits of little more than mere conjecture. In conformity with the principles which we have adopted in this work of avoiding all diffuse discussion of subjective views, and carefully abstaining from useless hypotheses, we can only permit ourselves to examine some few of those conjectures, regarding the formation of organic matter in the vegetable kingdom, which admit of being referred to definite experimental facts. The number of such facts, however, is very small, notwithstanding the many laborious researches which have been made in relation to this subject by some of our most distinguished inquirers. Our general remarks on the study of the vital processes hold good in a higher degree for the processes connected with the formation of matter in the vegetable kingdom; for although we possess some few good isolated observations, we are entirely deficient in quantitative determinations, without which we can make no certain progress in knowledge of the organic world. We are even ignorant of the relation existing between the carbonic acid which enters into the green parts of plants in solar light and the oxygen which is simultaneously given off. Yet how can we attempt to establish an hypothesis in reference to this process, before we have in some measure determined the numerical relations of the concurring substances? Very few numerical results have been obtained in phyto-chemistry, excepting some scanty determination of Saussure, from which it would seem probable that about 2 parts of organic matter are formed in sunlight for every 1 part of absorbed carbon. Were we even able, chemically, to trace the qualitative and quantitative relations of the different substances in the order in which they originate in the plant, we should find that our very imperfect knowledge



of the molecular forces, which play so important a part in organic processes, would prove very unfavorable to the comprehension of the chemical history of the gradual development of organic matter from such simple substances as carbonic acid, water, and ammonia. Whilst, on the one hand, the great simplicity observable in the more delicate structure of plants, and the constant occurrences of certain substances such as organic acids, the so-called carbo-hydrates, and albuminous matters in all plants, without exception, seem to afford an explanation of certain phenomena; the endless variety of those secondary products, which are peculiar to almost every plant, throws such obstacles in the way of our inquiries that we can scarcely hope to give even a hypothetical representation of the formation of organic matter within the plant.

The entire vegetable organism is scarcely anything more than a system of cells, within which various substances are undergoing metamorphoses, and organic matter is passing through the earliest stages of its formation. The ammonia which penetrates into the roots, combined with sulphuric or carbonic acid, according to Liebig, or with humic acid, according to Mulder, must have passed through the cells of the fibrils of the roots. The decomposition of carbonic acid can only take place within the green cells of the plant, for the most torn leaf may continue to exercise the function of absorbing carbonic acid and giving off oxygen; but when once its cells are crushed or otherwise destroyed, this vital process ceases. Hence we are led to conclude, that in the cell-membrane, or, in other words, in the morphological relations of the cell, there is as important an agent for this process of metamorphosis as in the chemical character of the cell-contents. We have already frequently remarked that our present knowledge of endosmosis and diffusion is not sufficient to lead us to the correct interpretation of vital processes. Discoveries such as Graham's, that the chemical union of certain substances may be broken by simple diffusion, lead us to anticipate that many obscure points connected with these vital processes may be elucidated, and that we may at length be enabled to determine with some degree of accuracy, the results which would be produced by bringing heterogeneous matters in contact with a cell of certain dimensions, definite thickness of the cell-membrane, known contents, &c. At present we are only able to conjecture in the most general manner the mode in which certain physical and chemical processes are effected by the agency of cells. We are especially indebted to Mulder<sup>1</sup> for pointing out the various modes in which cell-formations may possibly contribute towards the vital economy of the plant.

We next pass to the consideration of the *formation of those non-nitrogenous substances*, which are common to all plants, and are especially characterized by containing, in addition to carbon, hydrogen and oxygen in the same proportion as they exist in water, and which have, therefore, received the irrational designation of *carbo-hydrates*. The first origin of these substances, which we meet with in their more advanced stages of development as dextrin, sugar, starch, and cellulose, has, with apparent correctness, been referred to the decomposition of carbonic acid under the influence of light. The opinion can scarcely be maintained in

<sup>1</sup> Vers. einer physiol. Chem. S. 781-791 [or English translation, pp. 716-725].



these days that the carbonic acid in the green cells of the plant is instantaneously decomposed, and that the separated carbon combines with undecomposed water to form dextrin, or sugar. Unless we have recourse to the direct intervention of a vital principle, or to some metabolic force of the cell, we must admit it to be highly improbable that the bonds which hold the oxygen and carbon in close combination should be suddenly rent asunder. As we are still very ignorant of the proportion existing between the absorbed carbonic acid and the exhaled oxygen, we can only regard the view as tenable in very general terms, that a decomposition of water is associated with a partial deoxidation of the carbonic acid. Liebig has indicated the special grounds which support the view, that the decomposition of water exerts an influence on the separation of oxygen during the action of solar light upon the leaves. Liebig's opinion that these organic acids which we meet with in various quantities in all plants, as oxalic, tartaric, citric, and malic acids, may be originally formed by the simultaneous decomposition of water and carbonic acid, gains a certain amount of probability from the confirmation or explanation which it furnishes in relation to several other facts. This hypothesis derives special support from the fact, that the alkalies occur in accurately limited quantities in plants, and especially in their green parts; for if only a definite quantity of certain bases is necessary to the life of the plant, we may readily understand that they will in the first place be employed for the saturation of the acids, and that when the acid by subsequent forces has been converted into dextrin, sugar, or other indifferent matters, the same amount of bases may again serve for the saturation of newly-formed acid; and it may even be assumed that the alkali itself contributes towards the metamorphosis of the acid into these indifferent substances. We should find no lack of attempted explanations drawn from analogies of better known chemical processes, were we to advance further into the domain of pure hypothesis; but it must be borne in mind, in endeavoring to support such conjectures, that this process of deoxidation extends its activity beyond the final generation of dextrin and similar neutral carbo-hydrates.

In addition to these substances, we find many which are widely distributed in the vegetable kingdom, and contain far less oxygen than the carbo-hydrates; as, for instance, the oleaginous fats, wax, and resins, and several which are entirely without oxygen, that is to say, a large number of ethereal oils, caoutchouc, &c. When, moreover, we perceive that oxygen is given off, whilst carbonic acid is taken up, it would seem as if the developed oxygen were the combined result of the quantities of the gas yielded by several very different substances. Several phyto-physiological facts seem to indicate that the vegetable fats and wax are especially generated from the carbo-hydrate known as starch, whilst daily experience proves that those ethereal oils, which are either deficient in oxygen or entirely without that substance, can only be produced under the prolonged action of solar light. It is, therefore, not only not impossible, but even in some degree probable, that a number of different processes of deoxidation which extend to substances which have previously been more or less freed from oxygen, are simultaneously called into activity under the influence of solar light. Do differently consti-



tuted cells co-operate in these various reductions? Is it only one, or are there several matters which, under the influence of light, effect the elimination of oxygen from highly oxygenous substances? These, and numerous other questions of a similar nature, force themselves upon our notice, but, unfortunately, in the present state of our knowledge, they do not admit of satisfactory replies.

In considering the processes of deoxidation, which are connected with the life and growth of plants, we should bear in mind that some instances may occur in which the deoxidation is accompanied by a development of carbonic acid instead of a separation of oxygen. Liebig long since noticed during the prosecution of his experiments on fermentation, putrefaction, and decomposition, that oxygen was taken up by the organic substances during some of these processes of decomposition, and that then several atomic groups of carbonic acid were liberated from this combination. It depends entirely upon the relations existing between the oxygen that is absorbed and the carbonic acid which is developed, whether the remaining substance is richer or poorer in oxygen than the original body. If the volume of oxygen which is added be less than that of the carbonic acid which is evolved, the remaining organic body will be less oxidized, and will therefore appear as if it were deoxidized, exhibiting a decided process of reduction, notwithstanding the absorption of oxygen. Liebig made observations of this nature on the formation of carbo-hydrates from organic acids; if, for instance, 6 equivalents of oxygen be added to 6 equivalents of tartaric acid, and if 12 equivalents of carbonic acid are developed therefrom, we obtain grape sugar, which is relatively much poorer in oxygen ( $6 \text{ C}_4\text{H}_2\text{O}_5 + 6 \text{ O} = 12 \text{ CO}_2 = \text{C}_{12}\text{H}_{12}\text{O}_{12}$ ). Starch might be similarly formed from tannic acid ( $\text{C}_{18}\text{H}_6\text{O}_{10} + 8 \text{ O} + 4 \text{ HO} = 6 \text{ CO}_2 = \text{C}_{12}\text{H}_{10}\text{O}_{10}$ ). If more complete observations and experiments should enable us to prove that this kind of deoxidizing process has a more general application in the vital economy of plants, many points might be explained which still present considerable obscurity; we might thus comprehend why, notwithstanding the reversed interchange of gases which takes place during the night, organic motion pursues its undisturbed course after the restoration of the less oxidized matters; that is to say, why the evolution of oxygen during the day is not exactly balanced by the nocturnal absorption of that gas. We need then no longer wonder that a plant may drag on a miserable existence in an inclosed space, since it generates for itself through the day the oxygen necessary for it during the night, and, conversely, exhales the carbonic acid during the night, which is again to serve for its nutrition through the day. This circulation of the oxygen is only apparent, for the oxygen which has been separated from its combination with carbon during the day, serves in the night to extract a larger amount of oxygen, together with some of the carbon of the organized matter. Thus we see by Erdmann's admirable experiments on *Tradescantia discolor*, that a plant may continue for years to vegetate in an unhealthy condition, although without entirely dying, when placed in a hermetically closed vessel. The death of some few leaves or stalks serves in these cases merely to prolong the life of the plant, and to promote the formation of new buds. The air within the inclosed space where such plants had for a long time vegetated, would at length



become very rich in oxygen, if the above-mentioned parts, which die off, did not contribute by their decomposition to supply the new buds with carbon in the form of carbonic acid. If the nocturnal interchange of gases in plants depends upon the process to which we have here referred, the necessity of oxygen for the life of the plant would be obvious, and we should have a simple explanation of those experiments in which plants are found to vegetate in a non-oxygenous air only so long as the oxygen which is exhaled by day is suffered to remain in the atmosphere surrounding the plant, and is not removed by the agency of chemical means.

It still remains for us to notice an hypothesis advanced by Mulder in explanation of the process of deoxidation in plants, as it leads us to the consideration of a point to which we have scarcely made a distant allusion in the above-mentioned hypotheses. As the property of absorbing carbonic acid and of exhaling oxygen is limited to the green parts of a plant, the idea naturally presents itself that the chlorophyll on which this color depends plays a very important part in this process of reduction; although we are unable to decide, from the facts before us, whether the chlorophyll acts in the manner of a ferment or whether this interchange of gases is dependent upon the formation of the chlorophyll from bodies richer in oxygen. Mulder has advanced the following hypothesis, which presents considerable plausibility. According to his view, new chlorophyll is always being formed under the influence of light, whilst the more richly oxygenous starch is simultaneously converted into wax, which is poorer in oxygen, wax being, as is well known, constantly present, together with the chlorophyll. On the other hand, microscopical observations of the development of cells and their contents render it very probable that granules of starch are gradually converted into globules of chlorophyll, which are rich in wax. Mulder supposes that the oxygen which is developed during the formation of wax from starch goes partly to the colorless chlorophyll, to convert it into the green variety, and that is partly given off, in a free state, to the surrounding atmosphere. Draper is more disposed to regard chlorophyll as a ferment, and he urges, as a proof of the decomposition of the (nitrogenous) chlorophyll, the above-mentioned fact that plants always develop some nitrogen in addition to the oxygen which they give off in solar light.

The *nitrogenous compounds* generally, and more especially those which are included under the term protein-bodies, play no less important a part in the life of plants than in that of animals; and there is no living cell in the plant which does not contain albuminous substances, either in the primordial utricle, or in some other form. Wherever the vital activity of the plant is most powerfully developed, the cells are found to be most richly endowed with these substances; as, for instance, in the fibrils of the roots, as well as in the flower and leaf-buds, in the pollen granules, in the embryonic sac, and more especially in the seeds. Although these local relations sufficiently indicate the importance of these substances, they do not afford the slightest explanation of their mode of origin. Mulder does, indeed, conjecture, from the more abundant occurrence of these substances in the cells at the apices of the roots, that they are formed here from the ammoniacal compounds of the



humus acids (as they are conversely decomposed into these acids and ammonia by the action of concentrated hydrochloric acid); but even if it be granted that the ammoniacal salts reach the plant only or principally through the roots, and if, further, it be shown that many of these absorbed substances undergo chemical metamorphoses in the fibrils of the roots, the frequent occurrence of ammoniacal salts in the rising sap of the plant seems rather to prove that their metamorphosis must be effected at some other point. It is not improbable that the protein-bodies are principally formed wherever the process of reduction is most practicable, as, for instance, in the leaves. On the one hand, we know that all protein-bodies, and especially those obtained from the vegetable kingdom, contain a considerable quantity of sulphur; and, on the other hand, we learn from E. Wolff's<sup>1</sup> carefully conducted ash-analyses of the different component parts of plants, that the sulphates, as already observed, are accumulated in early spring in the buds and leaves, whilst they disappeared from all other parts of the plant; and that the quantity in which they occur in these parts is too large to admit of the supposition that they are derived from the protein-substances already present in the leaves; we are, therefore, naturally led to the idea that the sulphates must be already accumulated in the leaves at a very early period, and that they undergo only a gradual reduction in order to be applied to the formation of albuminous substances in proportion to the quantity of ammonia with which the plant is supplied. We can hardly refer the deoxidation of the sulphates to any part of the plant except the leaves, and, on this account, we may assume that these organs afford the final stimulus required for the complete development of these salts. If it would not be carrying us too far into the region of conjecture, we might hazard the remark that as the alkaline carbonates contribute to the formation of non-nitrogenous bodies, the sulphates and phosphates may also take an important share in the formation of protein-bodies, such a conjecture deriving plausibility from the simultaneous occurrence of phosphates in all those vegetable organs which are rich in protein-bodies, and from the generally recognized importance of the phosphates in reference to the life of the plant.

Although there may be innumerable possible modes by which ammonia may be converted by the co-operation of other organic matters into albumen and vegetable gluten, we have not even the faintest support to offer in favor of any one or other of these hypotheses. The disappearance of ammonia, as such, from a compound, and its complete resolution into a new non-saline body, are familiar to the chemist, who—besides the metamorphosis of formate of ammonia into prussic acid and of cyanate of ammonia into urea—besides the formation of pigments from ammonia and orcine, phlorrhizine, hæmatoxyline, or erythrine—and besides the formation of alkaloids, according to Wurtz or Hoffmann—would call to mind innumerable instances in which the ammonia more or less lost its original character and assisted in forming new and very complex bodies, water being at the same time produced. But notwithstanding this pliability of ammonia, which enables it to incorporate itself with all forms of organic groups, we are wholly deficient in the facts necessary to afford spe-

<sup>1</sup> Journ. f. pr. Chem. Bd. 51, S. 1-82.



cial proof of the formation of a nitrogenous substance in the living vegetable organism.

When we have seen Dumas's beautiful idea, that organic nature generates its own elements, confirmed by the most recent investigations in the domain of theoretical chemistry, and now that we may look forward to the attainment of a more profound knowledge of the arrangement of organic atoms and of the internal connection of the endless number of organic bodies, through the brilliant discoveries of Kolbe, Hoffmann, Wurtz, Laurent, and others, and when, finally, the ingenious experiments of Liebig on fermentation and decomposition, on putrefaction, dry distillation, and other processes of decomposition, have enabled us to gain a deeper insight into the forms of the gradual regression of organic matter,—we may fairly hope that the time is not far distant when we may be enabled to trace the order of arrangement in which organic matter becomes fully developed. Then, too, we might hope to acquire a more intimate acquaintance with the requirements and circumstances under which the simpler molecules are accumulated and arranged into more complex atoms, until we might perhaps be enabled to form to ourselves as correct an ideal representation of the mode of origin of organic matter as we possess in reference to geological processes. But although the chemist may with pride refer to the great conquests he has achieved in science during the last ten years, much yet remains to be done beyond what qualitative chemical experiments or even the most perfect theory of organic chemistry can supply; for notwithstanding the brilliant results attained in the science of phytotomy and phyto-physiology, we are still entirely deficient in exact experiments on the individual processes of vegetative life, we require a more perfect method of quantitative chemical analysis than we now possess, and we need scarcely make further allusion to our ignorance of the conditions and circumstances under which other molecular forces besides chemical affinity influence the metamorphosis and formation of matter in the vegetable kingdom. Yet notwithstanding the distance at which the aim of our inquiries presents itself to our notice, we are convinced that the time will soon arrive when that vital force, to which many have ascribed, together with chemical phenomena, an active participation in vegetable life, will be thoroughly eliminated, and when it will be finally laid aside, never again to become the subject of scientific consideration.

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#### GENERAL REVIEW OF THE MOLECULAR MOTIONS IN THE ANIMAL ORGANISM.

We have already (in the first volume) considered the material substrata of animal life, in as far as they can be separated by chemical means from the diversified group of substances which combine to form animal bodies, and can be tested and accurately determined by chemical reagents. We also endeavored in the same portion of our work to estimate the value of each separate substance for animal life generally, as well as



for the special purposes of life, after having considered its origin and ultimate disposition in the living organism, and indicated the position which it is entitled by its physiological importance to occupy amid this great number of chemical agents. It therefore only remains for us to notice in more general and more comprehensive terms the reciprocal actions of these individual parts during the vital activity of the organism, and their arrangement into a system of masses, constantly acting upon one another and inducing definite results.

In the first volume we turned our attention to the animal juices, which from their mobile and fluid nature have been regarded by many as the essence and seat of all vital activity. In endeavoring to trace the intimate relations existing between these mutually allied substances from a chemical as well as a physical point of view, we were necessarily led to the consideration of the continuous metamorphosis which they had undergone during life, and of the causal connection of those phenomena which seemed to correspond with definite purposes in the living organism. It only remains, therefore, for us to take a collective and general view of the mutual relations in which the different juices stand to one another, the interchange of their constituents, and the dependence of the changes of any one upon another, or upon all the others, and thus to arrive at a general conclusion regarding those processes known as the metamorphosis of animal matter.

Finally, in this, the second volume, we have treated of the mechanical and chemical relations of the masses, which are consolidated into cells, fibres, and membranes, as far as this is possible in the present very imperfect state of our knowledge; and in these structures we have recognized not merely the hollow skeleton or framework between the parts of which the separate currents of these fluid masses move and circulate in uninterrupted motion in order to satisfy the different requirements of life, but we have also discovered in them the apparatus by which the most intense and peculiar actions of the animal organism are manifested.

Many might be led at first sight to suppose that we had accumulated a sufficient mass of materials from all directions to enable us to gain a deeper insight into the vital phenomena of animal life, or at all events to delineate in few but characteristic outlines the chemistry of the animal organism; but the more deeply we penetrate into the obscurity of the metamorphosis of animal matter, and the more carefully we investigate the materials in our hands, the more plainly do we perceive the deficiencies with which we have to contend. We have already frequently taken occasion to notice how little aid we had derived from previous scientific investigations in establishing general conclusions regarding any special group of animal molecular motions. It is therefore wholly unnecessary to enlarge upon these deficiencies, which we have already noticed in detail in the methodological introduction to the first volume (see vol. i. p. 22). We shall certainly not exceed the bounds of truth, if we maintain that we are still entirely deficient in the very first principles necessary for a scientific treatment of the theory of the metamorphosis of matter in the animal organism. It is merely to clear ourselves from the imputation of exaggeration or the love of paradox in establishing this proposition, that we again refer to those points



which we noticed under the head of Exudations (p. 273), and again in treating of the molecular forces which are active in the animal body (pp. 303-307), where the lamentable condition of our positive knowledge is too plainly showed. Qualitative analysis fails us when we attempt to investigate the different stages of transition and metamorphosis of the most essential substrata of the tissues in a state of change, whilst the extractive matters, in the absence of any rational explanation, have received the most various interpretations, in accordance with the imaginative ideas formed in reference to them by different observers. We have more than once admitted our fear that there is no speedy prospect of any great advance in qualitative chemical analysis, notwithstanding the light which various departments of this branch of science have derived from the genius of Liebig; and we have, on the contrary, expressed our conviction that it required numerous and more carefully conducted estimates of the quantitative relations of the constituents of the different animal juices, before the mechanical metamorphosis of matter could be placed on a sufficiently secure foundation to admit of our studying its chemical nature. We observed, in conclusion, that even the most exact measurements of the masses and velocities of the molecular movements of matter, in which vital activity is manifested, did not enable us to attain to a truly scientific theory of the metamorphosis of matter as long as we were constantly surprised by new and unexpected observations on the action of the molecular forces. Even if we had mastered all the elements of this inductive inquiry, and could trace the mechanical and chemical features of the metamorphosis of matter, we should still be unable to comprehend the internal connection of the individual links of this great chain of phenomena—we should be unable to master the causal dependence existing between the different factors of vital motions—in short, we should be unable to give a *scientific explanation* of the mechanico-chemical processes in the living organism, until we had acquainted ourselves with the yet unknown laws of molecular forces.

Before we attempt to take a general review of the molecular movements in the animal organism, we think it will be expedient to add to the above remarks upon the formation of organic matter in the vegetable kingdom, a *comparison between the action of these forces* in the two great divisions of living bodies—the *vegetable* and *animal kingdoms*. A comparison of this kind has frequently been attempted and carried out with more or less success, and pains have been taken to trace through their minutest modifications the differences presented by the specific methods of combination occurring in the two kingdoms, and the peculiar results of the individual forces manifested in these different spheres; but an exaggerated zeal for sharply-defined distinctions of objects has frequently led to assertions which have rather tended to retard than advance the course of investigation. It almost seems like a satire upon Liebig's thoughtful researches, when we find the distinctions between the two kingdoms of nature laid down in such a manner as the following:—"The plant *generates* neutral non-nitrogenous bodies, such as fats, sugar, starch, and gum; *decomposes* carbonic acid, water, and salts of ammonia; *developes* oxygen; *absorbs* heat and electricity; is an apparatus of *reduction*, and is immovable. The animal *consumes* neutral-nitrogenous



bodies, such as fats, starch, sugar, and gum; *generates* carbonic acid, water, and salts of ammonia; *absorbs* oxygen; *developes* heat and electricity; is an apparatus of *oxidation*, and is movable." But nature will not be restricted within such narrow bounds, and in the teeming richness of her forms and phenomena, she speedily burst the bonds with which the human intellect capriciously attempts to restrain her.

Many of these distinctions are applicable when considered only in their most general bearings. The idea of a perpetual circulation in nature is most forcibly expressed in these two series. It is undoubtedly true that the organic matter which is generated in the vegetable kingdom is for the most part again destroyed in animals, but the idea that animals consume only protein-bodies, fats, and carbo-hydrates, and cannot also in part generate them, is an assumption which partly is false, and partly does not admit of proof. No one can any longer doubt that the animal body possesses the power of forming fat from other matters, such as protein-bodies or carbo-hydrates (see vol. i. p. 229). It yet remains an open question whether protein-substances may not also be generated in the animal organism under certain conditions, although it is most probable that such substances cannot be generated in the animal body (vol. i. p. 309). If we except the lower animals, we certainly are compelled to deny that the animal organism possesses the property of forming starch and cellulose; but sugar and dextrin are constantly generated within the bodies of the herbivora during digestion by the action of the saliva and pancreatic juice on the other carbo-hydrates (see vol. i. pp. 430-505); and even in the bodies of the carnivora the liver has been recognized as a seat of the formation of sugar, which most probably is solely produced from the metamorphosis of nitrogenous substances (vol. i. p. 483), as I have recently proved by careful observations.<sup>1</sup> We must remember too what a number of substances are formed in the animal body which never occur in the vegetable kingdom. It has indeed been stated that these substances are only the products of a process of oxidation; but what an essential difference there is between xanthine or uric acid, and their homologues, theine and theobromine! and who could determine, on seeing taurine or cystine, whether it were derived from the vegetable or the animal kingdom, if he were ignorant of the origin of these substances? Those complex substances, the biliary acids, have no analogues in the vegetable kingdom, nor can we deny to the animal organism generally the property of generating new organic matters within itself; but in this respect the animal organism is very much in the same condition as the chemist in his laboratory; both require, for the most part at least, ready-formed organic matter, from which to generate new substances foreign to, but analogous with the products of the vegetable kingdom. As many of the excreted matters of the animal body contain somewhat complex atoms of organic matter, the proposition that animals give off to the external world carbonic acid, water, and ammonia, is only half true: for although we regard the urine collectively as an ammoniacal salt, and even take the same view regarding the taurine of the solid excrements—and although, further, we comprise under the same head, and as of equal value with the carbonic acid and water, the formic, butyric, acetic, and caproic acids of

<sup>1</sup> Ber. d. k. sächs. Ges. d. Wiss. zu Leipzig, 1851, S. 130-164.



the sweat—it yet cannot be denied that men and animals daily give off directly to the external world no inconsiderable amount of protein-bodies; since the solid excrements are never free from mucus, and since the desquamation of the epithelium and the abrasion of other horny tissues occasion a loss in these complex bodies, the amount of which may even be ascertained by moderately careful investigations.

It is also perfectly true that the vegetable cell, which is capable of overpowering the strongest chemical combinations, eliminates oxygen from the atmospheric ingredients, carbonic acid and water, and is able to fix the indifferent substance, nitrogen, whilst the animal germ can only be developed by the co-operation of atmospheric oxygen. It cannot be denied that the separation of oxygen in the vegetable organism constitutes one of the principal momenta of chemico-vital activity, and that a progressive motion is induced in the chemical molecules by the action of the vegetable cell, the object of which is to separate the oxygen as far as possible, and to restore the most complicated radicals (the most perfect organic matter), whilst the animal organism borrows this matter from the plant for the purpose of finding a main support for the most important animal functions in the regressive motion which the oxygen generates in the oxidizable matters. Hence it is true that oxygen is the excitor of animal life; through its agency the primary mucus of the plasma becomes converted into a cell, the cell is developed into fibre, and animal matter into the animal.

Yet however much truth may attach itself to such abstract assertions, we always find in association with the truth the germs of many errors. In treating of the formation of organic matter in the vegetable kingdom (p. 317), we noticed the concurrence of several processes of oxidation with the deoxidation going on in the plant; in like manner we also find in the animal organism, in addition to the oxidation in the blood of the capillaries, numerous processes of reduction, scarcely less intense than those which we meet with in plants; thus, for instance, in the *primæ viæ* we have seen that substances, such as sulphates, which require the most powerful agents for their reduction, were completely deprived of their oxygen (see vol. i. p. 399); that the oxides of iron and mercury, and similar substances, were deoxidized in the intestine; whilst we elsewhere drew attention to the fact that the fats and lipoids, which are first formed in the animal body, can only be produced by a process of deoxidation. Even if we assume that oleic and margaric acids are formed from starch or sugar by such a process of cleavage as that by which alcohol is generated from sugar (so that reduction is only an apparent one, since the body is simply decomposed into one richer in oxygen, namely, carbonic acid, and into one poorer in oxygen, as alcohol, fusel oil, margarin, or olein); yet stearic acid, which is very rarely taken up by animals in vegetable food (hitherto it has only been found in cacao-butter), must be formed by a direct process of deoxidation, as both its composition and its chemical qualities show that it can only be regarded as a lower stage of the oxidation of the radical or margaric acid. Nor can we assume that a substance so poor in oxygen as cholesterolin, which so readily accumulates in the stagnant fluids of the animal body, can be formed from the simple decomposition of some organic matter. The oxidizing force of the animal organism is bounded by tele-



rably narrow limits; sulphide of potassium, when present in sufficient quantities, passes, in part, in an unoxidized form into the urine through the blood which is so rich in oxygen; saligenin is not even converted into salicylic acid in its passage through the blood. We can scarcely refer cystine, which is so rich in sulphur, to any other source than a process of deoxidation; whilst the great amount of sulphur present in many horny tissues, which contain a perfectly identical group of atoms with albumen, can hardly be ascribed to any cause but a mere local deoxidation. If it be true that the iron contained in hæmatin may be extracted by sulphuric acid and water under the development of hydrogen, a reducing apparatus must be employed in some part of the animal body, by which the iron, which only reaches the body in an oxidized condition with the vegetable food, can be deprived of its oxygen. We shall meet with many other processes in the animal organism which, without intentionally setting aside the ordinary chemical terms, we can only designate as reduction-processes. Generally speaking, however, the restoration in the animal organism of bodies which are deficient in oxygen, is effected in a different manner from what is found to prevail in vegetable structures. Thus, for instance, in the formation of most of the fatty acids from sugar, a larger or smaller number of atoms of oxygen combine with the corresponding number of atoms of the hydrogen in the sugar, whilst a certain number of atoms of carbonic acid are simultaneously liberated, leaving a body which is always poorer in oxygen than the starch or sugar which was exposed to decomposition. We shall revert on a future occasion to this hypothesis, which was first advanced by Liebig, and which certainly appears to be confirmed by the most remarkable analogies with known processes of fermentation. In every case of the formation of a body poor in oxygen the animal organism presents greater similarity in its action to the chemical process of reduction than to the process going on in plants, by which oxygen is directly separated. As the chemist only calls into play other affinities of oxygen in order to remove it from certain combinations, so the animal body places the carbo-hydrates in a circle of circumstances, under which other affinities of oxygen come into action, and give rise, as products of the process, to one or more comparatively non-oxygenous substances, together with a body rich in oxygen.

We shall pass over the other distinctions which it has been attempted to establish between plants and animals, as they are alike unstable and indefinite.

We will now include in one general *resumé* the leading propositions presented to our consideration by the three main divisions of physiological zoo-chemistry. If we pause for a moment to contemplate the great series of the chemical substrata of the animal body, we at once perceive that there are four principal groups of substances in which the vital processes are manifested with the greatest intensity. Amongst these the *albuminous substances*, or the so-called protein-bodies, and their *derivatives* are the most conspicuous. A mere superficial glance at the occurrence of albumen is sufficient to show that this must be one of the most important substances in the whole animal body; we have met with it in the largest quantity in the blood, and in all those animal juices which



contribute directly towards the nutrition of the organs, and a more careful examination of many of the animal tissues shows that albumen requires only some very slight modifications to become consolidated under different forms; as, for instance, when it contributes towards the formation of the solid contractile parts, under the form of syntonin (muscle fibrin), by which alone both the voluntary and involuntary movements of the animal body are effected. We found it both in a dissolved and an undissolved form in the most delicate organic combinations, as, for instance, in the contents of the nerve-tubes—structures by which the animal essentially differs from the plant, and in which the highest force of all animal life may be said to be located. While we are compelled to admit that chemistry is still unable to furnish the long-looked-for explanation of the internal constitution of albumen and of the substances most nearly allied to it, as syntonin, fibrin, and casein, or to trace the numerous morphological metamorphoses to which they are subjected, we are still less able to answer the question, wherein lies the capacity of these substances to preside over the highest functions of life. As long as the chemical questions regarding the difference of albuminous substances of identical or similar composition remain undetermined, we have no immediate prospect of solving the physiological problem of what it is which capacitates these substances for different vital functions.

We find that the animal germ is surrounded by albumen and casein, containing salts, together with a little fat and traces of sugar; hence it is to the albuminous contents of the egg that we must refer the development of the organs of animals, including even those structures whose substances do not appear very similar to albumen. Animals obtain during the period of lactation, besides fat and sugar, a substance which, with the exception of a smaller amount of sulphur, contains the same elements, and in the same proportions, as albumen; at the period, therefore, when the growth of the gelatigenous, non-albuminous tissues requires the largest supplies from without, the body is supported by the same organic compounds which occur in such large quantities in its true nutrient fluid, the blood. Herbivorous animals do not find any substance analogous to gelatin in their vegetable food, and hence they must generate it from the albuminous substances of plants. All the solid bases of the animal organs consist of nitrogenous matters, which can only originate from the albumen, on which account we have named them derivatives of protein. Although we may entertain no doubt that the albuminous substances are gradually metamorphosed into the non-sulphurous constituents of the gelatigenous tissues through the agency of the oxygen which enters the blood, we are not able to advance anything beyond mere conjecture in reference to the mode in which these processes of metamorphosis are effected. We are still ignorant of the intermediate stages through which the albumen or the casein undoubtedly passes before it appears in the form of a chondrigenous substance, nor do we comprehend the internal connection, although the metamorphosis of chondrigenous into the glutigenous tissue takes place almost directly under our eyes. Although we may succeed in exhibiting the result of these metamorphoses by very simple formulæ, we do not by that means the more clearly determine the actual nature of the process.



The question whether the blood-fibrin constitutes the necessary transition-stage from albumen to chondrin and gelatigenous tissue, has been more than once propounded in the preceding pages (see vol. i. p. 360, and vol. ii. p. 284), and we might with equal justice inquire, whether the chondrin must everywhere precede the glutin in the formation of connective tissue, the tendons, the skin, &c.? A very simple scheme of these forms of metamorphosis might readily be deduced from a theoretical combination of the formulæ representing the composition of these substances; but even if we were accurately acquainted with the rational composition of all these complex substances from a chemical point of view, our ignorance of the individual conditions of the process would prevent our being able to decide with certainty which of the many possible combinations and modes of representation expressible in formulæ should receive the preference. We have here to inquire if *that* formula is the correct one, which imitates a process of decomposition (or indicates the metamorphosis) in which atoms of oxygen are added, and water and atoms of carbonic acid are abstracted; or whether the preference is due to that formula by which the substance undergoing metamorphosis yields known excretory substances in addition to the main product; or whether that is the correct one which derives a new substance from the original one by the mere substitution of individual elements. There is one circumstance, however, which appears, at all events, to prove that the simplest chemical equation is not always the most correct in these processes, which seem to depend upon such highly complicated conditions. For, when we find that a concurrence of many different substances is necessary to the accomplishment of many processes, as, for instance, that nutrient matters are only imperfectly, if at all, digested without the presence of fat,—that no cell, fibre, or membrane can be formed without the presence of fat, phosphates, &c.,—we can scarcely suppose that a simple formula, based upon an unestablished atomic composition, can express the true process of the metamorphosis. There are certain substances which never occur isolated in the animal organism during chemical metamorphoses; thus, for instance, wherever albuminous matters occur, non-nitrogenous carbo-hydrates are always present, however small may be their amount; wherever fats are formed or decomposed we always meet with albuminous matters; whilst free acids and alkalies occur in almost every part of the animal body. Although we may not admit the necessity of the concurrence of two or more entirely different substances in the case of individual processes, we rather conjecture that such a necessity obtains from the analogy of those processes which we are able to induce in organic substances that are not included in the sphere of vitality. We perceive very clearly from a study of the process of fermentation, that one organic substance cannot exist together with another undergoing the process of metamorphosis, without being implicated in an analogous molecular motion, corresponding to its constitution. May we not conjecture that the substances formed under these conditions possess the tendency to combine together in their nascent state, and thus give occasion to the formation of certain complex atoms, in which chemistry has recognized proximate constituents, conjugated compounds, haloid salts, &c.? It is here that the recent chemical theory of the sub-



stitution of certain elements by other more simple or compound molecules will find the most extended application, and where we shall discover new proofs of the generally recognized proposition, that nature, under all circumstances, accomplishes the most varied ends by the simplest means. Hence it would be difficult to prove, and indeed it appears almost improbable, that those nitrogenous matters which have less affinity with albumen, as for instance, the animal pigments, the resinous acids of the bile, &c., are the simple remains of the decomposition of albumen or gluten; and, on several grounds, it might even be supposed that these matters have been formed from the products of the simultaneous decomposition of nitrogenous and non-nitrogenous bodies. The result of these considerations and of all the attempts made to explain the formation and decomposition of all these nitrogenous substances, keeps us within a circle of mere probabilities and possibilities, without affording any solid support for the maintenance of any one view in preference to another. The only fact which we deduce from a simple comparison of the empirical composition of these substances, and from corresponding statistical investigations regarding the metamorphosis of matter in the animal body, is, that the different phases under which nitrogenous molecules appear in the animal organism must be essentially dependent upon the inspired oxygen, and that the latter, under the most various circumstances, gives origin to the numerous metamorphoses which the molecules of albumen undergo before their final change into urea and similar substances.

In a second group of substances which we have learnt to recognize as important agents in the metamorphosis of animal matter, we must place the *fats*. We considered their physiological importance, origin, and final destruction so fully in the first part of this work, that very little remains to be said on this subject. We learnt (vol. i. pp. 232-242) that the fats, besides the manifold mechanical services which they render the animal organism, also take part, through their chemical metamorphoses, in the most varied animal processes, that they take an active share in the process of digestion in the *primæ viæ*, and that they preside generally over all the processes by which the fluid nutrient substances are converted into the solid substrata of the organs. The formation of the colorless blood-corpuscles seems also to owe its first impulse to the metamorphosis of fat, which thus serves as the most important auxiliary in the formation of blood. We also, in the same place, drew special attention to the fact, that no animal cell and no fibre was formed independently of the presence of fat. Indeed, the fat appears to possess the property of predisposing the animal organism to the formation of cells. Thus, for instance, whenever very large quantities of fat are introduced into the organism, as in the fattening of live stock, the connective and subcutaneous tissue of different parts exhibit an extraordinary number of cells, all of which contain fat. A cell-formation of this kind requires, however, the concurrence of albuminous substances, which are derived from the albuminates introduced into the organism with the food, as long as these are supplied in sufficient quantity. When the organism does not find in the food sufficient materials to form the investing membranes of the fat-cells, it borrows from the muscular fibre the substance with which it surrounds the fat in these protein-capsules. When this source of ma-



terials for cell-formation is no longer sufficient, the fat begins to accumulate in the blood and other animal fluids. These results were deduced by Persoz and Boussingault,<sup>1</sup> from a series of most carefully conducted observations on animals which were being fattened. A similar series of metamorphoses may be frequently observed in different morbid conditions; all the stages induced from excess of fat may be traced in the bodies of drunkards, for here a large amount of material forming fat is, as a general rule, introduced into the body, with only a very small quantity of substance that can be applied to the formation of cells; and in the artificial fattening of animals, the fat has the greatest tendency to collect in cells that are already formed, as for instance, in the liver, and this gives rise to what is termed the fatty liver—a morbid change which induces a certain group of disturbances. In short, we see that the fat, even considered from this point of view, stands in the closest relation to the formation of cells.

Whilst in the above-mentioned cases fat gives occasion to the formation of cells in the animal body, we see a tendency to the accumulation or new formation of fat in existing cells and tissues whose nutrition has been to a certain extent altered (see vol. i. p. 239). This tendency is most clearly manifested in those pathologico-anatomical cases which have been commonly known under the name of fatty degeneration. These frequently occurring phenomena may be interpreted in two different ways; for it may be assumed, either that the fat which is already present may be disposed by certain molecular forces to accumulate in the older and less vitally active cells, where it replaces the disappearing nitrogenous tissues; or that the fat arises directly from the nitrogenous substrata of the cells or fibres, and that their nitrogen disappears under the form of ammoniacal salts or other simple combinations, leaving fat as the secondary product of the decomposition of albuminous matter.

It must be observed, in reference to the latter hypothesis, that hitherto all attempts made to convert protein-bodies into true fat by chemical means have proved unsuccessful, although there is nothing, in a chemical point of view, at variance with such an assumption (see vol. i. p. 231); indeed Liebig<sup>2</sup> has especially shown that it is not only possible, but also probable, in a chemical point of view, that the albuminous substances of the animal body may be converted into fat. We find that in the putrefaction, as well as in the gradual oxidation of albuminous substances, there are formed, in addition to butyric acid, a number of acids which belong undoubtedly to the group of the fatty acids, and are thus closely allied to the fats; indeed fat may, under favorable conditions, be converted into ammonia and such fatty acids (butyric and valerianic acids); hence it may fairly be assumed that under the peculiar conditions presented by dead cells and tissues in the living organism, the process of decomposition takes the same course in nitrogenous matters as in the butyric or valerianic fermentation of the protein-bodies, with only this difference, that in the former case, where there is only a small supply of oxygen, oxides having higher carbo-hydrogen radicals are formed. If the formation of adipocire were more carefully exa-

<sup>1</sup> Ann. de Chim. et de Phys. 3me Sér. T. 14, p. 413-435.

<sup>2</sup> Chem. Briefe. 1851, S. 491 [or Letters on Chemistry, 1851, p. 379.]



mined, we should find that it presented the most striking instance of a true fatty fermentation of albuminous bodies. Chevreul, as is well known, found saponified fats combined with ammonia and lime in adipocire, which led to the conclusion that the nitrogenous constituents of the muscles undergo the process of putrefaction during the formation of this adipocire, and that the ammonia which is formed combines with the fat existing during life to form soaps, whilst the greater part of the oleic acid is destroyed, or carried away, or converted into margaric acid. Recent experiments made by Quain<sup>1</sup> and Virchow<sup>2</sup> on the conversion of muscular tissue into adipocire in macerating troughs seem rather to give some weight to the older opinions, that it was not merely the pre-existing fat which was saponified in this process, but that the albuminous constituents of the muscles were separated into fatty acids and ammoniacal salts. This subject requires, however, to be more carefully investigated before we can venture to decide to which of these hypotheses we ought to give the preference.

Virchow<sup>3</sup> has long been one of the most zealous supporters of the view that albuminous substances are converted into fat *within the living organism*. This observer was the first pathological anatomist who studied the so-called fatty metamorphosis in certain cellular organs, as for instance, the kidneys, spleen, liver, &c., and recognized it as one of the more frequent terminations of the process of inflammation, whilst Schultze<sup>4</sup> regarded it as the product of excessive plastic activity (see vol. i. p. 227). Virchow has attempted, with considerable ingenuity, to show that an accession of fat from without is scarcely conceivable during the fatty degeneration of entire organs and individual cells; but still we can hardly consider this view fully proved, owing to the extensive diffusion of fat in most animal fluids, and the frequent depositions of fat in organs enlarged by morbid processes. The interesting experiments of R. Wagner<sup>5</sup> appear, however, to furnish the most decisive proof in favor of this view. When Wagner found that testicles which had been introduced into the abdominal cavity of hens were completely changed and converted into a shrivelled fatty mass, he introduced crystalline lenses, portions of coagulated albumen, and similar non-fatty protein-bodies into the abdominal cavities of pigeons and other birds, and these, after a lapse of time varying from twenty-five to fifty-four days, were also found to be wholly changed, leaving a residue, the quantitative analysis of which yielded, in addition to some traces of nitrogenous matters, a larger proportion of fat than the substance originally employed had contained. Donders<sup>6</sup> and Middeldorpf<sup>7</sup> have subsequently made similar experiments with tendons, cartilages, and bones, and obtained very nearly the same results as Wagner; Donders, however, maintained that the fatty metamorphosis must be limited to the cells; but this opinion seems to be refuted by the observations of Wagner and others. As, however, Wagner himself had started the objection, that

<sup>1</sup> Medico-chirurgical Transactions. 1850, Vol. 33, p. 141.

<sup>2</sup> Verh. d. phys.-med. Ges. z. Würzburg. Bd. 3, S. 369.

<sup>3</sup> Arch. f. path. Anat. Bd. 1, S. 30-64.

<sup>4</sup> De adipis genesi pathologica, Comm. præmio orn. Gryphæ, 1852, p. 47.

<sup>5</sup> Göttinger gel. Anz. 1851, No. 8.

<sup>6</sup> Nederlandsch Lancet, 3 Sér. Jaarg. 1, p. 556.

<sup>7</sup> Günsburg's Zeitschr. f. klin. Med. Bd. 3, S. 59.



fat might be introduced from without, that is to say, from the exudation forming itself (from fat) around the foreign body, and might pass into the disappearing nitrogenous matter, more especially as in some, although not in all cases, the fat presented the appearance of having been infiltrated from the external surface, it was necessary to alter the experiments by cutting off every supply of fat from without. For this purpose Husson,<sup>1</sup> who had repeatedly confirmed Wagner's earlier observations, undertook a series of experiments under the direction of that physiologist, introducing into the abdominal cavity of pigeons portions of albumen or crystalline lenses enclosed in gutta serena bags. These experiments, in which there was only a very small increase of fat where the gutta serena bags were well preserved, seem rather to speak against the formation of fat than to confirm such a view. Schrader<sup>2</sup> employed crystalline lenses enclosed in stoppered glass tubes for similar experiments: he did not, however, make any quantitative analyses, but merely thought he had discovered the presence of fat by examination with the microscope. F. W. Burdach<sup>3</sup> has recently carried on some very circumstantial experiments, in which according to Wagner's method, portions of albumen or crystalline lenses, enclosed in collodion or caoutchouc, were introduced into the abdominal cavity of animals, and examined after an interval of a month or even a longer period of time; from these observations Burdach convinced himself that where the animal juices were entirely cut off, the protein-body was not metamorphosed into fat, nor did it undergo any essential alteration from the simple action of the animal heat; whence it followed that if the protein-substances are actually converted into fat within the animal body, the free access of animal juices is at all events indispensable to the process. Burdach also found that when the albuminous substances were enveloped in collodion, a very fatty yellowish layer of exudation was formed upon the latter, in consequence of the exudative inflammatory process, in precisely the same manner as when such a mass is deposited directly upon the protein-substance. It is, therefore, obvious that the yellow fatty rind observed in Wagner's experiments is not the result of the decomposition of the protein-substance, although it is possible that the whitish fat which appears as if infiltrated into the object (but seems to be always more copiously deposited on the circumference than at the centre) may derive its origin from the decomposition of the protein-body. With the view of determining this question, Burdach employed porous vegetable matters, such as wood and elder-pith in place of the protein-substances in his experiments, and the results obtained were very nearly the same as those observed in the case of nitrogenous animal matters, the yellow fatty exudation being deposited round these substances, and the fat having been imbibed, through the intercellular spaces of the periphery, into the innermost part of the wood or elder-pith.

As this method did not afford any prospect of deciding the question of the formation of fat from protein-substances in the animal body, Burdach has attempted another method, which, as far as we are able to judge at present, appears likely to furnish definite results. Comparative

<sup>1</sup> Göttinger gel. Anz. 1853. No. 5.    <sup>2</sup> Ibid.    <sup>3</sup> Dissert. inaug. med. Regimontii, 1853.



analyses of undeveloped and already developed ova have been instituted, with a view of ascertaining the increase or decrease of certain salts or of sugar during the development of the embryo; and the first question which presents itself for consideration is whether the embryo does or does not contain more fat and less protein-bodies than the egg from which it is developed. If the amount of fat in the egg increased in a definite ratio to the diminution of the protein-substance, or of the nitrogenous matters generally, the conversion of protein-matter into fat during the metamorphosis of matter would be demonstrable, at all events for this case. Burdach certainly found in some experiments which he made on the ova of the *Limnæus stagnalis*, that there was no inconsiderable increase of fat during the development of the embryo; but as these few observations did not coincide perfectly as to their results, the question must still be regarded as undecided.

The third group of the most important substances of the animal body (comprising the *carbo-hydrates*) stands in such an intimate relation to fat, that in noticing these bodies we shall at the same time have occasion to make many additional remarks regarding the value of fat in the animal economy. We are only acquainted with four substances of this group as constituents of the animal body, namely dextrin, milk-sugar, inosite, and grape-sugar (glucose). We have already seen that the carbo-hydrates, with the exception of the cellulose deposited in the outer integuments of the *Tunicata* (see vol. i. p. 267) never constitute the basis of tissues. Sugar, which was formerly considered to be almost limited to the *primæ viæ*, has recently been discovered in nearly all the animal fluids which contribute towards nutrition, such as the blood, the transudations, lymph, chyle, the white of egg, &c. The sugar which we find in the intestinal canal of the herbivora and omnivora owes its origin to the metamorphosis of the starch and other carbo-hydrates through the influence of the saliva and pancreatic juice; but sugar is also met with in no very inconsiderable amount in the blood of the carnivora (see vol. i. p. 589), and must, therefore, be dependent upon some other source besides the carbo-hydrates which are introduced into the body from without. I have been enabled by a number of comparative analyses of the blood of the portal and hepatic veins to give considerable probability to the view,<sup>1</sup> that the sugar which is formed in the liver—a fact which was originally discovered by Bernard, and subsequently confirmed by Frerichs (see vol. i. pp. 258, 483)—owes its origin to the decomposition of albuminates, and more especially of fibrin. The possibility that a carbo-hydrate may be contained in albuminous substances as an intimate constituent or adjunct, as in salicin, phlorhidzin, and amygdalin, was first conjectured by Berzelius, and has since been clearly demonstrated by Liebig. The tendency of albuminous substances to pass into the butyric fermentation, which is especially noticed in fibrin and casein, may also, perhaps, be interpreted in the same manner. Hence not merely the sugar which is conveyed into the bodies of herbivorous animals with the food in the form of starch, but especially that which is generated in the organism itself, must possess high importance in the metamorphosis of animal matter generally. It is a striking

<sup>1</sup> Ber. d. k. sächs. Ges. d. Wiss. 1850, S. 130-146.



fact, however, that notwithstanding this abundant supply both from without and from the liver, sugar is found only in comparatively small quantities in the blood of herbivorous animals, although it is present in scarcely smaller quantities in the blood of the carnivora, even after the use of a purely animal diet. It is not less remarkable that nature has provided the egg with a small quantity of sugar, and that the amount of sugar in the hen's egg is increased rather than diminished with the development of the embryo. These facts undoubtedly indicate that the sugar or the carbo-hydrates generally, as well as the fats, must serve some other purpose than that of maintaining the heat of the animal body by their simple, although gradual oxidation. It will be presently seen that by these remarks we do not by any means intend to deny that the development of the heat, which is generated by the consumption of these substances is one of the most important objects of their introduction into the animal organism; but if the sugar served solely to generate heat, we can scarcely explain why the quantity should increase in the egg during incubation, whereas we should rather expect that it would wholly disappear during the oxidation which accompanies this process of development. The question further arises, why the sugar, which is certainly present in far smaller quantities in the blood of the carnivora than in that of the herbivora, should not be immediately consumed in the former, and rendered unamenable to our reagents, since the sugar occurring in considerable quantity in the herbivora is so rapidly removed from the blood either by respiration, or where this is inadequate for the purpose, by the urine.

We are still very imperfectly acquainted with those carbo-hydrates and their metamorphic products which occur in the animal juices; but it is very probable that in addition to Scherer's inosite, we may find other similar indifferent substances amongst the extractive matters of the animal body. We are, however, acquainted with many of the acids which are formed in the animal body from the carbo-hydrates, as for instance, formic, acetic, and butyric acids, which occur in large quantities in the sweat, and, in addition to these, lactic acid, which is associated with them in the muscular juice, in the parenchymatous juice of the smooth muscles of the stomach, of the intestinal canal, and of the bladder, as well as in the middle arterial coat.

We have already seen that in the small intestine free acid is commonly found as far as the middle of the ileum, notwithstanding the access of pancreatic juice and bile; here its use is assuredly not merely to dissolve the nitrogenous substances which were not digested in the stomach, but also essentially to promote the resorption of the soluble constituents of the chyme. The admirable experiments of Jolly<sup>1</sup> have shown us, that the endosmotic equivalents of the acids are extremely small, as compared with the equivalents of the alkalies, for he found the equivalent of hydrated sulphuric acid = 0.350, but that of hydrated potash = 215.725, and Graham<sup>2</sup> found the diffusibility of the acids extremely great, and that of the alkalies very small; it, therefore, stands in an inverse relation to the endosmotic equivalents. Graham observed amongst other

<sup>1</sup> Zeitschr. f. rat. Med. Bd. 7, S. 83-147.

<sup>2</sup> Ann. de Chim. et de Phys. 3 Sér. T. 29, p. 197-229 [or Phil. Trans. for 1850, p. 1].



things that an acidified albuminous fluid was much more diffusible than an alkaline solution of albumen. Whenever, therefore, an alkaline and an acid fluid are separated by a membrane, the main current of the interchanging fluids will always be directed towards the alkaline side, and hence it is most obvious that the acid of the small intestine must aid in essentially promoting and facilitating the resorption of the contents. There can therefore be no doubt that the carbo-hydrates, or rather their acid products of metamorphosis, control some important function in the intestinal canal which does not stand in any direct relation to the process of respiration. We need hardly have recourse to facts well known to the physician to prove the truth of this proposition, since the phenomena of indigestion in gastric catarrh, and the temporary benefit derived in these conditions from the use of acids, are now explained by these purely physical relations.

This proposition acquires still higher importance in reference to the animal functions, when we consider the antagonism of the reactions of the different animal fluids, a condition which we shall more fully consider at a future page. We will here simply observe, that we find, when we examine the mixture of the animal juices already noticed, that on the one hand the free acid is associated with phosphates and potash-salts, and on the other hand a strongly alkaline reaction with soda-salts and chlorides. These occurrences are not the result of accident, and Liebig, as we shall presently see, has with his usual ingenuity and success elucidated the object and necessary results of this peculiar grouping of the acid and the alkali, and of the different salts in the animal organism. If we attend only to the constant difference in the reactions of the different juices, we shall have to admit, that the alkaline nutrient fluid of the blood must, in accordance with this physical law, transude far less readily than the acid parenchymatous fluids through the walls of the vessels. Even if the remarkable play of affinities in the phosphate of soda might often give rise to an acid reaction, such an effect could scarcely be produced unless carbo-hydrates were introduced into the body, or generated within it, by whose conversion into acids a part of the base would be abstracted from the phosphates taken with the vegetable food in order to convert them into acid salts, until the alkali, after being freed by combustion from its organic acid, might recombine with the phosphate.

If we deny this function to lactic and other organic acids, we could not admit the occurrence of an acid reaction, or what is the same thing, the formation of an acid phosphate in the organism, if the carbo-hydrates without forming acids, were consumed in the same manner as in our furnaces or crucibles. The ash of plants always exhibits an alkaline reaction (excepting in the case of some seeds), and consequently the food of herbivorous animals could only generate alkaline fluids within the body if the carbo-hydrates were not, partially at least, converted into acids, and distributed with the phosphoric acid amongst the bases, thus serving to restore the acid salts and the acidly reacting fluids. Nature has, therefore, provided by this beneficial distribution of acids and alkalies for the removal of all effete matters from the tissues in the most rapid manner, and for their transference to the blood, where they are employed in maintaining animal heat, or are entirely removed from the body with the urine and sweat, whilst on the other hand equally



efficient means serve to render the passage of deleterious matters from the blood into the parenchyma of the organs extremely difficult, and to facilitate in an equal degree their expulsion from the organism by the aid of the urine and sweat.

Moreover, the carbo-hydrates, or rather the sugar, may very probably accomplish some other less striking functions before their conversion into acids; thus for instance, the sugar in the alkaline fluid of the blood certainly contributes its share to the solution of the carbonate and phosphate of lime, as is very obviously manifested in the development of the embryo in the egg of the bird. It long remained a mystery to the older observers, how the salts of lime could be augmented in the embryo, and it was believed or assumed that the lime must be derived solely from the shell of the egg; but even if some acid salt of lime may be formed during the period of incubation, and may pass into the juices of the developed germ, yet the sugar, when present, combines with the alkali or lime in the alkaline fluid, and may then dissolve the carbonate of lime as a compound of sugar with lime or soda, a fact which has been long known and has been recently brought to notice by Barreswill.<sup>1</sup> May not the capacious size of the liver of the chick during the latter days of incubation be the cause of the greater amount of sugar which is found in the albumen of the egg at that period than before incubation? And may we not conjecture that the liver of the foetus of the mammalia, which notwithstanding its size, secretes very little bile, may serve to generate sugar from the protein-bodies? This sugar, which I have determined with the greatest exactness in the foetal blood of calves, is assuredly not formed in the liver simply to be consumed, for even if the albuminous substances in the foetus are partially appropriated to the maintenance of internal heat, they would hardly be first decomposed into sugar and other substances in order to effect this purpose. The foetus which requires sugar quite as much as the young animal during lactation, generates it in the organs designed for that purpose, and the blood of the foetus with its small amount of alkali has less tendency to decompose sugar than the more alkaline blood of breathing animals.

We have already frequently referred to the application of sugar to the formation of fat, and we will, therefore, simply observe that according to Liebig,<sup>2</sup> the formation of fat from sugar may be explained in two different ways. It may in the one case be analogous with vinous fermentation, or with the formation of fusel oil, the atom of sugar being decomposed into carbonic acid, and into a substance poor in oxygen; or in the other case, the sugar may undergo a process analogous with the butyric fermentation, by means of which the hydrogen is in part abstracted from the carbo-hydrate, and carbonic acid escapes, while a substance poor in oxygen remains in the form of one of the known fatty acids. In the butyric fermentation, one atom of sugar is decomposed into hydrogen, carbonic acid, and butyric acid ( $C_{12}H_{12}O_{12} = 4H + 4CO_2 + C_8H_7O_3 \cdot HO$ ); in the formation of caprylic acid within the animal body, two atoms of sugar become decomposed into the above-named acid, carbonic acid and

<sup>1</sup> Moniteur Industriel. 1850, No. 1542.

<sup>2</sup> Thierchemie. 1846, S. 102. Chemische Briefe. 1851, S. 486-492 [or Letters on Chemistry. London, 1851, p. 377].



hydrogen, the latter combining to form water with the oxygen which it meets with in the blood ( $C_{24}H_{24}O_{23} + 4O = 4HO + 8CO_2 + C_{16}H_{15}O_3.HO$ ). Liebig adduces an interesting experiment in support of the view to which we have already referred, that the formation of fat is effected in the liver. When pieces of calves' liver are chopped up in water, and suffered to stand at a temperature of  $39^\circ$  or  $40^\circ$ , an extraordinary amount of pure hydrogen gas will be developed in about four or five hours; some ferment must, therefore, be developed here, which is capable of separating the hydrogen from the oxygen. In every case the deposition of fat within the animal body betrays a certain deficiency of oxygen showing that the amount of oxygen respired was insufficient to allow the complete separation of the sugar into water and carbonic acid.

The part taken by the *fats* in the metamorphosis of animal matter has already been very fully considered in the first volume. We there showed (after discussing the mechanical objects fulfilled by the fats in different parts of the animal body), that these substances accomplish definite purposes in the *primæ viæ*, and that they appear to be powerful auxiliaries in the formation of cells and tissues, whilst their ample supply of carbon and hydrogen, and their gradual oxidation, enable them to contribute essentially towards the generation of animal heat. We shall refer in a future page to the special value of the fats in relation to the generation of heat.

We now pass to another group of substances, whose occurrence in the body, and whose importance in the animal economy have already been considered in detail in the first volume of the present work. On taking a general retrospective view of the substances which occur in the ash, or which we assume to exist preformed as *inorganic salts* in the animal juices, certain general considerations which we have not hitherto noticed demand our attention. We have frequently had occasion to refer to the numerous defects which still appertain to the chemical analysis of the incombustible constituents of vegetable and animal substances, and which necessarily oblige us to exercise great caution in applying the results of ash-analyses to the explanation of the physiological actions of the substances which are found preformed in the living body. It is sufficiently evident, however, that these substances play a very important part, and that notwithstanding these defects in our analytical methods, they are more accessible to exact investigation than any other constituents of the organism. If any doubts still exist as to the necessity of their presence for animal life, we need only refer with Liebig to the series of experiments instituted by French investigators, in which animals were destroyed in more or less brief periods of time when fed upon substances containing no salts, although otherwise nutritious. We also learn from other experiments, in which animals were fed on substances which were deficient in certain mineral constituents, that a certain group of these bodies contributes essentially towards the nutrient power of the different articles of food. Liebig has especially drawn attention to this obscure and much-neglected question, which he has made the object of numerous experiments, and has again recently studied, with his accustomed care and completeness,<sup>1</sup> ably elucidating the numerous relations borne by these

<sup>1</sup> *Chemische Briefe*. 1851, S. 495-544 [or *Letters on Chemistry*. London, 1851, pp. 382-440.]



substances to individual processes, as well as to the entire economy of the animal organism.

It is a singular circumstance that it should have been reserved for our own day to define with greater exactness the inequality in the distribution of the *free acid* and of the *alkali* in the juices of the animal body. Andral,<sup>1</sup> who was the first to institute observations in relation to this subject, prosecuted the inquiry purely in relation to medical diagnosis, and hence they did not yield any actual benefit to physiology; here, too, Liebig was one of the foremost in the field. If we revert to the experiments on the different animal juices described in the first and present volumes of this work, we shall perceive that the blood constitutes the main representative of those animal fluids which are distinguished by a decided alkaline reaction, whilst the juices of the most vitally active organs have a decided acid reaction. Besides the blood, there are only few of the animal fluids which are constantly alkaline, as, for instance, the lymph, the chyle, and the transudations. Among the secretions, the saliva alone exhibits a strongly alkaline reaction under certain physiological conditions, whilst the bile and the pancreatic juice are so slightly alkaline that they are often unable, under ordinary conditions, to neutralize the acid masses which enter the duodenum from the stomach. On the other hand, we know to what a degree the gastric juice is distinguished for its acidity, and that the acidity of the muscular juice varies directly with the activity of the corresponding organs; the most recent experiments of Du Bois Reymond and Liebig showing that the muscles, when at rest, contain no acid juice. The parenchymatous fluids of the spleen, the thymus gland, the smooth muscles, the liver, and the supra-renal capsules, all contain free acid. This antithesis in the preponderance of the alkali and the acid is not only apparent in the mass of the coarser organs, but shows itself on a close examination even where we should not expect to meet with such differences, as for instance, in the egg and the blood. Although the fluid of the yolk exhibits no acid reaction towards vegetable colors, yet it is found on a closer examination, to differ essentially from that of the white, which is so rich in albuminate of soda and alkaline carbonates as always to color turmeric brown, whilst the yolk-fluid is so poor in alkalies that the casein contained in it is separated in granules. We might certainly regard this casein as the free acid of the yolk, if the ash-analyses of the latter did not show that the mineral bases are insufficient to saturate half of the phosphoric acid contained in it (see p. 79). In examining the blood, we find that a difference exists between the serum and the blood-cells precisely similar to that which we have noticed between the yolk and the white of the egg. If we are not mistaken, C. Schmidt has somewhere suggested that the contents of the red blood-cells may have an acid reaction; the numerous experiments which I have made in relation to this question have not enabled me to arrive at any definite results; but if we consider the composition of the mineral constituents belonging to the blood-cells as first determined by Schmidt, and if we bear in mind the facts<sup>2</sup> which have been recently established regarding the behavior of the

<sup>1</sup> Compt. rend. T. 26, p. 650-657.

<sup>2</sup> [See vol. i. p. 344 (on the crystalline matter contained in the blood-cells).]



crystalline substance of the blood, its acid reaction on coagulation, the amount of metaphosphates which it contains, &c., it becomes highly probable that the contents of the blood-corpuscles have either an actually acid reaction, or that, analogously with the yolk-fluid, they contain substances which are able to saturate the alkalies.

When we consider all that has been ascertained in reference to the nature of the free acids in the different animal juices, and all that has been set forth in different parts of the present work, we find that wherever free acids occur in the parenchyma of the organs acid *phosphates* are invariably present, or that where an acid reaction cannot be directly recognized, phosphoric acid is always met with, either conjugated or simply combined with casein, globulin, or glycerine. The proposition may, therefore, be established for all animal juices, which are neither secretions nor excretions, that in all juices which exhibit an acid reaction the soluble phosphates are especially accumulated, for it has been found that whenever the mineral constituents were determined by the ordinary method of incineration, the ash of all these juices, whether they exhibited an acid or a neutral reaction, was much richer in phosphates, and especially metaphosphates, than the ash of alkaline animal juices. As all these juices naturally originate in the blood, it would appear very singular, although by no means incomprehensible, that certain of these juices, as for instance the muscular juice, and the fluid bathing the contractile fibres, should exhibit such a strongly acid reaction if free organic acids and their alkaline salts were not also simultaneously present with the acid phosphates. This free acid, which as we have already seen, consists essentially of lactic acid, together with a smaller quantity of volatile organic acids, is originally generated in the parenchyma of the organs by their own functions, and the neutral phosphate which has passed from the blood is here first converted into an acid phosphate; such at all events is the case with the muscles, which Du Bois found to be without free acids when in a state of rest. We are, therefore, disposed to adopt the view advanced by Berzelius many years since, that this acid reaction is not the requirement, but the result of the function of the muscles.

Moreover the earthy phosphates are also brought into solution in larger quantity by the occurrence of free acids, than would have been the case by albumen or casein alone. It need not, therefore, excite our surprise, if we find large quantities of these phosphates present in the ash of the animal juices, for such a fact would at first sight appear to be the mere result of a chemical necessity; but we have already shown that although no free organic acids are formed anew in the parenchyma of the organs, the occurrence of acid phosphates in them, although striking and inexplicable, is yet not inconceivable. After the wonderful discoveries of Graham in reference to these complicated endosmotic phenomena, which have hitherto been so imperfectly reduced to definite laws, we need no longer be surprised when we see an acid fluid separating from the alkaline blood, or an acid phosphate separating from the neutral phosphate, and permeating the coats of the vessels. A similar view must be taken of the faintly acid or neutral fluids in which, at all events at present, no organic acid has been recognized, as for instance, the yolk and the con-



tents of the blood-cells; for it is certainly not very probable that these adjuncts, or faintly acid bodies, such as casein or glycerine, should be capable of decomposing the neutral alkaline phosphate.

We must here refer to an observation which is intimately connected with the above-described facts, and which bears upon the influence of these unknown laws of diffusion and endosmosis; we allude to the fact first observed by Liebig during his investigation of the muscular fluid, and subsequently confirmed by C. Schmidt in his investigation of the contents of the blood-corpuscles, namely, that these fluids, which are so rich in phosphates, and which exhibit an acid reaction, contain only a small amount of soda-salts and alkaline chlorides, while they are very rich in potash. This observation I have been able to confirm (see pp. 228 and 241) in examining the parenchymatous juice of the different contractile tissues; for I found that acid sweat, which was almost entirely free from phosphoric acid, contained a much larger quantity of potash-salts than were contained in the alkaline animal juices, which were richer in phosphoric acid. The experiments hitherto made on endosmosis and diffusion have indeed afforded some indications of the readiness with which the potassium-compounds transude, although they have not yielded any more precise results; Graham's<sup>1</sup> most recent experiments have merely demonstrated that hydrated soda and the soda-salts in general are diffused somewhat more strongly than hydrated potash, and the corresponding potash-salt. Here again, therefore, we are deficient in the elements necessary to furnish an explanation of these phenomena; that is to say, we are ignorant of the physical laws, whose application to organic nature, and whose utility in proving that all vital phenomena are results of a physical necessity, constitute the true essence and the ultimate aim of physiological chemistry and physiology. As long, therefore, as we continue in ignorance of the leading physical premises, we should abstain from having recourse to less efficient agents, such as nervous force and electrical endosmosis (although, as Du Bois Reymond has shown, these are not without their influence); least of all, however, should we conceal our ignorance by calling to our aid any peculiar vital forces.

But if we do not regard the occurrence of free acids, acid phosphates, and an excess of potash-salts as purely accidental, in so far as we recognize their presence as *the result of a necessity*, that is to say, as the effect of physical laws, we are also equally bound to consider that their presence may not be accidental when examined in a teleological point of view; that is to say, we ought also to inquire what purposes are accomplished by the occurrence of the free acid, the phosphates, and the potash-salts in the fluids of these organs; or rather, what effects are necessarily produced by the presence of these substances in the organs under consideration. The present state of our knowledge does not, however, enable us to decide this point with more certainty than we have already indicated in the first volume, when treating of lactic acid and the phosphates. We are entirely unable to conjecture the effect which may be produced by the simultaneous presence of the phosphates and potash-salts on the metamorphosis of matter, either in the organs or in the surround-

<sup>1</sup> Chemical Gazette. 1851, pp. 256-258.



ing parts; for mere surmises and hypotheses regarding polar antitheses, and the like, call for no further notice till we are more conversant with the effects of polarity.

There is, however, one point of view which must not be wholly neglected in our considerations of the antagonism of the reactions, and of the different salts occurring in these organs and in the blood, since it may, in this respect, possibly present the idea of an antagonism between the organ and the blood under such an aspect as to necessitate our relinquishing it entirely. Here, for instance, the question especially arises, whether the acid reaction and the amount of phosphates in the fluids are solely dependent upon the quantity of fibre-cells or smooth muscular fibres contained in the organs, or whether they are definitely associated with the organs as such. This question must certainly be answered before we enter into further discussions or investigations, since so many facts appear to show that this free acid, and this abundant supply of phosphates and potash-salts, which we have found to be the constant associates of the smooth muscular fibres, occur in the various organs solely in proportion to their number of contractile fibre-cells; we need here only refer, by way of illustration, to the fact, that organs, such as the spleen and the muscular layer of the intestinal canal, which are especially rich in contractile tissues, are also especially distinguished by the amount of free acid, &c., which they contain; whilst, on the other hand, the juice of the salivary glands and of the pancreas, in which Kölliker discovered few or none of these fibre-cells, are distinguished by their alkaline reaction and by their poverty of potash-salts. I have ascertained from direct observation that the middle coat of the aorta and the A. innominata yields far less acid, phosphates, and potash, in proportion to the amount of fibre-cells, than the same tissue from middle-sized arteries. It requires, therefore, further and more exact investigations to determine whether the juice of the spleen and similar organs exhibits an acid reaction, &c., simply because it is blended with the juice belonging to the fibre-cells, or whether the presence of these substances is inherent in the organ as such; but still it must be confessed, that our histo-chemical investigations render the former view by far the more probable.

We likewise meet with accumulations of *phosphates* independently of the presence of free acid, or the formation of acid salts, in parts of the animal body where their presence has either served certain definite purposes, or where it is still regulating certain functions; instead, however, of recurring to the observations we have already made in relation to this subject (see vol. i. pp. 373-378 and 395), we will here merely refer to the following facts. All histogenetic substances are almost inseparably combined with considerable quantities of phosphates, so that the two are always dissolved together, and are again associated in all coagula or precipitates obtained from their solutions. The bases of all completely developed tissues always contain in their ash considerable quantities of phosphates, which for the most part are in the proportion of 1 equivalent of phosphoric acid to 1 equivalent of base, and therefore occur as metaphosphates; as for instance, in the case of the muscular substance, and the substance of the connective tissue of the lungs and of the liver, after being thoroughly rinsed in water according to Liebig's directions. Hence



we may conclude, that acid phosphates must have been present in the recent tissue, or rather that a portion of the phosphoric acid was combined with organic matters. We have further seen (see p. 282) that all secretions from the blood, which are distinguished by their plasticity, exhibit phosphates, which although not always present in large quantities, never fall below a certain amount; and the admirable observations of C. Schmidt have shown that a certain quantity of phosphates is required to supply the first basis for the new tissue, even in the case of those organs which subsequently exhibit an excess of carbonate of lime. After considering all these facts, we can scarcely entertain a doubt of the positive influence which the phosphates exert on the formation of the tissues and organs. The effects and counteractions reciprocally induced by the phosphates and organic matters in the development of the tissues and in their maintenance, are subjects which still require elucidation. If any doubt still exist as to the share taken by the phosphates in the formation and functions of certain tissues, the observation made by Liebig must, we think, finally set them at rest; we refer to the fact noticed by that observer, that herbivorous animals take up a very small quantity of phosphates in their food, and although their blood is very poor in those substances, their tissues and organs contain as large a proportion of these salts as the corresponding parts of the carnivora. The phosphates must, therefore, be especially attracted and retained by the tissues in the organism of the herbivora, in order that they may there fulfil definite effects corresponding to the objects of the several organs, which could not be fulfilled by the other substances which are supplied in abundant quantities in the vegetable food of these animals. The very variable amount of these salts which we meet with in the blood of herbivorous as well as carnivorous animals, and which obviously depends only upon the nature of the food, or, in other words, upon the quantity of phosphoric acid which it contains, led Liebig to adopt the view that the phosphates do not exert any perceptible influence upon the process of the formation or the main functions of the blood, that is to say, upon nutrition and the development of heat. The facts we have already considered, and those which still demand our notice, coincide so fully with Liebig's view, that future investigations are not likely to modify it. We shall revert at the proper place to the relations of the phosphates in secretion, excretion, and similar processes.

The *alkali* and the carbonates predominate in the liquor sanguinis (serum+fibrin), in the same manner as the free acid and phosphates in the fluids of the tissues. We have seen that the alkalinity of the liquor sanguinis is not induced by the free alkali, but by certain saline compounds of alkalies, and more especially of *soda* with albuminous substances on the one hand, and with carbonic acid, and in part also with phosphoric acid, on the other hand. The albumen of the blood-serum is combined with soda in at least a twofold proportion, constituting an acid and neutral, or a neutral and a basic compound, according as we calculate its atomic weight. We have already described, under the head of Albumen (vol. i. p. 297), and under that of Blood (vol. i. p. 587), the reactions which show that the blood-serum contains two albuminates of soda, one of which is rich and the other poor in alkalies, and that these



are mixed together in variable proportions; it is only in diseases that free albumen, held in solution solely by the salts of the serum, can be obtained. This relation even might of itself aid us in conjecturing the effects of the alkali, or in other words, the purpose it accomplishes in the blood. The somewhat lax combination between soda and albumen will always be disposed to give off the alkali, as soon as acids are formed in the blood, or are conveyed to it from other parts of the body. The provision by which the blood is surrounded by acid fluids, and which enables it to expend a portion of its alkali in destroying the acids without by that means losing its alkaline character, is one which demands our fullest consideration; this alkalinity of the liquor sanguinis would, however, very rapidly be destroyed, owing to the abundant supply of acid fluids, and the great tendency of the latter to be converted into alkaline and neutral fluids, if the newly formed salts were not readily and quickly decomposed into carbonates, and in part also were removed unchanged from the blood.

The following seem to be the only considerations which are able to assist us in determining the causes which maintain the alkalinity of the blood at a tolerably constant degree, and the objects which are effected by this constancy. We need not here seek for any complicated modes of explanation, for the question to be determined is simply this: what effect will the alkali necessarily exert on organic bodies under the relations prevailing in the living blood? As far as these relations are known to us, it would appear that the one which especially claims our attention is *the simultaneous presence of oxygen*. The first principles of chemistry teach us that the tendency of oxygen to combine with certain elements is extraordinarily strengthened by the presence of alkalies, but it is scarcely necessary to enter more fully into the chemical laws and experiments which refer to this subject, and which have been already considered in various parts of this work. We will, therefore, limit ourselves to a brief notice of the most important experiments, which show the necessity that the collective organic constituents of the blood should be subjected to a process of gradual oxidation by the simultaneous presence of oxygen and loosely combined alkalies in the blood. The oxidation thus gradually proceeding extends itself in organic substances, not merely to the disintegration, step by step, of one atom after the other, but also to the individual atoms of their constituents; that is to say, it is not, for instance, one atom of sugar after the other which is directly converted into carbonic acid and water, but whilst the separate atoms of hydrogen of the sugar are oxidized, there are formed various derivatives before we obtain the final results of carbonic acid and water. The length of time which, Liebig<sup>1</sup> has shown, is required for the completion of many chemical processes external to, and independent of, the influence of living organisms, makes the gradual and slow course of chemico-vital processes less remarkable than it was formerly supposed to be. In order that we may take our stand on direct observation, we will pass in review the individual constituents of the blood, and briefly consider their relations whilst they are simultaneously subjected to the influence of the free or

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 65, S. 350-352.



slightly combined alkalies and of the oxygen at the temperature of the living body.

We will begin with the *organic acids*, which readily and in no inconsiderable quantity transude into the blood. Every one who has spent even a short time in a chemical laboratory is aware of the rapidity with which organic acids, or rather the salts which they form with alkalies, begin to decompose when there is an excess of the alkali, even where there is a very slight excess of oxygen. Fluids previously colorless become brown; we generally remark the formation of vegetable growths; and a closer examination shows that products of oxidation, such as succinic acid, &c., are generated. Liebig has even recommended gallic and pyrogallic acids as the best eudiometric agents, owing to the high oxidizing capacity exhibited by their alkaline salts. The well-known discovery of Wöhler, which has justly excited so much attention, is, therefore, nothing extraordinary, and certainly does not prove that the animal body possesses an altogether special oxidizing capacity, equalling in intensity our strongest oxidizing agents. The means are precisely the same by which organic acids are consumed both within and without the organism; the apparent intensity of the oxidizing power in the blood is not owing to any special force, but is the mere result of a peculiar complication of circumstances.

We have, moreover, seen that the *carbo-hydrates* contained in nutrient matters for the most part reach the blood in the form of grape-sugar. We can hardly wonder at the rapidity with which the latter disappears from the circulation, if we remember that this sugar, when associated with an alkali, is capable of taking up combined oxygen, and of withdrawing it from oxide of copper and many other oxides.

Our experiments show that a less striking influence is exerted by the alkalies on the oxidation of the *fats* and *fatty acids*; indeed, direct observations appear to show that the fats in the blood are oxidized much less rapidly than the carbo-hydrates, or even than the albuminous substances. Urea may be detected in urine as a product of the oxidation of the nitrogenous matters of the food, long before the combustion of the fats can be recognized in the augmentation of the expired carbonic acid (see Nutrition); whilst facts may be advanced in proof of the gradual oxidation experienced by the fats under the action of an alkali and oxygen. We need only refer to the occurrence in the blood of acids homologous to the solid fatty acids, as for instance, in certain secretions, and more especially in the sweat, where the whole series of acids, from formic to caproic acid, has been exhibited with tolerable certainty. Thus, too, butyric fermentation, like lactic fermentation, requires the addition of equivalent quantities of the alkalies for its perfect accomplishment. Although we may deny the appellation of fats to those lipoids, such as cholesterin and serolin, which most probably are formed only in the blood, they betray in many of their properties so near an affinity with these bodies, that in our ignorance of their origin, it would scarcely seem at variance with the truth, were we to refer them to the oxidation of the fats as residua poorer in oxygen, in the same manner as we refer humus to the decomposition of wood.

Chevreul and Scherer have recently shown that *hæmatin* (the coloring



matter of the blood) when dissolved in alkalies is able to continue unchanged for a prolonged period, and that on the access of atmospheric air it instantly attracts oxygen, and becomes converted into a colorless body. The want of a more careful examination of these facts has hitherto prevented the exact comparison of this form of metamorphosis with that which occurs in the blood.

No one can doubt that the *albuminous substances* of the blood undergo a gradual oxidation before they can be employed in the formation or renovation of the tissues, although we certainly are still unable to determine the extent to which the alkalies influence their oxidation and further metamorphosis. We know only this much, that the alkali of the blood must aid in abstracting and oxidizing the sulphur which is peculiar to all protein-bodies; and we need only refer to the method recommended by Mulder for the exhibition of the albumen-protein and the fibrin-protein, to show the importance of the alkali in this form of metamorphosis. Hitherto, at least, we have not arrived at any proof of the co-operation of the alkali in the further oxidation of the albuminates.

It certainly would seem probable, from a careful examination of the chemical facts in our possession, that this simultaneous action of the alkali and of the free or imperfectly fixed oxygen upon readily oxidizable substances, might afford an explanation of the entire process of oxidation in the animal organism. But this is by no means the case, and the present affords an instance of the danger of being led astray, by perfectly correct but isolated facts, to adopt extreme and exclusive conclusions. The highly complex chemical processes which prevail in the lower sphere of vitality, are not of a kind to be comprehended in their entire complication of actions and reactions, by one individual function taken indiscriminately from amid the involved and inseparable links of the great chain of causes and effects; for even when, by the strictest application of the inductive method, we have thoroughly investigated the most important factor of a process, we have by no means elucidated the process in all its bearings. We frequently enough encounter contradictory phenomena, which sufficiently show that we are deficient in the elements necessary for tracing the whole of these phenomena in their causal connection. Such is the case here. If, for example, we were to draw the conclusion from these facts, that the process of oxidation could not be accomplished in the animal organism without the concurrence of free oxygen and an alkali, we should err quite as much as if we were to conclude from the same premises that all oxidizable matters which have once reached the blood must be consumed, provided only there were enough oxygen and alkali present for their oxidation. The following examples will serve to show the erroneousness of such a deduction. Starting from the proposition above referred to, the opinion has been advanced that diabetes mellitus depends solely on the absence of the necessary quantity of alkali in the blood in this disease, and that consequently the sugar is no longer consumed in the blood (Mialhe). So far as my direct investigations of the blood of diabetic patients extend, the most careful ash-analyses do not show that there is any such diminution of the alkali, nor do the analyses of the serum exhibit any diminution of the albuminate of soda. But as comparative analyses of this kind are attended with considerable



difficulty, and as the concurrent circumstances might possibly invalidate the correctness of this view, we will turn to other investigations connected with this subject. Bernard, who, as we have already stated, injected a solution of grape-sugar into the veins of dogs and rabbits, thought he could perceive that the sugar not only did not pass into the urine, but that the latter secretion was even rendered alkaline. Without including my previous experiments, which led to precisely opposite results, I have very recently injected grape-sugar, prepared from starch, into the jugular veins of 37 rabbits and dogs;<sup>1</sup> but in no single instance was the previously acid urine rendered alkaline; and in no single case was grape-sugar absent from the urine. Quantitative determinations showed that even 0.1 of a gramme of grape-sugar could be detected in the urine of a rabbit weighing 2,150 grammes. The greater part of this (0.1 of a gramme) of grape-sugar passed into the urine, even when the rabbits had fed before and after its injection on cabbage-leaves, carrots, grass, and other substances rich in alkalies, and the alkaline urine of these animals did not retain its alkaline character, notwithstanding the abundance of alkalies contained in the food, but acquired, in opposition to Bernard's assertion, an acid and often a very intensely acid reaction. Finally, I convinced myself in two cases that rabbits into whose veins very small quantities of starch-sugar had been injected (which might in other cases be detected in the urine) did not void any sugar, provided they had received no succulent food either shortly before or after the experiment, and hence did not require to pass urine. A similar result was observed when urine was artificially discharged by pressure on the region of the bladder. It appears that sugar can only be separated from the blood when there is an excess of water in the latter, for it is only by the prolonged continuance of sugar in the blood that it can be thoroughly consumed; but the urine here is not rendered alkaline, but strongly acid, as is always the case with fasting rabbits. The sugar, moreover, passes so rapidly into the urine that it may frequently be detected five minutes after its injection (and that even when only 0.1 of a gramme has been injected). This rapid separation of the sugar from the blood, and its decomposition in this fluid, if from a deficiency of water it be retained sufficiently long, seem to favor the hypothesis that the cause of the appearance of sugar in the urine is solely owing to the blood not being sufficiently rich in alkali to aid in the oxidation of the sugar. With a view of determining this point, I injected caustic alkalies or their carbonates, in association with grape-sugar, into the veins of rabbits; but even in these experiments the wholly unexpected result ensued that, notwithstanding the caustic alkalies or their carbonates, the urine not only contained sugar, but also exhibited an acid reaction. More exact and often-repeated experiments on rabbits afforded the following explanation of this remarkable phenomenon. When 1 equivalent of sugar with 1, 2, or 3 equivalents of caustic potash or its carbonate, was injected, or when the sugar and potash compound artificially prepared from alcoholic solutions was injected in such quantities that 0.1 of a gramme of sugar reached the blood, the urine remained alkaline for at least ten minutes after the injection, becoming then decidedly acid, in

<sup>1</sup> Ber. d. k. sächs. Ges. der Wiss. Jahrg. 1852.



which state it continued for at least five hours, even when the animals had been fed in the interval upon green food. In the seventh hour the free acid diminished when food of this kind had been taken; it continued, however, although in a less intense degree, when the animals had been kept fasting. In all cases, however, sugar could be detected in the urine from the first five minutes after the injection to the eighth, and even often to the eighteenth, hour. If in these cases the alkali does not act in the manner one might be led to expect from the above hypothesis, the cause is to be ascribed partly to the circumstance that the alkali is removed from the blood more rapidly than the sugar, and partly, and perhaps mainly, to the fact of an acid being formed in the blood (as we see by the constant acid reaction of the urine after the injection of sugar) by which the alkali is saturated, and its action on the sugar thus interfered with. I have unfortunately been unable, from the small amount of material for investigation, to decide what is the acid which is thus produced, but it certainly is neither phosphoric or hippuric acid. We at all events learn this much from these experiments, that no one perfectly correct chemical fact can enable us to foresee and correctly prejudge the result of chemical effects in the living body; and it would, therefore, be no less unsuitable to endeavor to elucidate the mystery of life by rude chemical hypotheses, than it would be senseless to banish chemistry from the sphere of vitality merely on account of some few unsuccessful experiments. The following experiments, which I have instituted in relation to this point, will show the correctness of these views. On gradually injecting very dilute solutions of tartaric and citric acids into the stomachs of rabbits and dogs (concentrated solutions must necessarily be avoided, as they always induce a morbid condition in the animals), the result to be expected would naturally be, that when the animals had been fed on oats only, or on some food equally poor in alkalies, the normal alkalinity of the blood would be so much diminished that the sugar which had now been conveyed to the blood from the intestine or the liver would not be perfectly oxidized, and would therefore pass into the urine in an undecomposed state. This conjecture has not, however, been verified by my experiments. The urine does not even exhibit any trace of sugar when attempts are made to remove the alkali from the blood by artificial means. Similar but variously modified experiments have also been made by Uhle,<sup>1</sup> with precisely similar results. It would, of course, be an utterly useless experiment to attempt to gain the same object by injecting acids into the blood.

We must not, however, form too high an opinion of the oxidizing force of the blood, however important it may be to the entire animal economy. Thus, for example, we meet with numerous phenomena which indicate the co-existence of a deoxidizing process with the process of oxidation; of these we need only instance the formation of substances so rich in sulphur as taurine and cystine, and of others so poor in oxygen as cholesterolin, castorin, &c. The most striking illustration of this fact is afforded by the well-known experiment, which has recently been confirmed by one of my pupils, Ranke,<sup>2</sup> that the animal organism acts upon indigo in the same reducing manner as the hot or cold vat; ordinary indigo blue is converted in the *primæ viæ* into sub-oxide of isatin

<sup>1</sup> Diss. inaug. med. Lips. 1852, p. 19.

<sup>2</sup> Journ. f. pr. Chem. Bd. 56, S. 17.



(reduced indigo), and may, when dissolved in an alkaline solution, pass through the blood without being perfectly oxidized; hence it may reappear in an unoxidized state in the urine. If we observe the urine that is discharged after the administration of a few grammes of indigo, we perceive that the fluid assumes a light blue color, which becomes gradually more intense if it is shaken for a time in the air, until a blue sediment of pure indigo blue is finally formed. This reduction does not originate in the urine itself, since the alkaline fermentation must be set up in the fluid before it can dissolve indigo. This urine, however, has always an acid reaction. If we had not the most evident proof before us that free oxygen was contained in the blood, an unphysiological chemist might consider himself justified in concluding from these facts, that oxygen cannot be contained in the blood either in a free or loosely combined form. We can only assume this much, that the process of oxidation in the blood does not possess any high degree of intensity, and that the manner in which the process is here accomplished is more involved than we should at first sight be disposed to believe.

Although we may not overrate the importance of the alkali in connection with the process of oxidation in the blood, the above experiments might probably lead us to the erroneous conclusion, that no oxidation can take place within the organism, independently of alkalies. We call such a view erroneous, for independently of the circumstance, that it cannot be denied that a certain oxidation takes place in many acid fluids as well as in the substance of the organs, there are many points which indicate that other conditions may probably contribute to increase the oxidizing capacity existing in the blood. Many of the salts of the organic acids, as for instance, the alkaline lactates, tartrates, and citrates, do not become so rapidly oxidized in the air, even when an excess of alkali is present, as the gallates or pyrogallates; for if solutions of the salts be injected into the blood, they not only become much more rapidly oxidized than would be the case externally to the animal body in the atmosphere, but almost more quickly than if the salts were directly incinerated (see vol. i. p. 97). Other substances again, such as salicin, theïne, &c., are very rapidly oxidized in the blood, whilst they continue for a long time to resist the action of alkalies or oxygen, when exposed to their influence at a temperature of  $37^{\circ}$  externally to the living organism. The rapidity and readiness with which so many substances are oxidized or changed in the blood cannot be solely referred to the simultaneous presence of a mass of bodies undergoing various metamorphoses, to any peculiar condensation in which the oxygen occurs in the blood, or to any similar relations which control the effects of the alkalies; but they must rather be referred to conditions which we are still unable to deduce from any definite physical or chemical processes, owing to the extremely complicated nature of the chemical changes going on in the blood. We will here only refer, by way of illustration, to that condition of oxygen in which it exhibits, as ozone, a far more energetic force of affinity.

However much we may differ from some of Schönbein's modes of explanation and the conclusions he deduces from his discoveries, the majority of the results which he obtains are indubitable facts, whilst it is almost a necessary deduction from his most recent observations,<sup>1</sup> that the

<sup>1</sup> Journ. f. pr. Chem. Bd. 52, S. 135-149, u. Bd. 53, S. 321-331.



oxygen in the blood must undergo a change resembling that which it experiences when retained for some time in intimate contact with phosphorus, oil of turpentine, &c. If we fail to recognize the presence of ozonized oxygen in the blood by the ordinary tests, as for instance, iodide of potassium with starch, &c., this is obviously no proof of its absence, for in the presence of a large number of oxidizable matters in the blood, it must necessarily disappear almost as quickly as it is formed. The recent investigations in physiology, which seem at length to approximate towards the solution of the mysterious connection between electricity and nervous action, while they hold out a prospect of being able to determine more definitely the phenomena of free electricity in the animal body, render it more than probable, that the oxygen within the living body—if not in the blood, at all events in other parts—passes into this state of special attractive force, and that in this condition it takes part in the vital processes. At all events we feel that Schönbein's admirable discoveries ought not to be disregarded by physiologists, notwithstanding the obscurity which still appertains to the principles from which we must deduce an explanation of these facts.

But whatever difference of opinion may exist as to the more immediate relations in which the inspired oxygen combines in the body with individual substances, every one must admit the correctness of Liebig's ingenious hypothesis, that the alkalies in the blood promote and maintain the combustibility of the respiratory constituents of the food, and that they consequently serve as essential conditions for the maintenance of animal heat. In the absence of a positive proof of this proposition, we should not wholly reject the negative evidence in its favor. We have often alluded to Wöhler's discovery, that organic acids, such as tartaric, citric, and gallic acids, when they had been introduced in a free state into the body, reappeared unchanged in the urine after their passage through the organism, whilst their alkaline salts, under similar relations, are burnt within the body. We cannot surely explain this fact, except by assuming that the presence of the alkali induces, in the one case, the oxidation of the organic acid, whilst in the other case, the free acid, if present in sufficient quantity, suspends the alkalinity of the blood, and consequently also its oxidizing capacity, until it is removed from the organism through the kidneys.

A series of experiments were made some years ago in my laboratory (by R. Buchheim, now of Dorpat, among others) with the view of determining the quantities of alkaline carbonates, tartrates, citrates, &c., which are necessary to destroy the free acid of the urine, and further to ascertain the quantities of free tartaric or citric acid which must be taken at one time to allow of a portion appearing unchanged in the urine; but notwithstanding every attention to the quality and quantity of the food taken during equal intervals of time, the bodily exercise, and other physiological relations, these observations have failed in leading us to any sharply defined numerical results. In experiments of this nature, a number of conditions exert an influence, the determination of which is in part beyond the power or the calculation of the experimentalist. If we could succeed in determining these intricate relations, we should, at all events, have a check upon our calculations regarding the mechanical metamorphosis of matter in the animal body, in as far as the one series



of experiments shows the amount of the free acid which is excreted by the kidneys from the body within definite periods of time, whilst the other series might enable us to determine, at least approximately, the quantity of alkali in the blood, and consequently also the amount of blood in the animal body. Although these experiments have not hitherto advanced the science of physiology, they promise to yield more certain results to therapeutics. As far as we are aware, the relations subsisting between acids and alkalies or the salts of the vegetable acids, and the reactions and constitution of the urine and the sweat, have not yet been considered from a physiological point of view. Physiology has not hitherto been sufficiently applied to medicine, whilst the pharmacologist is ever striving to explain the presumed action of the most irrational agents by apparently rational means, and to defend their respective applications.

With the view of forming some estimate of the oxidizing capacity of the animal organism, I formerly turned my attention to the study of the metamorphoses which salicin undergoes in its passage through the body; and I formerly inferred from the reaction which the urine exhibits towards the persalts of iron after the use of salicin, as well as from other experiments, that the organism can only so far oxidize saligenin as to lead to the formation of salicylous acid. Städeler was led to conclude from his experiments on the volatile acids of the urine of the herbivora, that phenylic acid passed into the urine, and that the blue color imparted to the alcoholic and ethereal extracts of urine, induced by the salts of iron after the use of salicin depends upon phenylic acid. Ranke,<sup>1</sup> who commenced under my direction a more minute examination of this subject, has now obtained the undoubted result, that salicylic acid is formed in addition to salicylous acid; he also obtained considerable quantities of phenylic acid by the distillation of the alcoholic extract of such urine with water. I have, however, not convinced myself that this acid is contained preformed in this urine; it may very readily occur here as a product of distillation. Phenylic acid exerts an extremely poisonous action, so that some symptoms of indisposition ought to manifest themselves after the use of salicin, if this acid were formed from salicin; such, however, is not the case. As it might be conjectured that phenylic acid was separated from the kidneys immediately on its formation, I injected the alcoholic extract of this urine into the jugular vein of a rabbit, but the animal exhibited no morbid symptoms whatever.

I may here observe in reference to the decomposition of salicin in the animal organism, that this substance, which, like amygdalin, is decomposed by synaptase, does not behave in the blood in the same manner as amygdalin, which on being injected into the blood is not decomposed, and hence does not produce poisoning by prussic acid; although when salicin is injected, a portion only passes in an unaltered state into the urine, whilst the larger quantity is decomposed in the blood; for after the injection of salicin into the veins, the urine is affected in the same manner as after its introduction by the mouth. Sugar, which, as is well known, is formed in the decomposition of salicin by synaptase, cannot be recognized in the urine, even when as much as 0.943 of a gramme of

<sup>1</sup> Op. cit.



salicin has been injected into the blood. Ranke also found saligenin in addition to those acids in the urine, but no saliretin.

The previous observations leave no doubt as to the function of the *alkaline carbonates* in the blood, and we have already treated circumstantially of carbonate of soda in the first volume of the present work (see pp. 392-394); we will, therefore, only observe, that these salts are able to maintain their function as agents in the process of combustion for an infinitely long period; that is to say, an infinite quantity of organic acids and carbo-hydrates may be reduced by one and the same quantity of these salts into carbonic acid and water; for scarcely is an alkaline carbonate decomposed by a substance of this kind, and deprived of its carbonic acid, before it is reconverted into a carbonate by the combustion of the organic substance; hence we are able to explain how the proportionally small quantity of alkaline carbonates which are present in the blood of the carnivora, and which are only very slightly increased or replaced by the food of such animals, should be sufficient to adapt the materials of respiration for oxidation. We shall revert to the alkaline carbonates and phosphates when we enter upon the more special consideration of the processes of nutrition and secretion.

In treating generally of the distribution of *chloride of sodium* in the animal organism (vol. i. pp. 387-392), we drew attention to the well-established fact that the quantity of this salt varies very slightly in most of the animal juices, especially in the blood, and is restricted within tolerably narrow limits for each class of animals, being wholly independent of the nature of the food and of the quantity of this substance taken up with the food (see vol. i. pp. 388, 569); we have also found that the quantity of salt in the excretions, and more especially in the urine, corresponds very closely with the quantity in the food, whilst direct experiments have shown that this salt when it is injected into the blood, is rapidly excreted through the salivary glands, the mucous membranes, and the kidneys. We think that these well-established facts give great probability to the idea that this substance is necessary for the animal vital process. Even if we attach little weight to the instinct which leads certain domesticated animals eagerly to lick up the salt placed before them, and induces the natives of certain districts where salt is scarce to barter slaves and gold-dust for this substance, yet certain experiments on the quantity of salt contained in the blood, together with Boussingault's investigations,<sup>1</sup> sufficiently show that the use of salt with the ordinary food is an indispensable requisite towards the healthy condition of domesticated animals. Boussingault instituted experiments on two lots of oxen (each consisting of three), one of which he fed for a month on food with which salt had been mixed, and the other on fodder containing no salt, and found by accurate weighing that the salt produced no effect upon the formation of the flesh and fat, or on the quantity of milk, but that towards the close of the period of observation the external appearance and activity of the animals which were being fed upon food to which salt had been added were very superior to that of the animals which were fed without salt, for the latter presented a less smooth and

<sup>1</sup> Ann. de Chim. et de Phys. 3me Sér. T. 19, pp. 117-125, et T. 22, p. 116; or Compt. rend. T. 25, p. 729.



shining coat, while their hair was matted and in part fell off; their gait was also heavy, and they exhibited a cold temperament. The utility of common salt to the animal organism cannot therefore be questioned, and its importance is further shown by the fact, that during fasting, or when there is a deficient supply of nutriment, in diseases, as pneumonia, &c., the separation of common salt by the urine soon ceases, whilst in those cases in which the blood is deficient in this substance, all the chloride of sodium entering the organism from without is retained until the normal amount is restored.

We have now, however, to consider the more difficult question of the manner in which chloride of sodium contributes towards the metamorphosis of animal matter. We have endeavored to refer the importance of this salt to the peculiar relations which it exhibits towards the albuminous matters of the blood and of the animal body generally; and it seemed to us that its special use may be to dissolve the pure albumen (or serum-casein of Panum),<sup>1</sup> together with the albuminate of soda, and thus render it amenable to chemical agencies. Liebig, has, however, drawn attention to a very important fact connected with this subject. Gluten is dissolved as readily as muscle-fibrin in water containing hydrochloric acid (see p. 239), and is precipitated from this solution not only by more hydrochloric acid, but also by the addition of a solution of chloride of sodium of less strength even than 4%. From these and similar experiments we may assume that the amount of common salt in animal fluids exerts a certain influence on the separation as well as the solution of albuminous substances, although we are unable to demonstrate the individual details with any great exactness.

The mode of action of chloride of sodium in the metamorphosis of animal matter was the more difficult to determine, as it was known to the chemists as an extremely indifferent substance, with very little tendency to form further chemical combinations, urea and grape-sugar being almost the only substances with which it combines chemically. These two facts sufficed, however, to lead Liebig to a very ingenious view regarding the function of this substance in the metamorphosis of matter. It is very probable that the union of urea with chloride of sodium may be far more intimate than its ready decomposition by re-crystallization in water would lead one to conjecture. Thus, for instance, urea is only imperfectly separated by nitric acid from a moderately concentrated aqueous solution, if chloride of sodium be present; urea, moreover, occurs associated with chloride of sodium, even in positions where its presence would not be suspected, as for instance, in the crystalline lens of the eye, as was observed by Wöhler, and in the sweat, according to the investigations of Schottin and Favre. Liebig's conjectures may therefore be perfectly correct, that the absence of urea as well as of common salt in the muscular juice, and the passage of urea into the circulation, and its excretion by the kidneys, have a close relation with the presence of chloride of sodium in the blood.

Liebig observes, in relation to the combination of grape-sugar with chloride of sodium, that we are instinctively led to add salt to amylaceous food (which during digestion yields much sugar) in far larger pro-

<sup>1</sup> Arch. f. pathol. Anat. Bd. 3, S. 251.



portion than to other food. The saliva and the pancreatic juice, which more especially conduce towards the conversion of starch into grape-sugar, contain a preponderating quantity of chloride of sodium in their solid constituents.

Diabetic urine always contains, in addition to free grape-sugar, the compound of this sugar with common salt, and it frequently happens that this is the only compound which separates in crystals from diabetic urine. It is not, therefore, an irrelevant question to inquire, on the one hand, into the relation of the chloride of sodium to grape-sugar in the digestion of amylaceous substances, and, on the other, into its separation through the kidneys in diabetes.

Slightly based as the assumptions may be, which can be deduced from the chemical affinities of chloride of sodium in reference to the purposes which this substance accomplishes in the animal organism, there are some facts which can only be explained by a decomposition of this salt in the animal body, and which may therefore throw additional light on its utility, in the animal economy. The most striking of these facts is the occurrence of free hydrochloric acid in the gastric juice; at all events, it appears from the most recent investigations of C. Schmidt that free hydrochloric acid may be present in this secretion, without lactic acid or lactates. It certainly remains a mystery for the present how this decomposition of the chloride of sodium is effected. Another less obvious, but not the less remarkable fact is, that even in the blood of herbivorous animals, which take up almost solely potash salts in their food, there are in every 4 parts of alkaline carbonate in the blood-serum at least 3 parts of carbonate of soda, and only 1 part of carbonate of potash, whilst in the muscular juice of carnivorous as well as that of herbivorous animals chloride of potassium is almost solely found. This fact, which was discovered and mainly established by Liebig, shows, on the one hand, that the chloride of sodium in the blood must necessarily undergo an interchange of constituents with the carbonate and phosphate of potash, and on the other hand, that nature has assigned very different parts in the animal organism to the alkalies which are otherwise so similar when considered from a chemical point of view. Similar conclusions may be deduced from the experiments made at Giessen on different terrestrial animals, which showed that the bile, notwithstanding a food rich in potash, contains a large amount of soda, which is combined with the biliary acids. The great persistence of this distribution of these two alkalies in the various animal juices precludes the idea that we have here to deal with a phenomena which is merely incidental. As we have already observed, it still remains for us to discover the properties to which the soda owes its place in the blood-serum and the bile, and to explain the purposes which are effected by the accumulation of potash in the juice of the muscular and of all the contractile tissues, as well as in the blood-cells, the plastic exudations, and the yolk, &c.

The constant presence in the blood of a tolerably uniform amount of chloride of sodium has led Liebig to the ingenious idea that this very constancy exerts an essential influence on the absorbing power of the blood. The assertion of Liebig that the constant amount of chloride of sodium present in the blood is an essential agent in the organic process of



absorption, must be universally admitted as correct by all who have witnessed even a single endosmotic experiment, and who are moreover well aware that the substances which are actually dissolved in the intestinal canal generally present a far less dense fluid than the blood, and that the kidneys possess a property, which has not yet been explained, of immediately carrying off any excess of water that has entered the blood. If we further add the peculiar relation of acids and alkalies first noticed by Jolly and Graham in diffusion and endosmosis (see p. 345), we shall be disposed, with Liebig, to admit that in the animal body are united all the conditions for rendering the circulating system, by means of the blood, a most perfect suction-pump, which performs its duties without stop-cocks or valves, without mechanical pressure, nay, without regular canals or passages for the transmission of the fluids.

In conclusion, we must again refer to the remarks which have been previously made (vol. i. p. 390, and vol. ii. p. 283) in reference to the influence of chloride of sodium upon the development of cells in secretions and exudations. Amongst the latter we found that the most plastic were those which contained soluble phosphates and potash-salts, together with moderate quantities of chloride of sodium, whilst those exudations which exhibited a tendency to the formation of pus-corpuscles and cancer-cells always contained very large quantities of chloride of sodium in addition to these salts. It was first observed by Heller,<sup>1</sup> and subsequently by Redtenbacher,<sup>2</sup> that in pneumonia, a disease, in which the exudation is generally transformed into cytoïd corpuscles (gray hepatization), chloride of sodium is constantly retained in the body, and can scarcely, therefore, be detected in the urine. We find, moreover, in mucus (a fluid which consists almost entirely of a humid mass of cells) the animal juice, which contains a far larger quantity of chloride of sodium than any other animal fluid, whilst even in the cellular tissues as well as in the permanent cartilages and the still unossified bones, we meet with the largest constant amount of chloride of sodium. We also learn, from Frerichs<sup>3</sup> that the synovial fluid, which is so rich in cells and epithelium, contains a large amount of chloride of sodium in solution; and Schottin's recent experiments on the constitution of the sweat have unquestionably shown its richness in this salt. When we consider that the scales of the epithelium of the mucous membranes as well as of the epidermis are moistened by a fluid which is more richly charged than any other with chloride of sodium, and when we observe that the greatest amount of this salt is found in the structures which are richest in cells, we shall scarcely be falling into error if we seek to establish a very intimate relation between the presence of this salt, and the formation of cells. Now the horny tissues and the hair, which consist to a great extent, or almost wholly, of cells, contain no very large amount of common salt; but this fact does not prove that the presence of this substance is immaterial to their formation; for the cells of the hair and other horny tissues are either atrophied or destroyed, whilst those of the cartilaginous tissues are still fresh, and hence serve to convey chloride of sodium. If the presence of this salt be necessary for the

<sup>1</sup> Arch. f. Chem. u. Mikrosk. Bd. 1, S. 214.    <sup>2</sup> Wien. Zeitschr. Bd. 6, No. 8.

<sup>3</sup> Handwörterbuch der Physiologie. Bd. 3, Abt. 1, S. 463-468.



development of the horny tissues, and especially of the hair, we have a simple explanation of the fact observed by Boussingault in his experiments, that the growth of the hair was injuriously affected in those cattle which were fed without any admixture of salt in their fodder.

In respect to the other mineral constituents which occur in the animal body, we need only refer to what has been stated in reference to this subject in the first volume, since they take a less important part in the more general functions of life.

Now that we are approaching towards the termination of the general considerations of the arrangement of the most important chemical substrata observable in the metamorphosis of matter, we are forcibly reminded of the ancient saying of Aristippus, that the most probable is often untrue, and the most improbable true. If we are correct in forming a low estimate of the amount of our *positive* knowledge, we ought to exercise extreme caution in the selection of the *principles* by which we regulate our judgment regarding the positive results of our observations and experiments. In our application of chemistry to physiology, we must be especially mindful of the fact that most of the fundamental propositions which at the present time have attained to a general recognition in chemistry, by no means possess such a degree of scientific, or rather of logical, exactness as to place them beyond all dispute. We must not forget that chemistry, like medicine and theology, although perhaps in a more limited degree, possesses a dogmatism of its own. How many of the modes of consideration which are now valid in scientific chemistry, are the mere provisional modes of expressions of certain groups of phenomena, whose analogy is obvious, but whose internal connection and relations of causality are alike incomprehensible and unknown! A chemist of the old school would be indignant if any one were to hint at the faintest doubt of the correctness of the hypothesis that chemical combinations can *only* be effected in accordance with definite numerical proportions, or should venture to assert that gradual metamorphoses, which are alike independent of mathematical laws, and perfectly foreign to the ordinary chemical affinities, might run their course in the highest spheres of vitality. Yet every chemist who regards chemistry and physics as inadequate for the science of life, and on that account deems it necessary to call vital forces to his aid, must of necessity admit the cogency of these doubts; for experiments have alike failed to show that albuminous and histogenetic substances generally are constituted in accordance with perfectly definite numerical relations, or that any supervising agent has been appointed to control the economy of the living organism.

We need not, however, encroach upon the sphere of vitality to show the uncertainty and purely dogmatic nature of many of the more general principles of chemistry. Many principles which have been established, and are highly useful in investigation, are utterly devoid of any theoretical basis; for many methods have been sanctioned by chemical use which would not stand the test of a logical inquiry. Thus, for instance, no one hesitates to employ predisposing affinity as a means of explanation, although this is nothing more than the personification of an obscure idea. Does not affinity in the mass contradict the fundamental idea of



chemical affinity? We do not speak of the theory of the organic radicals, for the constant alterations and the uninterrupted modifications to which this theory has been subjected, sufficiently attest the slight degree of stability which it possesses. And has not the most prolific of all new theories, by which chemical science has been enriched to such an extraordinary extent with the most important facts—the theory of the conjugated compounds, notwithstanding the noble experiments and the brilliant discoveries to which it has led—been in turn subjected to every form of modification?

We must therefore never forget, in applying our chemical ideas to the elucidation of vital phenomena, that the basis on which they are reared is far less firmly established than the fundamental propositions of physics. We find that even in physics new observations and discoveries are daily being made, which long continue to excite our wonder before we are able to reduce them to known physical principles. How many futile attempts have been made to explain Leidenfrost's experiments! And are there not many even at the present day who regard with wonder the experiments of Boutigny? Is the doctrine of molecular attractions so well developed in physics as to preclude the possibility of being further called in question? It is only in the present day that we have had a direct proof of the motion of the earth afforded us by Foucault. Yet how far is chemistry behind physics in its fundamental principles? In endeavoring, therefore, to decide questions of physiology in chemical modes of expression, we cannot exercise too great caution in our deductions; for we know but too well that in most cases we are only supporting one hypothesis by means of another, and that truth in chemistry is very often little more than an idea embodied in a systematic form.

When, mindful of our fallibility, we once more review the character of the substances which nature employs to produce the most varied effects in the living organism, and to realize the most multifarious purposes, we are struck here, as everywhere, by the wonderful simplicity of the means or the forces by which the world of external phenomena is maintained in a state of incomprehensible alternation. There are only three groups of organic substances through which all the vital phenomena are manifested, and even these groups exhibit the most important internal correlations. May we not conjecture, although we are still unable to prove the fact, that members of the group of fats may be formed, like those of the group of carbo-hydrates, from histogenetic bodies? And do not the members of the individual groups present such uniformity and analogy in their composition, and even in their properties, that the diversity of the processes to which they give rise is perfectly incomprehensible? We are thus obliged to have recourse to isomerism and polymorphism as a prop to our ignorance, and as the means of affording us at least some clue to the manner in which protein-bodies, which appear almost identical, can be exhibited under such numerous modifications of form, and can so variously influence the mechanism of the living organism. There are almost inappreciably small differences in the composition and qualities of the substances which, as far as we know, are most homologous with ethereal bodies, viz., the fatty substances; yet the different fats do not produce the same or even analogous effects in the animal body. The carbo-



hydrates, which to a superficial observer might seem to be destined solely to undergo disintegration in the animal body, exhibit the most various metamorphoses and subdivisions before they are fitted to perform their part beneficially in the apparent intricacy of the vital phenomena. Potash and soda, for instance, are substances which the chemist finds it extremely difficult to keep asunder in his systems, and which frequently appear to replace one another in the mineral kingdom; yet they are employed in life to maintain the most strikingly opposite conditions; whilst carbonic acid, the weakest and most volatile of all acids, is occasionally made to perform the same service in the organism as the powerful and solid phosphoric acid.

It might here be asked whether nature has not employed forces peculiar to itself in regulating, with these few means, the internal economy of animal life, while we are admiring the insignificant expenditure of force which is required to convert these changeable bodies from one form to another. When we see how readily the largest quantities of starch or cane-sugar are converted into grape sugar by almost inappreciable quantities of diastase or of acids,—when we further bear in mind what slight means suffice to convert oxide of ethyl into methyloxalic acid, or oxide of amyl into valyloxalic acid,—and when, finally, we consider the various modifications which the protein-bodies experience under the action of the ordinary atmospheric influences, causing them even in some cases (as we see in putrefying cheese) to be partially regenerated,—we can scarcely conceive that any special expenditure of force is necessary to move these masses in the manner indicated. Although we must not suppose that isomerism and polymorphism, or even the laws of ordinary chemical affinity, are able to afford a true explanation of these metamorphoses and modifications of known materials, it cannot be doubted that the same forces are employed within the sphere of life as those which act in the external world, and that a very slight increase of intensity is alone necessary to produce the effects which we perceive in life. If, however, the organism requires so slight a development of force to effect these changes in matter, we shall hardly deem it necessary to assume the existence of a special force of great intensity and applicability to effect the ever-marvellous movements of organic matter; but are rather led to the belief that the same simplicity which nature exhibits in the use of material means, is unfolded on a grander scale in the application of her forces.

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## DIGESTION.

As in the present volume of this work, we have treated of the different juices which take part in the digestive process, and have attempted to determine the functions which nature has assigned to each of them, it might appear advisable, before reviewing this process as a whole and in a general point of view, to examine more closely the objects of digestion, that is to say, the nutrient matters themselves in their relation to this process; but as we have there assumed that the reader possessed a general



knowledge of the subject of nutriment, it will here be our best course to discuss the process itself, before entering upon the digestibility of individual articles of food, and the action of the various digestive agents upon them.

From the earliest period at which it was attempted to apply chemistry to physiology, and to afford a scientific explanation of the animal processes, it has been believed that the digestive process, sooner than any other, would be more or less elucidated by these means. Every one recollects that the iatro-chemical school based a great part of their philosophy on the facts which they believed that they knew regarding the digestive process. Since then scarcely any department of the physiology of vegetative life has been made the subject of such brilliant scientific labors as the digestive process. It is needless to name the great work of Tiedemann and Gmelin, for even to the present day we constantly find in this rich treasury of admirable observations, fresh motives to new experiments and to new views; witness the numerous meritorious investigations which have been pursued in the Giessen laboratory, on the chemistry of the juices, and of the materials on which they act. The barbarous experimental physiology of the French created new ways and means, in order to penetrate into the obscure mystery of the digestive process. The very names of Blondlot and Cl. Bernard are indelibly associated with the ideas of well-directed vivisections, performed with extraordinary dexterity. Science has scarcely had time to rejoice over the admirable monograph of Frerichs (written under the superintendence of Wagner) when reports reached us of wonderful discoveries emanating from the Dorpat laboratory, and throwing an unexpected light on many points connected with the digestive process.

But if, in such a department as this, where we seem to be dealing with the most direct actions of chemical forces, we are obliged to admit that the results which to-day we appear to have obtained by the most direct experiment and the most positive observation, are to-morrow rendered doubtful by other experiments and other observations, we should at all events, learn to exercise caution in expressing our opinion even on apparently the most exact observations. Did it not appear to be an established fact that lactic acid is always present in the gastric juice?—and yet, in many cases, C. Schmidt has demonstrated its absence and the presence of free hydrochloric acid; and even at the present time does not Blondlot still retain his earlier view regarding the presence of acid phosphate of lime in this fluid? Who could expect that after Bernard's most recent experiments on the influence of the pneumogastric nerves on gastric digestion, their influence would be disproved, or, at all events, rendered questionable by the most positive experiments? When fat is brought in contact with the pancreatic juice, French observers recognize its immediate disintegration into fatty acids and glycerine, while Germans can scarcely perceive that the two substances form even an emulsion. To speak candidly, we are unable to find any motive for the action of the bile, or for its infusion into the intestine, from the many conflicting opinions on the subject, all of which, however, have been deduced from observations; and do we even to this day know what actually becomes of the resinous biliary acids in the intestine? Who



could have anticipated from our previous knowledge, that an isolated loop of intestine, with its slightly alkaline contents, would be able to digest flesh? and finally, what rich although as yet inexplicable results may we not hope to obtain from Ludwig's continued experiments regarding the influence of the nerves on the secretion of the digestive juices! In short, the intestinal canal always presents itself to us as the scene of a number of highly mysterious processes, and our ideas still range unsatisfied around the as yet unopened portals of this almost impenetrable subject. Hence, if we see even the most acute investigators rapidly passing from one view to another, we must recollect that what we regard as true is in this case always dependent on the stage of development which scientific inquiry has attained at the time.

In the digestive process, as in many other phenomena in the living body, it might seem possible to anticipate the laws according to which these processes, which are still obscure to us, run their course; but we are as little able to draw any conclusions regarding the causal connection of the phenomena as regarding the primary object of each perceptible action. Hence we must rest satisfied, according to the manner of our forefathers, with a mere representation, when we are unable to apprehend the internal connection of different phenomena. Thus we have such a representation when, for instance, we compare the digestive canal with its minutest absorbents to the roots of a plant, and then show that the animal carries about and contains within itself the roots or radicles by which it absorbs its proper nourishment, while the plant is firmly rooted in the soil from which it draws its nutriment. The more striking and apparently applicable such a picture may at first sight appear, the more glaringly obvious become the differences on closer investigation, and hence we may perhaps be permitted to devote a few moments to the consideration of the above comparison. If, in the first place, we take into consideration the radicles, which in the higher animals pass into the internal surface of the intestine, we come upon the capillaries, which envelope the whole canal with the most delicate network, and then upon organs which in their finest ramifications terminate blindly in minute projections of the inner surface of the intestine, and seem to be specially designed for the purpose of absorption: besides these innumerable media for absorbing the soluble substances from the chyme, we likewise find in the intestinal tube certain glandular or capsular organs, which according to recent views are regarded as being connected with absorption rather than with secretion.

At the first glance it might appear inappropriate to begin our consideration of the digestive process with its actual termination, that is to say, with absorption; but independently of the fact that we have already, in the first volume, entered somewhat fully upon many subjects having reference to digestion, in our remarks upon the digestive *juices*, we are the more resolved to commence here with the final result, inasmuch as we can thus better take a general review of the whole process. If by the term digestion we understand that process by virtue of which nutriment is transmitted, in accordance with chemical and physical laws, into the circulating system for the renovation of those portions of the organs which have become effete,—and if we further establish the fact, that by



digestion the food is reduced to a soluble state, or generally speaking, to such a condition that it is capable of being absorbed into the mass of the juices of the animal body,—we take the most natural starting-point, not merely for forming an opinion regarding the proximate object of digestion, but likewise for attaining a deeper insight into the different actions and reactions between the food and the digestive juices. For if we only establish the proposition, that the intestinal absorbents possess no specific indwelling property totally different from other physical forces, and that they no more enjoy a distinct elective power than the radicles of plants, it obviously follows that in the various arrangements which occur in the intestinal canal in connection with the process of absorption, the difference in the agents of absorption must correspond with the different physical and chemical characters of the substance to be absorbed; and this leads us to the idea, that food (whose nutrient power, moreover, has nothing to do with the question of digestion) stands in as close a relation to the organs of absorption as to the solvent and digestive juices. The group of molecules entering into the composition of a substance, whether we consider the point chemically or physically, must regulate its general behavior in relation to the agents concerned in digestion as well as in absorption; and hence the agents concerned in digestion, that is to say, the juices effused into the intestinal canal and the organs of absorption, must necessarily stand in a far closer relation to one another than has generally been supposed to be the case. If, for instance, we attempt to classify the articles of food according to the manner in which they are absorbed in the intestinal canal, such an arrangement must coincide pretty closely with the changes which the different articles of diet undergo through the different digestive fluids. Hence it would be by no means an irrational proceeding, if we divided the different articles of food, first, into such as are introduced in a state of solution into the intestinal canal, and consequently are at once diffused and distributed generally through the animal juices; secondly, into such as are rendered soluble by the digestive fluids, and in this condition are, like the former, more or less diffusible; and lastly, into such as, either dissolved or undissolved, must be first metamorphosed by certain digestive fluids, and even if soluble, do not undergo a simple diffusion, but are conveyed by some special routes into the blood and the body generally—by routes on which they undergo certain, although perhaps small changes before their entrance into the blood.

If, therefore, we would study the digestive process in the more highly organized animals, and would not merely consider the food in connection with the juices to whose digestive action it is submitted, but also in reference to its passage into the blood, we must especially take into consideration the organs of digestion, and the laws or conditions under which absorption proceeds. If further it would appear that the mechanical arrangements which are exhibited in the organisms of the higher animals for the purpose of aiding the chemical actions of the digestive fluids, and of promoting the transition of the materials prepared for nutrition into the general mass of the juices, do not directly pertain to the department of physiological chemistry, we must not overlook the fact, that on the one hand, no definite limits can as yet be drawn between the



actions of affinity and purely mechanical molecular motions, and on the other, that a scientific comprehension of the whole process from a purely chemical point of view would be impossible. If we here recur to the previous comparison between the absorbing organs of the intestinal tract and the roots of the higher plants, it at once follows that it is only a system of organs for resorption that can be compared with the roots of plants, and that even here the similarity is less between their mechanical configuration than between the laws according to which the absorption proceeds. These resorbing organs are the minute capillaries which run through the whole intestinal canal, almost from its beginning to its termination.

In the root-fibrils of the higher plants, whose leaves, twigs, stems, and coarser roots are, as is well-known, invested by a membrane that possesses only little permeability for liquids, we find no canals or special organs corresponding to our ordinary ideas of absorption, but rows of cells which from the delicacy of their walls are specially adapted to endosmotic actions. It requires no very profound knowledge of vegetable physiology to comprehend that during the life of a plant, and even for some time after its death, the cells of the root-fibrils continue to have the opportunity of absorbing water and aqueous solutions from the moist soil surrounding them, while they continue to be deprived of this fluid by the cells lying immediately superior to them. If we only consider the enormous evaporating surface which plants present in their leaves and their stomata, and how these organs are exposed to relatively higher degrees of temperature and a perpetually varying atmosphere, we shall readily perceive how the juices occurring in the leaves and in their vicinity gradually become concentrated, and how the cells enclosing them must collapse if those in their immediate vicinity do not transfer to them a portion of their water; their own fluid contents thus becoming more concentrated, and a necessity for a continuous transmission of a similar kind downwards to the cells of the root-fibrils being thus established. At certain periods the formation of organic matter from the previously liquid or gaseous nutrient matter of the plant may also, in no slight degree, contribute to the increased concentration of the cell-juices, and may thus react on the absorption through the roots. Finally, if we bear in mind that the cells contain solutions of protein-substances, dextrin, sugar, &c., substances which possess far less diffusibility than the salts which are contained in the moisture of the soil, we are compelled to admit that plants present all the conditions necessary for calling into play the most active endosmotic currents, and that the terminations of the roots are excellently adapted for the most abundant absorption. The admirable experiments of Hales may serve to corroborate the correctness of the view, that it is only mechanical laws which are here in force, although some individual points still require elucidation in respect to the process of absorption through the roots.

We have already taken an opportunity of remarking that the capillaries, which form a network around the intestinal canal, constitute the medium through which a great part of the fluid portion of the intestinal contents is absorbed. We see that here also the known mechanical laws suffice to explain the absorption by capillaries and veins, and we may



readily convince ourselves that the same laws of endosmosis here come in question which guided us in our explanation of the absorbing capacity of the roots of plants. We here refer less to the systems of cells, between whose contents endosmotic currents are established, than to the cylindrically shaped membranes in which a tolerably concentrated fluid is continually moving forward—an arrangement which is far more favorable to endosmotic motion than the rows of minute closed sacs which constitute the vegetable cells. We have already mentioned (see p. 364) that the blood, as compared with the fluid contents of the intestine, is so concentrated a solution that the chief current must be directed from the intestine towards the capillaries, and that this direction must moreover be always maintained in consequence of the intestinal fluid generally containing free acid. While we must admit, from these few experimental propositions on endosmosis, that this mechanism in the intestinal canal exerts a suction or pump-like action, we must moreover take into account that the denser fluid of the capillaries is constantly flowing onwards, whilst the liquor sanguinis, which is attenuated by endosmosis, is replaced by a fresh and denser blood-wave. Kürschner<sup>1</sup> has demonstrated by an excellent experiment, which easily admits of repetition, the extraordinary manner in which this process favors endosmosis. We must take a cleaned portion of small intestine (that of a rabbit, for instance), and place it in a basin filled with a solution of sulphocyanide of potassium, in such a manner that one end of the intestine hangs over the edge, while, by the aid of a funnel, we gradually pour a moderately dilute solution of perchloride of iron into the other end, so that a current of the solution of the salt of iron continuously runs through the gut lying in the solution of sulphocyanide of potassium. When the two fluids which are separated by the animal membrane are relatively at rest, more of the sulphocyanide of potassium passes into the perchloride of iron than conversely (as may be readily seen by the deeper red color of the fluid on the side of the perchloride of iron); if, however, the solution of the perchloride of iron only run in a slow current, we observe that the solution of sulphocyanide of potassium is far less colored, while if it run through the membranous tube in a very rapid stream, we can scarcely observe even a faint red tint in the solution of sulphocyanide of potassium.

If we observe far more favorable conditions in the sources of absorption in the intestine than in the roots of plants, this is mainly owing to the circumstances by whose reaction the continuance of the absorption is controlled. It need hardly be observed that the rapid absorption of aqueous fluid would very soon thin the blood and the whole mass of the juices to such an extent as finally to put a stop to any further endosmotic action. But the animal, and more especially the human body, presents two means for removing the excess of water from the blood; one of these is tolerably analogous with what occurs in vegetables, whilst the other is peculiar to certain of the higher animals, including man. Like the leaves of plants, the lungs, and in part also the skin of animals, present so large an evaporating surface to the atmosphere, that here, as in the leaves, an extraordinary quantity of water is volatilized. According to Lindenau's approximate calculation, the surface of the lungs of an

<sup>1</sup> Handwörterbuch der Physiologie. Bd. 1, S. 64.



adult man amounts to 2,642 square feet, whilst the surface of the skin cannot be estimated at more than 12 square feet, and even if we assume the area of the much-plaited internal surface of the intestine to measure 24 square feet, the excessive difference between the absorbing and the evaporating surface will be sufficiently manifested to elucidate this admirably contrived mechanism. The evaporating surface is not, however, so readily exposed to the air in animals as in plants; for, even under ordinary circumstances, large portions of the evaporating membranes are so closely approximated and even collapsed together, that they are rendered almost inefficient; for the pure, comparatively dry atmosphere does not come in direct contact with these evaporating surfaces, but in general only a mixture of air considerably impregnated with aqueous vapor. To this we must add, that the ingestion of fluid food is, to a certain extent, a voluntary act in animals, and hence a much larger mass of fluid may be readily conveyed to the intestine than the pulmonary and cutaneous evaporation can remove,—a circumstance which might readily induce a disturbance in the whole mechanism. Finally, we must remember that a large quantity of water is generated in the animal even by its vital processes, which must contribute towards the attenuation of the juices, whilst organic substances are generated in the plant by the decomposition of water, and the juices of the cells are thus rendered more highly concentrated.

Owing to these relations, it may readily and frequently happen that the evaporation is insufficient to counteract the absorption in *the higher animals*; and to meet this condition, we find in these animals a mechanism which we are at present unable to explain, but the purpose of which is to remove, in a fluid condition, the excess of water from the blood. We need scarcely refer here to the part taken by the kidneys in accomplishing this function in the higher animals, although this is absent in birds, which drink only little fluid, whilst they exhale a large quantity of aqueous vapor during rapid evaporation, and in the lower animals, which do not drink, and exist under peculiar relations.

This brief notice of the mechanical relations existing between evaporation and the ingestion of fluids into the animal body, is sufficient to show that by the clearer exposition of several physical laws, with which we are still but imperfectly acquainted, we have made an important advance towards the knowledge of the mechanical effects exhibited in the animal body. The process of absorption appears to be so wonderfully simple in all its details, that we can scarcely comprehend at the first glance why nature has thus superfluously added to the capillaries other and special absorbing vessels, namely, the lacteals. Whilst in a past age the transition of fluids from the intestine to the kidneys was conjectured to take place through "*viæ clandestinæ*," we may now examine the "*viæ apertæ*," through which the liquefied nutrient matter passes into the blood, and which, although not entirely devoid of purpose, appear to us almost superfluous when we remember the power of absorption possessed by the bloodvessels. Our knowledge of this fact should teach us not to overlook those phenomena which we cannot freely deduce from the known propositions of the statics and dynamics of molecular motions, and should remind us that cases very frequently occur in physiological as well as pathological conditions, where the capillaries will appear to be either



unsuited or inadequate for the purpose of absorption, when judged by the endosmotic actions with which we have already become acquainted. It too often happens, that when a beautiful physical discovery has been made, it has been hastily applied to all analogous relations in the living organism, without considering that the sum of the existing conditions must give rise to the most various modifications of the newly discovered physical proposition. Thus, for instance, on considering more carefully the process of resorption through the intestinal veins, we are struck by a succession of contradictions, which do not admit of being referred simply to known endosmotic relations. We shall meet with a considerable number of substances which, although they are extremely soluble, and occur in very dilute solution, are unable to enter directly into the intestinal capillaries, while there are many substances which only reach the blood indirectly through the lacteals. Although such facts as these strike us at the first glance as singular, we must not forget that the relations existing between the dissolved parts of the intestinal contents and the veins of the intestine are less simple than the above description might lead us to infer. These fluids, and the walls of the intestinal capillaries, are separated by at least one dense layer of epithelial cells, which are further surrounded by a more or less dense network of filaments of connective tissue. We are unable at the present time to determine *what* modifications these thick layers of organic matter induce through the results of endosmosis, and consequently also of absorption, but that they do effect such changes has been proved beyond a doubt by numerous experiments on endosmosis, which agree in showing that an endosmotic motion is succeeded by numerous alterations depending upon the thickness of the membrane, its morphological and chemical character, the chemical constitution of the fluids between which the interchange is going on, &c. We know that the difference between animal membranes exerts an essential influence on the endosmotic process, although we are still far from knowing how a mucous membrane, a serous membrane, &c., is able to induce or to modify an endosmotic process. We know, further, that external pressure powerfully influences endosmosis; and Liebig's beautiful investigation affords an example how, in consequence of different pressure, we obtain an opposite result from what the fundamental principles of endosmosis would have led us to expect; but we are not acquainted with any mathematical connection between the amount of the pressure and the velocities of endosmotic motion. The influence exerted by the force of different pressures is of the greatest importance in the process of absorption by the intestinal capillaries, for we need scarcely observe that the pressure to which the blood is exposed in the capillaries must contribute very essentially towards the abundant absorption of matters from the dilute solution of the chyme-constituents. If we know the law of endosmosis, in its simplest expression, we are still totally unable to classify, according to simultaneously prevailing conditions and definite general formulæ, the differences of its actions. Notwithstanding the efforts of the most distinguished inquirers, such as Poisson, Magnus, Brücke, Liebig, Jolly, Ludwig, &c., we have no comprehensive theory of endosmosis; yet without such a theory we are as little able to comprehend the causal connection of the complicated endos-



motie processes exhibited in the living body, as to deduce *à priori* the result of certain endosmotic effects depending upon definite external circumstances. We cannot hope to establish a theory of endosmosis before the laws of the diffusion of liquid fluids discovered by Graham have been elucidated, and the influence of the different nature of porous intermediate walls upon diffusive fluids, that is to say, the relation between diffusion and endosmosis, together with all the circumstances by which the latter is determined, has been adequately investigated. Not until then will it be possible to prove or refute the co-operation of the vital capacities of the organs during absorption. If, however, we still continuously encounter a number of phenomena in the living body, which seem to be at variance with the endosmotic laws with which we are at present acquainted, and if many interesting experiments (as, for instance, those of Böcker<sup>1</sup>) still appear to defy explanation by simple molecular motion, this merely proves that we are still deficient in the physical knowledge necessary for the comprehension, in a physical sense, of the causal connection of such phenomena. We are further taught that, in order adequately to comprehend the mechanism of absorption, our first task ought to be that of accurately examining the physical conditions of endosmotic actions, and comparing them with the relations which exist in the living body. A great step forwards in science is, however, always made, when we arrive at a clear conception of the problems which we are especially called upon to solve.

As we cannot discover the slightest logical justification in the still imperfectly elucidated processes of absorption for the assumption of vital forces having the power of directing one substance hither and another thither, or of taking up what is useful and rejecting what is noxious, we are thrown back upon the proposition from which we started, namely, that the capacity of a substance for absorption stands in the same intimate relation to its chemical quality as all its essential qualities do to one another (compare vol. i. p. 367). If the capacity of a substance for absorption be not a mere irrelevant property, those substances which are exposed to similar relations of absorption must generally present very definite analogies with one another; the capacity for absorption does and must always coincide with certain other qualities in the same substances. We will here only refer, by way of example, to a group of properties exhibited by soluble bodies which stand in the most intimate relation to one another for each individual body. It cannot surely be denied that the degree of solubility of a substance stands in a definite relation to the coefficient of condensation occurring during solution; and who, moreover, could venture to question that the diffusibility of a substance must stand in certain relations of dependence to its solubility? and do we not proclaim our belief in the intimate connection between endosmosis and the diffusion of fluid bodies, when we regret that we should hitherto have followed a wrong direction, and studied the more complicated processes of endosmosis before we had attempted, as Graham has now done, to refer the phenomena of diffusion to definite laws? Our knowledge is indeed not yet so far advanced as to enable us sharply to define these conditions and relations of dependence, or the connection

<sup>1</sup> Rhein. Monatsschrift. 1849, S. 754-759.



existing between these different properties; but, at all events, this much is clearly shown, that all these properties are not merely connected together, but that they are also placed in the most intimate connection or relation with certain fundamental qualities in each individual substance. The undeniable importance which this relation of the integral properties of a substance must exert upon it during its entire passage through the animal body, must serve as our apology for entering somewhat fully into this question. It has generally been customary to understand by the term *solution* simply a uniform distribution of the molecules of the dissolving substance amongst the molecules of the dissolving menstruum; and on this account it has been proposed to apply the term *dissolution*<sup>1</sup> (*Auflösung*) to those cases in which the solution (*Lösung*) is evidently accompanied by simultaneous chemically attracting forces. But, in point of fact, such a distribution of the molecules of a solid body amongst those of a fluid never occurs, as far as our knowledge at present extends, unless we at the same time observe, on comparing the sum of the original volumes of the substances to be mixed with the volume of the mixed body, that the entire volume has been diminished by condensation. The merit of having confirmed this fact appertains to C. Schmidt, who has also determined for many substances the degree of condensation exhibited in their solution in certain quantities of water, that is to say, their coefficients of condensation (see vol. i. p. 409). Schmidt is therefore disposed to assume the existence of a chemical attraction even in the solution, and a "hydratation" in the case of a solution in water. If we conceive the idea of chemical affinity in the more limited sense which has hitherto generally been attached to it in chemistry, and continues for the most part still to prevail, we do not think that the condensation which is here observed affords any stringent proof of the activity of chemical attraction in simple solution. We may certainly give any wider extension that we please to the idea of chemical affinity, but a narrower and stricter limitation of an idea can never do any injury, and cannot in the present case be without a certain significance. The mere condensation of two bodies when they are mixed, is no argument for their chemical combination; for if we are unwilling to admit that the condensation of gases on the surfaces and in the pores of solid bodies presents a proof against this view, Pettenkofer's admirable investigations on metallic alloys must convince us that, in addition to condensation, a development of light may occur, together with an altered condition of many physical properties, without the occurrence of any true chemical combination. An attraction for the water is manifested when a solid body becomes fluid; an attraction is manifested when a solid body, having thus become fluid, undergoes condensation with the water; forces of attraction are manifested when different substances require different periods of time in order to spread or diffuse themselves through a given volume of water.

It might, therefore, be conceived, that the degree of this attraction, manifested in the solution of a solid body in water, would admit of determination, either by comparing together the quantities of the bodies which

<sup>1</sup> [I merely use this word for want of a better. We have no two words which bear precisely the same relation to one another as the two German words.—G. E. D.]



are able to absorb a definite quantity of water, that is to say, by determining the degree of solubility; or by the calculation of the coefficients of condensation, using the quantities of the heat that is developed as a controlling check; or that we might ascertain the readiness with which a substance is disposed to diffuse itself during perfect rest through a larger quantity of water. It might be supposed, that as all these three momenta speak in favor of an attraction between solid and fluid bodies, the degree of this attraction might be calculated from the different quantities obtainable by the three methods of investigation, and that one method must control another. Such, however, is not the case. It must be regarded as one of the theoretical deficiencies of chemistry, that the degree of solubility of substances has not yet admitted of being brought into definite relations to their chemical constitution, or even to any other of their properties. Even the coefficient of condensation cannot be regarded as a standard for the amount of this attraction between water and a solid body; for even in the attraction which regulates the chemical combination, it is of no consequence in reference to the determination of its amount; nor has any definite relation been discovered between the modulus of condensation of these bodies and any one of their integral properties. Even the degree of diffusion of soluble bodies does not readily give the amount of attraction between the solid and the fluid; but its dependence upon weight seems to be very clear from Graham's investigations. Although no definite connection can be established even from these three intimately allied relations between water and soluble bodies, we yet learn from previous observations, that certain relations, which are at all events analogous, may be determined for different well-characterized groups of bodies. These relations, however, acquire so much the higher signification, since they are more especially reflected in the groups of substances which play a considerable part in the animal body, and are thus of great importance in our discrimination of the products of the metamorphosis of matter and of absorption generally. C. Schmidt found that the coefficients for 10 per cent. solutions of chloride of sodium, grape-sugar, and albumen, were 1.505, 0.766, and 0.420. Graham observed the following proportion for the diffusibility of these three substances in 20 per cent. solutions, namely, 100, 45.36, 5.24. The analogy is here very great, although we may not be able to recognize any equal proportion in these numbers. Moreover, Graham's provisional investigations show distinctly enough that there is a definite relation between the diffusibility and the specific weight of the diffusing fluid; hence the coefficient of condensation must have a direct relation to the diffusibility; at any rate we cannot at present overlook this relation. Urea here presents itself as an important exception; the coefficient of condensation of its 10 per cent. solution was found by Schmidt to be less than in any other substance ( $=0.160$ ), while its diffusibility is, according to Graham's determination, exactly equal to that of chloride of sodium.

Owing to the generally recognized and very comprehensive relation existing between the capacities for diffusion and transudation, it will not surprise us to find that the endosmotic equivalents, when calculated by Jolly's provisional method, should correspond tolerably closely with the



equivalents of diffusion. The definite attraction towards water, which we see so variously expressed in the above cases by solid *soluble* substances, and the attraction shown in the last-named case of solid insoluble bodies to water, equally lead us into a domain of inquiry, in which we receive no aid whatever from empirical bases; although the long-known, as well as the more recent investigations regarding hygroscopicity by Blücher,<sup>1</sup> by Schwede,<sup>2</sup> and by Buchheim,<sup>3</sup> and the provisional results obtained by Brücke, Liebig, and Ludwig, agree in showing that even in this relation between the three important bodies already referred to, the most essential differences are observable in respect to the attraction towards water. No physiologist can doubt that all the relations of solid bodies to water must be involved in the explanation of the phenomena of absorption and of the mechanical and chemical metamorphosis of matter; but even if we admit that absorption is nothing more than a function of these various relations, we are not thereby enabled to explain the process of absorption, for we have not yet succeeded in expressing by a mathematically demonstrable formula any of the different kinds of attraction between water and solid bodies, or of establishing the relations which exist amongst them. For how is any explanation practicable, or, in other words, how can we refer phenomena to laws, when we are ignorant of the laws themselves? We may, however, conclude from the scanty facts before us, that the movements of soluble matters within the living organism, and more especially the phenomena of absorption, must be supposed to depend upon certain physical laws. Thus tremble and fall the last feeble supports of the old and naïve belief in an instinct, or a certain spiritual capacity of the absorbing organs. The time may, however, come, and perhaps is not very remote, when we may include amongst "comprehensible ideas" the properties of every substance whose relation to the animal body may be brought into question; when the zoological department of physiological chemistry will no longer be limited to the enumeration of a few qualities of bodies, either arbitrarily or accidentally selected, but will indicate all without exception—the coefficients of condensation of their solutions as well as their absolute solubility, their diffusibility as well as their volatility, their endosmotic as well as their chemical equivalent, their hygroscopicity as well as their fusibility, &c., &c.; and when all these qualities will be elucidated in their most intimate relations to one another. None of these properties should for the time to come be regarded as accidental, for in nature nothing is accidental; the different properties of matter are the necessary result of certain fundamental conditions. When once we shall be able to form a logical judgment of the nature of those substances in which vital phenomena are manifested, when sharply defined ideas of the diversity of matter can aid our judgment regarding the relations of each individual substance to the whole, we may perhaps be able to express, in the simple but clear language of mathematico-physical conception, those conclusions which are deducible from our sensuous observations of the movements of matter in the living body. We shall not on that account be

<sup>1</sup> Pogg. Ann. Bd. 50, S. 541-562.

<sup>2</sup> De Hygroscopicitate, diss. inaug. Dorp. Livon. 1851.

<sup>3</sup> Arch. f. physiol. Heilk. Bd. 12, S. 217-243.



less able to contemplate the wise arrangements of the animal organism, although we may no longer indulge in visionary dreams of the spirituality of matter, or seek to conceal our own inactivity in the incomprehensibility of nature ; for these very arrangements are merely the perfected expression of that which may be attained by the co-operation of simple physical forces, when acting upon differently formed and qualified matter under the most various mechanical conditions.

Although such a future may yet be far distant, and the attainment of such aims may require the most arduous efforts of many zealous laborers in science, we yet know the direction in which our endeavors will secure a satisfactory result in this department of our inquiries. We know what we have to seek, and, emancipated from a belief in supernatural forces of matter, we feel that we are not striving for that which is unattainable, but that every step and every scientific result, once gained, will bring us nearer to the goal of our desires.

This being the point of view from which we began our analyses of the movements of matter in the animal organism, it will not appear singular if we commence the consideration of the process of digestion by establishing the qualities of the objects to be digested. The qualities which principally demand our attention are those which involve the different relations of such matters to water ; for these essentially control the form and the nature of the absorption which the matters undergo in the intestinal canal. Now as all the properties of a substance stand in the most intimate relations to one another, we scarcely think that we shall be in error if we insist upon the existence of a certain relation between the capacity of a substance for absorption and its other relations in the alimentary canal, more especially to the so-called digestive juices. Those substances which have already undergone special molecular displacements before their transition into the mass of the juices, must be conveyed by a different channel from that by which unchanged or only slightly modified substances pass into the blood. We must presume that it depends upon certain more or less prominent properties whether a substance passes directly and without change into the blood, or whether it only reaches its destination by indirect channels and after undergoing various changes. It cannot be owing to accident that those substances which undergo no essential alteration in the intestinal canal from the action of the digestive juices, should be especially qualified for direct absorption through the bloodvessels ; the one qualification does, and must undoubtedly stand in some definite relation to others, although we do not clearly understand its nature. It is not only their saline character which renders the alkaline salts so easy of resorption ; for there are many other salts which are not resorbed by the capillaries, whilst on the other hand, urea, alcohol, and certain poisons, pass with equal or perhaps greater rapidity into the mass of the juices than many of these salts ; nor is it the mere solubility of a substance which influences this easy transition ; but it is the combination of several qualities depending upon the fundamental relations of each individual substance, which induces the capacity for absorption in the same manner as these fundamental relations also influence the resistance against the action of the digestive fluids. When, therefore, we find some poisons rapidly absorbed in the intestinal canal,



while others are not taken up, we should seek for the reason of these facts, not in a certain and definitely limited instinct in the absorbing organs, but in certain definite, although, unfortunately, not perfectly elucidated fundamental relations in these substances. It, therefore, seems most appropriate to divide the objects to be digested into groups, which, instead of being based upon their nutrient power (and this belongs to the theory of dietetics and nutrition), or with regard to their utility or their injuriousness to the living organism, should be arranged according to their digestibility, that is to say, their greater or lesser capacity for being absorbed.

Before we consider those matters individually, whose absorption is solely or principally effected by the capillaries, we must clearly ascertain in what manner a proof can be adduced that a substance does not reach the general mass of the juices through the lymphatics, but passes directly through the capillaries. After it had been anatomically proved that the lymphatics and lacteals only communicate with the bloodvessels through the thoracic duct, the following experiments were instituted. The lymphatics or the thoracic duct having been tied, a substance was introduced into the intestine or into a loop of gut, which could either be easily detected chemically in the blood, or whose passage into the blood might be recognized by certain phenomena of poisoning. Experiments of this nature were undertaken by Magendie,<sup>1</sup> Brodie,<sup>2</sup> Westrumb,<sup>3</sup> Emmert,<sup>4</sup> Segalas,<sup>5</sup> Mayer,<sup>6</sup> Bischoff,<sup>7</sup> v. Dusch,<sup>8</sup> Kürschner,<sup>9</sup> and others, the principal object being to determine as far as possible the capacity of the bloodvessels for resorption. Another method employed to prove the transition of certain substances into the blood without passing into the lymphatics, consisted in examining the blood and the chyle a short time after certain substances had been introduced into the intestinal canal of an animal. It was shown that many of the matters which will subsequently be enumerated, might be found in the blood, but not in the chyle. Experiments of this kind were made by Flandrin,<sup>10</sup> Tiedemann and Gmelin,<sup>11</sup> Mayer,<sup>12</sup> and more recently by Bernard;<sup>13</sup> the latter observer, moreover, essentially improved this method, by seeking in the blood of the portal vein for substances which had been introduced into the intestinal canal. As the lacteals convey the fluids which they contain with comparative slowness, it must be assumed that those substances which reappear very rapidly in the blood and in the excretions must be resorbed through the intestinal capillaries, and not previously through the lacteals. We may therefore, according to Westrumb, Stehberger, and others, recognize matters which are resorbable through the bloodvessels, by the extreme rapidity with which they reappear in the urine or in the pulmonary exhalation.

<sup>1</sup> Précis de Physiologie. T. 2, pp. 203 et 279. <sup>2</sup> Philos. Trans. for 1811, p. 178.

<sup>3</sup> Physiol. Untersuchungen über die Einsaugungskraft der Venen. Hannover, 1825; and Meckel's Arch. Bd. 7, S. 525 u. 540.

<sup>4</sup> Meckel's Arch. Bd. 1, S. 178. <sup>5</sup> Magendie's Journal de Physiologie. T. 2, p. 117.

<sup>6</sup> Meckel's Arch. Bd. 3, S. 485.

<sup>7</sup> Zeitsch. f. rat. Med. Bd. 4, S. 62-71, und Bd. 5, S. 293-305.

<sup>8</sup> Ibid., Vol. 4, pp. 360-374. <sup>9</sup> Handwörterbuch der Physiologie. Bd. 1, S. 48.

<sup>10</sup> Magendie's Journal de Physiologie. T. 13, p. 65.

<sup>11</sup> Versuche über d. Wege, auf welchen Substanzen aus dem Magen und Darmcanal ins Blut gelangen. Heidelberg, 1820.

<sup>12</sup> Op. cit.

<sup>13</sup> L'Union méd. T. 3, pp. 445, 457 et 461.



What are the substances which, according to these experiments, may be directly absorbed by the bloodvessels of the stomach and intestine? Among these numerous and, at first sight, very various matters, we meet, in the first place, with certain tolerably soluble salts, which, whether noxious or innoxious to the animal organism, experience no essential changes whilst within it, and do not exhibit any great affinities towards any constituents of the animal body, namely, all the neutral alkaline salts, whose acid shows no peculiar tendency to enter into special combinations with other matters. To this class, therefore, belong the chlorides of sodium and potassium, iodide and bromide of potassium, the alkaline phosphates, sulphates, chlorates, nitrates, borates, and arsenates, yellow prussiate of potash, sulphocyanide of potassium, and the combinations of the alkalis with non-nitrogenous organic acids. A second group of those substances which are especially resorbed by the intestinal capillaries, are the acids, both mineral and organic. A third group consists of alcohol, ether, wood-spirit, and fusel oil (Schlossberger).<sup>1</sup> A fourth group contains many volatile oils, including the non-oxygenous as well as the oxygenous and sulphurous oils, as, for instance, camphor, oil of radish, oil of assafoetida, &c.; to these we may probably also add, combustible and natural odoriferous substances, as musk and the constituents of Dippel's animal oil, &c. A fifth group comprises several alkaloids, whether volatile or non-volatile, as, for instance, strychnine, brucine, morphine, theïne, nicotine; and finally, there remain to be enumerated certain pigments, which cannot be detected in the chyle, although they may be recognized in the urine, as for instance, the pigment of alkanna, of gamboge, whortleberries, black cherries, rhubarb, logwood, madder, litmus, cochineal, sap-green, and tincture of indigo.

The great diversity of the substances above enumerated would make it appear difficult, if not impossible, to discover in them any common aggregation of properties by which their capacity for absorption through the bloodvessels might be influenced; but certain other matters, which far exceed in solubility many of those already described, do not, as it would appear from direct experiments, show the slightest disposition to enter through the capillaries into the blood, although they are very readily absorbed by the lymphatics, or else, notwithstanding their great solubility, traverse the entire intestinal tract without being resorbed. We shall subsequently become better acquainted with those substances which are exclusively or principally absorbed by the lacteals, whilst in the present place we will simply refer to such extremely soluble matters as gum, turmeric, &c., which are not absorbed from the intestinal canal either by the bloodvessels or the lymphatics. To the last-named substances belong both the curare-veneno (which is probably identical with the woorara) and the poison of serpents. If from this we were to conclude, as has actually been done, that nature in her wisdom has closed the passage of this poison to the blood by both channels, the fact would scarcely impress us very powerfully, when we remembered that all access to the capillaries or the chyle was alike forbidden to the comparatively harmless gum or turmeric as well as to serpents' poison, which could only rarely find its way into the stomach, whilst it opposes no

<sup>1</sup> Arch. f. physiol. Heilk. Bd. 9, S. 267.



hindrance to the absorption of other poisons which rarely enter wounds but are of common occurrence in the intestine. These considerations, together with the experiments of Boussingault and Bernard (which certainly still require confirmation), according to which an animal membrane that readily permits the endosmotic passage of saline solutions is completely impervious to curarine, emulsin, and diastase, sufficiently show that the law of a physical necessity is here involved. Considering the striking diversity of the above-named materials, we may still hope, notwithstanding our slight knowledge of the laws of diffusion and of endosmosis through membranes, to discover certain properties common to all these matters, on which we may suppose this great capacity for absorption to depend. It is generally admitted that it is only soluble substances which admit of resorption; but the degree of solubility in these substances is so different, that if there were not a number of very soluble bodies which were not capable of resorption, we yet could not ascribe to their solubility alone the capacity which they exhibit of being absorbed by the capillaries. Unfortunately the greater number of these substances have as yet been so imperfectly investigated in reference to their capacity for diffusion and to the endosmotic equivalent which is undoubtedly connected with it, that we are still unable to demonstrate the dependence of their capacity for absorption upon these properties; but the analogy between substances found by Graham to be very diffusible and many of the bodies already referred to, lends the greater probability to our conjecture; for we find that those substances which are very little disposed to be absorbed through the veins, are precisely those which Graham found relatively little capable of diffusion, as, for instance, albumen, and in part also, sugar.

Considering the near relation in which the volatility of these substances undoubtedly stands to their diffusibility, we can hardly wonder that there should be so many volatile matters in the class of easily resorbable bodies. The third and fourth groups of these transudable substances especially belong to this class; but there is no group in which we more distinctly perceive the dependence of resorbability upon these physical properties than in the second one; for Graham's experiments on diffusion, as well as the numerous endosmotic experiments which have been made with the acids, explain their easy transition into the capillaries. If we could suppose that the diffusibility and similar properties of a substance were alone dependent upon certain fundamental properties pertaining to it, we should find a certain simplicity in the form of composition of most of the above groups. These substances have either a mere binary composition, or, at all events, like the haloid bases and alkaloids, they have, according to the most recent chemical investigations, a very simple constitution, approximating to the binary law; while such soluble matters as do not belong to the above groups, as albumen, emulsin, gum, and even sugar, have hitherto baffled all the efforts of chemists to comprehend their composition in accordance with the ordinary views of chemical affinity or polarity.

Although we have endeavored in the above remarks to consider from purely physical points of view the absorbing capacity of the capillaries and the capability of certain substances to be absorbed by them, we hope



that our feeble attempt will not be so far misconceived as to leave the impression that we would wish to characterize the process operating in the animal body as actually physical in its nature. We are, on the contrary, far from entertaining such an opinion; for the physical facts presented to our notice do not, in our opinion, present sufficiently strong indications to enable us to establish with completeness any such purely mechanical mode of consideration; we will therefore merely repeat, that the simplicity of the physical principles of explanation are better adapted to give a safe direction to our conjectures and further investigations, than if we were credulously to trust to a transcendental mode of reasoning, without the aid of earnest and profound reflection.

In passing from these provisional remarks to the process of digestion, and the comportment of different substances while subjected to this process, we have nothing to add to the observations already made, excepting to remark that we shall not here have to notice the digestive fluids with which these groups of substances are brought in contact, since these substances pass from the intestinal canal into the mass of the juices in the same unchanged state in which they entered it. The combinations into which some of these substances enter with acids during the process of digestion, can scarcely come within the scope of the present inquiry, since no essential change is produced by their action.

In turning to the consideration of the individual objects of digestion, our attention is in the first place directed to a group of substances which have been distinguished by the irrational name of the *carbo-hydrates*, amongst which are included cellulose, the different kinds of gum, starch, inulin, lichenin, and the different kinds of sugar.

It must be observed, in reference to *cellulose* or the substance of the vegetable cell, that it belongs to those substances which resist all the digestive fluids and other solvents; and, on account of this property, all those vegetable substances which essentially consist of this substance reappear unchanged in the excrements of herbivorous and omnivorous animals. It must, however, be borne in mind that this substance (which Mitscherlich,<sup>1</sup> in his more recent experiments, found to be perfectly isomeric with starch, and is represented by the formula  $C_{12}H_{10}O_{10}$ , although its composition had been previously assumed by Mulder to be  $C_{24}H_{21}O_{21}$ ) is very frequently found to be incrustated with some other perfectly insoluble substance, such as lignin or suberin. When, as in the case of the Beaver, we find the whole stomach, and more especially the cæcum, plugged, as it were, with fragments of wood and bark, without being able at the same time to detect any easily soluble nutrient substances—as, indeed, E. H. Weber<sup>2</sup> and myself have frequently observed—we can scarcely avoid adopting the opinion that the digestive juices, at all events, of these animals, are capable of exerting a metamorphic and solvent action upon cellulose. This view of the subject seems also to gain confirmation from a circumstance especially noticed by E. H. Weber,<sup>3</sup> that in the beaver, those organs whose secretions more especially contribute towards the metamorphosis of the carbo-hydrates are developed in a remarkable degree; thus, for instance, the salivary glands are exceedingly large in

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 75, S. 305–314.

<sup>2</sup> Ber. d. königl. sächs. Gesellschaft d. Wiss. 1850, S. 192.

<sup>3</sup> Ibid. p. 193.



the Beaver, amounting, according to Weber's estimate, to 1-118th of the whole weight of the body, whilst in man, for instance, they do not exceed the 1-895th part of the entire weight. In the same manner the pancreas is remarkably voluminous in the Beaver (Weber found that it measured 18 inches in the case of a tolerably large animal). It seems more doubtful, whether the well-known large gastric gland, which is peculiar to the Beaver, bears a direct relation to the animal's digestion of cellulose.

If we should be disposed to ascribe to the secretions of this apparatus, which exert so powerful an action on starch, the property of converting cellulose into dextrin and sugar, it must, at least, be admitted that the chemical relations of cellulose to certain solvent and metamorphic agents are in no respect opposed to this view. It is a well-known fact, which was first observed by Schleiden, and has been admirably elucidated by Mulder, that cellulose, by treatment with the second or third hydrate of sulphuric acid, is converted into a substance very similar to starch, and which is colored blue under the action of iodine. According to Mulder, syrupy phosphoric acid may, in such cases, be used in place of the sulphuric acid. Notwithstanding the acid nature of the contents of the stomachs of Beavers, and however much this large gastric gland seems to imply that the free acid is destined for the metamorphosis of the cellulose, the acids which occur here are always too much diluted to justify us in ascribing to them such a metamorphic action. At any rate, on accurate micro-chemical investigation of the fragments of wood, bast, and bark found in the stomach and duodenum of the Beaver, I have never been able to perceive that the addition of iodine induced a blue coloration in the cellulose fibres and cells, although this color always appeared very beautifully after repeated applications of sulphuric acid. The alkaline juices of the salivary glands, the pancreas, and the cæcal glands, probably exert a stronger influence on the conversion of cellulose into starch, and its further decomposition into sugar, than the acid juices of the stomach. For the admirable experiments of Mitscherlich<sup>1</sup> show us that even very dilute alkaline solutions act upon cellulose, whilst concentrated solutions act more readily and completely than concentrated acids in converting this substance into starch. Hence we must suppose that the greater part of the cellulose undergoes its metamorphosis and solution in the lower portion of the small intestine and in the large intestine, because the contents of these parts in the Beaver exhibit a strongly alkaline reaction. We must here also notice a conjecture, which has derived some degree of support from another beautiful experiment by Mitscherlich. There exists a peculiar ferment for cellulose which is generated during the putrefaction of potatoes, and destroys the cellulose-cells without attacking the starch. Since, moreover, it is impossible to assume that the conversion of starch into dextrin and sugar by the saliva and pancreatic juice can take place without a special ferment, some probability certainly seems to attach itself to the conjecture that a ferment which can decompose cellulose also exists in these juices of the Beaver, and co-operates simultaneously with the alkali in the digestion of this substance. But although anatomical facts, as well as chemical experiments, speak in favor of the digestibility of cellulose (at

<sup>1</sup> Op. cit.



least, in the case of the Beaver), we cannot regard the view as perfectly proved until more direct proof of its correctness can be adduced. With a view of elucidating this question, I have frequently made a microscopical and micro-chemical examination of the contents of the small and large intestine of the Beaver, but I have unfortunately never been able to determine with certainty that the cellulose-cells obtained from thence exhibited chemical corrosion, or had been converted into a starch-like substance.

*Gum* is another carbo-hydrate, concerning whose uses in the animal organism, notwithstanding its solubility, there is still considerable doubt.

Although this substance is of such rare occurrence in the ordinary nutrient matters, even of the herbivora, that its co-operation in the process of digestion, and its application to the metamorphosis of matter, can be of no great importance, its frequent therapeutical application as a dietetic remedy would entitle it to some degree of notice, even if its peculiar chemical and physiological relations did not demand our attention. In the obscurity which still involves the question regarding the digestion of gum, three possible modes of explanation present themselves, namely: that it is converted into sugar before its resorption; that it is resorbed directly and without alteration; or lastly, that it is not at all resorbed, and is consequently completely eliminated with the solid excrements. The first of these hypotheses is entirely disposed of by the result of our former experiments. We certainly know that gum, like other carbo-hydrates, is converted into grape-sugar after prolonged digestion in the dilute mineral acids; but all experiments which have hitherto been made to convert gum into sugar, or into any other substance, by means of the digestive fluids, such as natural or artificial gastric juice, mixed saliva, or pancreatic juice, have yielded thoroughly negative results. Frerichs<sup>1</sup> found that gum remained entirely unchanged when digested as long as 48 hours with saliva and gastric juice, nor was it altered after having remained for 3 hours in the stomach of a dog, both when it was introduced through a fistulous opening and by the mouth. Blondlot<sup>2</sup> instituted a similar experiment. I found<sup>3</sup> that the gum not only always remained unchanged during lactic acid fermentation, and during the conversion of starch into sugar by diastase, saliva, or pancreatic juice, but also convinced myself, by parallel experiments, that the presence of this body invariably retarded that process. I found, from quantitative determinations, that after the gum had been digested for three or four days in a fermenting or digesting mixture, nearly the original quantity might be again recovered. These experiments, therefore, render it very improbable that even a small portion of the gum is converted into sugar during digestion. If, then, gum be actually subservient to the purposes of animal life, it only remains to be assumed that this body may be resorbed in an unchanged state from the alimentary canal, either by the bloodvessels or the lacteals. Tiedemann and Gmelin<sup>4</sup> fed a goose exclusively on gum for sixteen days, when it died; they found in the excrements unchanged gum, which was also present in

<sup>1</sup> Handwörterbuch der Physiologie. Bd. 3, Abth. 1, S. 806.

<sup>2</sup> Traité de la Digestion, p. 297.

<sup>3</sup> Simon's Arch. f. Chem. u. Mikrosk. Bd. 1, S. 76-82.

<sup>4</sup> Verdauung nach Versuchen. Bd. 1, S. 186.



the acidly reacting contents of the small and large intestine. Boussingault<sup>1</sup> caused a duck to swallow 50 grammes of gum-arabic, and in the course of nine hours 46 grammes were recovered from the excrements. I daily injected into the stomach of an old rabbit, which was otherwise fed on cabbage-leaves, 10 grammes of gum-arabic dissolved in 90 parts of water; the excrements retained their ordinary form and consistence, but gum was easily recognized in them. The daily urine was collected, strongly concentrated, and treated with absolute alcohol, and the undissolved residue was then extracted with cold water. The aqueous solution, even in its most concentrated state, did not give any reaction corresponding to the presence of gum, either when treated with silicate of potash, with borax, or with sulphate of iron (Lassaigne).<sup>2</sup> The animal was killed at the end of three days, four hours after it had taken the last dose of gum (10 grammes at a time), but no trace of gum could be discovered by means of these reagents, either in the very small quantity of chyle that was collected from the thoracic duct, or in the blood after the coagulation of all the coagulable matters and the exhibition of the aqueous extract. We cannot doubt, therefore, that even if this substance admitted of resorption, it must only pass in extremely small quantities, and very slowly, into the mass of the juices; nor can we assume the probability of its rapid conversion in the blood, since all chemical experiments prove that gum is far less easily decomposed than other carbohydrates, as, for instance, sugar, which, notwithstanding its ready decomposition, may yet be detected in the blood.

If we are not disposed to believe that the absorbing organs possess the property of resisting the absorption of this extremely soluble substance, the question arises, whether the facts hitherto ascertained from physical experiments on the diffusion or transudation of gum, afford any explanation of the above-named physiological experiments. According to Graham, the diffusibility of gum is only half that of starch-sugar, and four or five times less than that of chloride of sodium, whilst, on the other hand, it is more than four times greater than that of albumen. Jolly found that the endosmotic equivalent of gum was considerably higher than that of sugar. The simplest endosmotic experiments with gum are, however, sufficient to show that animal membranes are not impermeable to that substance. Physical experiments only prove, therefore, that gum penetrates through animal membranes less readily than many other substances; and it only remains to show by further experiments what are the mechanical conditions which cause so small a portion of gum to pass from the intestinal canal into the blood; for the experiments which I have already mentioned, do not by any means lead us to the conclusion that positively no gum is absorbed, for silicate of potash, borax, and sulphate of iron are such slightly sensitive reagents, that when applied to a mixture of organic bodies (such as we have here to deal with), they may fail in detecting very considerable quantities of gum. It has also been asserted that turmeric is not resorbed in the intestine; but in my experiments I have detected small quantities of it in the blood of rabbits, which had been made to take daily a concen-

<sup>1</sup> *Ann. de Chim. et de Phys.* 3 Sér. T. 18, p. 444.

<sup>2</sup> *Journ. de Chim. méd.* 3 Sér. T. 7, pp. 580-582.



trated solution of this pigment. It must, for the present, remain undecided whether there is any substance soluble in water, for which the ordinary animal membranes would be absolutely impermeable; for Cl. Bernard's experiment, which appeared to show that the curara poison could not penetrate through an animal bladder, requires to be repeated, whilst Bernard is no doubt in error, when he believes that he has convinced himself that emulsin and diastase are incapable of penetrating animal membranes; these bodies, like albumen, undoubtedly, however, possess only a small capacity for penetrating animal membranes. With regard to the curara poison, its chemical qualities have been so imperfectly investigated, that we are not yet justified in assuming anything more than that the reason why it exerts no poisonous actions in the intestinal canal may probably be due either to the fact that it undergoes decomposition in that region, or that it enters into combinations which are innoxious to the animal organism. If, moreover, gum, emulsin, diastase, and curara are, in point of fact, resorbed in much smaller quantities than we should have expected from endosmotic experiments, we must not regard it as impossible that the physical constitution of the intestinal coats may here exert a special influence; for we know that endosmotic experiments often yield different results, according as the mucous or the serous surface of a membrane be turned to the salt that is to be diffused, and that (for example) membranes of caoutchouc and animal membranes act quite differently from one another in regard to water and alcohol. All such relations as these should be clearly comprehended before we venture to form a definite opinion with respect to the behavior of gum in the intestinal canal, or to assume the existence of vital forces opposing its absorption. At present, therefore, we know nothing more than that the *Potiones gummosæ*, which are such favorite medicines with the physicians of the rational school, can yield to the animal organism only an extremely small quantity of material, and *that* only of a nature to support the respiratory process; and that their uses—if they are of any use—can be merely negative in acute diseases.

As an object of food, *starch* is well known to be the most important of all the carbo-hydrates; we know that it is one of those substances which must undergo a preliminary metamorphosis in order to be resorbed, that it is converted into dextrin and sugar (lactic acid being produced only in a limited degree), and finally, that the saliva and pancreatic juice are the means by which this rearrangement is effected in the atoms of starch. We have so fully discussed these points in the first volume, when treating of the functions of the saliva (pp. 430–438) and of the pancreatic juice (p. 510), that very few additional remarks are necessary.

If we briefly review the history of starch within the animal organism, commencing with its introduction into the mouth, we find that in this cavity it is more or less impregnated with saliva, according to the intensity of the movements of mastication, its own dryness, and other circumstances. Powerfully as normal saliva occasions the transformation of boiled starch into sugar, its influence on the raw starch during the short time that each morsel remains in the mouth must be extremely slight. In the ruminating animals, on the other hand, where the food is for a



long time retained in the paunch, and where, from the continuous flow of saliva, it is exposed to the prolonged action of this secretion, a great part of the starch contained in the food must certainly be metamorphosed; and the same must be the case in the crop of the bird. In all other animals, the greater part of the starch passes unchanged into the stomach, where the further action of the saliva upon it is, to a certain degree, suspended by the gastric juice, when secreted in sufficient quantity. After a due sojourn in the stomach, this substance passes into the duodenum, where it is brought in contact with the powerfully acting pancreatic juice, and the commencement of its metamorphosis ensues. Towards the ileum the pancreatic juice disappears, and in its place we find the intestinal juice, which acts somewhat less energetically in effecting the metamorphosis of the starch. The conversion of the starch into sugar gradually follows; the starch-granules become softened on their surface, and, as they dissolve, become converted into dextrin and sugar. Individual lamellæ become separated from the granules, and undergo more or less disintegration, isolated shreds being often perceptible by the microscope after the application of iodine. The farther the starch passes onwards from the jejunum into the ileum, so much the smaller do the granules appear in consequence of the above-mentioned solution of their surface. The enormous development of the cæcum in herbivorous animals, seems to indicate that the amylaceous matters are here again exposed to the action of a ferment which exerts some change upon them; but the experiments which have been hitherto made afford no evidence either in favor of or against the view that the glandular secretions which are there poured forth, actually yield such a ferment. We know that the first product of the decomposition of starch, dextrin, is so rapidly converted into sugar, that we only rarely find it in the intestine, and then merely in small quantities. Since, however, we always find sugar in the intestine in association with starch, it is probable that the dextrin, as such, is, like gum, absorbed only in very small quantities. Although it can scarcely be doubted that a great part of the starch taken with the food, passes from the intestine into the blood in the form of sugar, yet we may very readily convince ourselves that a by no means inconsiderable quantity of starch is metamorphosed in the small intestine into lactic acid, and in its lower portions, but especially in the large intestine, into butyric acid, and in these forms is more rapidly absorbed than as sugar.

*Inulin* is affected by the digestive fluids in precisely the same manner as starch: indeed it may be concluded, from the investigations which I have instituted (which, however, were not of an accurate quantitative character), that this substance undergoes even a more rapid metamorphosis than ordinary starch.

We now proceed to the consideration of *sugar*, and especially of *glucose*, which, while it certainly demands our notice in consequence of its frequent occurrence in articles of vegetable diet, is of greater importance from its being, as we have just seen, the most ordinary and normal metamorphic product of that most important non-nitrogenous nutrient matter, starch. The question here at once presents itself,—does true glucose undergo any further changes during the digestion of other sub-



stances or when digested alone, or is it resorbed unchanged? And after this question has been answered, the following suggests itself,—by what organs is the glucose absorbed from the intestinal canal?

Many references have been made in the preceding pages to the metamorphosis of glucose into lactic acid, butyric acid, and fat; and hence we should scarcely have occasion to refer more fully to the subject if we had not here to determine, at all events approximately, the magnitude or extent of these metamorphoses. It is commonly assumed that the sugar which is introduced into, or first formed within the intestinal canal is absorbed without further change, and very speedily, by the capillaries,—a view which seems to us very far from being satisfactorily established. That a portion of the sugar before it is resorbed undergoes one or other of these changes is almost generally acknowledged, but no direct investigations have as yet been made regarding the quantity that is thus altered, and it has commonly been regarded as extremely small. The reason why it has been supposed that only a small quantity of sugar is converted into lactic acid is probably dependent in part on the observed fact that the acid reaction of the intestinal contents is not very great, and in part on the belief that sugar which is so readily soluble, and is regarded as highly diffusible (not being found in large quantities even in the small intestine) must be resorbed with extraordinary rapidity. Since, as has been observed, direct observations on the quantity of the lactic acid formed in the intestinal canal are not practicable, we must look around us for other positive facts, which may support either the one or the other view; such, for instance, as, if we could accurately determine it, the proportion of sugar that passes in a definite time into the blood or into the chyle, as its quantity in these fluids might be compared with the quantity of the sugar-yielding carbo-hydrate taken with the food. Although such calculations certainly might be made from the investigations previously in our possession, yet I preferred instituting certain experiments bearing directly on this question.<sup>1</sup>

The experiments were made on horses, whose food consisted of a mixture of equal parts of boiled and raw potato-starch; this was mixed with about one-twelfth of rye-bran, and formed into balls, of which from 2,000 to 3,000 grammes were daily given to the horses at intervals of two hours. The quantity of starch in the dried balls was determined by the method of Liebig and Horsford. They had, additionally, about 1 kilogramme [nearly 2·2 lbs.] of sugar in the 24 hours. This feeding was continued for three days, and on the last day the amount of starch in the excrements discharged in 24 hours was ascertained by digestion with dilute sulphuric acid, and the subsequent determination of the carbonic acid developed by fermentation. The animals were killed about an hour or an hour and a half after the last feeding, when the intestinal contents were examined, and the chyle as well as the portal blood was submitted to a careful analysis in reference to the quantity of sugar contained in those fluids.

The horse A took in the last 24 hours 1584 grammes of dry starch in balls; as 234 grammes were found in the excrements, the animal had consumed 1350 grammes in 24 hours; consequently 1500 grammes of

<sup>1</sup> Ber. der k. sächs. Gesellsch. der Wiss. Jahrg. 1850, S. 130.



sugar must have been resorbed [nine parts of starch being converted into ten of glucose or grape-sugar].

The horse B consumed 1235.3 grammes of starch on the third day of the experiment; as 321.5 grammes of starch were found in the excrements, 914.8 grammes of this substance, or 1016.4 grammes of sugar, must have been resorbed.

The horse C took 1871.8 grammes of starch on the last day of the experiment, and 413.2 grammes were found in the excrements; hence 1458.6 grammes of starch, or 1620.6 of sugar, must have been absorbed into the mass of the juices.

Hence in these animals, if the starch was converted solely into sugar, 1382 grammes of sugar were, on an average, formed in 24 hours, and transmitted into the bloodvessels and lacteals. As the animals were fed at short intervals of 2 hours, we may assume that 57.58 grammes passed into the chyle or into the portal blood in 1 hour, and consequently nearly 1 gramme in 1 minute. Now the movement of the fluid is not so rapid either in the lacteals or in the portal vein as to lead to the belief that the absorbed sugar is too quickly removed from the neighborhood of the intestine, or from the abdomen generally, to admit of this substance being qualitatively, if not quantitatively, determined in one of these fluids.

It has been formerly mentioned that it was only sometimes that I could obtain even traces of sugar in the portal blood of horses, there often being no indication of this substance. If previous observers believed that they had detected sugar in the blood of this vessel, and found that the properties of this fluid generally were different from those which I have described, the reason of these discrepancies is very probably to be sought in the methods of obtaining the portal blood. The proper method of proceeding is not at first to lay open the whole abdomen, and then to make a regular dissection of the portal vein; for the blood of the hepatic veins in this case regurgitates, and a portion of it makes its way into the branches of the portal vein; and as the hepatic blood presents peculiarities in its morphological elements, and contains sugar, the experiment must be more or less marred. We should make only a small opening in the abdominal walls, and reaching the portal vein as speedily as possible, we should tie it at the point where it enters the liver. Even Bernard,<sup>1</sup> when he collected portal blood in this manner, never found a trace of sugar in it. In procuring the portal blood of the horses in these experiments, I guarded against the above-named source of error, and I never found sugar or even a trace of dextrin in it.

Although I have often previously stated the procedure which I adopt for the recognition of sugar, yet I would here remark, in consequence of the importance of the case, that I obtained from one of the horses 69.4, from another 53.3, and from the third 77.2 grammes of portal blood, and that I employed at least two-thirds of it for the determination of the sugar. The following was the method of proceeding: The blood, after being neutralized with dilute acid and treated with four times its quantity of water, was coagulated by heat, the expressed and filtered fluid was evaporated, the residue extracted with spirit of 85%, and the

<sup>1</sup> Nouvelle fonction du foie, &c. Paris, 1853, p. 23.



spirituous fluid precipitated by an alcoholic solution of potash. The portion insoluble in water was mixed with a little water, filtered, treated with dilute sulphuric acid, for the purpose of effecting the metamorphosis of any dextrin that might be present, and then examined for sugar.

We feel inclined to regard as incapable of proof these singular facts (it being in direct opposition to the previously received belief, that the sugar passes with facility into the blood of the intestinal veins), and either to doubt the accuracy of the chemical analysis, or to get over the difficulty by assuming that there is an extremely rapid decomposition of the sugar in the blood. With regard to the first objection, which might be, and actually has been, brought against this experiment, scarcely a larger quantity of blood is necessary for the quantitative determination of sugar in the normal fluid than was employed for this purpose in the above experiments; but there must in every case be more sugar in the blood of the portal than in that of any other vein, and its existence there could not be altogether overlooked. If we should further assume that the sugar absorbed by the intestinal capillaries is rapidly decomposed before it can reach the trunk of the portal vein, we must produce evidence that the decomposition of sugar proceeds far more rapidly in the blood of the intestinal veins than in any other blood. We have already seen in another place, that glucose, like all other kinds of sugar, when it is injected into a vein, very soon reappears unchanged in the urine; even when very small quantities of glucose are injected, it admits of easy recognition in that fluid. Since it has been maintained that portal blood is rich in alkaline carbonates, we might be led to believe that it was the presence of the alkali which caused a more rapid decomposition of the sugar in the portal than in any other blood. This abundance of alkalies in the portal blood might probably give some support to this view, if it did not happen to be a mere incidental circumstance, that is to say, if it were constantly present in portal blood without reference to the nature of the food which the animal had previously taken; this, however, is by no means the case. In my latter investigations regarding the composition of the blood in different vessels, I have on several occasions (after feeding the animal abundantly on bran) found the serum of the portal blood even far poorer in salts than the serum obtained from the blood of the arteries or of the *vena cava*; thus, for instance, in one case the serum of the arterial blood contained 0.853%, that of the blood of the *vena cava* 0.887%, and that of the portal vein 0.521% of salts; these numbers calculated in relation to the solid residue of the serum in each case give a similar result; in the solid residue of the serum of arterial blood the salts amount to 8.392%, and in that of the *vena cava* to 8.501%, while in that of the portal vein they only reach 4.895%. Even in this portal blood, which was so poor in salts, not a trace of sugar could be found.

It has been already mentioned (p. 357) that sugar, even when injected with one or two equivalent of alkaline carbonates, still passes into the urine.

Since, therefore, it appears probable that only little sugar is resorbed by the bloodvessels of the intestine, the question suggests itself, whether the sugar is not probably taken up in so much the larger quantity by the lacteals. But my earlier observations, as well as those recently



made on the chyle of the above-mentioned three horses, are opposed to this supposition. It has been already mentioned (vol. ii. p. 21) that it was only after the use of highly amylaceous fodder that I could detect small quantities of sugar in the chyle of horses, and in my latest experiments with the three horses, I arrived at no result which would favor the view that the sugar is absorbed by the lacteals. If we assume that the average quantity of chyle which is poured into the subclavian vein of the horse in 24 hours amounts to 50 kilogrammes [110·23lbs.], as might be inferred from what has been already stated (see vol. ii. p. 25), then in these cases, when digestion was constantly going on, 37·4 grammes of chyle must have passed through the thoracic duct in one minute. The quantities of chyle which I obtained from the thoracic duct in the horses A, B, and C, was 22·567, 18·184, and 25·616 grammes respectively. Now, according to our calculations, we see that about 1 gramme of sugar was resorbed by each horse in 1 minute. If, therefore, the sugar has neither been taken up by the bloodvessels, nor has been previously metamorphosed in the intestine, there must be about 1 gramme of sugar in 37·4 grammes of chyle; but if only 0·1 of a gramme of sugar were contained in this quantity of chyle, it would readily be detected if we had from 18 to 25 grammes of the fluid for the purpose of analysis. In the chyle of the horse A only 0·029% of sugar was found, and in that of the horses B and C even less. The quantity of sugar passing into the lacteals is consequently very inconsiderable.

Do we then find in the intestinal canal itself any proof that the absorption of sugar takes place so rapidly as is commonly believed to be the case? Direct experiments, which I have instituted with the view of determining this point, do not by any means support the above view. From 1 to 2 grammes of sugar obtained from starch (dissolved in 5, 10, 15, and 30 parts of water) were injected into the stomachs of rabbits weighing from 1·5 to 2·5 kilogrammes [from 3·3 to 5·5 lbs.], and the animals (which had been allowed to take solid food both immediately before and after the injection) were respectively killed half an hour, 1 hour, and 2 hours afterwards. Sugar could always be still found in the stomach, the duodenum, and the jejunum; in the animal that was killed after one hour, sugar was still found in the lowermost part of the ileum; if the animal were killed in 1 hour after taking 2 grammes of sugar, this substance was found in no inconsiderable quantity in the cæcum. The contents of the duodenum and jejunum, which were generally tolerably fluid and even limpid, had a very strong acid reaction, which was less strongly manifested, but was still very distinct, in the contents of the ileum. The contents of the cæcum always presented a very strong acid reaction. Further, if rabbits were fed for several days solely with red beet, or solely with carrots, sugar (namely glucose) was found not only in the stomach but also in the duodenum in very considerable quantities; in the jejunum the quantity of sugar that could be detected was smaller, and at the lower part of the ileum this substance had entirely disappeared. The contents of the stomach exhibited a strong acid reaction, and those of the duodenum were rather less decidedly acid; on the other hand, the contents of the jejunum reddened litmus paper very intensely, while those of the ileum were less acid, although stronger than those of the cæcum.



These observations which were formerly made by myself on cats, horses, and rabbits, have recently been confirmed by numerous investigations conducted in my laboratory, partly by Uhle<sup>1</sup> and partly by von Becker.<sup>2</sup>

It needs no circumstantial numerical proof, which indeed could never be decisive with such uncertain grounds of support, to show that the gastric juice cannot be the cause of this acid reaction; on this point we would rather trust to the evidence afforded by well-known experiments, which show that even after a flesh diet, which gives an additional quantity of free acid to the gastric juice, the acid reaction often entirely disappears in the jejunum. Putting aside altogether my own observations and experiments, I would here refer exclusively to the very admirable investigations of Bidder and Schmidt<sup>3</sup> on this subject. After the common biliary and the pancreatic duct had been tied in a young dog, an intestinal fistula was formed, which on the subsequent dissection of the animal was found to communicate with the end of the upper third of the small intestine. A week after the operation, when the wound might be regarded as healed, and all general irritation seemed to have subsided, the following experiments were instituted on the animal: After feeding the dog with flesh, a grayish-white mass, with a strongly alkaline reaction, issued from the fistula; in this case, therefore, the free acid of the gastric juice and that of the flesh itself was not only neutralized, but so much intestinal juice was secreted that the alkalinity preponderated. In this case the alkalinity cannot be referred to a formation of ammonia consequent on putrefaction, which might perhaps have ensued from the suspension of the flow of the bile; for when the bile and pancreatic juice are allowed free access to the intestine, we likewise find the chyme in the jejunum and ileum equally alkaline. This much, however, may be inferred from the above experiment, that the free acid which we observe in the whole of the small intestine during a vegetable non-acid diet, or after the use of sugar, does not depend upon the gastric juice, but must have its source in the food itself.

If the fact be confirmed that a portion of the starch and sugar in the intestinal canal be converted into acid, we have then to ascertain what substance, or what constituent of the intestinal contents it is which induces this change. We have seen that when the saliva, gastric juice, pancreatic fluid, and bile are totally excluded, the intestinal juice itself is able to effect the metamorphosis of starch into sugar, and of the latter into lactic acid. Moreover, starch was observed by C. Schmidt to be completely changed by the intestinal juice into sugar in 30 minutes, and into lactic acid in 5 or 6 hours. While we do not mean to deny that gastric juice (Bouchardat and Sandras), bile (van den Broek) or other fluids that make their way into the stomach, or, indeed, that even normal mucus, may not possess this property, or, at all events, may not attain it at the temperature of the animal body, this, at all events, is certain, that all these materials collectively do not so rapidly excite the lactic acid fermentation as the special intestinal juice.

I agree with Frerichs and Schmidt that the pure acid gastric juice of

<sup>1</sup> Diss. inaug. Lips. 1852.

<sup>2</sup> Zeitschr. f. wiss. Zoologie. 1853, Bd. 5, S. 123.

<sup>3</sup> Verdauungssäfte und Stoffwechsel. Mitau, 1852, S. 271 u. 281.



dogs, in the state in which we obtain it from gastric fistulæ, does not convert sugar into lactic acid even after several hours' digestion; but if the gastric juice be mixed with much saliva, or if we add to it a small piece of the glandular coat of the stomach of the pig, lactic acid may certainly be detected in the mixture after 3 or 4 hours. Hence we believe that, at all events at the present time, the possibility of a formation of lactic acid in the stomach cannot be altogether denied, although it is not at all probable that, under ordinary conditions, any appreciable quantity of starch or sugar undergoes this change.

If we allow saliva to remain in contact with sugar of milk, or even with starch, at a temperature of from  $30^{\circ}$  to  $40^{\circ}$ , a little free acid is certainly formed, but so long a time (often from 16 to 32 hours) is required for its development, as almost to exclude the idea that the saliva in any degree contributes to the conversion of the sugar into lactic acid.

Heintz and van den Broek<sup>1</sup> support the view that the bile contributes in a special manner to the conversion of the sugar into lactic acid, and the well-known observation, that we generally find the contents of the duodenum more intensely acid than those either of the stomach or of the jejunum, favors this view; but, notwithstanding this, I cannot unconditionally adopt this opinion, for altogether independently of the circumstance that, as has been already mentioned, the intestinal juice alone, without the bile, can induce the lactic acid fermentation, and that the intensely acid reaction of the duodenal contents admits very readily of another solution, the action of the bile on sugar is of so slow and gradual a nature, that we cannot regard this function even as a secondary object of the flow of bile into the intestinal canal. Every one who has repeated Meckel's experiment of allowing bile to ferment with sugar, in the same manner that Schiel has done (see vol. i. p. 230, and vol. i. p. 494), must have convinced himself that it is only very slowly that the acidity is developed in the bile; and this is especially the case when we employ for the experiment bile that has been filtered, or that has been removed with extreme care from the gall-bladder. Bile that has been freed by alcohol from mucus, and from which the alcohol has afterwards been removed by evaporation, may be kept for months without undergoing the lactic acid fermentation; mucus is indispensably requisite in this process of fermentation, and this substance acts independently of the bile, and not more slowly when alone than when associated with that fluid, but a far more prolonged action is necessary than within the intestinal canal. It cannot be supposed that any of the lactic acid which is formed in these fermentation-experiments could be saturated by the alkali of the bile; for the quantity of alkaline carbonate in bile is extremely small, and the acids, soluble in ether, which are liberated by the decomposition of the bile (and amongst which I could never detect lactic acid with certainty after twenty-four hours' fermentation) exhibit a very strong acid reaction. I found that ox-gall containing mucus, to which I added sugar of milk, and which was kept at a temperature varying from  $20^{\circ}$  to  $40^{\circ}$ , deposited in the course of two or three months a sediment of crys-

<sup>1</sup> Zeitschr. f. rat. Med. Bd. 8, S. 343.



talline cholic acid (Strecker's cholacic acid); the supernatant fluid contained an alkaline acetate and comparatively little alkaline lactate.

Lassaigne<sup>1</sup> was the first to observe that the pancreatic juice does not possess the property of effecting the metamorphosis of sugar.

If we introduce a solution of grape-sugar into a tied loop of gut (at about the middle of the small intestine)—an experiment which Funke often attempted at my suggestion—we find that in the course of 2, 3 or 4 hours the solution, even if it was very concentrated, has for the most part disappeared, while the intestine itself is very pale and never inflamed (whereas loops of gut into which solutions of chloride of sodium of moderate concentration have been introduced, often exhibit a strong inflammatory injection); the portion of fluid remaining in the loop never, however, exhibits an acid reaction. At the first glance this experiment appears to be in entire accordance with the view held by van den Broek and Heintz, that it is solely by the influence of the bile that the metamorphosis of the sugar into lactic acid is effected; but if we simultaneously introduce bile and sugar into the loop of gut, there is still, after the lapse of the above-mentioned time, no acid reaction in the remaining fluid; it might therefore be regarded as a fair conclusion, that the intestinal juice is as powerless as the bile in inducing this metamorphosis, and further, the view that sugar is partially converted into lactic acid, might be held as thoroughly controverted. But we must not limit ourselves to isolated facts, if we wish to obtain a deeper insight into the phenomena of the living organism; for the fact remains beyond all question, that after the use of sugar an acid reaction forthwith occurs in the whole of the small intestine and in the first half of the large intestine, and that saliva, gastric juice, and the pancreatic fluid exert no metamorphic power on sugar, this power being possessed in a slight degree by bile, and in a high degree by the intestinal juice. It is easy to see why, notwithstanding the presence of intestinal mucus and bile, no acid is observed in the isolated loops of gut; for the lactic acid is no sooner formed than it combines with the alkali of the intestinal juice and is rapidly absorbed; hence it is only seldom that the contents are alkaline, being for the most part neutral. It is still, however, difficult to understand how it is that the chyme, when its passage is not impeded by any loop, so constantly exhibits an acid reaction—a fact, to the discovery of which we have not been led by any special predilection for lactic acid; moreover, Schmidt and Bidder have indeed observed it (without, however, attaching any special value to the observation). If the passage of the food through the intestine be interrupted by a ligature, so much bile collects in a short time above it that the intestine becomes much distended at the spot; but even here, after sugar has been taken by the mouth, we find no free acid. We wait, therefore, for further investigations to elucidate the cause of the interruption in the formation of lactic acid, which occurs when a single ligature is applied to the intestine. Unfortunately we have been unable to include the consideration of the enormously large intestine of the herbivora in this investigation: my discovery, that after sugar has been taken by the mouth, it may after a very short time be detected in the cæcum, and that it is there that the greatest formation

<sup>1</sup> Journ. de Chim. méd. 1851. No. 2, pp. 69-71.



of acid occurs, would seem to indicate that this portion of the intestine possesses more active functions than we have been led from former investigations to ascribe to it. Certain experiments by von Becker, which have a bearing in this direction, have yielded the most decisive evidence in favor of this view.

If we regard it as an established fact, that even after the abundant use of amylaceous food, neither dextrin nor sugar can be detected in the portal blood or in the chyle, and that we can for a long time trace the presence of sugar in the intestine, even as far as the cæcum, after sugar itself or saccharine food has been taken, the supposition that starch is not merely changed into sugar in the intestine, but that it very soon undergoes still further alterations, seems to present a greater probability than the assumption that it is merely on account of its great solubility and diffusibility that it passes with extraordinary rapidity into the mass of the blood. But is the diffusibility of sugar actually so great? Graham's experiments, which were instituted with crystallized and fused cane-sugar as well as with glucose, coincide in this point, that sugar has less than half the diffusibility of chloride of sodium; while 58.7 parts of salt are diffused, only 26.6 parts of sugar are diffused under precisely the same conditions. Moreover, the endosmotic experiments which have been made by Jolly and others entirely correspond with the above results; thus Jolly found the endosmotic equivalent of sugar to be almost twice as great as that of chloride of sodium, and twenty times greater than that of hydrated sulphuric acid. Hence these physical experiments do not by any means justify us in concluding *à priori* that the resorption of sugar in the intestine is an extraordinarily rapid process.

Amongst the numerous contradictions which we meet with in the consideration of the phenomena connected with the behavior of sugar in the intestinal canal, it seems to be especially necessary to institute further and more accurate investigations regarding this circumstance. Several series of experiments have been carried on at my suggestion by von Becker<sup>1</sup> on rabbits, which at all events have thoroughly cleared up some of the points in question. I deemed it necessary to put aside for the time the consideration of starch, cane-sugar, &c., and to employ only that sugar in these experiments which is formed in the animal body from these carbo-hydrates before they undergo resorption. In the consideration of the results of Becker's experiments even this point must not be wholly overlooked; for we have introduced into the intestinal canal and the blood far more sugar than is ever found there during the digestion of the amylacea under normal relations; and from this very circumstance several objections have arisen which affect not only Becker's investigations, but likewise several experiments made by myself or Uhle. In the first place, it was established beyond all doubt, by three series of experiments, that after the introduction of large quantities of grape-sugar into the intestinal canal, this substance passed directly into the blood, where, indeed, it often accumulated in such large quantity as to show itself in the urine. In the first series, saccharine solutions of various strengths were introduced by the previously described

<sup>1</sup> Zeitschr. f. wis. Zool. Bd. 5, S. 123.



methods into tied loops of intestine, when an augmentation of the normal quantity of sugar was constantly found in the blood; in some cases it even rose to 0.6%, and could therefore be detected in the urine (see note to p. 138). The same results were obtained from a second series of experiments on rabbits, in which solutions of sugar were injected through the œsophagus into the stomach. The value of the experiment was often diminished by the circumstance that the abnormal distension of the intestine with an aqueous fluid loaded with sugar induced morbid phenomena and interfered very considerably with the resorption of the sugar. The third method of detecting the direct passage of the sugar into the blood, consisted in allowing the animals a free supply of highly saccharine food. In this case also there was found to be a constant augmentation of the quantity of sugar in the blood; it was, however, only when the animals had been very voracious that any sugar could be observed to have passed into the urine. Thus there can be no doubt that a great part of the sugar taken with the food or formed in the intestine during digestion, passes unchanged into the blood: and hence, although sugar is also formed in the liver, the quantity of this substance in the blood is directly proportional to the quantity of carbohydrates that have been taken—a fact which Bernard<sup>1</sup> has been led to deny, from his determinations of the amount of sugar in the livers of various animals, although his own investigations show that the liver of herbivorous animals and birds always contains more sugar than those of carnivorous animals.

Another question of much importance in relation to the resorption of sugar is, regarding the quantity which an animal of known size or weight can take up in a given time. Boussingault<sup>2</sup> found in his experiments on ducks, that one of these birds (the weight not being stated) was able to resorb 5.62 grammes of sugar, or 5.26 grammes (the equivalent quantity) of starch in one hour. Von Becker found, in several experiments in which saccharine solutions were injected at intervals of a quarter of an hour into the stomachs of rabbits, that for every kilogramme's weight of the animal there were about 4.5 grammes of sugar absorbed in the hour. No importance should, however, be attached to this determination, since, as we learn by direct experiments, the quantity of sugar resorbed in a given time is very dependent on the concentration of the saccharine solution in the intestine.

The circumstance that has been just mentioned leads us to a most important question in connection with the general process of digestion. We have pointed out in the introductory remarks to this section, that very little light has yet been thrown upon the manner in which those substances are resorbed which are known to pass, as products of digestion, into the blood. In order to obtain an insight into this obscure subject, it seemed advisable to commence the investigation with the simplest and least complicated part of the inquiry, namely, with the determination of the laws affecting the resorption of sugar. The following means were employed to determine this point. Solutions of grape-sugar, of various but accurately determined strengths, were introduced into tied

<sup>1</sup> Nouvelle fonction du foie, p. 48.

<sup>2</sup> Ann. de Chim. et de Phys. 3 Sér. T. 18, p. 460.



loops of gut of different lengths, and the animal being killed after 1, 2, 3, or 4 hours, both the quantity of sugar remaining in the loops of gut and the quantity contained in the blood were determined. The following may be regarded as the most interesting of the results which von Becker obtained from this series of experiments, which amounted to nearly 60 in number; *the quantity of the absorbed sugar is altogether independent of the length of the loop of gut or of the superficial extent of the absorbing surface.* This thoroughly unexpected result was confirmed in all the experiments; the quantity of sugar injected into the loop being the same, the resorption remained the same, however large the portion of intestine over which the solution of sugar was distributed; if, however, a very short loop were taken, the rule would not hold good. Thus, for instance, 8 grammes of a saccharine solution, containing 0.278 of a gramme of sugar in 7.722 grammes of water, were injected into tied loops of intestine in two rabbits of equal size; in one of the animals the cubic contents of the tied gut amounted to 27,720 cubic millimetres [about 1.6 cubic inches], and in the other to only 6,800 cubic millimetres [0.4 of a cubic inch]; and yet, after four hours, only 0.231 of a gramme of sugar was resorbed from the former, while 0.225 of a gramme (or very nearly the same quantity) was taken up from the latter. In several experiments it was actually found that rather more sugar was resorbed from the smaller than from the larger loop.

A second fact which von Becker established by parallel experiments with two rabbits of similar size, was equally unexpected. While there is a general tendency to believe that the resorption of the intestinal contents proceeds with a rapidity and freedom proportional in a certain degree to the dilution of the solutions contained in the intestine, he found that, at all events, for saccharine solutions, precisely the opposite rule held good; for it appeared that when equally large quantities of fluid were injected, the absorption of the saccharine solution stood in a *direct* ratio to its concentration; that is to say, that the more concentrated the solution is, the larger will be the quantity that is resorbed. Thus, for instance, in several experiments with solutions of sugar, one of which was four times more concentrated than the other, there were four times as much sugar taken up from the former as from the latter, in equal times; or, while in the former case 90.6% of the sugar injected into the intestinal loop disappeared, in the latter case only 80% were resorbed during the same time.

These rules, as well as the previously mentioned fact, that the intestinal loop absorbing the saccharine solution must have a size proportional to the quantity of sugar, while an excess of size in the loop exerts no influence on the absorption, are explained by those experiments of von Becker's, which were instituted with the view of ascertaining the amount of absorption in different intervals of time, when equally large quantities of equally concentrated saccharine solutions were injected. If we lay down a curve representing the amount of the absorption of sugar in the different intervals elapsing between the injection into the gut and the complete emptying of the loop, and based upon the sixteen experiments which were made upon this point, we see at the first glance that the absorption of sugar proceeds most rapidly at first, and afterwards



more gradually. Four rabbits of equal size were always used in these experiments, and equal quantities of the same saccharine solution having been injected into equally large loops of gut, the animals were killed in 1, 2, 3, and 4 hours after the injection. (Inflammation was recognizable about 4 hours afterwards, at the places where the ligatures were applied.) Now if we perceive that the most abundant absorption took place at the commencement, that is to say, during the first hour, this is only a confirmation of the above law, according to which the resorption proceeds with a rapidity proportional to the concentration of the solution. If, after the death of the animal, we observe the degree of fulness of the loop, we find that after the first hour it is thoroughly filled and distended with fluid, if the solution that had been injected was tolerably concentrated; the volume of the fluid within the loop must, therefore, have considerably increased by the absorption of water from the blood of the intestinal capillaries. It follows from a careful comparison of the numerical results which have been thus obtained, that the penetration of the fluid into the cavity of the intestine proceeds with a strength proportional to the concentration of the saccharine solution contained within it; and further that the absorption of the sugar varies directly with this concentration. If the solution within the cavity of the intestine be very much diluted by the absorption of water, the further absorption of sugar only proceeds slowly. The previously mentioned exceptions to the first of these laws strengthen the evidence in favor of this law; for if a concentrated solution of sugar be introduced into too short a loop, into which the influx of aqueous fluid from without is consequently difficult or impossible, we find even after 4 hours that it is strongly distended, and that very little sugar is absorbed. Thus, for instance, from 8 grammes of a solution containing 0.982 of a gramme of sugar, 0.889 of a gramme (or 90.53%) of sugar was absorbed by the loop containing 30,800 square millemetres of superficial area, while only 0.182 of a gramme (or 18.534%) of sugar was taken up from the loop presenting 11,160 millemetres of surface, after the lapse of 4 hours.

It is sufficiently apparent, even from this simple statement of the positive results of von Becker's labors, that unexpected as at first sight many of the facts appear, they are yet in the most perfect accordance with the laws of endosmosis in so far as they are yet known. For if we only remember, for instance, the method by which Jolly determined his endosmotic equivalents, in which, in the place of the dissolved salt, a definite and corresponding quantity of water always enters into the endosmometer, and where 1 part by weight of sugar is always replaced by 7 parts of water, we can at once understand the augmentation in the contents of the loop, which we perceive during the first hour after the injection of a concentrated solution, while the absorption of sugar is going on most actively. If the loop be too short for the concentrated saccharine solution, it can only take up a small quantity of water, and hence only a small quantity of sugar, corresponding to the absorbed water, can be given off; and we thus have an explanation why we observe only a very slight absorption of sugar, associated with considerable distension of the loop, in such cases. Finally, we see from this endosmotic law, why the size of the loop (unless when it be too small) exerts



no influence on the absorption of sugar; for if the loop be sufficiently great to allow the equivalent quantity of water to enter, no more sugar than the quantity corresponding to this water can ever escape, however great the loop may be. Since the quantity of water which enters is dependent upon the amount of sugar in the injected solution, the absorption will be precisely the same in loops of the most varied size, provided the concentration of the solutions be the same.

These few indications are sufficient to show that the recognized laws of physics are perfectly sufficient for the explanation of the resorption of sugar in the intestine, and that we are not justified, from the facts in our possession, in referring intestinal absorption to special vital forces. Hence von Becker's persevering labors have advanced us a further step in the knowledge of the physical phenomena in animal life.

Before we proceed to consider the relations of the fat conveyed from without into the intestine in the process of digestion, we must briefly direct attention to certain carbo-hydrates and non-nitrogenous bodies which have not yet been mentioned. To begin with *cane-sugar*, Frerichs maintains, in opposition to Bouchardat and Sandras, that this sugar is not converted into any other form of sugar (as, for instance, glucose), either by the saliva or the gastric juice. My own observations do not lead me to accord with Frerichs' view. It was only recently that I found in repeated experiments, that after rabbits had been fed with beet-root, glucose was invariably present in the stomach and duodenum, while cane-sugar was never found; even when large quantities of cane-sugar were dissolved in water and injected into the stomachs of rabbits, glucose was the only kind of sugar that could be found an hour afterwards in the stomach and in the whole of the small intestine. Perfectly similar results have likewise been obtained by von Becker in the numerous experiments which he instituted on this subject; it was only rarely that he could trace cane-sugar so far as to the middle of the jejunum, even in those cases in which large quantities of this substance had been introduced into the stomachs of animals (cats and rabbits). Since neither the saliva nor the gastric juice is able to effect a rapid conversion of cane-sugar into grape-sugar (or glucose), it only remains for us to assume with von Becker, that this transformation of cane-sugar into glucose is produced by the action of the substances in a state of change which are always present in the intestine.

*Sugar of milk* appears, both from my own experiments and from those of von Becker, to comport itself in the intestinal canal in precisely the same manner as glucose; it distributes itself very rapidly throughout the whole of the small intestine, and in about an hour after it has been swallowed may be traced as far as the cæcum; but like glucose and cane-sugar, it occasions an intensely acid reaction in the jejunum and ileum, which remains for three or four hours after the injection of the sugar.

*Vegetable mucus (Bassorin)* was made the subject of several experiments by Frerichs,<sup>1</sup> who found that during the process of digestion, at all events the greater part of it was not altered, and reappeared unchanged with the excrements. [Gum tragacanth, in which bassorin

<sup>1</sup> Handwörterbuch der Physiologie. Bd. 3, Abt. 1, S. 807.



exists abundantly, was the substance actually experimented upon by Frerichs.—G. E. D.]

Like Blondlot, Frerichs convinced himself that *vegetable jelly* (*pectin*, and its derivatives) is totally unaffected by the digestive fluids.

No group of nutrient matters has presented so many difficulties to physiologists as that of the *fats*, and even in the present day we must not flatter ourselves that we perfectly understand the process of their digestion.

We shall, in the first place, notice the successive changes which may be perceived to take place in the fat in its passage from the mouth downwards in the different parts of the intestinal tract. We could scarcely expect to observe any changes in the fat while in the mouth and in the stomach; for we have already seen that both the saliva and the gastric juice are devoid of any influence either of a mechanical or chemical nature upon it; and in point of fact, we find on examining the contents of the stomach after the use of fat (whether it has been taken alone or in conjunction with other substances), that the fat itself has not undergone the slightest change. Every physiologist, moreover, coincides in this point, that the digestion of fat commences in the duodenum.

In the duodenum, and still more in its further course along the small intestine, we find that the fat ceases to appear in large drops or semifluid masses; the further we descend in the small intestine, so much the smaller do we find these drops becoming, till at length the fat appears very finely comminuted, and the chyme presents an emulsive appearance. Since we see the lacteals distended with white (fatty) chyle after the use of fatty food, it is obvious that the principal course by which the fat makes its way into the blood is through the lymphatics of the intestinal walls. If, however, we follow this fat, which is easily recognizable with the microscope, in its course from the cavity of the intestine to the finest branches of the lacteals in the villi, we find that notwithstanding repeated rinsings with water, fat-globules may be perceived at intervals on and between them, which, however, only adhere externally to the epithelium of the intestinal mucous membrane. The occurrence of these external globules on the epithelium is a perfectly natural phenomenon, and there is no difficulty in distinguishing them from fat-globules within the epithelium and from other cells. Now if we consider the epithelial cells themselves, whether they are still adherent to the villi, or have peeled off in large thimble-like shreds, we very frequently find fat-globules in them, which, however, are not to be observed, or are few in number, after the use of food free from fat. During digestion the cylinder epithelium is often somewhat distorted in form, and presents a distended appearance; the broad margin of the base of the conical cylinder epithelium is raised up into an extremely thin and hyaline, strongly convex, or perfectly hemispherical cover. Below the epithelium we perceive the lacteals commencing in small club-like dilatations, and surrounded by a layer of vesicular or cellular bodies, which appear as if they were imbedded in an undefined fibrous mass, the true parenchyma of the villi; more externally, near the peripheral investment of the villi with cylinder epithelium, there are not only the contractile fibre-



cells which were first seen by Brücke, but also the small trunks of the bloodvessels which communicate with one another by a very fine network of capillaries. According to E. H. Weber,<sup>1</sup> there is, however, a layer of roundish cells, in addition to the bloodvessels and lacteals, between the epithelium and the true parenchyma of the villi; in the fasting state these cells present a collapsed appearance, but during digestion they become filled and much distended. It is, moreover, worthy of remark, that very often (but not always) some few of these vesicles are filled with a dark granular matter, while the great majority amongst which they are interspersed, are distended with a light fluid exactly resembling oily fat; we very often see a large vesicle (dark in transmitted, but white in incident light), and by its side another vesicle equally distended with a strongly refracting fluid; in addition to the very distended cells of these two kinds, which are for the most part situated on the apices of the villi, we always remark gradual transitions to minute granules, some of which are light and others dark, as far as the immediate neighborhood of the finest ramifications of the lacteals in the villi. While Weber regards these light and dark vesicles as a layer of true cells between the epithelium and the parenchyma of the villus, and is consequently of opinion that the epithelium cannot be regarded as in a normal condition without this layer of germs, other investigators, and especially Kölliker,<sup>2</sup> Bidder and Schmidt,<sup>3</sup> and Frerichs,<sup>4</sup> look upon these vesicles, as well as the branching lacteals of the villi, only as masses infiltrated into the spongy parenchyma, and consider that these vesicles, whether filled with refracting or granular matters, possess no true walls. Bruch<sup>5</sup> adopts this view in a memoir which he has very recently published, and shows that in all probability the branching lacteals running towards the margins of the villi are merely bloodvessels, which are able to resorb fat during the process of digestion equally well with the lymphatics.

As there has hitherto been much uncertainty regarding the morphologico-objective facts connected with the resorption of fat, so also has there been much obscurity and controversy in the views that have been brought forward regarding the mechanical processes by which the transition of the fat from the intestine into the lacteals and bloodvessels is effected; and the reason of this will be readily understood when we take the following points into consideration. The animal body is everywhere permeated by an aqueous fluid; the fats are, however, absolutely insoluble in water and aqueous solutions; hence they cannot undergo diffusion in the ordinary sense of the word, and the irresistible evidence of daily experience demonstrates that oily fluids cannot penetrate through membranes moistened with water. Viewing the case chemically, we may say that the fats are, in a certain sense, somewhat easily decomposable; but independently of the circumstance that stronger reagents are necessary for this decomposition than we are accustomed to find in the intestine, a closer investigation shows us that the fat found in the lacteals is in precisely the same condition as that which is contained in the chyme,

<sup>1</sup> Müller's Arch. 1847, S. 399.

<sup>2</sup> Mikrosk. Anat. Bd. 2, S. 163.

<sup>3</sup> Op. cit., p. 230.

<sup>4</sup> Handwörterb. d. Physiologie. Bd. 3, Abt. 1, S. 854.

<sup>5</sup> Zeitsch. f. wiss. Zool. Bd. 4, S. 282-298.



and, consequently, that the assumption that the fat is decomposed during its resorption through the lacteals is inadmissible. We are led, therefore, to the view, that certain special cells in each of the villi are solely devoted to the absorption of fat; the appearance of some transparent vesicles filled with fat, and of other opaque ones distended with granular matter, seeming to confirm this view. The chemist who is in the habit of separating the fat from aqueous fluids, sometimes by a filter saturated with water, and sometimes by one saturated with oil, will probably regard this mode of explanation as satisfactory. Thus, indeed, the absorption of fat in certain superficial parts of the villi could be explained; but not the admixture of fat in their interior, since the fat in the minutest branches of the lacteals is seen to be in a state of extreme comminution, and is mixed with an albuminous fluid. Although the admixture of fat with an aqueous fluid is regarded as impossible upon the surface yet its possibility is here being assumed where we can no longer make direct observations. All the former attempts to explain the digestion and resorption of fat are open to the same objections, since as we have already mentioned (in vol. i. pp. 492 and 506), the property of forming emulsions with oily fat, and, consequently, of promoting the resorption of that substance, has been ascribed by some physiologists to the bile, and by others to the pancreatic juice, although we know that the fatty particles of an emulsion very imperfectly, or scarcely at all, penetrate through a moist filter or a moist membrane. It is, however, impossible to deny that the emulsive condition of the fat essentially facilitates its resorption; the bile may, at all events in association with the pancreatic juice and with the co-operation of the intestinal movements, reduce the fat to a state of emulsion, that is to say, diffuse it in minute particles through the watery fluid; but this in no degree serves to explain the mechanical process of resorption. Since Bidder and Schmidt first proved by their experiments that bile was unquestionably necessary for the digestion of fat (see p. 494 of vol. i.), von Wistinghausen<sup>1</sup> has succeeded, under their directions, in discovering the physical conditions under which the resorption of fat occurs. He has ascertained that oil cannot be made to penetrate through animal membranes without considerable pressure, but that it may be forced through with comparative facility when the membrane is saturated with a fluid which adheres to, or has an affinity for oil. When the membrane was moistened with a solution of potash, an abundance of saponified oil appeared on this side of the membrane in the course of 10 hours, under the pressure of a column of mercury of from 1.75 to 3.37 millemetres [or from .068 to .132 of an inch], and associated with it was free fat which had been mechanically borne along by the soap. When a mixture of equal parts of potash-lye and albumen was employed, the oil passed through the membrane even without pressure, although in very small quantity, while in this case also a soap was formed. The oil, however, passed through animal membranes, without being saponified, when they were saturated with such fluids as a solution of soap or bile.

Even if these experiments cannot be considered as having entirely elucidated all the conditions affecting adhesion, they place it beyond a

<sup>1</sup> Diss. inaug. Dorp. Livon. 1851.



doubt that the presence of bile is essentially necessary for the resorption of fat, since this fluid renders these delicate membranes permeable by the fat. It is, however, obvious, that if the membrane or cell-wall be once saturated with a bilio-oleaginous fluid, it will the more readily permit the passage of more fat, and consequently that the inequality in the filling of the individual vesicles either with fat or with a granular aqueous fluid admits of a very ready explanation. These differences may, however, manifest themselves more in the outer portion than in the interior of the villi, since the pressure which at intervals is exerted by the organic muscles of the villi on the interior, obviously contributes very much, as von Wistinghausen's experiments show, to the intimate admixture of the oil and the aqueous fluid, which must, therefore, take place at the very commencing points of the lacteals.

If, as we learn from Bidder and Schmidt's experiments, a small fraction of the fat is resorbed, even without the co-operation of the bile, this is to a certain degree explained by the subsequent experiments of von Wistinghausen, even if we are unable specially to indicate the exact pressure or the exact substance which effects the transition of this small quantity of fat.

After the preceding remarks it is obvious that no further proof is required that the fat is principally resorbed by the lacteals. It must, however, be obvious from Schmidt's and my own observations (vol. i. p. 619), that the capillaries also take up fat, although in less considerable quantities; for the augmentation of fat which we observe in the portal blood of animals a few hours after they have been fed, cannot with any probability be explained by such an assumption as that the carbo-hydrates resorbed by the intestinal capillaries become converted into fat in their passage from the intestinal cavity to the portal vein. The above-mentioned observation of Bruch's, who saw fatty chyle-like masses beside blood-corpuscles in the capillaries of the villi, seems (as there does not appear to be any possibility of error in the observation) to afford the most distinct proof that there is a direct transmission of fat into the blood of the capillaries from the epithelial cells and the parenchyma of the villi.

We now proceed to that group of substances which must undergo an essential change in the intestinal canal before they are capable of being resorbed; to this class belong not only the *albuminous substances*, but also their more or less remote derivatives, as for instance, many gelatinous substances, and likewise a number of less-known matters, as synaptase and diastase, the poison of serpents, curarine, &c. Hitherto attention has naturally been, for the most part, directed to the behavior of the albuminous matters in digestion. We have already, when treating of the function of the gastric juice (in vol. i. pp. 449-456), considered this subject somewhat in detail. We there showed that the albuminous matters are not merely dissolved by the gastric juice, but are likewise converted into matters which, although similar in their elementary composition to the substances from which they were derived, yet differ essentially from them in their physical, and in several of their chemical properties. We have proposed the term *peptones* for the albumen, fibrin, casein, &c., after their metamorphosis by the gastric juice, and we believe that it is



these peptones which undergo resorption in order to be again very soon converted in the lymphatics into the well-known coagulable albuminous matters. We have been further taught by the experiments of Bidder and Schmidt, that the gastric juice which is secreted is far from being sufficient for the digestion of the protein-bodies necessary for nutrition (see "Gastric Juice"), and that the intestinal juice possesses in a high degree the faculty of dissolving the protein-bodies, and thus preparing them for being resorbed (vol. i. p. 510). This metamorphosis of the protein-bodies, and their subsequent resorption, should, however, be confined solely to the small intestine, which is the only part of the intestinal tract in which true villi occur; for if we had no evidence from comparative anatomy that the cæcum and colon exerted only very little influence on the digestion of the albuminates in carnivorous animals, the direct experiments which have been recently instituted, partly by Steinhauser and partly by myself, show that albumen and pieces of flesh when introduced into fistulous openings in the lower part of the jejunum, or into an artificial anus, pass off almost entirely unchanged by the rectum (see "The Intestinal Juice.")

We shall refer, under this fourth group of digestive objects, almost solely to the protein-bodies and their immediate derivatives; it is, however, not improbable that many other substances which do not possess the high physiological value of the albuminates, may yet comport themselves during digestion in a very similar manner, and we have already mentioned the gelatigenous tissues in connection with this point. Possibly also we should place in this category certain poisons, which, like the protein-bodies, cannot be directly resorbed by the bloodvessels, but must be first so changed by the gastric and intestinal juices, that after being absorbed by the lacteals they pass as innoxious matters into the blood. Diastase and emulsin are substances which in many points of view are very closely allied to the protein-bodies, although we cannot place them in this class. We know that emulsin undergoes the same changes during digestion as the true protein-bodies; for it has been shown by the experiments of Magendie and Bernard,<sup>1</sup> that pure amygdalin exerts no injurious effects upon the health or the life of animals, either when swallowed or when directly introduced into the blood; if, however, emulsin be simultaneously introduced into the stomach or into the blood, decomposition is set up in the amygdalin, and the prussic acid which is formed destroys the life of the animal. I allowed rabbits to eat sweet almonds, and injected amygdalin into the jugular vein, 1, 2, 4, and 6 hours after they had fed; the animals remained perfectly vigorous. I then reversed the experiment, and injected emulsin into the vein, while I introduced a solution of amygdalin into the stomach of the animal; symptoms of poisoning by prussic acid very soon presented themselves. Since, however, we cannot demonstrate in this manner that the emulsin has actually been metamorphosed by the digestive fluids, and has consequently lost its influence on the amygdalin, and since it is conceivable that emulsin, like gum, might be incapable of resorption, and passed off unchanged with the excrements, I collected the excrements of a rabbit which had been

<sup>1</sup> Arch. gén. de Med. 4 Sér. T. 16, p. 79.



fed for 48 hours on almonds, and mixed amygdalin with them; but I could detect no trace of any evolution of prussic acid; indeed no decomposition of the amygdalin was induced even by the cæcal contents of the same animal.

A number of other bodies, which have certainly been less accurately investigated, but which coincide in their quantity of nitrogen, in their insolubility in spirit, and in their solubility in water, comport themselves in an analogous manner with emulsin. Of all these substances, *curarine* has probably been most accurately examined, thanks to the labors of Boussingault and Roulin.<sup>1</sup> This substance, when introduced into the stomach and intestines, does not induce the slightest morbid phenomenon, whilst if it be conveyed into the blood, it causes the almost instantaneous death of the animal, without any premonitory symptoms; and very similar, both in a toxicological and in a chemical point of view, is the poison of the viper, as well as those poisons which are produced during contagious diseases, as hydrophobia, glanders, typhus, &c.; this view is, at all events, supported by the recent experiments of Renault,<sup>2</sup> who convinced himself that both carnivorous and omnivorous animals could, without any detriment, feed upon the flesh of animals which had been affected with these diseases, while the juices of such flesh or similar effluvia, when introduced directly into the blood or into a wound, occasion the most fatal effects.

This peculiar behavior of all these substances proves that they cannot be resorbed in an unchanged condition either by the capillaries or the lymphatics of the intestinal canal. Since most of them cannot be again recognized in the solid excrements, they must undergo so complete a change through the action of the digestive fluids, that when they at length make their way into the blood, they can no longer exert their former poisonous actions. Even if we cannot altogether agree with Bernard<sup>3</sup> in his view that animal membranes are absolutely impenetrable to these substances (emulsin, diastase, curarine, and the poison of the viper), this much, at all events, is certain, that these substances, like albumen, exhibit very slight endosmotic force. Mialhe and Pressat<sup>4</sup> have, moreover, recently attempted to show that the fresh albumen of the egg can only penetrate animal membranes, when the latter have attained a certain degree of putrefaction; but repeated experiments with various animal membranes (previously treated with alcohol, and afterwards rinsed with water) have convinced me that they are not perfectly impenetrable by albumen, emulsin, and diastase. The only point which is established beyond all doubt is, that all these substances pass with difficulty through animal membranes, and that their diffusibility is extremely small. (Graham found the diffusibility of sugar  $8\frac{1}{2}$  times as great, and that of chloride of sodium 19 times as great as that of albumen.) In the preceding remarks we can see the reason why the protein-compounds, which are apparently ready to be applied at once to the purposes of nutrition, must first undergo a metamorphosis, through the influence of the digestive juices before they are resorbed. If it were not for the gastric and intestinal juices, soluble albumen and casein would

<sup>1</sup> Ann. de Chim. et de Phys. T. 39, p. 24.

<sup>2</sup> Compt. rend. T. 33, pp. 532-535.

<sup>3</sup> L'Union méd. T. 3, pp. 445, 457, et 461.

<sup>4</sup> Compt. rend. T. 33, pp. 450-454.



be absorbed in far too small a quantity from the intestinal canal to suffice for the nutrition of the organism.

An observation made by Bidder and Schmidt,<sup>1</sup> although not very accurately carried out in all its details, may serve to give further support to the above view. These experimentalists have repeatedly observed that the contents of the thoracic duct did not coagulate for several hours, and then only imperfectly, in dogs, in which the pancreatic duct had been closed for a long time, whereas, ordinarily, these contents become coagulated in a few seconds. Will not this result, if its connection with the absence of the pancreatic juice in the intestine be confirmed by further investigations, serve to demonstrate that the pancreatic juice itself exerts an action on the metamorphosis of the peptones, even after their resorption into the lacteals, and that it probably contributes in some degree to the regeneration of certain albuminates from the peptones? At all events, this observation is in perfect accordance with the result of our experience, that the albumen-like bodies, as emulsin, diastase, &c., are not capable of resorption, as well as with the view, which we have boldly maintained, that the albuminates in their unchanged condition are only resorbed in an extremely small quantity, the greater part of them being previously converted into peptones.

We are as little able to explain the reason why special vessels exist in the organism for the resorption of the digested protein-bodies and their derivatives (that is to say, their peptones), as to recognize the physical conditions which direct these substances, although not exclusively, yet chiefly, to the lacteals in preference to the bloodvessels. To speak candidly, we must confess that we have no definite idea of the mechanism of resorption through the lacteals. All experiments made with the view of explaining the process of absorption by the lacteals, refer solely to the mechanism of the continuous motion of the fluids in them, but not to the true process of absorption. After having formerly determined all the incidental or indirect means by which the motion of the chyle and of the lymph is effected—the special *vis a tergo* which does not admit of a physical definition—we at length find Brücke's<sup>2</sup> discovery of fibre-cells in the intestinal villi (a fact which has been confirmed by Kölliker),<sup>3</sup> affording a sufficient indication regarding the *primum movens* of the motions of the lymph. Since, moreover, Lacaze de Mijoux,<sup>4</sup> Gruby and Delafond,<sup>5</sup> and more recently Brücke and Kölliker, have witnessed obvious contractions of the villi, we can hardly doubt that it is these contractions which communicate the first impulse to the motion of the chyle in the minutest ramifications of the lacteals. But although the discovery of fibre-cells in the villi has revealed to us the mode in which the commencing branches of the lymphatics are emptied, we have as yet made no advance towards the explanation of the manner in which these minutest lymphatic branches become filled. We have already mentioned that the capillaries of the villi present a closer resemblance than the lacteals to the root-fibrils of plants, in so far as absorption is concerned. In the lacteals there is neither any fluid which is so concen-

<sup>1</sup> Op. cit. p. 259.

<sup>2</sup> Berichte d. k. k. Akad. d. Wiss. zu Wien. 1851.

<sup>3</sup> Zeitsch. f. wiss. Zool. Bd. 3, S. 106; and Mikrosk. Anat. Bd. 2, S. 158.

<sup>4</sup> Compt. rend. T. 16, p. 1125.

<sup>5</sup> Ibid. p. 1195.



trated, nor any substance which is so soluble, as to occasion an attraction of the fluids from the intestine; and, indeed, the apices of the lacteals do not even float in the intestinal fluids, which must pass through several series of cells, and then come in contact with the minute capillaries, before they reach the true lacteals. One might almost wonder that, considering how great the absorbing power of the bloodvessels is, and that all the fluids must pass over them, so much important nutrient matter can find its way into the lacteals. It would appear, therefore, as if only those matters were taken up by the lacteals which the bloodvessels can only absorb with difficulty, or not at all. From these considerations, based on anatomical structure, as well as from certain experiments which showed that many membranes are only permeable for certain substances (as, for instance, caoutchouc for spirit, and not for water, the bladder of the pig for water, and not for spirit, &c.), we have been led to believe, with Lotze,<sup>1</sup> that the coats of the bloodvessels on the one hand, and those of the lacteals on the other, have a specific action, and allow one substance to pass through them, but not another. But even if we assume that there is such a specific difference in the membranes in question, we yet obtain no explanation as to the special agent which forces the matters through the walls of the lymphatics. The walls of the lacteals present opposition to the substances which are heterogeneous to them, but they do not on that account attract those by which they are permeable. The assumption of a specific permeability of the membranes does not, therefore, clear up the obscurity regarding the absorption by the lacteals.

We may not, perhaps, have sufficient grounds for the assumption of an altogether special (or specific) permeability of the different membranes; we may well suppose that differences in their thickness, tension, and other purely mechanical relations render the membranes, which in a chemical point of view are analogously constituted, more or less permeable for physically and chemically differing substances, so that no individual membrane could be characterized as absolutely impermeable. Independently of the great similarity in the chemical constitution of these animal membranes, those experiments on the resorbability of certain substances (poisons) through the bloodvessels or lymphatics, which have given rise to so much literary discussion, are opposed to the absolute impermeability of a membrane for the passage of certain matters. Thus, for instance, it appears to us that, contrary to Henle and Dusch's<sup>2</sup> view, it has been tolerably well proved by the numerous experiments of Bischoff,<sup>3</sup> Ludwig,<sup>4</sup> and Stannius,<sup>5</sup> that the lymphatics can absorb strychnine, and convey it into the blood, although far more slowly, and in smaller quantities, than the capillaries. Hence we also believe that the caution which is so necessary in this part of our inquiries demands that, instead of assuming that a perfectly specific relation is shown by different membranes towards different solutions, we should admit nothing more than gradual differences in this respect. On this account we have not ventured to maintain that albumen and fat, for instance, are solely resorbed through the lymphatics, whilst salts and alkaloids are alone

<sup>1</sup> Allg. Physiologie. S. 260.

<sup>3</sup> Ibid. Vol. 5, p. 293.

<sup>4</sup> Ibid.

<sup>2</sup> Zeitschr. f. rat. Med. Bd. 4, S. 368-374.

<sup>5</sup> Arch. f. physiol. Heilk. Bd. 9, S. 23.



resorbed through the bloodvessels. We must not forget, in endeavoring to form some idea of absorption from these experiments, that, on the one hand, we may probably still be ignorant of the physical laws by which those molecular motions are to be explained, and that, on the other hand, we may not be sufficiently well acquainted with the course of those phenomena which manifest themselves in the villi and in their elements during absorption. The comprehension of these phenomena is so extremely difficult, that even the best observers are not agreed in reference to many of them. It must be further borne in mind that chemical as well as molecular movements are here brought into play; but when we assume the concurrence of mechanical and chemical movements, we do not take into consideration the metamorphoses which the chyle undergoes in the vessels themselves before it reaches the subclavian vein. Still less would we refer to the very hypothetical conversion of sugar into fat within the villi; but we might be led to conclude, from the striking difference in the optical appearance of the cells described by Weber, that, in addition to the mechanical absorption, certain chemical alterations actually occur in the villi; thus, for instance, if we find in a certain portion of the intestine many strongly refracting vesicles, we shall also find, somewhat higher up, where the absorption is half completed, many others which are granular and dark (appearing white in incident light), and some of which are partially filled with a granular, and others with a lighter mass; and still higher up in the intestine we find only cells which are filled with granular matter. No conclusions ought to be drawn from these experiments of Weber, which we have only quoted for the purpose of showing that, even in an anatomical point of view, there is much to be done before we can hope successfully to arrive at any explanation of the process of resorption.

Bidder and Schmidt have at all events the merit of being the first to determine directly the *quantity of fluids* which are poured into the intestinal canal as *digestive agents*. The result of these investigations very considerably exceeds all the assumptions which had hitherto been made in reference to the amount of any of the secretions; who could have conceived, or ventured to assert, that the juices which flow into the intestinal canal in the twenty-four hours amount to almost the sixth part of the whole weight of the body? If we apply to the case of an adult man the quantitative relations of the individual secretions obtained for animals according to the above data, by Bidder and Schmidt, it follows from their calculations, that a man whose weight is about 64 kilogrammes [or about 10 stone] will secrete in the 24 hours,

Saliva amounting to 1.6 kilogrammes, containing 15 grammes of solid matter.					
Bile	"	1.6	"	"	80
Gastric juice		6.4	"	"	192
Pancreatic juice		0.2	"	"	20
Intestinal juice		0.2	"	"	about 3

The quantity of fluid which passes from the blood into the intestine during the 24 hours is therefore far larger than the amount of blood which, according to the most probable recent determinations, is contained in the body of an adult. This mass of fluid, which contains only 310 grammes of solid constituents (and therefore, 3.1%) is especially designed



to rinse and purify the absorbed food; and hence we may take the view, long since adopted by Berzelius, that digestion is a true process of rinsing. But however obvious the aim of this abundant secretion of aqueous fluid may be, since it not only favors the solution of the food, but essentially contributes towards its resorption, we ought not to forget that it at the same time imparts an extraordinary motion to the fluid masses within the animal body. The blood within the vessels not only circulates in the course of a few minutes through the whole of the body, but it also carries a considerable mass of fluid into the intestinal canal, from whence, in a longer or shorter time, it is again almost entirely restored to the vessels. This continuous ebb and flow of aqueous solutions can scarcely fail to exert an influence or to react upon the processes of nutrition and metamorphosis generally, which originate in the blood. We might perhaps have formed some idea of these relations from what we learnt of the destiny of the bile in the organism after its secretion, and of the purposes which the formation and secretion of bile were designed to fulfil in the intermediate metamorphosis of matter. We have seen that the bile is poured into the intestine in order to be again almost completely resorbed; and we have found that not only its water repeatedly circulated through the portal vein, liver, and intestine, but also that its solid constituents were for the most part returned into the blood through the lymphatics. A portion of the organic matters must, therefore, first pass through the stage of biliary formation, and then return from the intestine into the blood, in order that it may be applied to further purposes. As the bile shows itself to be not merely a simple secretion, designed for the digestion of definite substances, so also the other secretions, which are poured in such abundance into the intestine without leaving a trace of their solid or fluid constituents in the excrements, may serve to carry away with them from the blood into the intestine different substances which have become temporarily effete, in order that they may be carried back to the blood after having been subjected to metamorphosis, and rendered available for further purposes.

This transfusion of certain substances into the secretions, and their return into the blood, is not limited to the normal organic and inorganic constituents of the secretions; for we find, after the copious transfusion of water into the blood, that not only is the quantity of water in the secretions increased, but that there is often a simultaneous augmentation of their solid constituents, which are separated with them from the blood. The effete matters undoubtedly often pass through this course more than once; thus we frequently see iodide of potassium pass into the saliva (as witnessed by myself), ferrocyanide of potassium into the gastric juice (Bernard), arsenic, lead, and copper into the bile (Meurer and others), and iron into the intestinal juice (Buchheim), all of which often remain a very long time in the organism before they are returned to the external world through the special organs of excretion. The elucidation of the above relations is perhaps one of the most important among the numerous interesting contributions to science which have resulted from the investigations of Bidder and Schmidt, who have conducted these inquiries with equal intelligence and perseverance. We shall revert to this subject under the head of "Nutrition," when we shall have to consider the intermediate metamorphosis of matter—that process which to a certain



degree is effected in the living organism, independently of absorption and excretion.

Important to physiology as is the knowledge of the influence exerted by the *nervous system* on the molecular movements in the animal body, yet an inquiry of this nature, strictly speaking, scarcely belongs to the domain of physiological chemistry, seeing that we are still entirely ignorant of the chemical phenomena which are associated with the function of the nerves. Since, however, in the establishment of theories regarding animal metamorphosis, the existence of the nerves and their influence on the individual factors of this process have been almost entirely ignored from a chemical point of view, it might not be wholly out of place were we here to observe, that the more recent physiological investigations have established beyond all doubt the direct dependence of certain secretions upon definite parts of the nervous system.

We have already frequently had occasion to refer to Ludwig's<sup>1</sup> important investigations in relation to the secretion of the saliva. It appears from these observations, that there is not the slightest amount of saliva secreted independently of the influence of the nerves, and that the secretion is not effected indirectly by nervous excitation, that is to say, through the agency of contractile parts or by increased pressure of the bloodvessels, but directly through the special influence of the nerves.

The direct influence of the facial nerve upon the secretion of the parotid gland, the indirect action of the third branch of the fifth pair (by inducing the movements of mastication), and the reflex action through the glosso-pharyngeal nerve, have been investigated in rabbits by Rahn,<sup>2</sup> under the direction of Ludwig, with all the acuteness of experimental criticism.

Ludwig's admirable investigations afford some grounds for the belief, that all those secretions which only appear at certain times or in consequence of definite excitants, as for instance those of the gastric juice and of the pancreatic fluid, are only produced under the action of certain groups of nerves. The correctness of this view, in reference to the two last-named animal juices, seems to be confirmed by the observations recently repeated by Bidder and Schmidt,<sup>3</sup> that the gastric juice is copiously effused into the stomachs of dogs when flesh or any other attractive food is placed before them while fasting. But although we certainly cannot deny the influence of the nerves upon the secretion of the gastric juice, we are entirely unable to determine upon which nerve this secretion depends. It has generally been referred to the pneumogastrics, and in recent times with more certainty, since Ed. Weber's<sup>4</sup> admirable experiments (of which I was myself a witness) have proved beyond a doubt that these nerves exert a direct influence on the contractions of the muscular coat of the stomach. The direct observations which have been made in reference to the secretion of the gastric juice after the division of both the pneumogastrics have, however, led to entirely opposite results. Whilst Arnold, Reid,<sup>5</sup> Leuret and Lassaigne, as well as Longet,<sup>6</sup>

<sup>1</sup> Op. cit. and Zeitschr. f. rat. Med. N. F. Bd. 1, S. 255-277.

<sup>2</sup> Zeitschr. f. rat. Med. N. F. Bd. 1, S. 285-292.

<sup>3</sup> Op. cit. p. 35.

<sup>4</sup> Handwörterbuch der Physiologie. Bd. 3, Abt. 2, S. 41.

<sup>5</sup> Edin. Med. and Surg. Journ. Vol. 51, p. 310.

<sup>6</sup> Arch. gén. de Méd. T. 15, p. 230, and Compt. rend. T. 14, p. 266.



following the views of Joh. Müller<sup>1</sup> and Dieckhoff,<sup>2</sup> could not perceive any change in the character of the secreted gastric juice in consequence of the division of the pneumogastric nerve, Bouchardat and Sandras,<sup>3</sup> and subsequently to them Bernard<sup>4</sup> and Frerichs,<sup>5</sup> believed that they had convinced themselves that no acid gastric juice was any longer secreted after the interruption of continuity of the pneumogastric nerves in the neck, and that there was no longer any true digestion of the albuminates in the stomach (whilst the digestion in the small intestine continued its undisturbed course after such operations). In order more clearly to demonstrate this circumstance, Bidder and Schmidt<sup>6</sup> instituted very careful experiments on four dogs, in which fistulous openings into the stomach had been made; the result of these experiments was, that the quantity and the composition of the gastric juice, which was secreted after the course of the pneumogastric nerves had been interrupted, was precisely the same as in the normal state. In two cases, however, the quantity and the acidity of the gastric juice were not inconsiderably diminished, but after such an operation as the division of the pneumogastric nerves, so many of the vital functions of the animal become involved, that this diminution can only be regarded as an indirect effect of this action, more especially as in both the other cases a more abundant and more acid gastric juice was secreted than is even commonly observed in the normal state. Independently of the fact that the proportion and character of the constituents, both organic and inorganic, were entirely the same in the gastric juice after division of these nerves as before the operation, the above-named observers convinced themselves that such gastric juice, both within and external to the stomach, possesses precisely the same digestive powers as the ordinary secretion. Are we, then, justified, from these thoroughly exact experiments, in entirely denying to the pneumogastric the function of presiding over the secretion of the gastric juice? We believe not: for even the movements of the stomach, whose dependence on the pneumogastric has been quite decisively established, first by Weber, and subsequently by Reid, Bischoff,<sup>7</sup> and Volkmann, may often be perceived with scarcely any diminished intensity after division of the pneumogastrics. A nerve whose fibres form so abundant a network around the stomach can, however, hardly exert no influence either on its movements or on its secretion, especially when we recollect that Bidder and Schmidt have found that it is in no way connected with the sense of hunger. Volkmann<sup>8</sup> has certainly been led, from anatomical considerations, to the opposite view, in his experiments on the influence of the pneumogastric on the movements of the stomach, and there is this much in support of his views, that this nerve loses the greater part of its cerebro-spinal fibres within the cranium and in the upper part of the neck, and that its sympathetic fibres increase in proportion to its distance below the diaphragm; hence the pneumogastric in the abdomen is altogether different from the pneumogastric as it emerges from the

<sup>1</sup> Handb. d. Physiol. Bd. 1, S. 459 [or English Transl. 1839, Vol. 1, p. 597].

<sup>2</sup> De actione, quam nervus vagus in digestionem ciborum exerceat, Diss. inaug. Berol. 1835.

<sup>3</sup> Revue méd. Fébr. p. 159-180.

<sup>4</sup> Compt. rend. T. 18, pp. 783 et 995.

<sup>5</sup> Handwörterbuch der Physiologie. Bd. 3, Abt. 1, S. 822-825. <sup>6</sup> Op. cit. pp. 90-97.

<sup>7</sup> Müller's Arch. 1838, S. 496. <sup>8</sup> Handwörterbuch der Physiologie. Bd. 2, S. 584.



cranial cavity; the pneumogastric nerve in the abdomen contains fibres which cannot be irritated from its cervical portion, and whose action on the movements of the stomach cannot therefore be interrupted by dividing the nerve in the neck. In reference to this point, the same remarks are equally applicable to the movements of the stomach and the secretion of the gastric juice. It is, however, clear that further experiments, of an extremely difficult character, are requisite in order to decide the question on what nerve or group of nerves the secretion of the gastric juice directly depends. We must hope that the ingenuity of Ludwig may as brilliantly overcome these difficulties as those which were presented to him in the investigation of the salivary secretion.

Having considered the process of digestion in its most diversified conditions, and noticed the relations between the objects to be digested, the digestive agents, and resorption, it only remains for us to make some observations in reference to the *digestibility* of those objects which, in reference to the nutrition and regeneration of the animal body, have been named "compound," in contrast with the above-mentioned simple nutrient matters. There was a time when, notwithstanding the little that was known of the process of digestion, the digestibility of different more or less compound nutrient matters was a favorite subject for writers to expatiate upon. We shall see, however, that the further we advance in science, the more do we become distrustful of our own experience, and the more modest will be our pretensions. Whilst in former times the most decisive hypotheses or conjectures were unhesitatingly adopted in the absence of all direct observations, and merely on the strength of certain traditions, which, without having been tested, were derived in part from antiquity, the edicts of the schools of the middle ages, or even from the mere biassed notions of the people; we at the present day scarcely venture to give a decisive reply to the simplest and most ordinary questions regarding the digestibility of any nutrient substances, although we may be far removed from that forced scepticism which has in part become the fashion in medicine. Yet what, properly speaking, do we understand by the digestibility of a nutrient substance? The simplest mode of comprehending this idea will be to understand by the expression the facility with which the nutrient fluids are able to prepare the substance for resorption, or the shortness of the time in which the substance in question undergoes resorption, that is to say, the time at which it disappears from the intestinal tract. Yet how did inquirers formerly endeavor to decide the readiness and rapidity of the metamorphosis of nutrient matters? The determination of this question was mostly limited to this,—that the digestibility of compound nutrient matters was estimated by the subjective feelings which patients or convalescents experienced after having partaken of them. Even if we do not take into account the innumerable deceptions which must necessarily be liable to occur, either on the part of the subject of the experiment or of the person watching the result, an organism which is not in a state of health, and in which all the functions are not performed in a regular manner, cannot assuredly afford a measure of the greater or less digestibility of a substance; for the power of a patient to bear one or other article of food must depend upon the nature of his malady. Thus, for instance, it is *à priori* obvious



that one patient will find no difficulty in bearing certain kinds of food, which may induce indisposition in another individual; and every physician who has made it a point at the bedside to attend to the effects of different nutrient substances, as well as to observe the actions of medicines, must be familiar with innumerable instances of this kind. Experiments of this nature are, moreover, not practicable in the case of healthy persons, since they are not conscious from any sensations within themselves whether digestion is proceeding with slowness or rapidity. It is only in recent times, since we have begun to experimentalize scientifically, that attempts have been made to collect any definite positive facts, with the view of establishing the different digestibility of even the most ordinary articles of diet. Of this class of experiments, those of Gosse are the best known; he possessed, as is occasionally the case, the faculty of swallowing air, and of thus distending the stomach to such an extent as to induce vomiting; and he employed this peculiar power in order to bring up food which had remained for different lengths of time in his stomach. Spallanzani<sup>1</sup> introduced perforated tubes or linen bags filled with different varieties of food, through the œsophagus into the stomachs of cats, and observed in this way the time that elapsed before the various articles of food disappeared from the above-named receptacles. Beaumont<sup>2</sup> instituted a very extensive series of experiments, regarding the digestibility of different kinds of food, on a man (Alexis St. Martin), in whom there was a very considerable persistent opening from without into the stomach, in consequence of a gun-shot wound. Although Beaumont's investigations have led to many brilliant results in relation to gastric digestion generally, and have much facilitated the path for further inquiries, they do not yield many certain results regarding the question we are now considering. In the first place, all these experiments have reference solely to the time during which the food remains in the *stomach*, although we know that vegetable matters undergo their principal changes in the small intestine, and that a great part even of animal food leaves the stomach in an undigested state, and is only thoroughly digested by the intestinal mucus. These experiments would, however, have been of higher scientific interest, if only the time during which the food remained undigested could have been accurately determined; Beaumont has, however, generally (and Gosse always) regarded the gastric digestion as ended when the food in the stomach had been converted into a uniform pulp (*chyme*). But even this very uncertain determination would have its own peculiar value, if the experiments both of Gosse and Beaumont were not wanting in two essential points. They used very complicated, variously prepared, and for the most part half vegetable and half animal food, in their experiments (thus, for instance, Beaumont generally gave bread and vegetables with meat); and it is at once obvious that such a method is totally unfit for determining the digestibility of individual articles of diet; since Beaumont neither employed chemical means nor the microscope for the minute investigation of the matters that were presumed to be digested, he was naturally unable to decide which constituents of the food were

<sup>1</sup> Versuche über. d. Verdauungsgeschäft Leipz. 1785.

<sup>2</sup> Experiments and observations on the Gastric Juice and the Physiology of Digestion. Boston, 1834.



dissolved, which were partially digested, and which were altogether unaffected. Independently of certain other circumstances which should be taken into consideration, it is obvious that only a moderately satisfactory conclusion could have been drawn from Beaumont's experiments if he had employed the simpler articles of food, as albuminates, flesh, meal, bread, &c. His conclusions, even in that case, would less have had reference to the digestibility of individual substances, than to the time in which they are retained in the stomach. The retention of the food in the stomach is, however, extraordinarily different even for one and the same substance, as for instance, flesh, without our often being able to discover the cause of the difference; this being a point which daily observations on dogs with gastric fistulæ have placed beyond a doubt. It very much seems to depend on the quantity of the food taken at once; if, for instance, we allow a dog to swallow a large quantity of flesh, fragments may be still found in its stomach after six, eight, and even ten hours, while smaller quantities often disappear after less than two hours. And a further reason why the results of Beaumont's observations cannot be specially applied to physiology or even to dietetics, depends upon the circumstance that he has either not at all or very inaccurately described the quantity of the food that was taken; and upon this circumstance may partly depend the great differences which are often observed in his observations, when made under apparently similar conditions.

There are still to be mentioned the experiments instituted by C. G. Schultz,<sup>1</sup> who at a certain time after feeding dogs and cats with different kinds of food, killed them and examined the contents of their stomachs. These attempts, from the method by which they were carried out would deserve great confidence if their results did not differ in so remarkable a manner from those obtained by Beaumont and others, that we are almost compelled to presume that there must have been some essential errors in them. The same is the case with the observations which Lallemand instituted on men with gastric fistulæ. Blondlot, who first introduced into physiology the operation of artificial gastric fistula, was so far from being able to attain to definite results, notwithstanding that his observations were made under far more favorable conditions, that he was led to express the view that the digestibility of different articles of diet depended solely on the state of the stomach at the time of the experiment, and that it is pure waste of time to labor at the determination of the digestibility of individual articles of food.

These few instances are sufficient to indicate that moderately accurate determinations of the digestibility of varieties of animal food are involved in extraordinary difficulties even in relation to gastric digestion alone. At the present time we possess few experiments which can afford a fixed point of departure for the determination of the digestibility of different kinds of food.

My personal experiments, which have reference partly to dogs, in which gastric fistulæ had been formed, and partly to animals that were killed (generally with a view to other investigations) at definite times after taking food, are limited to the following facts, which increase rather than diminish the uncertainty of our knowledge.

<sup>1</sup> De alimentorum concoctione experimenta nova. Berol. 1834.

<sup>2</sup> Traité de la Digestion, p. 383-409.



As in the first place we shall only consider the retention of food in the stomach, we shall commence with the digestibility of the albuminous substances.

With regard to *soluble coagulable albumen*, it has been already mentioned (see vol. i. p. 450) that, according to my experience, this substance undergoes a change in the stomach, and is not resorbed unchanged, as Frerichs maintains. Blondlot saw the white of 4 eggs entirely disappear from the stomach in the course of  $2\frac{1}{2}$  hours. We can here very distinctly observe the influence which the quantity exerts on the relative digestibility of the food; if we introduce the white of one egg into the stomach of a dog with a gastric fistula, but otherwise healthy, after it has fasted for about 12 hours, we often find in the course of an hour no remaining trace of coagulable matter; but we are more certain to find such traces when the white of two eggs has been taken. If the white of eight or more eggs was given to the same dog, which was one of average size, weighing about 5 kilogrammes [or 11 lbs.], coagulable matters could always be recognized in the stomach after 3 or even after 4 hours, except in cases in which the dog had vomited a portion of the substance.

Densely coagulated *blood-fibrin* requires a longer period for gastric solution than the same substance in a finely comminuted state; a fasting dog swallowed 9.5 grammes of the moist fibrinous crust (buffy coat) obtained from coagulated horses' blood, and after  $2\frac{1}{2}$  hours fragments of it were still contained in the stomach; the same quantity of blood-fibrin obtained from the red coagulum of horses' blood disappeared, with the exception of a few flakes, from the stomach of the dog in the course of  $1\frac{1}{2}$  hours. It might have been expected from the simplest chemical experiments, that the degree of cohesion would essentially influence the more or less easy digestion of a substance, and this view is thoroughly borne out by further direct investigations. Fluid, finely divided, porous foods are much more open to the action of the digestive juices, and must necessarily be more readily digestible, than others which do not possess these properties in an equal degree.

In order to determine the digestibility of *coagulated albumen*, we have recently so far modified the experiments of Spallanzani, who introduced the food enclosed in muslin bags through the gullet into the stomach, as to introduce into the stomachs of dogs, through fistulous openings, portions of coagulated white of egg, of definite form and definite weight, enclosed in similar muslin bags. This method of procedure, which has been adopted by Bidder and Schmidt, as well as by Buchheim,<sup>1</sup> may be very advantageously employed in various investigations; the sole objection to it is that we can only employ extremely small quantities of the substance in question, and that even portions of the same albumen often require very different times for their solutions; this difference appears to depend as much on the varying density of the albumen (which may certainly differ even in one and the same egg), as on the different positions which the bag containing the albumen may happen to assume in the stomach. In Buchheim's experiments, which were made with cylindrical pieces of albumen weighing 1 gramme (the stomach having been filled three or four hours previously with bread and curdled

<sup>1</sup> Beiträge zur Arzneimittellehre. Leipzig, 1849, S. 15-112.



milk), it was found that in 1 hour sometimes more than 59%, and in 2 hours even 93% of the originally introduced moist coagulum of albumen were dissolved, although the amount was frequently far smaller. Here again we must give the widest scope to the idea of digestibility; in 1 hour half of the compact mass of coagulated albumen, which presented comparatively little surface, was dissolved, while the gastric digestion previously took from 3 to 4 hours. Further experiments show us, that far more coagulated albumen is digested in 1 hour in the stomach of a dog, when that organ is empty, or when a long time has elapsed since the last meal was taken, than under opposite conditions,—when albumen in small portions, or finely comminuted, is introduced into the stomach, than when a cylinder of albumen, of a gramme weight, is introduced,—when a freer motion is permitted to the pieces of albumen than was possible when they were enclosed in bags,—and lastly, when the experiment is instituted on a perfectly healthy dog, than when made on dogs with fistulous openings. Hence we may foresee that large pieces of coagulated albumen and long boiled or more or less dried albumen, must require a comparatively long time for their solution, especially when the stomach has been very much filled with food, and digestion has been going on for some time. Hence, independently of many other relations connected with special idiosyncrasies, it is extremely difficult, if not impossible, to find any definite unit of conditions, according to which a scale of the relative digestibility of different articles of food might be made out. And even if all the conditions were similar, a doubt would always remain as to the precise moment at which gastric digestion might be said to terminate. There can be no definite rule regarding the beginning of digestion, for the solvent process commences as soon as the gastric juice comes in contact with the object to be digested: if, for instance, we allow albumen which has been previously carefully rinsed with acetic acid to remain only five minutes in the stomach, a careful weighing will generally (although not always) indicate a loss, which in this case can only depend on actually digested albumen; a portion is, therefore, digested in the course of five minutes, or, at all events, a quarter of an hour, which shows that albumen obviously may be digested in so short a time. We find, however, that when coagulated albumen is introduced in considerable quantity into the stomach, remains of it may sometimes be detected in that organ, even after five hours; as we cannot regard the commencement of the process as affording a measure of the digestibility, the terminations may probably serve this purpose. But even the end cannot be always accurately determined; for while one part of the albuminous body commonly leaves the stomach in an undigested state, another often remains for a long time in the stomach, in consequence of the digesting force of that organ becoming gradually weakened, and its glands secreting less juice after it has been for some time in a state of functional activity—a circumstance which more than any other, is dependent on the individual constitution. In many animals, however, the stomach is never altogether empty, as for instance, in the rabbit. Even when these animals perish from hunger, the remains of their last meal may still be found in the stomach. Although this is not the case with the carnivora and omnivora, it shows that the termination



of gastric digestion and the emptying of the stomach cannot furnish any appropriate standard for the determination of the digestibility of a substance. It might perhaps appear superfluous to devote so much space to the consideration of a subject which is so simple of comprehension, but we must bear in mind these relations and the general vagueness of the idea in question, before we can even attempt to construct any scale of the digestibility of the simple and compound articles of food, which could be of use for purely practical purposes. C. Schmidt has never found all the albumen dissolved in the stomach, and after it had remained for six hours enclosed in muslin bags, he constantly found that half of it was still undissolved; similarly small quantities of albumen, when introduced into an empty stomach without being enclosed, never remained as long as six hours in that organ, but passed for the most part in an unchanged state into the intestine. Beaumont assumes from his observations, that the average period of digestion for hard-boiled eggs is about  $1\frac{1}{2}$  hours.

Frerichs has already shown by experiments on living animals, that *boiled fibrin* is dissolved in the stomach far more slowly than the *unboiled* material; we arrive at the same result when both kinds of fibrin are treated externally to the organism with natural or artificial gastric juice.

It is a well-known fact, to which we have already frequently referred, that soluble *casein*, as it exists in milk, is very rapidly coagulated by the gastric juice, and then only very gradually redissolved or digested; casein must, therefore, be the most indigestible of the unboiled protein-substances; a difference is, however, even here observable, according to the more porous or dense condition of the coagulum, for, as we have already remarked at vol. i. p. 451, the more gelatinously coagulating casein of women's milk is, according to Elsässer, much more rapidly digested than that of cow's milk, which forms in the stomach a compact lump, generally coagulated into a single ball. Frerichs found that clots of casein disappeared from the stomachs of cats and dogs in about  $2\frac{1}{2}$  hours. Beaumont, according to his observations, fixes a period of 2 hours for the digestion of milk. Gosse classes milk amongst the most easily digested articles of food, which include, according to him, substances which are converted into chyme within 1 hour or  $1\frac{1}{2}$  hours.

*Gelatin* belongs to those substances which are the most readily liquefied in the stomach; in Beaumont's experiments all the gelatinous character of this substance disappeared after it had remained for 20 minutes in the stomach; at the close of an hour no trace could be found in the stomach of 150 grammes of jelly which had been taken. The digestibility of the *gelatigenous tissues* depends, however, entirely upon their aggregate condition, and is very considerably facilitated by their being previously boiled. Frerichs saw the connective and fatty tissues (when enclosed in a thin muslin bag) perfectly dissolved in the stomach of a dog in 60 or 90 minutes after its introduction. It is obvious that tendons and cartilage, and those tissues generally which are abundantly intersected with elastic fibres, belong to the least easily digested class of substances, for we often find these parts only slightly altered, even in the excrements of the carnivora. True elastic tissue and elastic fibres completely resist the action of the digestive fluids.



Chemically pure *syntonin* appears, from several experiments which I have made, to be very readily digested, its digestibility being in fact greater than that of the blood-fibrin of the ox; when in a state of coagulation, it is tolerably similar in this respect to coagulated albumen and casein. Although this substance is perfectly identical in every kind of flesh, and also in the smooth muscles (see page 226), experience teaches us that the digestibility of the smooth and of the transversely striated muscles, and even of the latter in different animals, is extremely different. When we consider the histological conformation of these two kinds of muscle, we can readily comprehend why the flesh of organs which consist of smooth muscles is far more easily digested than the transversely striated muscles; we know that the smooth muscles are not provided with the same dense and insoluble, although thin investment (see page 239) which encloses the primitive bundles (and consequently the *syntonin*) of the transversely striated muscle, but are for the most part surrounded only with loose connective tissue, which is easily permeated and dissolved by the digestive juices. Hence it was that Beaumont found that tripe disappears with such rapidity (in an hour) from the stomach, and that oysters disappear at all events more quickly than beef and other kinds of meat. The difference in the digestibility of the flesh of different animals is probably for the most part dependent upon mechanical conditions, which are modified by the histological arrangement of the different elementary tissues. Thus the flesh of young animals is more easily digested than that of older animals, for (as we have seen at page 242) the primitive bundles of the former are far thinner than those of the latter, and on this account they present, in relation to their mass, a larger surface to the gastric juice than a similar piece of meat of equal size, taken from an older animal. Frerichs found that the flesh of old animals required (for its digestion) an hour or an hour and a half longer than that of younger animals. Fish is probably not easily digested (by persons whose digestive powers are not strong), since when introduced into the stomach in a state of fine comminution, and in contact with fluids, it forms an almost homogeneous mass, which can only be slowly acted upon by the digestive fluids from the surface inwards. This is indeed, as Frerichs has shown, more or less the case with every kind of flesh which is gradually acted upon from the surface, for it is not till the connective tissue has been dissolved that the gastric juice is able to act, through the openings made in it, upon the sarcolemma and primitive bundles (see vol. i. p. 320). On this account, true muscle does not actually belong to the class of easily digested substances. Frerichs found in the stomach of a cat, four hours after feeding, pieces of raw beef which were only softened on the surfaces. When portions of flesh, enclosed in a fine muslin bag, were introduced through a fistulous opening into the stomach of a dog, they did not thoroughly disappear until after an interval of from five to eight hours.

It has generally been regarded as an established fact that raw flesh is much more difficult of digestion than boiled or roast meat; the difference is not, however, very considerable, and it has been estimated by Frerichs at only half an hour. Nor need we wonder at this, for the advantage derived from the boiling or roasting, by which the connective



tissue is loosened and the organic structure is partly destroyed, is in part counteracted by the albumen of the muscular juice as well as the syntonin being reduced to a state of coagulation. The above-mentioned jelly-like swelling up of the syntonin in acid fluids may, perhaps, in a great measure, contribute towards the difficult digestibility of raw meat.

We have formerly had occasion to observe, that after an animal diet, muscular fibres, although in various phases of metamorphosis, may be distinctly recognized along the whole course of the intestinal canal; hence we see that the digestion of flesh is by no means completely effected in the stomach, and that its most important histological element, the true muscular fibre, in association with the sarcolemma, resists for the longest period the action of the digestive fluids; indeed, during an abundant flesh diet, we find a large number of muscular fibres, morphologically unchanged, in the excrements. Hence in the case of flesh we can form no conclusion regarding its digestibility from the duration of its retention in the digestive organs. When dogs are fed solely with flesh, we find that after 6 or 8 hours the greatest part has usually disappeared, although small portions often remain in the stomach for 10 or 12, or even 16 or 20 hours. In their observations on a dog with a fistulous opening at about the middle of the small intestine, Bidder and Schmidt found that most substances escaped in 5 or 6 hours after a meal; and very similar results were observed in a man who was a patient in our hospital, and in whom there was an intestinal fistula at the end of the ileum. We may therefore assume that in the normal state the stomach is not engaged in the digestion of flesh for a much longer period than four or five hours; and this view coincides tolerably closely with the experiments made by Beaumont. Thus, for instance, he found that boiled lamb disappeared from the stomach after  $2\frac{1}{2}$  hours, boiled beef after  $2\frac{3}{4}$  hours, roast beef after 3 hours, and broiled beef after 4 hours; on the other hand, roast pork did not disappear from the stomach for  $6\frac{1}{2}$  hours, while broiled pork disappeared after  $3\frac{1}{4}$  hours. If we are able, in some cases, to adduce scientific explanations for certain practical dietetic rules which accord tolerably well with Beaumont's observations, the far more considerable differences which present themselves in all results of this kind seem to invalidate such conclusions; hence we do not venture to enter minutely into the influence which the different modes of preparing the food, and the different species of animals, exert on the digestibility of the flesh. We must, however, not altogether omit to mention (what has so often been prominently brought forward) that flesh which has been kept lying in vinegar is rendered more digestible, since, as every microscopist knows, the connective tissue and muscular fibre are thus rendered of looser texture; and that smoked meat is generally far more difficult of digestion than unsmoked, since the pickle in which the meat was placed preparatory to the smoking not only extracts from the flesh a fluid containing certain easily digestible substances, but also renders the fibres themselves harder and more insoluble.

With regard to the *fats*, it is tolerably well agreed that they rank amongst the most indigestible matters; physicians have, indeed, always exhibited an extraordinary aversion to permit the use of fatty food to any of their patients, although they see that many fats, as, for instance,



the fashionable, but generally rancid, cod-liver oil, is very easily digested. It may readily be conceived from its physical characters, as, for instance, its insolubility in water, and the resistance which it offers to the most powerful reagents, that fat, as compared with the other simple nutrient substances, is only slowly absorbed; indeed, even to the most recent times, it has been difficult to form an idea of the mode in which fat undergoes resorption. It is sufficiently clear, from what has been previously stated, that the stomach is not the place where the fat is resorbed, or even where it undergoes any essential changes; but when it is taken in large quantity, either alone or with other food, it usually remains for a long time in the stomach; thus Beaumont found beef-suet in St. Martin's stomach after  $5\frac{1}{2}$  hours. It is not only not digested in the stomach, but often exerts an impeding action on the digestion of other substances in that organ, since, on the one hand, it liquefies in consequence of the high temperature, and, encasing as it were the individual particles of food, renders them proof against the digestive juices; and since, on the other, it becomes rancid during its long retention at that temperature, and forms volatile acids, which exert a very deleterious, although not duly investigated, action on digestion. It must, therefore, be admitted that large quantities of fat are prejudicial to gastric digestion, although, strictly speaking, there is no digestion of fat in the stomach. The digestion of fat does not commence, as we have already seen, until it reaches the small intestine, and even there it only takes place under certain limitations. We have seen from the accordant experiments of Boussingault on the one hand, and Bidder and Schmidt on the other, that the animal organism can only take up a limited quantity of fat in a given time; after animals were fed upon very fat flesh, we find that there were ejected from the fistulous opening in the intestine (in Bidder and Schmidt's experiments) gray masses which contained an abundance of fat, while only very slight remains of muscular fibres could be detected in them. Hence we can no more draw any inference from the retention of the fat in the stomach regarding the degree of its digestibility than from its passage into the small intestine and the solid excrements. Small quantities of fat meet with the means requisite for their digestion in the small intestine, and are there very rapidly resorbed. If we can draw any conclusion from the distension of the intestinal villi with fat, and the appearance of white chyle in their lacteals, we must regard the fat as very easy of digestion; for in the course of from half an hour to an hour after fatty food or oil has been taken, we find in the upper part of the jejunum in dogs, cats, and rabbits (as I have very often convinced myself), not merely the epithelium filled with fat-globules, but also the lacteals with glistening white chyle. We have, however, formerly shown (see vol. i. p. 236) that fat, when not mixed in too large quantity with the food, essentially promotes the digestion both of the albuminous and the amylaceous substances.

It has been already fully shown that most vegetable substances, like the fats, do not undergo gastric digestion; we cannot, therefore, judge regarding their digestibility from their longer or shorter retention in the stomach, in the same manner as in the case of the albuminous matters. We have already expressed an opinion, founded on our own experiments,



and differing from that of Bidder and Schmidt, that *starch*, the principal nutrient matter contained in vegetables, is in part converted in the stomach into sugar, and even into lactic acid; this metamorphosis of starch within the stomach is, however, so far as we can conclude from our former experiments, solely dependent upon the quantity of the saliva that is excreted; the greatest part of the starch is first metamorphosed in the intestine. We have already sufficiently alluded to the fact that the conversion of this substance in the intestine takes place most rapidly when it is finely comminuted and thoroughly saturated with water (in short, when it is boiled). If we confine ourselves solely to the question of the digestibility of starch, we should regard it as in general easy of digestion, although we very frequently meet with considerable quantities of it passing through the rectum of man and animals. This last-named fact is dependent partly on the circumstance of an excessive quantity of raw (unboiled) starch having been taken (for the saliva, pancreatic fluid, and intestinal juice are not secreted in such quantities, and with such powers, as to metamorphose any amount of starch), and partly upon the fact that the starch is enclosed in vegetable cells, through which the digestive fluid can only enter by endosmosis. Hence the digestibility of *vegetables* depends chiefly on the nature of the cells in which the starch and the vegetable protein-bodies are enclosed; if the cells are still invested with epidermis, no portion of them is dissolved, since the epidermis of plants is completely proof against the digestive fluids. Boiling is so far useful in regard to vegetable food, that it thoroughly loosens the intercellular substance of the parenchymatous cells, and hence allows the digestive juices to make their way more readily between the cells; moreover, the process of boiling causes the outermost layer surrounding the starch-granules to burst, and it is this layer which is the main impediment, in the case of raw starch, to the action of the digestive fluids. Since the protein-bodies occurring in plants exist in a state of the finest comminution, they offer far less opposition to the action of the digestive juices (when the latter once come in contact with them) than the corresponding animal protein-bodies. Hence, moreover, it is easy to see why bread is comparatively so easy of digestion. We must, however, again recur to the fact that in the case of vegetables we are even far less able to draw any conclusion regarding their digestibility, from their longer or shorter retention in the stomach, than in the case of animal food. The most important part of the digestion of vegetables assuredly takes place in the small intestine, and, to a certain degree, also in the large intestine; for even if, in accordance with the observations of Bidder and Schmidt, we regard the secretion of the intestinal juice in the latter as inconsiderable, the enormous size of the cæcum in most of the herbivorous animals indicates that a very essential act in the process of digestion must take place in this region. The chief difficulty in connection with the digestion of vegetables, therefore, does not lie in the stomach, and hence their retention in that organ cannot be strictly considered as a measure of their digestibility; and yet vegetables remain on an average longer in the stomach than animal food. Even after feeding an animal with bread, we may find the greater part of it in the stomach after a lapse of 3 hours, and the



quantity hardly perceptibly diminished till after 4 hours (Frerichs), and remains of bread are commonly found in the stomachs of dogs after 5 or 6 hours, and often even after 8 or 10 hours: potatoes and other vegetables remain in this organ for a far longer time; Frerichs, as well as Bidder and Schmidt, have frequently found the remains of vegetable substances in the stomachs of dogs after the lapse of 22 hours; and we have already mentioned that the stomach in many herbivorous animals is never completely empty. If we have thus established the point that the disappearance of an article of food from the stomach affords no proof of its digestibility, the next question that suggests itself is in relation to the conditions under which the stomach either retains or impels into the small intestine the more or less digested matters—a question to which, in the present state of our knowledge, we can give no satisfactory answer. This is one of the least important of the many problems whose solution must be left to future investigators, notwithstanding the admirable and comprehensive labors of Frerichs and of Bidder and Schmidt. We are, however, here forcibly reminded of the fact, that notwithstanding the brilliant triumphs of science in this direction, we have as yet only gained the outworks from which further advances must be made.

As we have limited ourselves in the former pages almost exclusively to the consideration of the principles which, in accordance with the present condition of science, ought to guide us in our judgment of the digestibility of the different articles of food, some of our readers may miss the important aids and special indications they may here have hoped to discover in relation to medical practice; for many physicians seem to entertain the idea that physiological chemistry must be able to decide all questions of a practical character, and accurately to determine the digestibility of every article of food, or at all events to furnish sharply-defined rules for its estimation; and some have even gone so far as to expect that this branch of our science should serve in every respect as a guide for a system of dietetics. But even if our physiological premises were sufficient for this purpose, and if our positive facts were less deficient than they are, we should consider a text-book of physiological chemistry as an inappropriate place for a comprehensive exposition of the relations involved in this department of science: purely scientific inquiry is bounded by definite limits; the application to practical life of the facts discovered by science must be left to the kindred but less strictly scientific branches of knowledge; all that is required for practical application must be supplied by the methods peculiar to the so-called practical sciences. Thus, for instance, there exists a large amount of material in reference to the digestibility of the different nutrient matters, which appertains exclusively to a medical inquiry. For we do not concur with those who denounce as unfounded every fact which has not been obtained by the exact methods of physical science, and who consequently often arbitrarily cast aside many striking hypotheses which may be advanced by physicians in reference to dietetic conditions; far from participating in such views, we do justice to the fruits which practical experience is able to furnish, and we are fully aware that a physician may do a great deal by the bedside towards the introduction of correct dietetics, without our being able to refer his mode of practice to scientific grounds. Thus,



for instance, we know that a number of substances, which present considerable analogy to one another in a physical and chemical point of view, exhibit great differences in reference to their digestibility under certain morbid conditions; there are a number of still more mysterious phenomena known to every attentive physician, which, although they owe their recognition to no exact scientific method, are yet as firmly established as if they were mathematical propositions. Yet the solution of these mysteries—the formation of comprehensive scales for the calculation of the digestibility of different articles of food in accordance with their chemical nature or preparation—and the determination of the causes by which a substance which is in itself easy of digestion may become less digestible under different external or internal relations (for the simple digestibility of a substance must be distinguished from the facility with which a patient is able to digest it)—these are all questions which it behoves the physician to determine, and which do not fall within the province of physiological chemistry. The latter science merely furnishes the physician with the fixed principles or scientific means necessary for enabling him to arrive at a more exact knowledge of carefully observed practical facts on which to base a system of dietetics. Until the appearance of Moleschott's admirable work,<sup>1</sup> most of the treatises on dietetics consisted merely of individual physiological facts carelessly connected with more or less well-grounded propositions; and while they were deficient in a logically strict treatment of these different propositions, they did not even give those minute observations with which many of the older practitioners had enriched the theory of dietetics; not unfrequently, indeed, we meet with an entire confounding of the ideas of digestibility, nutritive power, and the facility with which different articles of food can be borne. Such a proper elaboration of dietetics does not, however, fall within the province of physiology, but belongs exclusively to the practical physician.

We cannot avoid offering a few remarks on certain misconceptions which we occasionally meet with in reference to the value of physiological chemistry, in relation to Pathology and Therapeutics. Although we have endeavored throughout the present work to draw attention to the deficiency of our knowledge, to refer all views and assertions to their true foundation, and to check as far as possible the haste with which individual observations or discoveries have been applied to practice, we have been anxious to avoid those hasty and uncharitable judgments which we meet with from time to time both in literature and in medical practice. Physiological Chemistry has recently done more in destroying former illusions, than in furnishing physicians with new materials for further hypotheses. We may, indeed, instance many discoveries in Physiological Chemistry which have exerted a direct influence on medical practice, but the greater number of deficiencies which still exist in this respect, hold out a prospect of ample return to future laborers. It is not the province of Physiological Chemistry, as a special department of science and a branch of physiology, to guide the physician within narrow limits by which he must bound his own reflections and investiga-

<sup>1</sup> *Physiologie d. Nahrungsmittel.* Darmstadt, 1850.



tions, and regulate his practice; for our science presents too many deficiencies within its own domain to enter upon a foreign province, whose possession has already caused strife and jealousy. Physiological Chemistry no more constitutes a science of therapeutics and diagnostics, than pure physiology can be said to constitute the science of pathology. Technical Chemistry does not undertake to show what mordant will affect a certain organic tissue, or how the fire of a furnace can be kindled; the noblest discoveries in this department have been made, not by chemists, but by practical men with the aid of chemistry. A similar relation exists between physiological chemistry and the physician; the latter must not remain inactively waiting until physiological chemistry is ready to supply him with a diagnostic agent for every disease which is accessible to its investigation. It is the duty of the practitioner to apply every fresh conquest in the field of science to the benefit of medical practice, and to endeavor to extract by his own researches and labors all the practical results to be obtained from the treasures of science, instead of requiring that, under the pressure of his other avocations, all difficulties should be smoothed from his path, and the results of laborious research presented for his acceptance, cleared from their obscurity and divested of their difficulties.

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## RESPIRATION.

Although we have already considered the excretions of the animal organism, there is one of the most important of them which has not yet been noticed, namely, that from the lungs. The reason of this omission is obvious, for whilst pulmonary excretion challenges our attention as a process, the quality of the products of excretion does not demand any special notice, as they consist mainly of carbonic acid and water. The full exposition of this subject has been deferred to the present place, since it leads most securely to the development of that which we have already designated as the crowning point of physiological chemistry, to the attainment of which an accurate acquaintance with the process of respiration is indispensable. For since this process reflects almost all conditions of animal life, including even those which are not directly connected with the vegetative process, it not only throws considerable light on individual subjects connected with the nutrition and maintenance of the animal body, but it also furnishes us with the most stable supports for forming a scientific estimate of the quantitative metamorphosis of matter, and of the entire animal economy. On this account we consider it as the last link in the series in which we have treated of the solid and fluid parts of the animal body and its various functions.

We should greatly err, were we to regard the lungs simply as organs of excretion, for they differ from other excreting organs, inasmuch as they not only excrete gaseous bodies, but also absorb certain elastic fluid substances. An interchange of gases is therefore effected within the lungs. Although our notice of the respiratory process must neces-



sarily be especially directed to the higher pulmoniferous animals, we must bear in mind that that interchange of gases which we term respiration is by no means solely limited to the organs known as lungs. As is well known, there are many aquatic animals besides fishes which breathe through gills, while insects are provided with a system of tubes (tracheæ) which take the place of lungs, and which, like bloodvessels, are distributed through all the tissues on which vital activity depends in these non-vascular animals—a circumstance of great importance in connection with the theory of the respiratory process.

If the respiratory process depends essentially upon an interchange of certain substances within the lungs, an accurate acquaintance with the substances whose constituent parts are thus interchanged is indispensably necessary for the scientific comprehension of this subject. Thus, in considering pulmonary respiration, we must be accurately acquainted, on the one hand, with the constitution of the blood, and, on the other, with the character of the atmosphere, before we can venture to form a judgment regarding the interchange which takes place. We do not, however, purpose entering more fully into the close consideration of these two fundamental bases of the respiratory process, as we have already, in the first volume, considered the constitution of the blood and the amount of gases which it contained; and as we must presume that our readers are equally well acquainted with the chemical constitution of the atmospheric air, and with the physical laws of the motion of elastic fluids.

The causes which present themselves to our notice as essential agents in effecting that interchange of gases which takes place in the lungs of air-breathing animals may be of three different kinds, anatomico-mechanical, physico-chemical, and purely physiological, without, however, being fundamentally and completely distinct; for each cause must, from the nature of the case, merge into the others. We need scarcely observe that the *mechanical momenta* depend upon the manner and the degree in which the bodies acted upon, namely, the blood and the atmospheric air, are brought into contact with one another, and by which this interchange is rendered possible and promoted. We abstain from giving a systematic exposition of the anatomical relations and the entire mechanism of the respiration, since, in the first place, we must presume that our readers have some knowledge of anatomy as well as of pure chemistry, and, in the second, that the following remarks will suffice to afford some idea of these modifications in the quantitative results of the respiratory process, which depend upon differences in the mechanical relations.

In the first place, we ought to observe that no direct communication exists between the fluids which undergo this mutual interchange, for the elastic and fluid atmosphere and the liquid blood, are separated by an extremely delicate moistened membrane. Although the interchange of the gases may be somewhat retarded by these membranes, nature has compensated for these impediments by giving an extraordinary degree of expansion to the surfaces of contact. The extremely delicate distribution of the blood- and air-vessels affords an immense extent of superficies in a small space, and enables the processes to be widely diffused.



The fluids, however, do not stagnate at those surfaces (the membranes) which establish communication between them, but both are maintained by very different physical means in continuous motion and in constant interchange; and hence we have an additional condition which essentially facilitates this process. The heart, which, as is well known, sends forth the vessels of the lesser circulation into the lungs, constantly propels new blood through them, and is undoubtedly the most essential agent in circulating the blood through these organs; for even though the mechanism of respiration may exert some action on the movement of the blood in the lungs, pathologists have gone too far in maintaining, as some have done, that respiration is the sole cause of the motion of the blood. With regard to the motion of the air, on the other hand, it must be observed that the great increase of surface obtained in a circumscribed space (by the minute division of the air-vessels) renders its interchange with the gases of the blood less easy; we may compare the space filled with air within the thoracic cavity to a cone whose base is extremely large in proportion to its height; the base being constituted by the sum of the surfaces of the pulmonary vesicles, whilst we place the apex in the glottis; the interchange of air is therefore considerably impeded from the narrow calibre of the glottis being the only means by which air can enter into and be expelled from this wide, conically shaped cavity. The high diffusibility of the gases certainly contributes in some degree to counterbalance the effect of this narrow opening, and induces no inconsiderable interchange of air, both within and externally to this space; but this motion would be quite insufficient for the purposes of life (excepting in the case of the hibernating animals), and hence special provisions exist for the expulsion of the contained air by a partial diminution of this cavity and for the readmission of new air by its re-expansion. The mechanism by which this object is effected depends partly upon the peculiar structure of the thorax and the position of the muscles which move it, and partly on the peculiar elasticity of the pulmonary tissue. We should, however, form a very erroneous idea of the motion induced by this mechanism, were we to conceive that it was able to agitate the whole of the air contained within the cavity of the chest. For even when the contraction is relatively considerable, only a small fraction of the air is expelled, and an equally small proportion admitted by its expansion; hence it is only in the wider air-canals that the air can be absolutely changed, whilst in the narrower vessels there is only an undulating current of the stagnant air-column, induced by the contractility of the walls. The change therefore depends solely upon the different degrees of diffusibility of the gases. However simple this latter circumstance may appear, Vierordt has the merit of being the first who experimentally illustrated these physical relations.

A careful consideration of the above-mentioned mechanical relations shows how extensively this interchange of gases must be modified by slight alterations of the external conditions. We must not, therefore, believe that the difference in the characters of the blood and of the inspired air merely influences the final results of this interchange of gases, for it might rather be predicated as a physical necessity, that if the blood were pro-



pelled more copiously through the lungs, and the air was more frequently changed in this conical space (the latter being more considerably dilated and contracted), the results of the interchange would be different from what they would be in the opposite case. A more careful study of the mechanism of the respiration will not, however, always enable us to refer the modifications which it presents to proximate causes, based upon chemical and mechanical conditions; for these conditions are themselves often dependent upon so-called physiological relations, whose influence upon the character and motion of the blood, the frequency of the respiration, &c., have not yet been sufficiently investigated. We are, therefore, compelled, in endeavoring to deduce the laws of this interchange of gases, to trace the modifications to which they are liable, to the remote as well as the proximate causes from which they emanate. It is clear from the above remarks, that the proximate causes of those alterations which we meet with in the quantitative relations of the products of respiration are solely based upon the prevailing physical and chemical conditions; the more remote causes, those, namely, of a physiological character, can only influence this interchange of gases inasmuch as they modify those essentially physical and chemical relations. We cannot, therefore, hope to explain the influence exerted by any definite physiological relation on the products of respiration, until we have more clearly established its connection with the physical and chemical fundamental conditions of respiration. For this reason we shall in our further considerations of the process of respiration, at once enter upon the influences which purely chemical and physical relations exert on the interchange of gases, in order thus to elucidate the influence of the physiological conditions. Many difficulties here present themselves, one of the chief of which is the imperfect knowledge we possess of the constitution of the blood in ordinary cases, and the mere conjectural nature of our knowledge of the amount of gases which it contains, although, as we have already observed, this constitutes one of the two main factors of this process, and hence we are compelled to enter more fully into these physiological conditions than we should otherwise have done.

We must, however, devote a few brief remarks to the general results of the chemical investigation of the substances which meet together in the act of respiration, before we enter more fully into the causal connection of the modifications of the interchange of gases.

There is scarcely any portion of physiological chemistry which, notwithstanding the great difficulties that oppose its investigation, has been so circumstantially and exactly elucidated as the respiration. It would appear from the works of the older chemists, as Lavoisier and Seguin,<sup>1</sup> Humphrey Davy,<sup>2</sup> Allen and Pepys,<sup>3</sup> Humboldt and Provençal,<sup>4</sup> Prout,<sup>5</sup> and others, that attention had not hitherto been directed to this subject, but when physiologists endeavored to elucidate the mechanism of respiration from all points of view, the chemistry of the process obtained

<sup>1</sup> Mémoires de l'Acad. de Paris.

<sup>2</sup> Researches, chemical and philosophical, chiefly concerning nitrous oxide, or dephlogisticated air and its respiration. London, 1800.

<sup>3</sup> Philosophical Transactions for 1808.

<sup>4</sup> Mém. de la Soc. d'Arcueil. T. 2.

<sup>5</sup> Thomson's Annals of Philosophy. Vol. 2, p. 328.



some of the attention which it merited, and the most exact and admirable investigations were at once prosecuted by the aid of the most recent appliances of science. The beautiful experiments of Magnus (see vol. i. p. 570-574) on the amount of gases in the blood, may be said in some degree to have constituted the turning point in these inquiries, since it is only by the establishment of this factor that we can enter upon a satisfactory investigation of the interchange of gases in the lungs. Numerous investigations, of which the greater number are very admirable, have been instituted both on man and animals with a view of determining the relation between the inspired and expired air. Scharling,<sup>1</sup> Dumas,<sup>2</sup> Andral and Gavarret,<sup>3</sup> Valentin and Brunner,<sup>4</sup> Vierordt,<sup>5</sup> Malcolm,<sup>6</sup> and Hannover<sup>7</sup> directed their investigations for the most part to the excretion of carbonic acid in man under different physical, physiological, and pathological relations. Many of the difficulties which are inseparable from investigations on man, or which influence the accuracy of the method of investigation, were happily obviated in the series of exact and highly successful investigations of Valentin, Marchand,<sup>8</sup> Boussingault,<sup>9</sup> Letellier,<sup>10</sup> Ph. Zimmermann,<sup>11</sup> von Erlach,<sup>12</sup> Lassaigue,<sup>13</sup> myself, and especially Regnault and Reiset.<sup>14</sup> We are principally indebted to the labors of these chemists for the facts relating to the respiratory process, which we now proceed to consider.

Before we pass to the subject itself, we are led to notice some of the difficulties which attended these inquiries. It is extremely difficult to procure the special materials for our investigation (the expired air) in a state of purity, in sufficient quantity, and under perfectly normal conditions. Hence various methods were adopted to obtain the products of expiration, but the only mode by which the expired air could be collected pure and unmixed with the products of perspiration, consisted in the direct application (to the mouth) of an apparatus, by means of which the expired air was conveyed to suitable receiving vessels. This was the method which was usually employed in experiments on man (Dumas, Andral and Gavarret, Valentin, Vierordt). The advantages of this method over the one we shall presently proceed to notice, consisted not merely in the exclusion of the products of perspiration, but also in enabling the observer to determine the influence which certain physical conditions of respiration exerted on the numerical relations of its products. This method is, however, attended with some disadvantages, which although sufficiently serious, can hardly be foreseen; thus, for instance, a person conscious of the nature of the experiment which is being

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 45, S. 214.

<sup>2</sup> Essai de Physiologie chim. p. 160.

<sup>3</sup> Ann. de Chim. et de Phys. 3 Sér. T. 8, pp. 129-150.

<sup>4</sup> Arch. f. physiol. Heilk. Bd. 2, S. 372-417.

<sup>5</sup> Ibid. Vol. 3, pp. 526-588, and Physiologie des Athmens. Karlsruhe, 1845.

<sup>6</sup> Monthly Journ. of Med. Science. 1843, p. 1.

<sup>7</sup> De quantitate acidi carb. ab homine sano et ægroto exhalati. Havniæ, 1845.

<sup>8</sup> Journ. f. pr. Ch. Bd. 33, S. 120, and Bd. 37, S. 1.

<sup>9</sup> Ann. de Chim. et de Phys. T. 11, p. 433.

<sup>10</sup> Compt. rend. T. 20, p. 794-798, and Ann. de Chim. et de Phys. T. 11, p. 433.

<sup>11</sup> Comment. inaug. de respir. nitrog. oxydul. Marburgi, 1844.

<sup>12</sup> Vers. über Perspiration mit Lungen athmender Thiere. Bern. 1846.

<sup>13</sup> Journ. de Chim. méd. 3 Sér. T. 2, p. 477, et 751.

<sup>14</sup> Compt. rend. T. 16, p. 17, and Ann. de Chim. et de Phys. 3 Sér. T. 27, p. 32; also Recherches chimiques de la respiration des animaux des diverses classes. Paris, 1849.



instituted, cannot help breathing in so constrained a manner as to alter the number and depth of the inspirations, so that the normal relations of the ordinarily quiet and unconscious respiration are entirely changed. This inconvenience may, however, be completely remedied by long practice; and the brilliant results and investigations both of Valentin and Vierordt are a sufficient proof that this method does not merit the condemnation which was formerly awarded to it. The objections appertaining to it may indeed be almost perfectly obviated by careful attention to the construction of the apparatus.

The second method, which Scharling and Hannover employed on man, but which most other observers have used only in the case of animals, consisted merely in allowing a current of air constantly to pass through the apparatus in which the person or animal was placed, on whom the experiment was to be made; fresh air was thus continuously supplied, and the products of expiration carried off into a system of vessels, in which the constituents of the expired air might be absorbed, and at the same time quantitatively determined. However simple this method may at first sight appear, and however conformable it may seem to nature, it possesses many deficiencies which can only be fully understood by those who have themselves employed it. It is altogether unsuitable for the investigation of the influence exerted by the mechanical conditions of the respiration, or for the exact determination of the relations of volume existing between the inspired and the expired air, &c. For even if the apparatus is so constructed that the animals are not compelled to take deep or frequent gasping inspirations, if the air be sufficiently changed, and if the animal be removed from all keen draughts of air, and if the apparatus itself be free from a continuous alternation in the tension of the air, &c., we are only able by this method to ascertain with accuracy the absolute quantities of the carbonic acid and aqueous vapor exhaled in given times, for the quantity of the absorbed oxygen can only be determined approximately by weighing the animal both before and after the experiment, and determining the oxygen contained in the amount of exhaled carbonic acid and water, &c. The introduction of perfectly dry air, which is indispensable even to the moderate accuracy of the experiment, causes the animals to lose more water than under ordinary circumstances, in consequence of their breathing in an atmosphere to which they are unaccustomed, and hence they speedily fall into an abnormal condition. The admirable investigations which Marchand has made by this method on the respiration of frogs, indicate, however, that it is capable of leading to results of the highest value to science.

A third method was employed, first by Valentin, and subsequently by von Erlach under his guidance; animals were introduced into an enclosed space filled with atmospheric air, and they were suffered to respire there for some time, when the volume and the composition of the expired air were compared with those of the original atmosphere. As far as this object is concerned, the above method gives highly satisfactory results, as may be seen from the investigations of the above-named chemists; although, as is obvious, it cannot be employed for absolute determinations, or for the investigation of the influence exerted by mechanical and physiological relations on the respiration.



An apparatus has lately been ingeniously contrived by Regnault and Reiset, by which the second and third of these methods have to some extent been combined together. The animals here also breathe in a circumscribed space, from which the carbonic acid and a portion of the expired water are constantly being removed by a solution of potash, whilst a quantity of oxygen corresponding with the amount absorbed is continuously being supplied from another vessel, without the pressure of the air being on that account subjected to any considerable fluctuations. Although the advantages of this method are striking, it is not entirely free from objections, for the saturation with aqueous vapor of the air which the animal is inspiring, and the increased amount of nitrogen in the air after the long-continued respiration of animals, within a limited space, are elements which must speedily exert some influence on the respiratory process.

When we pass in review the most general results yielded by different investigations on the interchange of gases in the lungs, we find in the first place, that the blood in the lungs gives off carbonic acid and aqueous vapor to the inspired air, and takes up oxygen from the latter; a very small quantity of nitrogen also commonly passes from the blood into the respired air, although under special conditions, the opposite sometimes occurs. The first question which presses itself upon our notice is undoubtedly the determination of the relation existing between the exhaled carbonic acid and the oxygen from the inspired air which has disappeared in the lungs. It is well known that the volume of carbonic acid gas is equal to the volume of the oxygen contained in it; if, therefore, a volume of carbonic acid were found in the expired air, which was equal to that of the oxygen which had disappeared from the inspired air, we might be led to conclude with many of the older inquirers, that the oxygen absorbed in the pulmonary vesicles is exactly sufficient to form the carbonic acid which they exhaled. This, however, is by no means the case, for under ordinary relations, the volume of oxygen absorbed is much larger than the volume of carbonic acid which is exhaled. The oxygen does not therefore serve merely for the oxidation of the carbon, but also for that of the hydrogen of the animal constituents. If, for instance, animals be allowed to breathe in an enclosed space, and we then analyze the air which has been modified by their respiration, we find that more free oxygen has disappeared than could have been employed in the formation of the carbonic acid contained therein; we obtain the same result if, as was done by Marchand, we compare the loss of weight in the animal during the period of the experiment, with the oxygen contained in the expired air, and distributed in the carbonic acid and aqueous vapor; for in this case we find that the animal has lost less in weight than might be expected from the quantities of excreted carbon and hydrogen; consequently a substance appreciable by weight must be absorbed by the body of the animal during respiration, and this can be no other than oxygen, as the quantities of the nitrogen, which is either absorbed or given off, are on the whole too small to exert any special influence on this relation. Very numerous experiments have been made on this subject with all the best appliances of science. The individual results yielded by these investigations will engage our attention at a



future page, and we would here only observe, that on an average for every 1 volume of absorbed oxygen, there is only about 0.8516 of a volume of carbonic acid in the expired air. We shall presently see, on comparing the investigations of modern experimentalists, that this relation appears to be a somewhat variable one, while the experiments of Brunner and Valentin, and of von Erlach, give almost exactly this proportion between the gases. According to Valentin, the interchange of these gases (corresponding to the law of their diffusion) stands in an inverse ratio to the square roots of their densities.

Attempts have frequently been made to compare the *volume* of the expired with that of the inspired air. On examining both kinds of air when freed from water, we naturally find a diminution of the volume of air, corresponding to the volume of oxygen which has been absorbed and not converted into carbonic acid. (We must, however, here disregard the small quantity of exhaled nitrogen.) The result will certainly be different when both kinds of air are compared together in a moist state; since the inspired air is usually not saturated with aqueous vapor, while the reverse is the case with the expired air, it necessarily follows that the tension of the aqueous vapor taken up in the lungs must cause an increase in the total volume of the air.

We need scarcely observe that the elevation of temperature which the air commonly experiences in respiration, (from  $36.2$  to  $37.5^{\circ}$ , according to Valentin), must occasion a corresponding augmentation of volume.

The quantity of *water* exhaled by an adult man in a state of rest in 24 hours amounts, according to Valentin, to 506, according to Vierordt to 360, and according to Horn to 350 grammes; as, however, aqueous air was inspired in the experiments of the last-named observers, the actual loss of water is only 321 grammes.

We have already shown, that the *quantity of nitrogen* in the air does not remain precisely the same during respiration. Various views were long entertained in reference to the question, whether nitrogen gas was absorbed or exhaled during respiration; the more modern investigations of Brunner and Valentin, as well as those of Regnault and Reiset, have now placed it beyond a doubt that there is an excretion of nitrogen, although only in extremely small quantity. According to the former of these inquirers, the expired air was about 0.402% (by volume) richer in nitrogen than the inspired air; whilst the latter observers found in their experiments on animals, that for every 10,000 parts by weight of absorbed oxygen, from 8 to 133 parts of nitrogen were developed in the lungs. Boussingault<sup>1</sup> had already endeavored at an earlier period to prove this fact by an indirect method, namely, by comparing the quantity of nitrogen taken into the system with the food, with that contained in the fluid and solid excrements, and the result was, that the quantity of nitrogen present in the excrements was below the amount taken up with the food, and hence it was concluded that the deficient quantity of nitrogen must have been excreted from the organism through the lungs. Boussingault found that the relative weights of the exhaled nitrogen and the expired carbonic acid were nearly as 1 : 100. Barral<sup>2</sup> obtained the same result in

<sup>1</sup> Ann. de Chim. et de Phys. 2 Sér. T. 61, p. 128; and 3 Sér. T. 11, p. 433, and T. 12, p. 153.

<sup>2</sup> Compt. rend. T. 27, p. 361.



his experiments on men, for according to him the quantity of exhaled nitrogen amounts to about 1-100th of the quantity of the excreted carbonic acid. We have already observed (in vol. i. p. 405) that a portion of the nitrogen occurs in the expired air under the form of ammonia.

Dr. Reuling<sup>3</sup> has recently published a prize essay on the amount of ammonia in the expired air both in health and in disease, with especial reference to uræmia. The following are his most important conclusions:

1. The exhaled air of every one contains ammonia.
2. In health its quantity depends on the amount of ammonia in the inspired air.
3. In healthy men there is neither an absorption nor an elimination of ammonia by the pulmonary mucous membrane.
4. Fresh normal human blood contains no ammonia; but almost immediately after it has ceased to circulate in the vessels (whether obtained by venesection or from the dead body), carbonate of ammonia and other ammoniacal compounds begin to be formed in it.
5. Logwood paper is the most sensitive of all the tests for ammonia, and detects it when diluted 64 million times.
6. The amount of ammonia in the expired air is sometimes increased in the following diseases: In caries of the teeth, in angina tonsillaris, in typhus (in consequence of the formation of ammonia in the blood), in pyæmia (when ammonia is formed in the blood through the influence of pus), and in uræmia (either when ammonia is developed in the blood from the retained urea, or when the ammonia formed in the bladder from urea is taken up into the blood).
7. In all probability the amount of ammonia in the expired air is sometimes also increased in cholera and scarlatina.
8. The augmentation of the quantity of ammonia in the expired air occurs most frequently in uræmia, but is not a pathognomonic symptom of this disease.
9. The appearance of ammonia in the blood is certainly the most frequent, although it is not the sole cause of uræmia. Uræmia may be produced by the accumulation of the extractive matters in the blood in cases of suppression of urine.—G. E. D.]

In addition to these very slight traces of ammonia, the expired air not unfrequently also contains volatile substances which have been taken with the food, such as alcohol, phosphorus, camphor, and ethereal oils; and even when no such substances can be detected in the food, small quantities of an organic carbo-hydrogen are found in the expired air. The reddening which sulphuric acid undergoes when used for the purpose of drying the expired air also indicates this fact; but when, as in most experiments on animals, certain products of perspiration are intermixed with the expired air, this coloration may depend upon the gases of the intestinal exhalations, or in case the second of the methods above indicated have been employed, it may be owing to the presence of mechanically adhering organic parts, as, for instance, dust from the skin of the animal. But even where respired air, in which no impurities are present, has been employed, a slight coloring of the acid may be constantly observed after the air has been suffered to pass uninterruptedly through a sulphuric acid

<sup>1</sup> Ueber den Ammoniakgehalt der expirirten Luft, und seiner Verhalten in Krankheiten. Ein Beitrag zur Kenntniss der Uræmie. Giessen, 1854.



apparatus. It seems tolerably well established, from the very exact experiments of Regnault and Reiset, that the hydrogen and the carburetted hydrogen which they found in air which had served for a prolonged time for the respiration of animals, were not dependent solely upon the perspiration or the intestinal exhalation, but that an appreciable quantity both of hydrogen and proto-carburetted hydrogen was exhaled from the lungs when in a perfectly normal condition.

We will now proceed to establish several *absolute values* which the above-named investigators have obtained in reference to many of these points. We possess very different statements regarding the quantity of *carbonic acid* exhaled within a definite time by an adult man. The cause of this diversity may readily be comprehended, when we consider the methods by which these numbers have been obtained. With the exception of Scharling and Vierordt, all other observers have contented themselves with collecting the air of only a few respirations, and, after determining the amount of carbonic acid, have calculated the quantity of this gas for a definite period of time. We have already seen how easily we may be led into error, from want of practice, by the determination of individual respirations, and these errors augment in proportion to the length of time (as, for instance, 1 hour or 24 hours) for which we endeavor to establish the exhalation of carbonic acid. We will therefore pass over the older results, which vary considerably, merely observing that, according to Scharling, a very powerful adult man exhales in 24 hours 867 grammes, or at a temperature of  $0^{\circ}$ , and the barometer at 336''' [29.84 inches], 443,409 cubic centimetres [or about 27,058 cubic inches] of carbonic acid. Basing his calculations on Valentin's law, Vierordt therefore calculates that the amount of oxygen absorbed by an adult in 24 hours (and partly given off again with the carbonic acid and the water, and partly remaining in the body) amounts to 746 grammes, or 520,601 cubic centimetres [or about 31,740 cubic inches]; consequently about 116 grammes of the *absorbed oxygen* are retained in the organism. According to Boussingault's determinations, about 8 grammes of nitrogen would be given off to the atmosphere in the same period of time by the same individual, whilst, according to Valentin, about 500 grammes of water are exhaled on an average in equal intervals of time. The numerous and carefully conducted experiments of Vierordt show that the air exhaled by a healthy man in a state of rest contains on an average 4.334% by volume of carbonic acid.

The above remarks indicate that the frequency or depth of the respiratory movements must exert considerable influence on the interchange of gases in the lungs. Before we proceed to the other relations by which the pulmonary functions are modified, we will consider these purely mechanical relations somewhat more attentively, especially since many other physical and physiological influences affect the respiratory functions, and particularly the excretion of carbonic acid, only in an indirect manner by modifying the respiratory movements. Notwithstanding the attention which has been directed to the mechanism of respiration in its anatomical and physiological relations, and the number and excellence of the investigations made in reference to the chemical constitution of the expired air and the differences which it presents under the most different phy-



siological conditions, this most important factor in the process of respiration remained almost entirely unnoticed until Vierordt published his well-known work on the subject, which he has so thoroughly exhausted that all our knowledge of the relations in question may in fact be referred to him alone. We cannot, therefore, do better than follow him as our guide in these inquiries.

Vierordt first limited his investigations solely to the determination of the dependence of the amount of carbonic acid in the expired air upon the *frequency of the respiratory movements*; to ascertain this relation, he began by observing the quantities of carbonic acid excreted during perfectly quiet respiration, in order to obtain certain mean values and to establish the corresponding variations. All Vierordt's experiments were made upon himself, and as nearly as possible, under the same conditions. The duration of each experiment was limited to a minute, and the air collected during that period was tested for its amount of carbonic acid. Before each experiment a few respirations were made, corresponding in frequency as nearly as possible, to those made during the period of the experiment, since the air remaining in the lungs from the previous respirations might have induced a relative error in the result of the observation. These comparative observations on the different frequency of the respiration were not made consecutively, but at intervals of about half an hour, and, as far as possible, at the same time of the day. The volumes of gases given in the following table are calculated for a temperature of  $37^{\circ}$ , and the barometer at 336 Paris lines.

Vierordt found the following mean values, to which we add the maxima and minima, for the respiratory function for one minute during a state of perfect bodily repose.

	Mean.	Minimum.	Maximum.
Number of pulsations, . . .	75.52	54	101
Number of respirations, . . .	11.9	9	15
Volume of the expired air, . .	6034.0 c. c.	4206.0 c. c.	9331.0 c. c.
	[or 384.7 c. i.]	[or 256.6 c. i.]	[or 568.2 c. i.]
“ expired carbonic acid, . . .	261.52 c. c.	177.0 c. c.	452.0 c. c.
	[or 16.00 c. i.]	[or 10.8 c. i.]	[or 27.6 c. i.]
“ one expiration, . . .	507.0 c. c.	367.0 c. c.	699.0 c. c.
	[or 31.0 c. i.]	[or 22.4 c. i.]	[or 42.7 c. i.]
Carbonic acid in 100 parts of expired air, . . . . .	4.334	3.358	6.220

After having obtained these fundamental values, Vierordt tried the experiment of breathing with double the rapidity without diminishing the normal depth of the inspiration, and he then obtained the result that the relative quantity of carbonic acid was on an average about 0.907% less than in normal undisturbed respiration; when the number of inspirations were increased three times their former amount, this diminution was about 1.125%; when the number was increased fourfold, it was 1.292%; and finally, when they were increased eightfold, it was about 1.600%. When the number of the inspirations was diminished by one-half (when only 6 instead of 12 inspirations were made in a minute, which occasioned considerable difficulty of breathing, and hence could



not yield a perfectly pure result), the difference in the quantity of carbonic acid in the expired air was found to be 1.316%. This relation will be rendered more clear by the following comprehensive arrangement of mean values found by Vierordt, in which the mean quantities of the carbonic acid obtained during respirations of different rapidity, are calculated for one and the same normal quantity of carbonic acid.

Acts of respiration in one minute.	Carbonic acid in 100 vols. of expired air.
6	5.528
12	4.262
24	3.355
48	2.984
96	2.662

Vierordt was able, after a few corrections made in the numbers thus obtained, to show that the numbers of the respirations are functions of the numbers expressing the corresponding percentage of carbonic acid. Thus for every expiration, without reference to duration, there is a constant amount of carbonic acid (of 2.5%), to which we must add a second value expressing the quantity of carbonic acid exactly proportional to the duration of the respiration. We subjoin the following table in elucidation of this proposition :

Respirations.	Percentage of carbonic acid.	Constants.	Augmentation of the percentage of the carbonic acid for the duration of the respiration.
6	5.7	2.5	3.2
12	4.1	2.5	1.6
24	3.3	2.5	0.8
48	2.9	2.5	0.4
96	2.7	2.5	0.2

[The author here quotes Vierordt's formula, representing (as that chemist believes) the connection between the percentage of the carbonic acid and the number of respirations in a minute. As, however, it would not be intelligible to the general reader without a much fuller explanation than is given in the original text, we deem it advisable to omit it.—G. E. D.]

Stürmer,<sup>1</sup> who carried on a series of investigations on this subject under the direction of Marchand, obtained somewhat different results from those of Vierordt, although upon the whole they arrived at tolerably similar conclusions. As Stürmer and Marchand's results did not, however, admit of being expressed by Vierordt's formula, they attempted in some degree to modify it. Several objections were advanced against Vierordt's method, as, for instance, the expiration into the expirator with open nostrils, the employment of a solution of common salt as a separating fluid, and the neglect of the difference of the tension of its vapor from that of pure water, the inaccurate determination of the temperature of the air in the anthracometer, and the uncertainty in the reading of the water-line, &c. Most of these objections were, however, recognized and specified by Vierordt himself, and we agree with him in thinking that they do not materially influence the main results ; for although we by no

<sup>1</sup> *Observ. de acidi carbonici respiratione exhalati quantitate.* Halis, 1848.



means hold the view that a very large number of less exact experiments are able to give a better result than a few very accurate observations (since, if this were the case, an astronomer might as well content himself with taking the mean of the times of 100 clocks instead of employing one costly but reliable chronometer), Vierordt's experiments appear to as fully to merit the confidence which their author himself places in them. One of the most essential requirements towards the success of such experiments undoubtedly consists in the power of carrying on the normal respirations in a quick and undisturbed manner, and in this respect Vierordt has a decided advantage over Stürmer. The latter observer obtained the following mean quantities from eight or ten experiments with the expired air.

6	Respiratory movements in the minute yielded	5.45	per cent. of carbonic acid.
12	"	4.57	"
24	"	3.50	"
48	"	2.65	"

According to Vierordt's experiments, 500 cubic centimetres [or 30.5 cubic inches] are about the mean value for the volume of the air expelled by one expiration when the breathing is undisturbed. If now we assume, during hurried respiration, an equally large volume for the air expelled by each expiration, the absolute amount of carbonic acid exhaled in a minute may be very readily calculated from the above data. The following table plainly shows the relations deduced from this calculation.

Number of expirations in one minute.	Carbonic acid in 100 volumes of expired air.	The quantity of air expired in one minute.	The quantity of carbonic acid expired in one minute.	The carbonic acid exhaled in one expiration.
6	5.7	3,000 c. c. [or 183 c. i.]	171 c. c. [or 10.4 c. i.]	8.5 c. c. [or 1.7 c. i.]
12	4.1	6,000 c. c. [or 366 c. i.]	261 c. c. [or 13.5 c. i.]	20.5 c. c. [or 1.3 c. i.]
24	3.3	12,000 c. c. [or 733 c. i.]	396 c. c. [or 24.2 c. i.]	16.5 c. c. [or 1.0 c. i.]
48	2.9	24,000 c. c. [or 1,463 c. i.]	696 c. c. [or 42.5 c. i.]	14.5 c. c. [or 0.88 c. i.]
96	2.7	48,000 c. c. [or 2,928 c. i.]	1,296 c. c. [or 79 c. i.]	13.5 c. c. [or 0.82 c. i.]

Vierordt subjoins some interesting remarks on the number of respirations which must be made in a minute in order to remove the whole of the carbonic acid from the blood circulating through the lungs. If, for instance, we assume with him that the quantity of carbonic acid in the blood passing in one minute through the pulmonary capillaries amounts to 4300 c. c. [or 262 cubic inches], it would require, according to the above data, upwards of 300 respiratory acts for its entire removal; for 192 respirations would only remove 2496 c. c. [or 152 cubic inches], whilst twice that number might separate as much as 4896 c. c. [or 299 cubic inches], supposing that such excessive frequency of respiration were within the limits of possibility. In accordance, however, with his view of the quantity of carbonic acid contained in the blood of the pulmonary capillaries, six respirations within the minute would expel only 3.97% of carbonic acid; twelve would yield 5.72%; twenty-four 9.21%; and forty-eight 16.18%.

Although several causes, besides the frequency of respiration, exert



the most marked influence on the quantity of carbonic acid in the expired air, this law nevertheless remains in force for otherwise similar conditions, as Vierordt has convinced himself by numerous series of experiments instituted under the most various bodily conditions. We must, therefore, assume with him, that the rhythm of the respiration acts as the most powerful regulator of the excretion of carbonic acid.

The influence of the respiratory movements on the excretion of carbonic acid is equally manifested, when we consider the *intensity or depth of the individual respirations*. Notwithstanding the difficulty of drawing respirations of a certain depth, Vierordt has been able to obtain very decisive results in relation to this point, as may be seen in the following table :

If the air of normal respirations contain	4.60 per cent. of carbonic acid,
The air in respirations twice as deep contains	4.00    "    "
three times	"    3.70    "    "
four times	"    3.38    "    "
eight times	"    2.78    "    "
half	"    5.38    "    "

From these observations it follows, that in an expiration having double the normal volume, the absolute quantity of the exhaled carbonic acid is about equal to that which is exhaled by respirations having three-fold the normal frequency; whence it is further proved that the organism possesses two means of at the same time separating larger quantities of carbonic acid.

Vierordt adopted two methods of determining the question, whether the amount of carbonic acid in the air increases in the finer ramifications of the air-passages, as the experiments of Allen and Pepys, and of Jurine, seem to show. One method consisted in dividing each expiration into two as nearly as possible equal parts; the expired air in the latter half must have arisen from the deeper parts of the lungs, and Vierordt found in it 5.44% of carbonic acid as the mean of 21 experiments, whilst the first half contained on an average only 3.72%. The other method consisted in comparing the amount of carbonic acid in a normal expiration with that in the air obtained by an intensely forced expiration. He found as the mean result of eight experiments, that while the carbonic acid of a normal expiration (of 574 c. c.) amounted to 4.63%, a most complete and full expiration (of 1800 c. c.) contained 5.18%. Hence it follows that in the deeper strata (amounting to 1226 c. c.) of the strong expiration (the quantities contained in both expirations amounting to 26.57 and 93.34 c. c. respectively,) there are 66.67 c. c. (or 5.43%) of carbonic acid, and consequently 0.80% more than the amount contained in the volume of a normal expiration. As, however, there always remain about 600 c. c. of air in the lowest parts of the lungs even after the strongest expiration, the highest percentage amount of carbonic acid in the air in the pulmonary cells would be about 5.83%, that is, 1.2% more than is contained in the air of a normal expiration.

Vierordt made four series of experiments on the influence which *obstruction* of the respiration exerts on the secretion of carbonic acid. All these experiments generally exhibited a very considerable decrease in the absolute amount of carbonic acid, and a considerable increase in



its relative amount—a result to which Horn<sup>1</sup> has also been recently led in a series of analogous experiments.

We now proceed to the consideration of those changes which the expired air experiences from the indirect action of chemical agents, that is to say, more especially from the *inhalation of artificial atmospheres, or of different kinds of gases*. The latest experiments of Regnault and Reiset, on dogs and rabbits, show that the respiration of air which is richer in oxygen than the atmosphere, does not produce effects differing from those yielded under the normal relations; the animals did not exhibit any distress from the inhalation of air containing two or three times more oxygen than our atmosphere, and the products of respiration were precisely the same as when the animals had breathed atmospheric air. It is therefore the more striking, that the earlier experiments on respiration in pure oxygen should have led to tolerably decisive results; among these we must include the observations of Lavoisier and Seguin, as well as those of Allen and Pepys on man, and those of Marchand on frogs. According to these observers, the excretion of carbonic acid was only very slightly or not at all increased by breathing in pure oxygen, although far more oxygen was absorbed than under ordinary conditions. According to Marchand, for instance, there remained more oxygen in the blood (which was not expended in the formation of carbonic acid) than in respiration in ordinary air. The experiments of Allen and Pepys exhibit, moreover, no inconsiderable exhalation of nitrogen. Sir Humphrey Davy's experiments (according to which most of the vital functions are performed with augmented energy after the prolonged inhalation of oxygen) are worthy of being carefully repeated with such improved means as Lespasse<sup>2</sup> has lately employed in his observations.

The respiration of air *richer in carbonic acid* than the ordinary atmosphere, and the repeated inspiration of air which had already been expired, have been made the subject of numerous investigations. Marchand found that frogs which had been suffered to breathe in closed vessels, developed less carbonic acid and inhaled less oxygen towards the close of the experiments than at the beginning, and that at length they absorbed little more oxygen than was necessary for the formation of carbonic acid. The experiments made by Legallois<sup>3</sup> on animals, present results differing so essentially from those obtained by other observers, that one scarcely knows how far to trust them. The following facts seem, however, to possess some degree of probability. A larger amount of nitrogen is excreted in an atmosphere rich in carbonic acid than in the ordinary air, and when the air is very richly charged with carbonic acid some of this substance is even absorbed by the blood; the absorption of oxygen is in that case proportionally small.

Davy's experiments prove that pure carbonic acid cannot be inhaled, as the glottis spasmodically obstructs its passage; 60 or even 40% of carbonic acid are sufficient to render an atmosphere unfit for respiration, although air less densely charged with this acid may be respired for some time without producing any injurious effects, and the danger induced by its prolonged respiration depends less upon the actual amount

<sup>1</sup> Neue medic.-chirurg. Zeitung. 1849, S. 33–39.

<sup>2</sup> Compt. rend. T. 22, p. 1055

<sup>3</sup> Exp. sur le principe de la vie. Paris, 1812.



of carbonic acid than upon the insufficient supply of oxygen conveyed to the lungs by such an atmosphere.

It has been shown by Legallois' experiments on guinea pigs, that in air which is *richer in nitrogen* than the atmosphere, nitrogen is absorbed and less carbonic acid exhaled; the absorption of oxygen appears to be relatively greater than in atmospheric air.

The inhalation of pure nitrogen gas is speedily followed by symptoms of suffocation; according to Coutenceau<sup>1</sup> and Nysten,<sup>2</sup> rather more carbonic acid appears to be exhaled than in the atmospheric air.

The most careful experiments have been made on the respiration of *nitrous oxide* by its discoverer, Humphrey Davy, and these observations have been perfectly corroborated in recent times by Ph. Zimmermann. The first effects are manifested by pleasurable sensations, considerable excitement, and a state resembling intoxication, but this speedily (after the lapse of five or ten minutes) passes into asphyxia. According to Davy's analyses of the expired air, a large quantity of nitrous oxide is absorbed by the blood; carbonic acid and nitrogen being given off in no larger quantities than usual. Zimmermann made numerous experiments with this gas on pigeons and rabbits, and found that the pulse soon became irregularly quickened, and the respiration very frequent, these symptoms being followed after a time by slight convulsions and asphyxia. A strong rabbit was resuscitated by the artificial inhalation of atmospheric air, after the animal had remained for 3 hours and 20 minutes in an atmosphere of nitrous oxide. Zimmermann found that a rabbit which yielded on an average 0·8 of a gramme of carbonic acid in atmospheric air, exhaled 1·3 grammes, when respiring nitrous oxide.

Respiration may be carried on without injury for a tolerably protracted period in an atmosphere containing *hydrogen gas*, if a sufficient quantity of oxygen be present. Regnault and Reiset caused rabbits, a dog, and frogs to respire in an atmosphere whose nitrogen had been for the most part replaced by hydrogen (from 55 to 77% of hydrogen, from 1·1 to 14·4% of nitrogen, and from 21·8 to 28·8% oxygen); the rabbit remained in this atmosphere 20 hours and the dog 10 hours without any obvious injury, excepting that the respiration was augmented in force—a circumstance which these observers thought they might refer to the greater cooling power of the hydrogen. At the close of the experiment nearly the original amount of hydrogen was found; there was a more considerable absorption of oxygen than in the case of atmospheric air. Nitrogen appeared to be exhaled; but this might have been derived from the air already in the lungs of the animals, when they were introduced into the apparatus in which they were made to respire. The respiration of these animals proceeded, therefore, quite as regularly in this artificial atmosphere as in ordinary air—a circumstance which had already been observed by Lavoisier and Seguin, as well as by Humphrey Davy.

It is clearly shown by Regnault and Reiset's experiments that the only reason why respiration cannot be supported for any length of time

<sup>1</sup> Révision des nouv. doct. chem.-physiol., &c. Paris, 1814.

<sup>2</sup> Recherches de Physiol. et de Chim. pathol. Paris, 1811.

<sup>3</sup> Diss. inaug. med. Marburgi, 1844.



in pure hydrogen gas is, that the organism is thus deprived of the oxygen necessary for life. Marchand found that frogs died in from half an hour to an hour after being placed in pure hydrogen gas; they exhaled a much larger quantity of carbonic acid in this gas than in atmospheric air, for whilst 1000 grammes' weight of frogs exhaled about 0.077 of a gramme of carbonic acid in one hour in atmospheric air, they developed as much as 0.263 of a gramme of carbonic acid in the same time in pure hydrogen gas.

*Carbonic oxide gas*, when mixed even in very minute quantities with atmospheric air, gives rise to faintness, feelings of suffocation, stupefaction and death. The fact of this being the constituent to which choke-damp owes its fatal effects, has been especially demonstrated in recent times by Leblanc.<sup>1</sup>

We need hardly observe that sulphuretted hydrogen, seleniuretted hydrogen, phosphuretted hydrogen, arseniuretted hydrogen, ammoniacal gas, sulphurous acid, chlorine, &c., are not merely irrespirable, but are also poisonous gases, like carbonic oxide.

Like all the other functions of the animal organism, the respiration is acted upon in a definite manner by numerous influences of the external world. The animal body is brought into the most intimate relation with the atmosphere through the medium of the lungs; and hence the effects of various atmospheric conditions are discernible in the different respiratory functions. In consequence of these relations, we will investigate the alterations apparent in the composition of the expired air during different conditions of the atmosphere; amongst which the *temperature* first claims our attention. The earliest experiments made in relation to this point were for the most part limited to those animals which at low temperatures either fall into a state resembling hibernation, or whose vital activity is at all events more or less reduced. As Spallanzani, Saissy, Treviranus, and others had observed that insects and molluscs, as well as marmots, bats, and hedgehogs, exhaled less carbonic acid in a low than in a high temperature, it was at once assumed as a general proposition, that a depression of the surrounding temperature would constantly produce this effect in all classes of animals. The numerous and variously modified experiments which have since been made in connection with this inquiry have, however, proved that in the higher classes of animals at all events there is a diminution in the exhalation of carbonic acid corresponding with the rise of the temperature from the freezing point. Letellier<sup>2</sup> was one of the first of several observers who in recent times have made a series of determinations of the quantities of carbonic acid exhaled by different animals, as green-finches, turtle-doves, mice, and guinea-pigs, at various lower or higher temperatures. His results showed that the largest relative amount of carbonic acid was exhaled in a temperature between  $-5^{\circ}$  and  $+3^{\circ}$ , and the smallest at a temperature between  $+28^{\circ}$  and  $43^{\circ}$ . This ratio is more strongly marked in birds than in the mammals; the animals on which these experiments were made were unable to bear a temperature exceeding  $+43^{\circ}$ . Almost simultaneously with Letellier, Marchand obtained similar results with frogs; with this difference only, that these animals

<sup>1</sup> Compt. rend. T. 30, p. 483.

<sup>2</sup> Ibid. T. 20, p. 794.



already fell into a torpid state between  $+2^{\circ}$  and  $3^{\circ}$ , in which they excreted a remarkably small amount of carbonic acid, 1000 grammes' weight of frogs yielding only 0.039 of a gramme in one hour, whilst the largest amount was exhaled between  $6^{\circ}$  and  $7^{\circ}$ , 1000 grammes' weight yielding 0.124 of a gramme; the quantity of excreted carbonic acid then gradually sunk in proportion to the rise of the temperature. Between  $28^{\circ}$  and  $30^{\circ}$ , 1000 grammes' weight of frogs exhaled only 0.077 of a gramme in one hour.

Vierordt has calculated a scale of the values of the respiratory functions according to each degree of temperature between  $3^{\circ}$  and  $24^{\circ}$ , basing his numbers on the results of his numerous experiments on the excretion of carbonic acid, in which he noted the thermometric and barometric readings, as well as the pulsations and respirations, and the volumes of the individual expirations throughout the entire experiment. These tables afford a better insight into the influence of the temperature on the respiration than we obtain from any of the earlier observations on the same subject. For the better comprehension of these relations, we divide the mean result into two sections, of which the one represents the means of the values obtained in the lower degrees of temperature between  $+3^{\circ}$  and  $13^{\circ}$ , and the other those between  $14^{\circ}$  and  $24^{\circ}$ .

	Average temperature.		Difference.
	$8.47^{\circ}$	$19.40^{\circ}$	
Pulsations in one minute,	72.93	71.29	1.64
Respirations in one minute,	12.16	11.57	0.59
Volume of one expiration,	548.0 c. c.	520.8 c. c.	27.2 c. c.
	[or 33.5 c. i.]	[or 31.8 c. i.]	[or 1.7 c. i.]
Air expired in one minute,	6672.0 c. c.	6106.0 c. c.	656.0 c. c.
	[or 407.0 c. i.]	[or 367.2 c. i.]	[or 40.0 c. i.]
Carbonic acid in one minute,	299.33 c. c.	257.81 c. c.	41.52 c. c.
	[or 18.3 c. i.]	[or 15.70 c. i.]	[or 2.60 c. i.]
Carbonic acid in 100 parts of expired air, . . . .	4.48	4.28	0.20
State of the barometer, . .	334.60 Paris lines [or 29.73 inches].	333.82 Paris lines [or 29.64 inches].	

This table not only shows that the number and depth (volume) of the respirations decrease with the elevation of the temperature, but it also exhibits the indirect influence of temperature on the excretion of carbonic acid, from its absolute quantity being considerably diminished by the diminution of the number and extent of the expirations; in the meanwhile the percentage amount of this gas in the expired air is also decreased; whence the elevation of the temperature must necessarily influence the excretion of carbonic acid by some other means than by diminishing the mechanical functions of respiration.

Vierordt has also determined similar relations in regard to the quantities of water expired at different temperatures,<sup>1</sup> as may be best seen in the following table:

<sup>1</sup> Abhandl. bei Begründung der k. sachs. Ges. d. Wiss. Leipzig, 1846.



Temperature of the air.	Inspired air reduced to the corresponding temperature, and 366''' B.	Expired air reduced to 37° and 336''' B.	Water expired in one minute in grammes.	Quantity of water in the air inspired in one minute in grammes.		Loss of water in the body in one minute, in grammes.	
				Perfectly saturated	With the mean amount of water.	When breathing saturated air.	When breathing air containing the mean amount of water.
4°	5827	6634	0.27988	0.03997	0.02435	0.23991	0.25553
9°	5680	6334	0.26723	0.05219	0.02471	0.21503	0.24251
14°	5522	6034	0.25454	0.06760	0.02772	0.18696	0.22685
19°	5253	5734	0.24191	0.08682	0.03725	0.15509	0.20466
24°	5234	5430	0.22926	0.11164	0.04156	0.11461	0.18770

The degree of moisture of the atmosphere is not without influence on the respiratory functions, and especially on the excretion of carbonic acid. I have made several experiments in reference to this subject on wood-pigeons, green-finches, and rabbits. The weight of carbonic acid excreted in moist air greatly exceeds that eliminated in a dry atmosphere; thus, for instance, 1000 grammes' weight of male wood-pigeons yielded in one hour in the morning in a *dry* air 10.438 grammes of carbonic acid at 0°, 6.055 grammes at 24°, and 4.69 grammes at 37°; in a *moist* atmosphere they yielded 6.769 grammes at 23°, and 7.76 grammes at 37°.

In the same way 1000 grammes' weight of green-finches yielded in the course of one hour in the afternoon in *dry* air 7.260 grammes at 0°, 5.679 grammes at 17.5°, and 3.220 grammes at 37.5°. In *moist* air they yielded 5.351 grammes at 17.5°, and 6.851 grammes at 37.5°. Lastly, 1000 grammes' weight of rabbits exhaled in one hour before noon 0.451 of a gramme of carbonic acid in *dry* air at a temperature of 37.5°, and as much as 0.677 of a gramme in a *moist* atmosphere at the same temperature.

Few as these investigations are, they yet clearly demonstrate the importance of this influence on respiration, which we have frequently had opportunities of observing at the bedside, more especially in the case of pulmonary diseases. It is only when we proceed to inquire into the causal connection existing between the excretion of carbonic acid which is here observed, and the degree of moisture of the inspired air, that we are compelled to admit our insufficient knowledge of this subject.

The influence exerted by the moisture of the air on the respiratory movements is not a question of mere conjecture, since it admits of direct observation. The respirations of animals are more frequent in a moist warm atmosphere than in a dry one; but this result depends very much upon the change to which the animals are subjected at the beginning of the experiment; but when the frequency of the respiration is observed, 3, 6, or 10 hours after the commencement of the experiment, it is always found to be more considerable than in a dry atmosphere. It appears, however, from some experiments made by Buchheim in my laboratory, that the moisture of the air even more decidedly influences the depth of the inspirations. But although the augmentation in the expired carbonic acid, when breathing in a moist air, may be partially explained by the alteration in the respiratory movements to which we have already referred, the influence of moisture, like that of the temperature, pro-



bably also acts in some other way. Our knowledge of these relations does not as yet enable us to prove that the aqueous vapor exerts any direct influence on the excretion of carbonic acid from the blood. I have repeatedly made an observation in reference to this subject, which may, I think, prove of some interest towards the further elucidation of this question. I have found that frogs lose much less of their weight in a dry than in a moist atmosphere, the difference being very considerable. The two following of my numerous observations may suffice to demonstrate this difference. In one case 100 grammes' weight of frogs lost 1.820 grammes of their weight in twenty-four hours in a dry atmosphere, and as much as 4.376 grammes during the same period of time in moist air; in another experiment they lost 0.681 of a gramme in dry, and 5.340 grammes in moist air. It is very obvious that these conditions depend chiefly upon the perspiration, and do not, therefore, present a perfectly parallel case with the respiration of the higher animals; for the external appearance of the frogs which were in the dry air, showed that their skin was dry, and consequently in an unfit state for carrying on the process of respiration; but still this observation may not be entirely unconnected with these respiratory conditions. It also shows the necessity for practising caution in drawing our conclusions from experiments made on animals which have only respired a perfectly dry air. We cannot possibly observe normal conditions of respiration in experiments conducted merely in dry air, although this one element may not be of great importance in reference to the consideration of the whole process.

The *pressure of the air* is another of the atmospheric influences which reacts upon the respiration. We will here first refer to the most recent experiments made in relation to this subject, partly because they have led to the adoption of far more correct views regarding the influence of atmospheric pressure than could be obtained from the earlier observations on animals. Here too we are mainly indebted to Vierordt for our knowledge. His numerous experiments at different heights of the barometer yield the following values for the individual functions of respiration.

Height of Barometer.	Pulse.	Volume of one expira- tion.	Amount expired in one minute of		Relative amount of carbonic acid.
			Air.	Carbonic acid.	
332.04 Paris lines [or 29.48 inches].	70.9	528.9 c. c.	6121 c. c.	272.51 c. c.	4.450 per cent.
337.71 Paris lines [or 29.79 inches].	72.2	529.2 "	6607 "	271.16 "	4.141 per cent.

A rise in the barometer of 5.67''' therefore increases the pulsations 1.3, the respirations about 0.74, and the amount of expired air 586 c. c. [or 35.7 cubic inches] in a minute, whilst the carbonic acid of the latter sinks about 0.309%. Vierordt further remarks that these differences are made more apparent when respiration is carried on at higher temperatures.

Legallois placed dogs, cats, rabbits, and guinea-pigs in an atmosphere which was only one-third as dense as the ordinary atmosphere, and compared the results of these experiments with others obtained from obser-



vations conducted at the ordinary pressure of the atmospheric air. We cannot, however, attach any great value to these experiments, because the sudden change in the atmospheric pressure must necessarily have disturbed the other functions of these animals to so great a degree as essentially to vitiate the purity of the observation. Although my own experiments on rabbits and green-finches, in connection with this point, are not free from all grounds of objection, I have endeavored, as far as possible, to distinguish between the effects of the alteration in the pressure of the air, and those depending upon the constant atmospheric pressure. I found by direct observation, that every rapid change in the pressure of the air, whether this change were one of increase or diminution, gave rise to accelerated respiration both in birds and in mammals, and, consequently, that it was connected with increased exhalation of carbonic acid. My experiments were, therefore, conducted in such a manner as to accustom the animals to an increase or diminution of the ordinary atmospheric pressure, after which the quantity of carbonic acid expired within a definite time under such an increased or diminished atmospheric pressure, was determined. The results obtained presented nearly the same degree of variability, although in some cases the pressure was raised to 34'', and in others it fell to 22''. Although, for instance, in one case 1000 grammes' weight of green-finches exhaled 5.921 grammes of carbonic acid when the barometer stood at 739 m. m., and 6.313 grammes when the barometer was at 805 m. m., the temperature in both cases being  $+13^{\circ}$ , and in another case 1000 grammes' weight of rabbits exhaled 0.529 of a gramme of carbonic acid with the barometer at 704 m. m., and 0.600 grammes with the barometer at 801 m. m., the temperature in both cases being  $15^{\circ}$ , and there would, therefore, seem to be some ground for the hypothesis that an augmentation of the carbonic acid was due to increased atmospheric pressure; yet the most general result to be deduced from the tolerably accordant experiments made in reference to this subject seems nevertheless to prove that a diminution of pressure of the air gives rise to a slight decrease in the quantity of exhaled carbonic acid, whilst an augmentation of pressure occasions a slight increase in this gas, and that the absolute pressure of the atmosphere must consequently exert a very subordinate influence on the exhalation of carbonic acid. The animals which were employed for these experiments were, however, quite as lively and as much disposed to eat with the barometer both at 34'' and at 22'' as at the mean pressure.

Marchand made several experiments on the condition of frogs, when enclosed in a space from which *the air had been almost entirely withdrawn*. When the air-pump was worked slowly, the animals began to show symptoms of uneasiness, and their bodies swelled at a pressure of 54 m. m. [21.25 inches], and at a pressure of 4 m. m. [0.16 of an inch] they exhibited considerable inertia, and many of them became asphyxiated. After remaining for even half an hour *in vacuo*, the animals recovered on a readmission of air. If the animals were killed by complete abstraction of air, it was found that 1000 grammes' weight of frogs would eliminate about 0.600 of a gramme of carbonic acid.

Prout's experiments on the influence of the different *periods of the day* upon the exhalation of carbonic acid have been repeated by several



observers, amongst others by Scharling, Vierordt, and Horn,<sup>1</sup> who have noticed that the different periods of the day occasion decidedly appreciable differences in this respect. We fully concur, however, with Scharling and Vierordt in referring these differences far more to internal conditions of the organism, such as digestion, waking and sleeping, &c., than to cosmical relations, if indeed the latter claim any consideration. It would at all events appear from the experiments of these observers, that the influence of the different periods of the day, if the above physical relations be set aside, is reduced to a minimum. It must not, however, be forgotten, that the numerous experiments of Bidder and Schmidt<sup>2</sup> perfectly coincide with those of Chossat<sup>3</sup> in showing that animals, when fasting, constantly exhale far less carbonic acid during the night than by day, this relation continuing unaltered up to the time of death. As these oscillations were found by Schmidt to cease after the animals had been blinded, they cannot be entirely owing to sleeping and waking; for although light in itself may exert some influence on these corporeal conditions, it must be very indirect in its nature.

Marchand was induced to believe from his earlier experiments on frogs, that the difference between the diurnal and nocturnal excretion of carbonic acid was very considerable; he found, however, from his subsequent observations, that the apparent excess of the diurnal over the nocturnal excretion in his former experiments was entirely owing to the circumstance that the frogs were employed for the day-experiments immediately after their capture, while the same exhausted animals were again used for the night-observations. Marchand has, therefore, also been led to the conclusion, that the influences of day and night are very inconsiderable, and that the slight diminution in the excretion of carbonic acid during the night can only be referred to the more quiet condition of the animal during that time.

It might, *a priori*, be concluded that those *internal conditions of the animal organism* which are closely connected with *nutrition*, and which, therefore have a direct bearing upon the constitution of the blood, must exert the most marked influence on the respiration; and such indeed has been proved to be the case by various experiments on the respiratory functions during digestion, as well as during fasting, and after the use of certain articles of food and drink.

On passing to the consideration of the condition of the respiration *during complete abstinence from food*, we find that all observers coincide in this point, that fasting essentially influences all the excretions, including that of the lungs. Letellier found that 1000 grammes' weight of turtle-doves, which exhaled 5.687 grammes of carbonic acid in an hour when they were fed upon grain, excreted only 4.120 grammes of this gas within the same time after having fasted seven days. Boussingault<sup>4</sup> made a similar observation on the same animals, and found that 1000 grammes' weight of them, which hourly exhaled 4.169 grammes of carbonic acid when fed with millet, yielded only 2.050 grammes after a seven days' fast. Marchand has very carefully investigated the

<sup>1</sup> Op. cit.

<sup>2</sup> Op. cit. p. 317.

<sup>3</sup> Recherches expériment. sur l' inanition. Paris, 1843, p. 67.

<sup>4</sup> Ann. de Chim. et de Phys. 3 Ser. T. 11, p. 433.



diminution of the respiratory products and their relation to the absorbed oxygen in frogs while fasting. His numerous series of experiments, some of which embrace long intervals of time, appear clearly to show that these animals gradually exhale less carbonic acid, and absorb less oxygen; it is, however, worthy of notice that the ratio of the absorbed oxygen to the exhaled carbonic acid, always rises until it reaches the proportion of about 420 : 200, when the great quantity of oxygen must necessarily be employed for the oxidation of the hydrogen. This ratio becomes subsequently so changed (being 800 : 100, or even 270 : 100) that the oxygen is scarcely sufficient for the formation of carbonic acid. This lower ratio then remains tolerably constant.

It would appear from the extensive investigations of Regnault and Reiset, that there exists almost one uniform ratio for the most different animals in respect to the composition of the air which is expired during fasting. The consumption of oxygen is invariably less in fasting than in well-fed animals; thus, for instance, 1000 grammes' weight of rabbits, which when fasting absorbed on an average only 0.749 of a gramme of oxygen, took up when well fed as much as 0.877 of a gramme. A much smaller quantity of the absorbed oxygen reappears in the carbonic acid when animals are fasting than when they are abundantly fed upon amylaceous substances. Thus, for instance, in rabbits fed upon carrots, from 84 to 95% of the absorbed oxygen were expended in the formation of carbonic acid, while only from 76.2 to 70.7% were consumed in this manner when the animals were fasting. Regnault and Reiset frequently observed an absorption of nitrogen by animals during fasting; this being almost invariably the case with birds, but of rarer occurrence in mammals.

Bidder and Schmidt<sup>1</sup> have made two admirable series of experiments on the respiration of cats, when these animals were entirely deprived of solid food. A cat weighing 2464 grammes exhaled 699.52 grammes of carbonic acid (= 190.78 grammes of carbon) and 525.67 grammes of aqueous vapor during 18 days' inanition. A quantitative determination and analysis of the other excretions showed that here, almost exactly as in the case of Regnault and Reiset's direct observations, only 76.5 grammes of every 100 parts of the oxygen absorbed during inanition were eliminated with the expired carbonic acid; and further, that 75.15 parts of aqueous vapor were exhaled with 100 parts of carbonic acid (the animals were very rarely permitted to drink water), whilst 41.72% of the water exhaled were eliminated by perspiration. When we compare the observations made on individual days during this series of experiments, we obtain the following results: the absorption of oxygen decreases constantly to the death of the animal, at first very rapidly (about 2 grammes in the 24 hours during the first few days), and then more slowly and regularly (about 0.2 of a gramme in the 24 hours till the thirteenth day); this decrease is finally more rapid (about 2 grammes) till the close of the period of inanition. The quantity of inspired oxygen which is not expended in the formation of carbonic acid decreases at first very rapidly, but afterwards with tolerable regularity. At the commencement of the experiment 80% were expended in the formation of carbonic acid (on the second day 77.4%), and at the close of the experi-

<sup>1</sup> Op. cit. pp. 304 et 340.



ment only 73.0%. The quantity of daily excreted carbonic acid decreases with tolerably uniform rapidity during the first six days, but the diminution is much more gradual during the succeeding six days, and again more rapid during the remaining six days. If, however, we compare the daily excreted carbonic acid with the daily waste of tissue, as calculated by Schmidt, we obtain the following striking relation: at first the quantity of the excreted carbonic acid scarcely amounted to double the quantity of wasted tissue, in the middle of the experiment it was  $2\frac{1}{2}$  times as great, and at the close of the experiment it was even triple the amount. This waste of tissue yields, therefore, a relatively much smaller quantity of carbonic acid at the beginning than towards the middle of the period of inanition, but the largest quantity towards the close of the experiment. As we may already calculate from the composition of the fat and from that of the nitrogenous constituents of the body (after deducting the carbon accompanying the nitrogen into the urine and fæces), that the former supplies the respiratory process with 78.1% of carbon, while the albuminates yield only about 46.1%, it will be readily seen that we may easily compute, from the amounts of carbonic acid and nitrogen which are excreted, what are the relative quantities of fat and of albuminates, together with gelatigenous matter, which are daily submitted to metamorphosis. The relation between the quantities of excreted carbonic acid and the loss or waste of tissue, may therefore indicate what proportions of fat and albuminates are consumed during inanition; this is a subject, however, to which we shall presently have occasion to revert.

The quantity of aqueous vapor which is daily exhaled decreases during inanition with tolerable slowness and regularity, but this decrease is somewhat more rapid at the beginning and end of the experiment.

In the second series of experiments (the subject of which was a full grown male cat, into whose stomach a large quantity of water had been injected), the ratio of the absorbed oxygen to that which was exhaled with the carbonic acid was almost precisely the same as in the former case, namely 100 : 75.3. There were 95.7 grammes of aqueous vapor exhaled for 100 parts of carbonic acid; only 21.95% of the excreted water was eliminated by the skin and lungs. Whilst, however, in the first case, where no ingestion of water was allowed during inanition, there were daily exhaled on an average 21.641 grammes of carbonic acid for 1000 grammes' weight of the animal, and 16.281 grammes of aqueous vapor; while in the latter case, where water was freely given, 16.30 grammes of carbonic acid and 15.60 grammes of aqueous vapor were yielded by 1000 grammes' weight of the animal; the loss was therefore far less considerable when water was allowed than when both fluid and solid food were simultaneously withheld.

The omission of even a single meal alters the relations of the respiration very considerably, as is clearly shown by Vierordt's observations on the influence of *digestion*. This observer, who was accustomed to dine at half-past twelve, noted the following relations in his own person, which show that the principal meal exerts an influence in this respect which we could scarcely have anticipated.



Time of Day.	Pulsations.	Respirations.	Volume <sup>1</sup> of 1 expiration.	Air.	Carbonic acid.	Quantity of carbonic acid in 100 vols. of expired air.
				Expired in one minute.		
Noon, . . . . .	63	10	545.0 c. c.	5450 c. c.	270.22 c. c.	4.69
Two hours after dinner, At 2 P. M., when no dinner had been taken, . .	78.8	11.22	558.7 "	6162 "	307.36 "	4.74
	62.5	9.5	575.0 "	5479 "	258.18 "	4.73
Difference at 2 P. M., de- pending upon whether dinner has or has not been taken, . . . . .	16.3	1.72	163 "	683 "	49.18 "	0.01

We may see from this table that the individual respiratory functions constantly diminish in activity after the last meal (or in fasting), and that the ingestion of food very rapidly induces a very considerable increase in their intensity; the volume of each inspiration is, however, diminished in the latter case, as we may readily comprehend from anatomico-mechanical relations. Vierordt has, moreover, convinced himself that there is a similar augmentation in the excretion of carbonic acid whenever dinner is partaken of at a different time of the day, and that this increase is both relatively and absolutely greater in the *colder season* of the year. This observation corresponds with the result yielded by the experiments made by Barral<sup>2</sup> on his own person, in which he found that he excreted one-fifth more carbon through the lungs in winter than in summer.

Scharling also found by his method of experiment that man exhales more carbonic acid under like conditions when he has eaten a full meal than when he is fasting.

It has been proved by various experiments that the products of respiration must also be influenced by *the chemical nature of the food*. This might, indeed, have been conjectured from the experiments of Dulong<sup>3</sup> and Despretz,<sup>4</sup> on the differences in the respiration of herbivorous and carnivorous animals—results which have recently been confirmed. Dulong found that the ratio existing between the oxygen employed in the formation of carbonic acid and the oxygen which either remained in the blood or combined with the hydrogen, was altogether different in herbivorous and in carnivorous animals, for whilst in the former there was only about 1-10th more oxygen absorbed than was contained in the expired carbonic acid, as much as 1-5th or even the half of the absorbed oxygen, was employed in the latter for other purposes than that of forming carbonic acid. Lassaigne and Yvart thought they had convinced themselves that guinea-pigs absorb 1-5th more oxygen after nitrogenous than after vegetable food. Letellier found that 1000 grammes' weight of turtle-doves exhaled 136.5 grammes of carbonic acid in 24 hours when fed upon millet, 127.68 grammes after being fed for 3 days on sugar, and only 111.84 grammes of this gas after being fed for 5 days on butter.

The experiments of Regnault and Reiset afford us still further insight into these relations; for these observers found that a much larger

<sup>1</sup> [The *relative* being of more importance in this table than the *absolute* values, we have not deemed it necessary to reduce the cubic centimetres to inches.—G. E. D.]

<sup>2</sup> Ann. de Chim. et de Phys. 3 Ser. T. 25, p. 165.

<sup>3</sup> Magendie's Journ. de Physiologie, T. 3.

<sup>4</sup> Ann. de Chim. et de Phys. T. 27, p. 338.



quantity of oxygen was employed in the formation of carbonic acid when dogs had been fed on amylaceous substances than when the food had been of an animal nature ; in the latter case only 74.5 of every 100 parts of the absorbed oxygen were found again in the carbonic acid, while in the former case 91.3 parts of the oxygen were employed in the formation of carbonic acid. Nitrogen was also eliminated during a vegetable diet, although in far less quantity than during an animal diet. It is worthy of notice, that a dog which had been fed on mutton suet neither exhaled nor absorbed nitrogen, and that only 69.4% of the absorbed oxygen were employed in the formation of carbonic acid. A considerable absorption of nitrogen was observed in hens which had been fed on animal food after several days' starvation, but when they had become habituated to this kind of food they began again to develop nitrogen as in the normal condition : it was also found by experiments on these birds that a far smaller quantity of the absorbed oxygen was found in the carbonic acid when they had been kept on animal food ; in two cases there were only 63% of the absorbed oxygen present in the carbonic acid which was exhaled. On comparing the different experiments made on dogs and rabbits, we find that, when considered in reference to their dietetic categories, they agree perfectly with the results yielded by Dulong's observations on the respiration of animals. It is also found that after an animal diet the interchange of gases in the lungs is very similar to that we observe during fasting ; and this observation, which has also been made in reference to the urine and the other excretions, seems to be explained by the fact that fasting animals to a certain degree live upon their own flesh.

Although our attention is at present most especially turned to direct observations, and although we shall treat fully of the influence of diet upon the molecular movements in the animal body when we enter upon the subject of "Nutrition," the consideration of the question, how far the nature of the food partaken of influences the absorption of oxygen and the excretion of carbonic acid, can scarcely be deemed out of place in the present part of our work. In considering this subject, we have to take our stand upon a postulate, the inductive proof of which we defer for the present ; we assume that all the carbon and hydrogen of the fats and carbo-hydrates derived from the food are entirely oxidized in the living body into carbonic acid and water. It must be obvious to all who are acquainted with the composition of these substances, that very different quantities of oxygen are required for their perfect oxidation. The mean composition of the fats is about 78.13C, 11.64H, and 10.13O. The oxidation of the carbon (into carbonic acid) and of the hydrogen, which are contained in 100 grammes of fat, would require  $(208.35 + 93.92 \text{ grammes}) = 302.27 \text{ grammes}$  of oxygen ; but as the fat already contains 10.13 per cent. of oxygen, it would only require to absorb 292.14 grammes of oxygen to effect its entire combustion into carbonic acid and water. When we compare the composition of sugar with that of fat, we see at the first glance that the carbo-hydrates require far less oxygen for their perfect oxidation than the fats ; in the carbo-hydrates there is no hydrogen to oxidize, since the oxygen which they already contain is sufficient for the oxidation of the hydrogen : hence the carbon is the only substance in them requiring oxidation, and this substance is moreover



contained in far less quantity in the carbo-hydrates than in the fat for equal weights. Certain organic acids, such as tartaric acid, citric acid, and malic acid, which, as is well known, occur in many articles of food, contain so large an amount of oxygen that it not only suffices for the oxidation of the hydrogen, but in part also for that of the carbon also.

In reference to nitrogenous substances, we cannot, however, grant the postulate that all the carbon and hydrogen is consumed in the animal body, for we know that the greater part of the nitrogen in these substances is not removed in a free state as ammonia, but in combination with carbon, hydrogen, and a little oxygen, by other means than through the lungs. Hence we are led to inquire whether, and to what extent, the nitrogenous nutrient substances yield materials for oxidation, and consequently how much carbonic acid and water they are able to furnish to the respiratory process. As we have already seen that the albuminates and collagen are capable of supporting respiration, we are induced, in explanation of their respiratory value, to adopt the provisional hypothesis that these substances are merely decomposed into carbonic acid, water, and urea in the animal body, although we know that there are formed other nitrogenous products of excretion besides urea. But since the quantity of urea which is produced preponderates very much, and since in many organisms, as, for instance, in the carnivora, urea is almost solely formed, this hypothesis deserves some notice in our consideration of the average value of the amount of oxygen employed in the oxidation of the albuminates and the collagen. We therefore abstract from the composition of the albuminates and other nitrogenous nutrient substances an amount of urea equivalent to the quantity of nitrogen which they contain. If, for instance, we assume that the composition of the albuminates without the sulphur and salts is 54·36% C, 7·27% H, 16·05% N, and 22·32% O, there will remain, after the abstraction of the quantity of urea (= 6·88C, 2·29H, and 9·18O) equivalent to the 16·05 parts of nitrogen from 100 parts of an albuminate, 47·48 parts of carbon, 4·98 of hydrogen, and 13·14 of oxygen. The following table will give a clearer representation of these relations :

Substance.	Carbon.	Hydrogen.	Oxygen.	The quantity of oxygen required for the formation of CO <sub>2</sub> and H <sub>2</sub> O, in addition to the amount already present.
100 parts of fat, . . .	78·13	11·74	10·13	292·14
“ starch, . . .	44·45	6·17	49·38	118·52
“ sugar (C <sub>12</sub> H <sub>22</sub> O <sub>12</sub> ), .	40·00	6·66	53·34	106·67
“ malic acid (C <sub>4</sub> H <sub>2</sub> O <sub>4</sub> ),	41·38	3·45	55·17	82·78
“ albuminates, . . .	47·48	4·98	13·14	153·31
“ collagen, . . .	42·52	4·47	13·59	135·56
“ muscular substance (muscular fibrin + collagen) according to C. Schmidt, . . .	46·10	4·72	13·66	147·04

If we consider these relations in their bearing on the development of heat, we shall be able to construct a table such as Liebig long since suggested, which would indicate the different values of these substances in



supporting animal heat. Such a calculation may readily be made, if we take as the basis of our computations Dulong's determinations, according to which 1 gramme of carbon develops 7170 units of heat in its combination with oxygen to form carbonic acid, while 1 gramme of hydrogen gives off 34,700 units of heat during the formation of water. Although it cannot be denied that in an equation of this kind a number of functions must be taken into account which cannot be deduced from the chemical composition alone, it is, nevertheless, perfectly clear that this is the only point of view from which a rational theory of animal heat can be formed. The present, however, is not the fitting place to enter more fully into this subject. If we limit ourselves to the process of respiration, we obtain, from the above tabular exposition of the different amounts of oxygen required for the complete oxidation of these nutrient substances, certain numbers which may be regarded as *respiratory* equivalents. If, for instance, we assume that an organism in the full performance of its vital functions must absorb 100 grammes of oxygen within a definite time, the following quantities of the above-mentioned substances would be necessary, in union with 100 grammes of oxygen, to satisfy the requirements of vitality: namely 34.23 grammes of fat, 84.37 grammes of starch, 93.75 grammes of sugar, 120.80 grammes of malic acid, 65.23 grammes of albuminates, 73.77 grammes of collagen, or 68.01 grammes of (dry) muscular substance. No one who has followed our development of physiological chemistry can for a moment suppose that any one individual substance taken from this series can of itself serve the purposes of vitality, provided even it reached the organism in the equivalent quantity; and in the following section our attention will be especially directed to the inquiry of the proportion in which several of these substances require to be mixed in order to render them capable of supporting the vital functions. These numbers must, therefore, remain merely as proportional estimates of their relative values in respect to the functions depending upon the interchange of gases in the lungs.

This table suggests another consideration, which may throw some light upon the difference in the relations between the quantity of oxygen which is absorbed and that which is exhaled in the form of carbonic acid, after vegetable and animal food respectively, in as far at least as these relations have been made known to us by the experiments of the inquirers already referred to. If, for instance, we assume that the interchange of gases in the lungs is for a time merely the result of the combustion of a single one of the above-named substances, we should find, whenever pure fat was subjected to oxidation, that for every 100 parts of absorbed oxygen 71.32 parts are contained in the carbonic acid expired during the interchange of gases in the lungs, while in the case of starch and all the other carbo-hydrates 100 parts are found in the exhaled carbonic acid, in malic acid 110.53 parts, and in the muscular substance 83.60 parts. When we compare these numbers with the results obtained by Regnault and Reiset, Bidder and Schmidt, and other investigators, we discover the reason why, after vegetable food, a larger percentage of the absorbed oxygen is found in the expired carbonic acid than in the case of the carnivora, for the food of the latter class of animals has relatively more



hydrogen to be consumed than the food of the herbivora, and on this account we observe that the proportion exhibited in fasting animals, which to a certain extent may be said to live upon their own flesh, is very nearly the same as that noticed after the use of an animal diet.

The above remarks on the influence of the diet generally, show, however, that the *quantity*, as well as the *quality of the food*, exerts a very considerable influence on the amount of the interchange of gases occurring in the lungs. There must, however, be a certain limit for every organism, beyond which the absorption of oxygen and the excretion of carbonic acid cannot pass. We have already seen (pp. 368–384) that the absorption of nutrient matter from the intestinal canal can only be carried to a certain extent, and we have further convinced ourselves that notwithstanding this limitation of resorption, a far larger quantity of nutrient matters may enter into the mass of the fluids than is necessary for the maintenance of the vital functions; while we finally observe that this excess of absorbed food, when it consist of nitrogenous matters, is very rapidly decomposed in the blood, and that under these conditions large quantities of urea, far exceeding the normal mean, are excreted. But as we have already shown that only a fractional part of the albuminates is eliminated with the urine, while another portion is separated through the lungs, as water and carbonic acid, there can be no doubt that the pulmonary exhalation, as well as the other excretions, is correspondingly augmented after an excessive use of nutrient substances. All the experiments which have hitherto been made in reference to the excretion of carbonic acid in animals that have either been highly fed, or have been artificially fattened, confirmed the above proposition. As we purpose reverting at a future page to this subject, we will only adduce a couple of experiments made by C. Schmidt<sup>1</sup> on one and the same cat. When this animal was taking 142·41 grammes of flesh in the 24 hours (a quantity which was shown by numerous experiments to be sufficient to maintain the full strength and ordinary weight of the animal), it absorbed 60·14 grammes of oxygen, and exhaled 65·60 grammes of carbonic acid, together with 30·88 grammes of water; whilst during the consumption of 247·32 grammes of flesh it absorbed 103·84 grammes of oxygen, and expired 113·52 grammes of carbonic acid and 47·86 grammes of water. Regnault and Reiset's experiments also exhibit similar results in the case of the herbivora, for we there meet with several cases in which the excess of the absorbed carbo-hydrates may be distinctly recognized by the proportion existing between the absorbed oxygen and that which is excreted with the carbonic acid, this being in many cases as 100 : 95, or even as 100 : 99·7, consequently nearly the ratio (namely as 100 : 100) which accords with the requirements of theory after the use of pure sugar or starch.

The above circumstance leads us to a point, which although it will be considered with all the attention which it deserves under the head of "Nutrition," must not be suffered to pass without some notice in the present place. If, for instance, we consider the ratio of the absorbed oxygen to the oxygen which is again separated (with the carbonic acid), we perceive that it essentially depends upon the quality of the food; but yet after the abundant use of carbo-hydrates the ratio calculated from

<sup>1</sup> Op. cit.



the above considerations, will never correspond with that which is found by direct experiment: thus, for instance, if we feed an animal on pure starch, we shall never obtain the required ratio of 100 : 100, that is to say, the whole of the oxygen absorbed will never be contained in the expired carbonic acid, because a fraction of it will be expended in the formation of water, for the simple reason that this ratio does not depend solely upon the food, but is modified by the combustion of the nitrogenous organic parts which are destroyed during vital activity. During life those nitrogenous substrata which have been subservient to the functions of the organism, are continually becoming effete and unfitted for further use, and finally reduced to a state of oxidation, for the purpose of being eliminated; these bodies consume a portion of the oxygen in the oxidation of their hydrogen, and, consequently, this portion of the absorbed oxygen is not exhaled as carbonic acid, and the ratio of the absorbed oxygen to the exhaled carbonic acid differs, therefore, from that which we might assume from the composition of the carbo-hydrate. We have thus merely to inquire how much nitrogenous matter is destroyed during the normal course of the vital movements, and what fraction of the absorbed oxygen is consumed by it. To find the amount of this coefficient for every organism, constitutes a problem in the physiology of nutrition. We should, therefore, acquaint ourselves with the typical consumption of the organic constituents in order to find the proportion which essentially expresses the respiratory process, or this respiratory function. If, however, we knew the typical amount of the daily loss of tissue, we might very readily calculate from the quantity of the consumed starch, the relation existing between absorbed and exhaled oxygen. The loss of tissue, consisting of albuminates and collagen yields, as we find from experiments on inanition, the ratio of 100 : 83.6; if now we express the magnitude of the typical consumption of nitrogenous matter by  $c$ , and the quantity of the consumed starch by  $a$ , the proportional number for the excretion of carbonic acid might very easily be deduced from the formula  $\frac{c \cdot 83.6 + a \cdot 100}{c + a}$ . The experiments made on fasting animals warrant the conclusion, that the nitrogenous matters alone in their typical amount  $c$  do not suffice for the requirements of the vital functions, but that at the same time a certain amount of non-nitrogenous matter (distinct for each organism) must be subjected to oxidation; when, therefore, the carbohydrates are entirely wanting and the albuminates are only sufficient for the restoration of the tissues, the fat is expended in the accomplishment of this object; hence its quantity—the minimum of the necessary non-nitrogenous combustible materials—may easily be calculated, if we know the typical amount of nitrogenous materials undergoing metamorphosis, and the proportion which exists during a state of inanition between the absorbed oxygen and the oxygen which is excreted (in combination with carbon). From the above observations we learn, that the proportional number (for the oxygen in the carbonic acid) after the use of pure fat, is 71.32; if now we designate the typical expenditure of albuminates as  $c$ , and the proportional number in a state of inanition be found to be 75.0, we obtain according to the simplified formula  $\frac{(83.60 - 75.00) c}{75.00 - 71.32} = x$ , the quantity of fat which is consumed together with  $c$  albuminates.

We will not extend these remarks, since no further proof is necessary



to show how extensively the observations already made on the relation of nutrition to the process of the excretion of carbonic acid may be applied to many other momenta of the process of respiration. We, at all events, obtain some fixed point of support for numerous investigations on the metamorphosis of matter generally.

Although in our considerations of the influence exerted by ordinary food upon the respiration, we have deduced the results of the observations in question from purely chemical relations, we should greatly err were we to adopt the same method in reference to certain substances, which are occasionally introduced with the food into the organism, such, for instance, as the ethereal oils, alcohol, theïne, &c. We do not mean that these substances constitute any exception to this fixed law of nature, but the immediate effect which they produce reminds us that there are nerves in the animal organism which exert the most important influence on all its functions, on nutrition as well as on respiration, and that, consequently, they in some degree disturb that uniform course of phenomena which we might suppose would result from chemical laws. We cannot, therefore, believe that alcohol, theïne, &c., which produce such powerful reactions on the nervous system, belong to the class of substances which are capable of contributing towards the maintenance of the vital functions. We see this, for instance, in the case of alcohol, which when taken with the food diminishes the pulmonary exhalation instead of augmenting it.

Vierordt, like Prout, found that the excretion of carbonic acid is both absolutely and relatively diminished even after a moderate use of *spirituous drinks*. He has also confirmed Prout's observation, that the increased excretion of carbonic acid which accompanies digestion was considerably checked by the use of spirits. Strong tea exerts, according to Prout, precisely the same result on the respiration as spirituous drinks.

*Sleep* occasions a very considerable diminution in the excretion of carbonic acid, as we learn chiefly from the experiments of Scharling; thus, for instance, a man who during the day immediately after dinner expired 33.69 grammes, exhaled only 22.77 grammes in one hour during the night; in the case of another man, the ratio of the carbonic acid exhaled during sleep in one hour in the night to that eliminated in one hour in the day after dinner, was 31.39 : 40.74. In experiments on wood-pigeons, I found<sup>1</sup> that 6.156 grammes of carbonic acid were on an average exhaled during one hour in the morning by 1000 grammes' weight of birds, whilst the same birds expired only 4.950 grammes hourly in the night.

Regnault and Reiset have made observations on the relations of respiration during the hibernation of marmots, which exhibit an enormous difference, compared with the waking state of these animals; thus, for instance, 1000 grammes' weight of marmots absorb in their sleeping state from 0.040 to 0.048 of a gramme of oxygen hourly, whilst in their waking state they consume from 0.774 to 1.198 grammes. In the sleeping animals only 56.7% of the absorbed oxygen pass into the carbonic acid, whilst in the waking state the quantity amounts to about 73%. In two of the three experiments, these observers found that the marmots in their hibernating state exhibited a considerable absorption

<sup>1</sup> Jahresber. der ges. Medicin. 1844, S. 39.



of nitrogen, whilst they exhaled nitrogen like other animals when in their wakeful state. As a large part of the absorbed oxygen remains in the body of the sleeping animals (since only a small quantity is expended in the formation of carbonic acid, and the water which is formed does not evaporate, owing to the low temperature of the animal), and nitrogen is absorbed, we have an explanation of the fact first observed by Sacc, that the weight of the body is generally, although not constantly, increased during the hibernation of marmots.

These inquirers arrived at similar results in reference to the influence of hibernation, or the sleep induced by exposure to cold, in their experiments on lizards.

It may readily be seen, from the ratio of the oxygen contained in the expired carbonic acid to the inspired oxygen, that only a very small quantity of fat can undergo oxidation in the body of the hibernating marmot (while the nitrogenous substances are still less implicated in the process), for the substance consumed must be far richer in hydrogen; the carbon being to the hydrogen as 21.26 : 5.41, or, according to the atomic weights, very nearly as 2 : 3. (This substance would therefore exhibit a composition not very often met with in organic chemistry, namely,  $C_6H_9 + x H O$ .) If, with this abundance of hydrogen, ammonia or any ammoniacal alkaloid should be formed, we need scarcely wonder at the great absorption of nitrogen which Reiset and Regnault observed. At the same time we must beware of drawing too wide a conclusion; for besides the hypothesis already advanced, it would be conceivable, and perhaps more probable, that the oxygen absorbed by these animals during their hibernation combines with only the one part of the hydrogen in one constituent of the body, and thus generates relatively even more water than carbonic acid; thus the atomic aggregate  $C_2H_3$  would be abstracted from such a substance by the inspired oxygen, and the substance itself would not therefore be perfectly oxidized.

Regnault and Reiset found that marmots, when they awake from their hibernation, exhale an extremely large quantity of carbonic acid, and consume more oxygen than at a subsequent period of their waking state—an observation which corresponds with the fact noticed both by Prout and Vierordt in their experiments on man, that the act of waking was followed by a very abundant excretion of carbonic acid, which again diminishes in half an hour or an hour.

Bodily exercise increases the exhalation of carbonic acid in the same manner as we have shown that a state of rest diminishes it—a fact which might have been inferred from the above relations of the respiratory movements, but which is also proved by direct observation. Seguin,<sup>1</sup> one of our earliest observers, found that he consumed far more oxygen during violent bodily exercise than during a state of rest. Prout found that at the commencement of moderate exercise there was a relative excess of carbonic acid in the expired air, but during prolonged violent exercise there was less of this gas than in a state of rest. Vierordt convinced himself that the absolute as well as the relative quantity of carbonic acid was increased after moderate exercise, and this result is in perfect conformity with the experiments of Scharling. H. Hoffman<sup>2</sup>

<sup>1</sup> *Op. cit.* p. 357.

<sup>2</sup> *Ann. d. Ch. u. Pharm.* Bd. 45, S. 242.



found that the sum of the products of perspiration of the skin and lungs was much more considerable after prolonged motion than after prolonged rest. Every one who has instituted experiments on the respiration of animals must be aware that they expire far more carbonic acid when they are lively and active than during a state of repose.

Scharling's observations do not entirely exclude the supposition that *mental exertion* may induce an augmented excretion of carbonic acid.

The experiments instituted on man and animals, with the view of ascertaining whether *age* exerts any influence on the respiration, prove that considerable weight should be attached to this relation. Andral and Gavarret, who made tolerably complete observations on the absolute quantity of exhaled carbonic acid, found that the quantity daily expired increases, on an average, to the 40th or 45th year, agreeing mainly with the development of the muscular system. In Scharling's experiments, the two children experimented upon (one a boy aged  $9\frac{3}{4}$  years, and the other a girl of the age of 10 years) expired almost double the amount of carbonic acid exhaled by adults, if we calculate the excretion of carbonic acid for an equal bodily weight; but where the latter is not considered, we find that Scharling's results agree perfectly with those of Andral and Gavarret. The observations made by Regnault and Reiset on animals are also in accordance with these experiments on man, for it was shown that in animals of the same species, for equal weights, more oxygen was consumed by young than by adult animals.

With regard to the influence of *sex* on respiration, it appears, from the experiments of Scharling as well as from those of Andral and Gavarret, that males expire more carbonic acid than females—a relation which obtains even in childhood, for boys eliminate more carbonic acid than girls.

As Scharling's observations must, for the present, to a certain extent, be regarded as affording the normal numbers for the excretion of carbonic acid in man, we subjoin his average relations for one hour:

Subject.	Age.	Weight.	Carbonic acid expired in one hour.	Amount of carbonic acid expired in one hour for each 1000 grammes' weight.
	Years.	Kilogrammes.	Grammes.	Grammes.
Man, . . .	35	65.50	33.530	0.5119
Youth, . . .	16	57.75	34.280	0.5887
Soldier, . . .	28	82.00	36.623	0.4466
Girl, . . .	17	55.75	25.342	0.4546
Boy, . . .	$9\frac{3}{4}$	22.00	20.338	0.9245
Girl, . . .	10	23.00	19.162	0.8831

According to Andral and Gavarret, an adult man exhales on an average from 38.5 to 40.3 grammes of carbonic acid in an hour; an adult female, when not pregnant, from 22.0 to 23.8 grammes; during pregnancy, 29.3 grammes; and after the cessation of menstruation, from 27.5 to 31.2 grammes. Although Scharling included the products of perspiration with those of respiration, while Andral and Gavarret included only the latter, their numbers are yet higher than those of Scharling. It will be readily seen, from the preliminary remarks which we made on this subject, that the higher numbers obtained by Andral and Gavarret



are solely to be referred to the circumstance that in their experiments the respiration was less natural, or at all events more frequent, than in those of Scharling, who, by the use of a commodious apparatus was enabled to observe a more normal state of the respiration.

Although there can be no doubt that the *bodily constitution* influences the intensity of the respiration, we have no direct observations in proof of this fact, unless indeed we include under that head the fact noticed by Regnault and Reiset, that lean animals consume more oxygen and exhale more carbonic acid than very fat ones—a result which can readily be brought into harmony with the observation made by Schmidt and Bidder, that fat animals excrete far less bile than lean ones.

We now proceed to consider the differences which have been observed in the respiration of different *classes of animals*; for as the greater number of the experiments made on the respiratory functions have been instituted on animals, it is from them that we must derive our most valuable results, more especially from the experiments of Regnault and Reiset, who surpass all other observers in the value and importance of their results. When we consider, in reference to the *mammalia*, what influence the different food on which they live may have upon the quantitative relations of the interchange of gases in the lungs, we find, on referring to the remarks already made in relation to this subject, that the differences which have been observed in the respiratory relations of the herbivora and carnivora, do not depend upon any difference in their organization, but are almost wholly referable to the influence of the food upon which they subsist. For in the same manner as we observe that the urine of the carnivora, when fed upon vegetables, is similar to, if not identical with, that of the herbivora, and that the urine of herbivorous animals living on animal substances is analogous to that of the carnivora, we also find that carnivorous animals, which live principally on amylaceous matters, exhibit the same respiratory relations as the herbivora, and conversely. This fact has been proved beyond a doubt by the careful investigations of Regnault and Reiset, and more recently by Bidder and Schmidt. We subjoin a table of these relations as they are given by Regnault and Reiset. We have introduced it here merely by way of furnishing a general retrospect of the whole :

Species of animal.	Food.	Proportion of 100 parts of absorbed oxygen, which are given off to the carbonic acid.	Consumed Oxygen.	Exhaled Carbonic acid.	Exhaled Nitrogen.
			For 1,000 grammes' weight of the animal in one hour.		
		Per cent.	Grammes.	Grammes.	Grammes.
Dog,	Meat,	74.5	1.183	1.211	0.0078
Rabbit,	Carrots,	91.9	0.883	1.116	0.0036

The absolute quantity of absorbed oxygen and exhaled carbonic acid is, however, somewhat fluctuating, which partially explains the great discrepancy observable between these results and the numbers obtained by other observers in their experiments on rabbits and dogs. On instituting a comparison between the numbers obtained by different investigators, we



find that the results coincide in this respect, that the carnivora, when kept upon their ordinary food, exhale more carbonic acid and nitrogen in proportion to their weight than the herbivora when living upon their ordinary food.

It has long been supposed that the respiration of *birds* was far more active than that of mammals, but this is by no means an invariable law, and may very probably depend upon the mode of life of the animals; since hens, for instance, which seldom fly, consume very little more oxygen than rabbits, and not even so much as dogs; while the ratio of the absorbed oxygen to the oxygen reappearing in the carbonic acid is very nearly the same in hens which have been fed upon oats as in rabbits. Very different respiratory relations exist in those more active birds which sing much, are constantly flying about, and seldom at rest except during sleep. Birds of this kind consume more than ten times the amount of oxygen absorbed by proportionally more inactive birds, such as hens, whilst they also exhale nearly ten times more carbonic acid. The experiments of Regnault and Reiset also exhibit a great difference in this respect, that in the more active birds far less oxygen (only three-fourths) is employed in the formation of carbonic acid; but this ratio may, however, probably be dependent upon the fact that in the experiments in question the birds were fasting, being alarmed and off their feed. Regnault and Reiset, moreover, refer the great absorption of oxygen and exhalation of carbonic acid to the smallness of these animals, and connect it with the greater necessity for heat in the smaller animals. Although<sup>1</sup> I was long since led by my own experiments to express the view, that the excretion of carbonic acid in birds stood in an inverse ratio to their size, it appears to me that the necessity for heat may afford the most available ground on which to explain this fact. The cause must undoubtedly be sought in the greater activity, and in the consequently more rapid metamorphoses in the more active birds, although it is unfortunately only the smaller varieties which can be employed for such experiments. If we were able to investigate the respiratory equivalents of vultures and other large birds of prey, which continue for a long time on the wing, and if we could examine them under their natural relations, we should most certainly find them much greater than in the case of hens, ducks, geese, &c. Nature may, however, have endowed smaller birds with greater energy and a more rapid metamorphosis, in order to enable them to maintain the same temperature of body as larger birds.

The smaller birds whose respiratory equivalents we have given in the following table from the mean results of Regnault and Reiset, were greenfinches, cross-bills, and sparrows.

Animals.	Food.	Of 100 parts of absorbed oxygen, there pass into the carbonic acid,	Consumed Oxygen.	Exhaled Carbonic acid.	Exhaled Nitrogen.
			For 1000 grammes' weight of the animal in one hour.		
Hens.	Oats. Abundantly	Per cent. 80·7	Grammes. 1·053	Grammes. 1·320	Grammes. 0·0079
Small birds.	Sparingly	75·3	11·473	11·879	0·1296

<sup>1</sup> Jahresber. der ges. Med. 1843 u. 1844, S. 39.



The *eggs* of birds also maintain a process of respiration, even in the unincubated state; fresh eggs, on exposure to the air, continuously exhale carbonic acid and aqueous vapor, and hence they lose considerably in weight when kept for some length of time. But they also absorb oxygen, as is more especially shown by the circumstance that the air enclosed in the air-space contains more oxygen than atmospheric air, according to Bischoff<sup>1</sup> from 0.22 to 0.245%, and according to Dulk<sup>2</sup> from 0.25 to 0.27% (by volume); but this has been denied by Baudrimont and Martin St. Ange. The process of respiration becomes more active after incubation, as is obvious from the circumstance that the development of the embryo is very soon arrested and that death ensues in hydrogen or carbonic acid gas, as is shown by the experiments of Viborg, Schwann,<sup>3</sup> and Martin St. Ange. The greater part of the oxygen in the air-space disappears during incubation, and the air is then frequently found to contain about 6% of carbonic acid. The more recent experiments of Baudrimont and Martin St. Ange<sup>4</sup> have shown, in reference to the interchange of gases during the incubation of hens' eggs, that in proportion as the embryo becomes more fully developed, a larger amount of oxygen is absorbed from the atmosphere and more carbonic acid given back to it. Here also the quantity of oxygen contained in the carbonic acid falls far short of the absorbed oxygen. The experiments of Valenciennes have proved that here too the respiration is accompanied by a liberation of heat. The following table gives the results of the experiments, instituted by two of the observers already referred to, on eggs; but here the total loss of weight in the eggs, owing to the chloride of calcium in the apparatus, no doubt greatly exceeds the normal quantity.

In 1,000 grammes' weight of eggs.	From the 9th to the 12th day of incubation.	From the 16th to the 19th day of incubation.
The loss of weight amounted to . . .	26.26 grammes.	41.72 grammes.
The absorbed oxygen, . . . . .	5.74 "	10.70 "
The exhaled carbonic acid, . . . .	4.33 "	11.92 "
The exhaled water, . . . . .	2.88 "	3.66 "
The ratio of absorbed O to the O in CO <sub>2</sub> ,	100 : 54.9	100 : 81.0

Spallanzani also found that even the egg-shells alone absorbed a little oxygen and exhaled carbonic acid—a circumstance, however, which presents a much closer analogy with the decomposition of other substances, such as fibrin, &c., than with the respiration.

In considering the respiration of the *amphibia*, we shall merely refer to the experiments of Regnault and Reiset (notwithstanding the admirable observations of Marchand, which we have frequently noticed), as their results could alone furnish us with numbers admitting of comparison with the above tables, in as far as they have been obtained by one and the same method. In all main points, however, these observers perfectly agree with one another.

<sup>1</sup> Schweigger's Journ. N. R. Bd. 9, S. 446.

<sup>2</sup> Ibid. 1830, p. 363.

<sup>3</sup> De necessitate aeris atmosph. ad evolut. pulli in ovo. Berolini, 1834.

<sup>4</sup> Compt. rend. T. 17, p. 1343.



Animals.	The percentage of oxygen entering into the carbonic acid.	Oxygen consumed.	Carbonic acid exhaled.	Nitrogen exhaled.
		By 1,000 grammes' weight of the animal in one hour.		
	Per cent.	Grammes.	Grammes.	Grammes.
Frogs, . .	76.0	0.084	0.0880	0.0005
Salamanders,	82.4	0.085	0.0960	—
Lizards, . .	75.2	0.1916	0.1976	0.0025

We find, even amongst the amphibia, that the more active creatures exhibit greater rapidity in the metamorphosis of matter, and therefore consume more oxygen and exhale more carbonic acid and nitrogen, than the more sluggish animals, in which there is a less active metamorphosis of matter. This relation is very strikingly shown, in the above table, between lizards and frogs. This requirement of the amount of the respiration is further confirmed by certain experiments made on lizards; in the first experiment the animals were perfectly rigid, in the second they were not entirely rigid, and in the third, the results of which are given in the table, they were fully awake and lively. The half torpid animals consume about three times, and the perfectly wakeful animals nine times the amount of oxygen required by those which were in a perfectly rigid state. The same relation exists in respect to the absolute quantity of the excreted nitrogen, although we very frequently meet with the opposite condition in these animals, namely, with absorption of nitrogen, as was several times noticed in frogs by R  gnault and Reiset.

We now proceed to investigate the products of respiration of those animals which do not respire through lungs, namely, insects and fishes. Although the former of these absorb atmospheric air directly, the mechanism of inspiration and expiration is not the same as in lung-breathing animals. Their pneumatic apparatus consists of extremely elastic ramifying tubes, intersected by vessels of communication designed for the uniform distribution of the air. The expiration in insects is effected by muscular action only, while the act of inspiration is accomplished solely through the elasticity of the tracheal walls, which not only consist of chitin, but are surrounded by a spiral thread of that substance for the purpose of increasing their elasticity. The air in the trache   is brought into free and direct contact with the external atmosphere by means of the so-called stigmata, in which there is not often any appearance of muscularity. By every motion of the insect the universally distributed trache   are compressed, and a portion of the air which they contain is thus expelled; when the muscular contraction ceases, the trache  , in consequence of their extreme elasticity, resume their former volume, and fresh air again enters through the open stigmata into the spaces containing rarefied air. Insects are also provided with a special muscular apparatus for expiration, but this is limited to the abdominal rings, and exhibits in beetles only 15 or 25 contractions in a minute, corresponding pretty nearly with those of the dorsal vessel. The voluntary and irregular motions undoubtedly exert the most important in-



fluence on the expiration of the air in insects, and hence we find that the various degrees of animation in the motions of insects produce the most extraordinary differences in respect to the quantity of carbonic acid which they excrete, and the degree of animal heat which they exhibit. On this account pupæ expire only 1-190th or 1-160th part of the carbonic acid which is exhaled by a caterpillar of equal weight; but yet, according to Regnault and Reiset, the consumption of oxygen by the larva of the silkworm is only about 1-20th less than that by the caterpillar.

Regnault and Reiset, as well as myself, have experimented on the respiration of insects, as had been previously done by Spallanzani, Saissy, and Treviranus.

Reiset and Regnault employed cockchafers and the caterpillars of the silkworm when near the time of spinning, for their experiments on the respiration of insects. Their results were as follows:

Animals.	The percentage of oxygen entering into the carbonic acid.	Resorbed oxygen.	Exhaled carbonic acid.
		For 1,000 grammes' weight of the animals in one hour.	
Cockchafers, . .	80.8	1.0195	1.1372
Silkworms, . . .	78.2	0.8990	0.9600

In my own experiments on the excretion of carbonic acid in insects, I obtained<sup>1</sup> the following results for 1000 grammes' weight of the animals for one hour:

	Mean.	Minimum.	Maximum.
Cockchafers (5 experiments), . . . . .	0.729	0.650	0.832
Caterpillars of Phal. Bomb. Neustria (8 experiments), . . . . .	0.896	0.603	1.138
Caterpillars of Phal. Bomb. Dispar (7 experiments), . . . . .	1.077	0.835	1.303
Caterpillars of Pap. Nymph. Urticæ (2 experiments), . . . . .	0.0070	0.0069	0.0071

The respiration of animals breathing through *gills*, as fishes, crustaceans, &c., differs from that of creatures breathing through lungs or tracheæ, inasmuch as already dissolved oxygen is conveyed to the blood or the nutrient fluid, from which the dissolved carbonic acid must be removed. The mechanism by which the oxygenated water is propelled to the gills, and that which is loaded with carbonic acid is again removed, is so complicated, that mere indications of its character would carry us beyond our limits. There have unfortunately been but few experiments instituted with gill-breathing animals since Humboldt and Provençal prosecuted their experiments on the respiration of fishes. We find from

<sup>1</sup> Op. cit. p. 42.



these observations, which were most admirable for the time at which they were undertaken, that also in this form of respiration the oxygen which is absorbed exceeds that which is exhaled in the form of carbonic acid, the latter amounting in these experiments to scarcely four-fifths of the absorbed oxygen, and frequently to only half the quantity. These experiments yield, however, this remarkable result, that fishes constantly absorb very large quantities of nitrogen: and they show that fishes, like other animals, transpire copiously through the skin. These animals, moreover, are capable of breathing in atmospheric air as long as their gills are moist, the products of respiration presenting under these circumstances the same relations to the absorbed oxygen as in water, which is an obvious proof that respiration in water-breathing animals follows the same laws as those which control atmospheric respiration. Baumert<sup>1</sup> has recently, by the aid of an ingenious apparatus, made several interesting experiments on the respiration of the tench (*cyprinus tinca*), the gold-fish (*cyprinus aureus*), and the pond-loach (*cobitis fossilis*). It was shown by these experiments, in the first place, that 1000 grammes' weight of tench inspired on an average 0.0143 of a gramme of oxygen in one hour, and exhaled 0.0138 of a gramme of carbonic acid; while, on the other hand, the same weight of the more lively gold-fish absorbed 0.0409 of a gramme of oxygen, and eliminated 0.0419 of a gramme of carbonic acid in the same period of time. The ratio of the volume of absorbed oxygen to that of exhaled carbonic acid was very nearly as 10 : 7; for every 100 grammes of absorbed oxygen 72.3 grammes are again expired with the carbonic acid. In reference to the nitrogen, Baumert found sometimes a slight absorption, and sometimes a slight exhalation. In experiments with the pond-loach, results were obtained differing in several respects from those which we have been describing; thus, for instance, this fish, like some others, exhibits a special intestinal respiration, for it absorbs air through the mouth as well as by the gills, swallowing it on the surface of the water, and thus conveying it to the stomach. Baumert analyzed the air which was again eliminated through the intestinal canal, and found that it contained much less oxygen than the air which the fish had swallowed; the oxygen had, however, been replaced by much less carbonic acid than we usually meet with in bronchial or pulmonary respiration. The oxygen which is absorbed by the intestine passes, therefore, into the mass of the blood, and the carbonic acid to which it gives rise is not eliminated by the intestine, but through the gills; hence we also find, from Baumert's experiments, that in the branchial respiration of these animals there is a far greater exhalation of carbonic acid in proportion to the inspired oxygen, than in the previously named fishes. Special observations further showed that the pond-loach very seldom employs the intestinal respiration in fresh water, which contains a richer supply of oxygen, although in water which is poor in this gas, it very frequently comes to the surface in order to swallow air; yet these animals do not appear capable of supporting life by only one of these functions; they sicken when respiring through the gills only, almost as quickly as when they are limited to intestinal respiration. The experiments which were made upon pond-loaches by the

<sup>1</sup> Chem. Untersuch. über d. Respiration des Schlammpeizgers. Heidelberg, 1852.



same method employed with the tench and gold-fish yielded the following results: 1000 grammes of pond-loaches inspired on an average 0.0316 of a gramme of oxygen, and exhaled 0.0543 of a gramme of carbonic acid in the hour; these animals, therefore, gave off more oxygen in the form of carbonic acid than they had absorbed through the gills; since for 100 parts of oxygen absorbed through the gills, 124.9 grammes were eliminated with the carbonic acid. This result fully agrees with the comparative analyses made by Baumert of the air which was swallowed, and that which was again excreted through the intestine; for whilst the air in the intestine showed a diminution of the oxygen amounting to 8 or 11% by volume, the carbonic acid had only increased about 2% at most. Baumert's analyses have further shown the probability that pond-loaches always absorb a certain quantity of nitrogen during respiration.

Of those animals which possess no special organs of respiration, but accomplish their necessary interchange of gases by the skin only, the earthworm is the only one which has been made the subject of experimental investigation, and the only experiments of the kind, which we possess, were made by Regnault and Reiset. They prove that the respiration of these animals is very similar to that of frogs, which also respire vigorously through the skin. The consumption of oxygen, and the ratio of the oxygen contained in the carbonic acid, are nearly the same as in the latter animals: 1000 grammes' weight of worms absorbed in one hour 0.1013 of a gramme of oxygen, and exhaled 0.0982 of a gramme of carbonic acid; the ratio of the absorbed oxygen to that in the carbonic acid is as 100 : 77.5.

As in all these experiments on animals, the *cutaneous perspiration* has been investigated at the same time with the *pulmonary exhalation*, it might be supposed that no very exact result could be obtained for the latter, but the above numerical values are correct enough for the higher animals, as mammals and birds; for the inexactness is here so slight, that it generally falls short of the fluctuations in the errors of observation and other irremediable or incalculable conditions. In the case of rabbits, dogs, and hens, Regnault and Reiset have, indeed, adopted two methods for the more accurate determination of that portion of the gaseous excretion of the animal body which escapes through the skin; in both cases the animals were inserted in an air-tight bag, and their mouths alone were allowed to come in contact with the atmosphere; in one case the air within the bag was changed; in the other it was left undisturbed. In the first mode of experiment hens yielded only from 0.0047 to 0.18 of the carbonic acid resulting from the whole perspiration, rabbits only from 0.0102 to 0.0173, and dogs from 0.0035 to 0.0041. The second method also showed that the influence of cutaneous perspiration and intestinal exhalation is very unimportant when compared with the pulmonary function in the warm-blooded animals.

The relation between cutaneous transpiration and pulmonary exhalation must not, however, be considered so unimportant as it might appear from these experiments on thick-haired and densely feathered animals. The gaseous exhalations from the skin in man have scarcely been examined, but the quantitative investigations hitherto made, as for instance



those of Valentin, prove that the human skin takes a very considerable part in the separation of aqueous vapor from the body. This fact had already been rendered very probable by certain dietetic and other observations, and seemed to derive confirmation from Magendie's method of making the skin of animals wholly impermeable by means of glue, paste, varnish, &c.; and although the death of the animals thus experimented upon cannot be referred solely to the retention of gaseous fluids, the latter, although inconsiderable in quantity, are not devoid of importance in a physiological point of view. There are indeed many questions which still demand our earnest attention in reference to this subject; and even if the life of an animal of higher organization could continue to exist in a relatively normal state for any length of time after cutaneous exhalation had been suppressed, this circumstance would prove as little the unimportance of cutaneous gaseous transpiration, as the interesting experiments of Regnault and Reiset, on frogs whose lungs had been extirpated, could prove that the lungs of frogs are superfluous organs. In these experiments the frogs not only continued to exist for a very long time, but they also consumed a considerable quantity of oxygen (although scarcely as much as half the amount consumed by the uninjured animals): thus, for instance, 1000 grammes' weight of these animals consumed in one hour 0.047 of a gramme. The ratio of the oxygen to the transpired carbonic acid and to the nitrogen was nearly the same as in the uninjured animals.

This leads us to the consideration of the abnormal phenomena which the interchange of gases in the lungs occasionally presents, and which are consequent on anomalies, functional or other derangements of individual organs, or diseases. This subject is, however, beset with so many difficulties that we have hitherto been obliged to content ourselves with the determination of the absolute or relative quantity of excreted carbonic acid, and even these limited experiments have not yet led us to any important results.

In entering upon these *pathological* relations we cannot pass over an accurate observation made by Bidder and Schmidt,<sup>1</sup> although we shall recur to it more fully in the following paragraph; we allude to an experiment on the respiration of dogs, in which all the bile was carried off externally by means of a biliary fistula. For every kilogramme of this dog, which was kept almost entirely without food, there were absorbed in one hour 1.146 grammes of oxygen, and 1.146 grammes of carbonic acid were exhaled; hence, of every 100 parts of absorbed oxygen 77.07 were returned with the carbonic acid: for every kilogramme of a dog operated upon in this manner, but receiving an abundant supply of flesh, there were absorbed in one hour 1.153 grammes of oxygen, while 1.327 grammes of carbonic acid were excreted; hence, of every 100 parts of absorbed oxygen 83.7 parts were contained in the carbonic acid. We simply give these numbers in the present place as facts, since we purpose analyzing this experiment more fully in a future page.

Three different methods have hitherto been proposed for the investigation of the interchange of gases in the lungs during morbid conditions; but these are unfortunately nearly all equally open to objection. In the

<sup>1</sup> Op. cit. pp. 368-386.



first place, animals were experimented upon, in which certain abnormal processes had been induced by the operation employed, as was done by Regnault and Reiset, and in part also by Bidder and Schmidt. In these experiments, as in most cases in which animals were experimented upon, the whole amount of the perspiration was determined by enclosing the animals in a receiver to which fresh air was conveyed, while the air already used was carried off by a system of vessels for the purpose of being absorbed. I have myself<sup>1</sup> made experiments of this kind on the process of inflammation. The most important obstacle to such inquiries in the case of animals, is that many diseases which are of the greatest importance in the eyes of the physician, cannot be produced by operations, or any other artificial means. There are very few places, moreover, in which the experimentalist has the opportunity of carrying on a series of investigations on spontaneously diseased animals. On this account, the human subject has hitherto been most frequently experimented upon, for the sake of investigating the process of respiration and its effects on the excretion of carbonic acid in disease. Hannover<sup>2</sup> has partially co-operated with Scharling in employing the last-named method for determining simultaneously the pulmonary and the cutaneous perspiration. This method is undoubtedly the best adapted for examining the respiration during disease, provided the patients can, without any inhuman aggravation of their condition, bear to be moved and temporarily confined within a closed receiver. It cannot be denied that even in this mode of experiment, the true effect of disease upon the exhalation of gas is unavoidably modified, at least during an experiment of short duration, by the mental excitement of the patient; but this evil is far less completely rectified in Prout's method, which has been followed by Malcolm,<sup>3</sup> Hervier and St. Sager,<sup>4</sup> and Doyère.<sup>5</sup> It demands considerable practice to acquire the facility exhibited by Vierordt, in breathing with perfect calmness into an apparatus, however well it may be constructed; the disease may often run its course before the patient is able to acquire the necessary proficiency, while on the other hand humanity forbids us to torture a fever-patient for any length of time with such experiments. Hence great caution should be exercised in deducing scientific conclusions from any observations of this kind. Then, moreover, in the experiments made according to the last-named method, the determination has almost always been limited to the relative amount of carbonic acid in the air, without regard to the volume of the expirations, and hence we need hardly observe that such experiments are scarcely of any value.

My experiments on the *process of inflammation* and its influence on the perspiration have been unavoidably limited to rabbits, in whom it is very difficult to excite an acute inflammation. I found it was not sufficient merely to wound the animals, and that it was necessary at the same time to inject stimulating substances into the wounds; but notwithstanding these measures, I always had to make several fruitless attempts before any individual animal could be brought into the condition neces-

<sup>1</sup> Abhandl. d. Begründ. d. k. sächs. Ges. der Wiss. 1846, S. 465.

<sup>2</sup> De quantitate acidi carbonici ab homine sano et ægroto exhalati. Havniæ 1845.

<sup>3</sup> Monthly Journ. of Med. Science, January, 1843.

<sup>4</sup> Compt. rend. T. 28, p. 260; Gaz. des Hospitaux. 1849, p. 85.

<sup>5</sup> Compt. rend. T. 28, p. 636.



sary for these experiments. I subjoin only the results of those experiments to which I attach the greatest importance, and in which the morbid phenomena as well as the composition of the blood indicated the presence of the process of inflammation.

In (a) and (b) the lungs were the seat of inflammation, and in (c) and (d) the inflammatory process extended over several muscles.

(a) In every three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :

Before the animal was wounded, and during three hours		
in the morning, . . . . .	3.820	grammes.
Immediately after being wounded, . . . . .	3.877	"
On the first day, . . . . .	2.951	"
" second day, . . . . .	3.217	"
" third day, . . . . .	2.308	"
" fourth day, . . . . .	1.838	"
" in the evening, . . . . .	1.731	"

(b) In every three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :

Two days before being wounded, . . . . .	3.170	grammes.
Immediately after being wounded, . . . . .	3.392	"
On the first day, . . . . .	3.199	"
" second day, . . . . .	2.914	"
" third day, . . . . .	1.877	"

(c) In three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :

Two days before being wounded, . . . . .	3.592	grammes.
Immediately after being wounded, . . . . .	3.947	"
On the first day, . . . . .	3.533	"
" second day, . . . . .	2.711	"
" third day, . . . . .	2.179	"
" fourth day, . . . . .	2.098	"

(d) In three hours a rabbit excreted, at the mean temperature, the following quantities of carbonic acid :

Immediately before being wounded, . . . . .	3.004	grammes.
Twelve hours after, . . . . .	2.941	"
On the second day, . . . . .	2.986	"
" third day, . . . . .	2.213	"
" fourth day, . . . . .	2.347	"
" fifth day, . . . . .	2.066	"

According to P. Hervier and St. Sager, many acute inflammations, such as meningitis, peritonitis, metritis, and acute arthritic rheumatism, yield an excess of carbonic acid (*hypercrinie carbonique*), and all inflammations in which the respiration is implicated, as pneumonia, pleurisy, and pericarditis, yield less than the normal quantity of this acid (*hypocrinie carbonique*).

But what opinion can we form of experiments which, like those made by Hervier and Sager, have led to results diametrically opposed to the best observations, and which have exhibited distinctions of such extreme delicacy, that other observers have been unable to arrive at such nicety



of observation, even when employing more exact methods? What are we to think when we see that these experimentalists found that less carbonic acid was exhaled during the period of digestion than in a state of fasting; that they distinguished two maxima and two minima of the exhalation of carbonic acid, of which the one maximum occurred at 9 o'clock in the morning, the other at 11 o'clock at night, while the one minimum was observed at 3 o'clock in the afternoon, and the other as early as 5 o'clock; that they observed the quantity of excreted carbonic acid constantly rise with the pressure of air, and found invariably more carbonic acid exhaled after animal food than after a vegetable diet, and even without in any way investigating the proximate coincident causes?

According to these experimentalists, moreover, the excretion of carbonic acid is augmented in the cold stage of intermittent fever, and still more so in the hot stages. "When the patients perspire, the air they exhale hardly varies from the ordinary air. Again, the normal relations of the excretion of carbonic acid remain unchanged in all chronic diseases combined with fever, as in chlorosis, diabetes, the beginning of cancer, nervous affections, and chronic inflammations. The quantity of consumed carbon falls in measles, scarlatina, roseola, erythema, during the period of suppuration, in scurvy, in purpura, anæmia, anasarca, the last stages of cancerous, scrofulous, or syphilitic degenerations, in typhus, dysentery, chronic diarrhoea, and pulmonary phthisis. The temperature of the expired air rises and falls with the number of the respirations." This confused assemblage of names of diseases and symptoms, and of obsolete and recent titles of diseases, sufficiently attests the nature of these investigations.

Hannover has attempted to determine the quantity of carbonic acid exhaled in chlorosis; he employed four girls in these experiments, which so far admitted of comparison with Scharling's observations, that three of these girls were of nearly the same age as the girl experimented upon by the latter observer; the fourth girl, when in a state of perfect health, and at the age of 17 years, expired 0.4546 of a gramme of carbonic acid in one hour for every 1000 grammes of her weight. Hannover's three chlorotic patients, whose respective ages were 15, 16, and 18 years, exhaled, according to similar calculation, 0.6666, 0.6105, and 0.5874 of a gramme, and consequently, an amount of carbonic acid far exceeding the quantity eliminated by the healthy girl. This fact is the more worthy of notice as there is reason to believe that the blood-corpuscles participate in the absorption of oxygen, and in the formation of carbonic acid, although in those cases in which it has been proved with tolerable certainty that the blood-corpuscles are considerably diminished, it has been found that the excretion of carbonic acid is increased rather than diminished. Although we are not quite justified in concluding from this fact, that the blood-cells are devoid of all influence on the formation and excretion of carbonic acid, it is quite certain that they do not contribute very essentially to the interchange of gases, and that the source of the carbonic acid, as we learn from other experiments, has to be mainly sought in the metamorphoses of the tissues, and only to a very slight degree in the processes occurring in the blood-cells. Moreover, in these chlorotic patients, the absolute quantity of the excreted



carbonic acid stood in an inverse ratio to the number of the respirations, which, as we have already seen, is the reverse of what we observe in the normal state. Hannover was unable to discover any increase of animal heat, notwithstanding the great development of carbonic acid; indeed, chlorotic patients generally complain much more of cold than of heat.

All these experiments of Hannover were conducted with the greatest care in every respect; for besides making a very accurate examination of the special form of disease, he very carefully noted in each respiratory experiment the numbers of the pulsations and respirations, the temperature, the height of the barometer, the bodily weight, and the age and constitution of the individual. All the experiments were made in the middle of the day, between 10 and 1 o'clock, and the patient was in no case suffered to remain more than half an hour in the apparatus. The observations were made principally between the months of September and December.

Hannover instituted experiments on the respiration of five persons suffering from pulmonary tuberculosis; the tubercles being in part already softened and suppurating. The absolute amount of carbonic acid generally increases with the number of the respirations, while the relative amount (that which is contained in a definite volume of air) diminishes. [Dr. Malcolm<sup>1</sup> has just published "some experiments on the proportion of carbonic acid exhaled in phthisis pulmonalis." Fifteen patients, nine males and six females, in decided consumption, were operated on thirty-two times. The disease had reached the stage of softening in all but one, and in three there were cavities; the pulse averaged 104, the respiration 30. The result of the experiments in these cases was this: the percentage of carbonic acid averaged 4.467, the extremes being 3.7 and 5.5. The result of experiments similarly made upon twelve healthy individuals, six males and six females, at an average age of 29, showed an average percentage of 4.6916, ranging from 4.2 to 5.9.—G. E. D.] The other experiments made by Hannover on the excretion of carbonic acid in some other morbid conditions, are too disconnected to admit of our deriving any definite results from them.

Doyère repeatedly examined the air expired by a young girl who had cholera, and continued his observations till the death of the patient; he found that the excretion of carbonic acid was generally much diminished in this disease, and that this excretion was augmented as soon as the general condition of the patient improved.

Malcolm instituted a more exact series of experiments, according to Prout's method, on this relation in typhus, in which he, of course, determined only the relative quantity of carbonic acid in the expired air. This observer found that in nineteen cases of mild typhus the quantity of carbonic acid contained in 100 volumes of the expired air, varied between 1.18 and 4.15; the mean of all these observations gave the number 2.492%, but this quantity fell to 2.232% in seven more severe cases of typhus. Prout gives 3.96% as the mean number for persons in health; the relative amount of carbonic acid in the expirations is therefore very considerably diminished in typhus. The amount of carbonic

<sup>1</sup> Dublin Quarterly Journal of Medical Science, Vol. 18, p. 320.



acid in the air cannot be brought into any definite proportion either to the number of the respirations or of the pulsations.

Here again we perceive the great deficiencies of pathological chemistry, which does not even supply us with the necessary materials for establishing a system. On the other hand, it must be admitted that the charge of inapplicability to medical practice, which has been advanced against this section of physiological chemistry, is less just in the case of the respiration than in the theory of digestion (see p. 414). Until recently, the determination of the respirations, and of the contractions of the heart in cases of disease, were little more than mere symbols, which nothing but the rudest empiricism could venture to adopt as explanations for the recognition, diagnosis, and prognosis of diseases, whilst at the present time, although our knowledge of the interchange of gases, and the influence of the movements of the respiration and the circulation may not always afford definite conclusions, it can, at least, supply us with certain indications of the most essential constituents of the pathological process, by which we may regulate and modify our medical treatment. The more exact knowledge of the respiratory functions which we now possess has thrown a clearer light on the process of fever than any of the innumerable treatises which have been written on the subject. We are indebted to pure physiological investigations for numerous elucidations of some of those groups of symptoms which we meet with in certain diseases, such as pulmonary tuberculosis, emphysema, certain heart-diseases, diabetes, &c. No one can deny that the great advance which has been made in modern times in respect to our knowledge of respiration, has afforded us a deeper insight into these and many other pathological processes, but it would carry us too far were we to enter more fully into the results yielded in this respect by pure physiology to pathology. It is in his practice by the bedside that the physician obtains the most important aid from the physiology of the respiration. We do not exaggerate when we assert that there is scarcely a page of this section on the respiration which does not treat of facts from which the physician may obtain the most valuable hints for his treatment of various diseases, and more especially of pulmonary affections.

While the advances of the science of medicine have taught us that of all the vast accumulation of remedies which in the course of time have been collected together, very few are of any value at the bedside, and while the enlightened practitioner is disposed to attach at least as much importance to a rational dietetic as to a specifically therapeutic mode of treatment, the value of investigations on normal respiration, in reference to the science of medicine, can never be overrated; for when once the fact is universally admitted that the first thing to be considered in many diseases is to furnish a copious supply of oxygen to the blood which has been loaded with imperfectly decomposed substances, and to remove as speedily as possible the carbonic acid which has accumulated in it, these observations will have afforded us true remedial agents, which exceed almost every other in the certainty of their action. We may perhaps aid a tuberculous patient quite as much by recommending him to respire a moist warm air, as if we prescribed *Lichen Carragheen* or *Ol. jecoris*



*Aselli.* Instead of tormenting an emphysematous patient, suffering from congestion and hæmorrhoidal tendencies, with aperients and saline mineral waters, we might relieve him far more effectually by recommending him to practice artificial augmentation or expansion of the chest in respiration (filling the lungs several times in the course of an hour), or to take exercise suited to produce this result, while we should forbid the use of spirituous drinks, and not prescribe tinctures, which might hinder the necessary excretion of carbonic acid. We abstain, however, from offering any further illustrations of these assertions, since the reflecting physician will not blindly follow any guide; while the mere empiricist can never learn thoroughly to heal any disease, whatever may be his knowledge of physiology and pathological chemistry.

We endeavored, at the beginning of this section, to give a general representation of the interchange of gases which occurs within the lungs, tracing the movements of the atmospheric air into the pulmonary vesicles, where an opposite current of gases is developed from the fluid blood. What we then regarded almost *à priori* as a physical necessity in this occurrence of two opposite currents of air, has been proved, from Vierordt's experiments, to be an actual fact. Mechanical forces, considered in the strictest sense of the word, were insufficient to carry the oxygen into the pulmonary vesicles and the carbonic acid into the trachea, as has been most conclusively proved by the suggestive experiments of Hutchinson<sup>1</sup> and others. There is one portion of their course through which the oxygen and carbonic acid must be propelled by the aid of diffusion; and this, as Vierordt has shown by the numerous modifications of his experiments on respiration, is controlled by the same laws which Graham<sup>2</sup> has expounded in so masterly a manner. We may, therefore, hope that we have arrived at the recognition and physical explanation of the interchange of gases effected within the air-passages. We have thus, as it were, arrived at the boundaries of the blood in our theoretical consideration, and it now only remains for us to explain the physical or chemical laws by which the gases dissolved in the blood are liberated, and those of the atmosphere are condensed in the blood. Having acquainted ourselves with the constitution of the air at the place of its exchange—that is to say, in the pulmonary vesicles—we have next to ascertain the character of the blood which is affected by this interchange of gases; for without a knowledge of its character before and after this interchange, we shall be unable to form an opinion of the principles which control this most essential part of the process of respiration, that is to say, the interchange of gases between the blood and the air in the pulmonary vesicles.

Two questions present themselves to our notice regarding the manner in which, on the confines of the air and the blood, as it were, this interchange is effected between the carbonic acid and the oxygen: one of these questions is *whence does the blood derive its carbonic acid*, and in what form does it convey this gas to the lungs? The second question is, in what physical or chemical relations does the oxygen stand to the blood, or to this or that constituent, in its passage into the blood? In considering the

<sup>1</sup> Medico-chirurgical Transactions, Vol. 29, pp. 137–152; and Cyclopædia of Anatomy and Physiology, Vol. 4. pp. 1016–1087.

<sup>2</sup> Trans. of Roy. Soc. of Edin. Vol. 12, p. 222.



first question as to the sources of carbonic acid in the animal organism, we must, in the first place, remember that all animal fluids contain gases, and especially carbonic acid. We have already seen, in the second volume of the present work, that carbonic acid, oxygen, and nitrogen, are present not only in the blood, but also in the lymph, the transudations, the parenchymatous juices of many organs, and even in the urine. It is by means of these juices that all the animal tissues, as well as the parenchyma of the organs, are permeated by the gases in question, and there is not a single vital organ in the whole animal body from which we might not, by means of the air-pump, extract free carbonic acid, nitrogen, and some traces of oxygen. An experiment which was begun long ago in my laboratory placed this relation, as might readily have been conjectured *à priori*, beyond all doubt, by affording a positive proof of the quality of this gas; we are, however, still deficient in the more exact quantitative determinations for individual organs.

But when we investigate the source of the carbonic acid in the blood, and incline to the belief, after the most general examination of the vegetative vital functions, that it must, in part at least, be sought in the activity of the different organs themselves, we cannot wholly refute the objection which might be offered, that the carbonic acid may be formed in the blood itself, and be conveyed with the transudations of this fluid into the parenchyma of the organs. It is, therefore, in the first place necessary to prove *the pre-existence of this carbonic acid in the fluids of the tissue*. The probability of such a pre-existence may readily be seen by analogy, and the fact has been almost directly proved by positive observations. We have purposely devoted more time to the mechanism of the respiration of insects than we generally give to the mechanical relations of the animal processes; for it is precisely in these animals, which have no true blood, but merely parenchymatous juices, and no true bloodvessels, but at most mere rudimentary hearts, or a very limited analogue, the so-called dorsal vessel, that the atmospheric air penetrates directly through the most delicate tracheal ramifications to the very elements of the organs; here the air does not come first in contact with the blood, nor does it pass for any length of time with it through vessels, where it may undergo metamorphoses accompanied by a development of carbonic acid gas; the carbonic acid must here be formed in the parenchyma of the organs themselves, and through their vital activity; for the amount rises and falls in the exhaled air, as we learn from direct experiments, almost in equal proportion to the amount of the activity of these organs. It is, therefore, probable that also in the higher animals, endowed with true blood, the carbonic acid is almost entirely formed in the functional organs, and not in the liquor sanguinis. And should we then find such great differences in relation to the amount of gases, in the character of the blood flowing to and from the organs (the arterial and venous blood), if all the carbonic acid of the blood flowing to the right side of the heart were formed gradually and alone throughout the whole extent of the blood-column passing from the left to the right side of the heart through the capillaries? No further probabilities need be adduced to prove that the parenchyma of the organs is the seat of the formation of carbonic acid, as we obtain the most convincing proof of the correctness of this



view from the admirable investigations of G. Liebig.<sup>1</sup> Although many points may be susceptible of improvement in the method of experimenting adopted by G. Liebig, the main results must continue unaffected. We have already (p. 247) noticed the most essential facts which have been brought to light by these inquiries. We would here only repeat, that the carefully prepared frogs' muscles absorb oxygen and exhale carbonic acid so long as their irritability or contractility lasts, that the latter is lost in irrespirable gases, and finally, that a muscle completely deprived of blood continues to maintain this interchange of gases so long as it retains its contractility. We have here, therefore, not the mere representation, but the perfect expression of a respiration of the organ of a higher animal without blood, and even without any special air-passages; the interchange of gases and the formation of the carbonic acid originate here directly from the organ from which the carbonic acid is otherwise conveyed to the atmosphere by various indirect means (and necessarily through the blood and lungs). As, moreover, these experiments show that the muscles cannot retain their activity without an access of free oxygen, at all events, a large portion of this gas must, after its absorption by the lungs, be conveyed in a free state through the blood and the walls of the capillaries into the muscles. The blood is, therefore, quite as well adapted to convey to the muscles the free oxygen necessary for the accomplishment of their functions as to carry off the carbonic acid formed by this function; the *first interchange of gases* is, therefore, effected in the *parenchyma of the organs* themselves, or if we regard the interchange of gases between two different media as the process of respiration, the first act of this process—the first interchange—is effected between the parenchymatous juice and the blood in the capillaries. This act may be compared to the respiration of water-breathing animals; the difference consisting almost solely in this, that the medium conveying the oxygen is on an average denser than the medium which is destined to absorb oxygen, or that the difference in the density of both is on the whole very small, whilst in the true water-breathing animals, the density of the receiving medium exceeds that of the water very considerably, but principally in the circumstance that the blood differs essentially from water in its great capacity for the absorption of oxygen and carbonic acid. Notwithstanding this difference, we may hope that when the respiration of animals breathing through gills has been sufficiently elucidated (and this subject is at present occupying the attention of Valenciennes), we may succeed in bringing this interchange of gases, which is effected through the walls of the capillaries of the greater circulation, into accordance with the law of the transfusion of the gases absorbed by fluids. Then only can we establish the theory of this portion of the respiration on physical grounds.

Before we proceed to consider the second act of respiration in the higher animals, that is to say, the interchange of gases in the capillaries of the lesser circulation and the pulmonary vesicles—the interchange between the blood and the air—we must not omit to inquire *whether all the oxygen in the arterial blood is free*, and whether all the carbonic acid in the venous blood is only mechanically combined. The previous

<sup>1</sup> Ber. d. Akad. d. Wiss. zu Berlin, 1850, S. 339-347.



experiments, as well as the observations of Magnus and Marchand, to which we have already referred, and according to which the fresh blood exhibited no chemical attraction from oxygen, might incline us to believe that all the oxygen absorbed by the blood in the lungs passed unchanged, that is to say uncombined, into the capillaries of the greater circulation, and from thence into the parenchyma of the organs. This, however, is by no means the case, and we have already given the reasons, which seem to show that a part of the absorbed oxygen enters into chemical combinations even in the arterial blood. We need here only refer to the peculiar relation of the crystalline substance of the blood towards gases [see note to vol. i. p. 344], and to Liebig's apodictic proof, that as the blood considered as a fluid can mechanically absorb only a very small portion of oxygen, the greatest part of the oxygen which disappears during respiration must of necessity be chemically absorbed.

The very careful and admirable experiments of G. Liebig<sup>1</sup> appear at first sight to oppose the idea of a chemical absorption of the oxygen in the lungs; for he found that the differences of temperature in the different parts of the circulating system, including both the arterial and the venous systems, were solely referable to the physical laws of the radiation of heat, &c., and that in the lungs especially, the blood not only undergoes no elevation, but even a slight depression of temperature.

Here, therefore, we obtain for the first time, through G. Liebig's investigations, a direct confirmation of the early hypothesis, that the blood is cooled in the lungs by respiration. This fact appears, as has already been stated, to stand in direct opposition to the assumption that the oxygen is chemically absorbed, at all events in part, in the arterial system. This discrepancy is, however, merely apparent, as we may readily perceive, when we consider that only a part of the oxygen that enters the blood is chemically absorbed, that a great part of the free heat is consumed in the restoration of the carbonic acid to its gaseous form and in the evaporation of water, that the specific heat of water is very great, and that the difference of temperature between the blood in the left side of the heart and that of the right side is extremely small. If we follow G. Liebig's experiments in their details, more especially in reference to the testing of the methods of observation, and observe how the temperature of the blood in the different vessels is dependent upon external physical effects, we might rather wonder at the slight diminution of the temperature in arterial blood, and apply this observation in support of the assumption of a chemical absorption of oxygen.

Although we can scarcely any longer entertain the slightest doubt that a large portion of the absorbed oxygen enters into chemical combinations in the arterial blood, we are not on that account justified in assuming that *carbonic acid* and water are already *formed* within the arterial blood, for this is an assumption which has already led to many erroneous theories regarding the respiration. As the serum is only capable of absorbing a small quantity of oxygen, and as we find that the blood-corpuscles change so essentially in the capillaries, the more probable view will always be, that the oxygen is conveyed from the blood-corpuscles to the

<sup>1</sup> Ueber d. Temperaturunterschiede d. venösen u. arteriellen Bluts. Inaug. Abh. d. Med. Fac. zu Giessen vorgel. 1853.



capillaries in a loosely combined state, and that it passes from thence into the parenchymatous fluids in order there to commence effecting oxidations, among the products of which we find carbonic acid and water. We have already endeavored to show that wherever oxygen and organic matters enter into combination, they do not at once yield carbonic acid and water as the products of their combustion, and that these simple oxides (as in putrefaction and decomposition) are often only simply separated from the oxidized body, without the organic body being entirely destroyed, as in combustion. We must, however, beware of adopting such an exclusive view as to maintain that there is no generation of carbonic acid or even of water within the lungs, or between the left side of the heart and the capillaries after the oxygen has been absorbed in the blood. We might more readily adduce proofs of the formation of a part of the carbonic acid after the first contact of the blood with the atmosphere than the contrary. Magnus has certainly found relatively less, but absolutely more, carbonic acid in venous than in arterial blood; and although we may not regard this individual observation as one of constant occurrence, we can scarcely interpret it in any other way than that, at least in this case, carbonic acid is developed after the access of oxygen to the venous blood. In fact, we must obstinately adhere to a preconceived opinion, if notwithstanding the important differences recently made known to us in the arterial and venous blood, we should still maintain that the blood remains wholly unaffected by the oxygen with which it is charged in the lungs, and that any one of its constituents cannot intimately appropriate to itself the oxygen without losing it again in the capillaries. When we fully consider the differences exhibited in the blood before and after the absorption of the oxygen in the lungs (see vol. i. p. 620), we shall find some difficulty in yielding to the opinion, that the parenchyma of vitally active organs is the only destination of the oxygen.

We will simply remark in conclusion, that the very decisive influence of the different nutrient substances on the process of respiration, which we have shown to exist, cannot be reconciled with the view, that all oxidation must take place in the parenchyma of the organs. The carbohydrates, as well as the excess of albuminates, are very quickly oxidized, as might be conjectured, from the pulmonary and urinary excretion; these substances, which are absorbed in what may be termed superfluous consumption, are not first converted into constituents of the organs to be again excreted; but whether they are first conveyed from the blood and carried into the innermost parts of the organs in order to be consumed, is a question which we are not yet able to decide; there seems at the present day to be every appearance of probability that the greater part of the carbo-hydrates and fats, and the excess of albuminates, are decomposed and oxidized within the course of the blood.

Now that we have convinced ourselves, in the course of our inquiries, that that interchange of oxygen and carbonic acid, which we term respiration, is a process which is not limited to any individual part of the animal body; and now that we have seen how, on the one hand, an interchange of air is effected in the air-passages by the double means of mechanical transport and by diffusion, and how, on the other hand, an



active interchange of gases takes place in the parenchyma of all the organs and in their capillaries, it simply remains for us to ascertain *the laws* which control *the interchange* between the elastic gases of the air conveyed to the lungs and the condensed gases of the blood of the pulmonary capillaries upon the humid mucous membrane of the pulmonary vesicles.

We shall wholly pass over the older *theories* regarding the process of respiration, as they were almost exclusively mere hypotheses based on few facts, and consequently not explanations considered in a scientific point of view; nor, indeed, were such explanations possible at that time, when scarcely a conjecture had been hazarded in reference to the laws of absorption, of diffusion, and many other physical principles bearing upon this subject. Although we can scarcely yet venture to hope that we are acquainted with all the physical laws which may come into play in the interchange of gases in the lungs, our exposition of the positive facts referring to the respiration sufficiently show that we have nearly succeeded in tracing to their physical fundamental requirements the individual sections into which the respiratory process may be divided. The first attempt to determine the physical law according to which the blood and the air interchange their gases in the lungs was made by Valentin in conjunction with Brunner, and conducted with equal intelligence and perseverance. Valentin arrived at the result, that this interchange of gases corresponds perfectly with the *law of the diffusion of gases* established by Graham, and that consequently the oxygen and carbonic acid are interchanged in an inverse ratio to the square roots of their densities. As it does not fall within the limits of the present work to enter into more diffuse theoretical expositions, we will here content ourselves with briefly indicating the difficulties which oppose the unconditional assumption of this theory. In the interchange between the gases of the blood and the air in the lungs, we meet with external relations differing wholly from the conditions under which Graham observed the interchange of gases through a porous partition wall, and on which he based his law; after what has already been stated it would appear almost superfluous to observe, that in respiration an absorbed gas is opposed to an elastic fluid gas, while in the process of diffusion both gases must be in the elastic fluid state and under equal pressures, which cannot be the case in the respiration. These, and some other points, which are opposed to the direct application of the law of diffusion to the respiration, might perhaps be of less importance if this interchange of carbonic acid and oxygen occurred in the ratio required by the law of diffusion, that is to say, that 85.16 vols. of carbonic acid should be interchanged for every 100 vols. of oxygen. If this ratio very frequently exists during an animal diet, we have nevertheless encountered numerous facts in our previous observations which appear to be diametrically opposed to this law; a law cannot, however, tolerate an exception, and when the latter can be shown to exist, the law is without force. It seems to us at least that many of the facts which have been proved beyond a doubt by the most recent investigations, notwithstanding all the concessions which might be made in favor of the peculiar animal relations, cannot be brought entirely into harmony with Valentin's theory.



Vierordt has described the interchange of gases on the inner surface of the lungs in a manner corresponding entirely to known physical laws as well as to positive facts; there are few theories in physiology which have resulted from such numerous and carefully conducted experiments as those which Vierordt established, and which he based upon the laws of absorption discovered by Henry and Dalton. Henry has shown that the quantity or the volume of an absorbed gas depends entirely upon the pressure under which the gas above the fluid remains after the absorption has been completed; while Dalton has proved that in the mixed gases the pressure of each individual gas, which, as is well known, is entirely independent of that of the intermixed gases, alone determines the proportion in which this gas is absorbed by a fluid. If, therefore, there be more carbonic acid contained in the blood than the pressure of the carbonic acid in the pulmonary vesicles is able to maintain in a state of condensation, a corresponding quantity will escape from the blood, until the amount of carbonic acid in the blood is reduced to the number corresponding to the amount which would be absorbed by blood containing no carbonic acid, and exposed to a tension equal to the carbonic acid pressure on the pulmonary vesicles. The quantity of carbonic acid thus passing into the pulmonary vesicles would therefore depend, in part, upon the quantity of this gas condensed in the blood, and in part upon the tension of the carbonic acid gas already contained in the air of the pulmonary vesicles. Under the relations occurring in the animal body a motion in a directly opposite direction would be imparted to the oxygen. The blood, when it enters the lungs, is not sufficiently saturated with oxygen, and is able, under the pressure which it then experiences, to absorb a larger quantity of this gas; the tension of the oxygen contained in the pulmonary vesicles is so considerable, that a portion of it is transferred into the blood, and there condensed. Both gases are therefore quite independent of each other, as the more correct physical explanation would lead us to infer; their interchange is not effected by mutual displacement, but is determined for each gas by the quantity of condensed gas in the blood, and by the tension of the corresponding elastic fluid gas contained in the air of the pulmonary vesicles.

There can be no doubt whatever that this law of Dalton applies perfectly and completely to the free gas contained in the blood (whether mechanically combined or absorbed), and hence it must constitute one of the most important factors in the interchange of gases in the lungs; but we have already seen that a very large portion of the so-called free oxygen and carbonic acid gas in the blood is in a state of unstable chemical combination, and hence Dalton's law can, strictly speaking, only apply to the fraction of carbonic acid and oxygen contained in the blood which is only mechanically absorbed, or, to express the same thing in different words, is merely taken up by the water in the blood. The law of absorption is not, however, of less importance to the theory of respiration; and we may perhaps be justified in assuming that all the oxygen is mechanically absorbed (in accordance with the above-mentioned law) before it enters into this unstable chemical combination, and that the carbonic acid, before it is separated from the blood, is mechani-



cally dissolved from its chemical combination, when the diminished external pressure favors, or rather controls, its elimination. It cannot, however, as yet be strictly proved that the membranes which separate the blood and the air within the lungs may not manifest different degrees of permeability towards the gases or the fluids which saturate them, and may not, therefore, exert some influence on the interchange of gases proceeding in accordance with the law of absorption; for although these membranes may be extremely thin, they yet consist of at least three delicate layers of tissue, namely, the pavement epithelium and the *membrana propria* of the pulmonary vesicles, and the walls of the capillaries. The great difference of permeability shown by animal membranes towards fluids, having even the same character, makes it not unreasonable to conclude that, if we could once succeed in establishing a general formula for the expression of the interchange of gases in the lungs, this function would constitute a part of it.

The effects of the respiration on the entire metamorphosis of animal matter, and on the individual functions of the latter, will be systematically considered in the following section. It is customary to associate the theory of *animal heat* with that of the respiration, for, since the time of Priestley and Lavoisier, flame has not been regarded merely as a poetical symbol of life, but life and combustion have been regarded as two perfectly similar processes. Lavoisier's theory of animal heat has experienced various modifications in the course of time and from the pressure of advancing science, as has also the theory of combustion, although both are true in their fundamental principles. We will not here enter more fully into the theory of animal heat, since it still rests on a very uncertain foundation, and since further, an accumulation of the various facts and arguments bearing upon the subject would extend our work to an unreasonable size. Besides this, it is still questionable whether the theory of animal heat, which embraces so many purely physical and purely physiological laws and facts, can, strictly speaking, be considered as pertaining to physiological chemistry; for, if we admit its claim to this rank, we might with equal justice be called upon to enter into a more detailed exposition of the theory of animal electricity, since this, no less than the theory of animal heat, is based upon chemical inquiry. We ought to observe, however, that the special heat of every animal organism is merely the result of chemical combinations formed within it. No one has elaborated this proposition with more argumentative ingenuity and ability than Liebig; and nothing but excessive incredulity, combined with an inadequate knowledge of physical laws, could lead any one to doubt the correctness of his exposition. Dulong<sup>1</sup> and Despretz<sup>2</sup> are, however, almost the only inquirers who have afforded us any positive investigations in relation to the main point of this subject; and according to their observations, only from seven to nine tenths of the heat generated in the organism can be referred to oxidation. Too much importance must not, however, be attached to these results, for it must be admitted that the method of investigation employed by these inquirers was not entirely free from blame, while, moreover, they exhibited extraordinary instability in their estimate of the number of the

<sup>1</sup> Ann. de Chim. et de Phys. 3 Sér. T. 26, p. 1-86.    <sup>2</sup> Ibid. 2 Sér. T. 26, p. 54-110.



units of heat developed from the carbon, as well as from the hydrogen, during oxidation. If, however, future investigations should enable us to become better acquainted with the heat that is evolved from the combustion of the carbon and hydrogen (and especially to determine it with accuracy in those cases where, as in the animal organism, the elementary atoms to be burned must be only gradually dissolved by the oxygen from very complicated compounds), and if repeated zoo-calorimetric investigations, free from the errors of the above-named physicists, should lead to the desired result, that the animal heat which is developed entirely corresponds to the quantity of carbon and hydrogen burned in the body, then it would indeed appear most wonderful that other chemical excitants of heat, which are sufficiently obvious to every one, should be altogether excluded from the animal organism. Why should the chemical union of acid and base, and the many decompositions and other processes, which, as we know, are generally accompanied with the development of heat, lose this property in the animal body? This much is established and placed beyond all doubt by the labors of the most trustworthy observers, that the chemical movements in the living body are more than sufficient to explain the animal heat, and particularly that the process of oxidation which is carried on through the respiration yields by far the most important contribution to its excitation. Attempts have been made to ascribe to the nervous system a share in the production of heat, but, as we have already observed in vol. i. p. 30, we cannot form a conception of the nervous system in a state of action without chemical changes occurring in it. Any one may observe the depression of temperature that ensues in parts in which the connection between the nerves and the central nervous system has been interrupted; and we are well acquainted with the recent experiments of certain French physiologists, who, after dividing the sympathetic at a certain spot, have found the animal heat, at definite parts, considerably higher than the ordinary temperature,—an observation which I have myself had occasion to make; and while we do not overlook the difficulties which oppose an explanation of such phenomena in a special case, we must regard every view as unscientific, and therefore incorrect, which would refer the origin of animal heat, although only partially, to any other than chemico-physical forces.

If, however, the chemical theory of heat, as it has been generally understood, is open to objection, it seems to us that it can only arise from its having been regarded less as the consequence than as the object of all, or, at any rate, of most, of the chemical movements in the organism. Animal heat has, perhaps, been brought too prominently forward in the consideration of the metamorphosis of animal matter, so that it may almost have appeared as if a great number of the animal processes were accomplished solely for the purpose of generating heat in the living body. When we inquire into the objects accomplished in the organism, animal heat acquires a special significance from the fact, that most of the higher animals, however they may otherwise differ, are endowed with a power of compensation, which is so carefully adapted to each, that even the most different external or internal relations are scarcely able to produce the slightest fluctuations of temperature. The



conclusion which we might be led to draw from this fact, in reference to the importance of animal heat for the vital functions, is certainly somewhat shaken by the consideration, that many of the so-called cold-blooded animals from the agility of their movements, the nature of their food, their respiratory equivalents, the energy of their growth and nutrition, in short, from the amount of their metamorphosis of matter, are not so far different from mammals and birds as to establish the necessity of this high degree of temperature for the maintenance of life, and the energetic performance of the most essential vital functions. And are we not arguing in a circle, when we assert that animal heat is subservient to the metamorphosis of matter, and that the latter again is subservient to the promotion of animal heat? If we were to assume, that this high degree of temperature is necessary for the formation of the tissues from nitrogenous food, as well as for the functions of the organs, and that amylaceous substances are taken up in the organism merely for the purpose of generating this degree of temperature, the cold-blooded animals, which are not inferior to higher animals in rapidity of growth, and not unfrequently equal them in the energy of their vital functions, would, even under such limitations, refute these conclusions. If the carbo-hydrates were consumed by animals merely for the purpose of generating heat, it seems teleologically incomprehensible why certain fishes, whose animal heat never rises above the surrounding medium, even after the most active movements, should live almost exclusively upon amylaceous matters. (We need only instance the case of gold-fishes, which live for years on no other food than wafers.) We have already endeavored (pp. 344-348) to indicate the objects which may be fulfilled by the carbo-hydrates beyond that of generating heat in the animal body. We do not, however, intend by these remarks to disparage the importance of animal heat in relation to life. All the admirable investigations which have led us to recognize an internal connection between respiration, certain nutrient matters, and animal heat, have afforded us a deeper insight into the vital processes; and hence it is no poetical imagery to connect the life of respiring beings in reference to their production of heat with the process of combustion. Animal heat does not, however, on that account occupy a higher place than every other phenomenon, and every other result which is manifested in the active living organism; at once an effect and a cause, it proceeds, as in combustion, from processes on which it exerts a favorable reflex action; it is only one, but not the highest link of that immeasurable series of phenomena which constitute the true substance of corporeal existence, and is in certain organisms nothing more than the inevitable consequence of the chemical processes of the animal organism—nothing more than the final result of a movement regulated by definite laws.

We have purposely referred in brief terms to the different theories of the respiration, as a fuller exposition of theoretical questions and discussions would have been foreign to the plan of this work (as we have already observed in our methodological introduction); hence it has mainly been our object to limit ourselves to the notice of facts which have become incorporated with science, giving a critical opinion of their value wherever it was practicable to do so.



We have, therefore, endeavored, as far as possible, to consider the scientific bases on which physiological chemistry has been raised to the level which it *now* occupies. We purpose in the succeeding and closing section of this work, to notice the facts which have led to the deductions of this or that theoretical conclusion, without entering into a full exposition of the numerous theoretical questions which are discussed at the present day. Nor do we think that the time has yet arrived when a complete system of the metamorphosis of animal matter can be given in a textbook of physiological chemistry, and we should even be exceeding the widest limits allowed to such a work, were we to take part in the contest which is still waging concerning many of the leading questions of the metamorphosis of animal matter, for as we have already frequently remarked, the noblest labors of many distinguished physicists show that we are still deficient in the first exact physical and chemical bases of a theory of the metamorphosis of animal matter. We abstain the more readily from a further discussion of this subject, as we should otherwise be compelled to add to the two volumes, of which our work already consists, still another, which notwithstanding the exact bases laid down in the two former volumes, must of necessity be a mere repetition of the individual views of the author. All, therefore, who desire to acquaint themselves with the discussions on the more general views of vegetative life must familiarize themselves with the ground of the contest, and learn for themselves, by carefully testing the evidence on both sides, how to reach a higher and more comprehensive point of view. But those who do not feel that they possess the power of entering into such discussions, either as judges or combatants, will adopt the safest course if they accept the interpretations of one, who by his great discoveries in this department of science, as well as by his extraordinary powers of combination, has earned the right to be heard; we need scarcely say that we refer to Liebig. For even when facts were wanting, and when the empirical data were unsettled and vacillating, the acuteness of his intellect has frequently revealed secrets in nature which have rarely failed, on subsequent investigation, to verify the correctness of his views.

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## NUTRITION.

We have already, in the beginning of this work, advanced the proposition, that the study of the process of nutrition was the crowning point or final aim of all our researches in physiological chemistry; but although all our previous considerations and all our researches tended ultimately towards this point, we are still far removed from it, nor shall we find that our exertions have been rewarded with the success we might have hoped to achieve. Even here we are compelled to rest satisfied with a mere sketch, which notwithstanding a few sharply defined outlines, is still so imperfect that it must be left very much to the imagination of individual inquirers to fill up the deficiencies according to their own conception of what is needed for its completion, not forgetting that the



colors which are thus superadded must soon merge, according to circumstances, into other tints, and can only be fully realized by those who are familiar with the subject.

In the course of our considerations we have acquainted ourselves with all the substrata in which the animal processes are effected; we next endeavored to ascertain the mutual relations of the different substrata and processes in the accomplishment of the most essential functions of animal life, both in their general and special conditions, and we sought to study the parts assigned by nature to each of the four great groups of substrata, or to their individual members, within the animal organism. It would scarcely, therefore, appear necessary to enter into any elaborate exposition or investigation of those matters, which are necessary to the continuation or maintenance of vital motion when once induced, for that which has once been exhausted can necessarily be replaced only by something similar or identical. This restitution must be regulated according to the expenditure. Although these propositions are almost too self-evident to be advanced, yet it required the most extensive, laborious, and exact investigations of the most intelligent inquirers to arrive at the result which now seems to us to be so simple and so easy of attainment, namely, that the requirements of the animal organism in the accomplishment of the vital functions, must correspond with those four groups of substances which, as we have already delineated in the above sketch of the motions of animal matter, constitute their essential and fundamental elements. But this need scarcely excite our wonder, since it has required all the researches and investigations embraced within the entire compass of this work to effect this object. Is any one link of this long chain of so slight an importance that it does not stand in the closest relation to the general process of vitality? It is only by means of all these introductory propositions that we are able to comprehend how those substances, which we have learnt to know as the most important adjuncts in the metamorphosis of animal matter, must also be contained in those matters which the animal body takes up for the renovation and restoration of that which has been lost or rendered effete (whether it be a fluid or a tissue, a ponderable or an imponderable matter), and for the regular accomplishment of the vital phenomena.

There could scarcely be a doubt that the albuminous matters, the fats, the carbo-hydrates and salts, which we have learnt to know as the bases of the metamorphosis of animal matter, must at the same time serve as the nutrient matters of the animal body; yet the opinion that one of these groups was more important than another to the vital process has led to many errors in reference to the physiological value of the nutrient matters. It was long before it could be conclusively shown by experiment, that the value of any of those bodies could only be expressed by the combination of these four categories. How far we were removed, even a short time since, from comprehending this simple truth, is sufficiently proved by the various experiments prosecuted under the direction of different learned societies, in which animals were fed exclusively on nitrogenous matters, as for instance, albumen or animal jelly; and the result of these observations excited general surprise, when it was found that in those experiments, which had been conducted with the greatest



exactness, the animals perished under symptoms of inanition, and exactly as if they had been deprived of all food. The nutrient quality of any one substance depends upon the intervention of some other body; and it is only by the reciprocal action of these four fundamental substances that life can be maintained, even as it was originally begun and influenced by the same means. We ought, therefore, to distinguish, in our consideration of the absorption of matter necessary for the maintenance of life, between those essential *nutrient matters* which we have learnt to know as adjuncts in the metamorphosis of matter, and those *articles of food*, which originating either in the vegetable or animal kingdom, generally contain the former in combinations of the most varied proportions. This is, however, so obvious, that after what has been already advanced, it would be superfluous to enter further into the subject. But if the various articles of food differ to so extraordinary a degree in the amount of nutrient matters belonging to these four groups, it would not seem out of place to estimate the value of food by the proportion in which these substances are combined in them, so as best to promote nutrition. However justly the albuminous matters may be termed histogenetic or organo-plastic, and however indispensable they may be to the vital organs, we must necessarily ascribe a very limited nutritive force to all articles of food which in addition to the albuminates contain neither fats nor carbohydrates, and even if all these matters were combined together in one article of food, we could scarcely ascribe to it any great degree of nutrient force, unless there were also phosphates and other salts present in it, for no cell or fibre could be formed or regenerated without the co-operation of these salts. If, therefore, all four groups of nutrient substances are equally necessary to afford compensation to the animal organism for the matters which have become effete, or to supply materials for the establishment of new manifestations of force, those articles of food will be the best and the most invigorating which consist of such substances combined in the proportion which is best adapted to the animal organism. Hence we see, that the idea of *the nutritive value of any article of food* is entirely relative, as it depends partly upon the proportion in which the fundamental bases of nutrition are mixed in it, and partly upon the individual requirements of the organism that is to be nourished.

There are, therefore, two points which specially demand our attention in entering upon a scientific consideration of food generally, and of its nutritive qualities specially; the first refers to the amount of these four elements, which it contains; and the second, to the circumstances under which the organism exhibits a greater or lesser necessity for one or more of these elements, for the maintenance of its integrity, as well as for the production of certain effects of force. These questions must be solved by quantitative determinations, for the physiologico-chemical statistics of the living organism are not alone competent to elucidate this subject. We need scarcely observe, that in judging of the nutritive value of an article of food, we must not lose sight of the quality of the nutritive elements belonging to the different groups, since this in a great measure determines its digestibility. Hard-boiled white of egg, meat that has been boiled for a long time, and hard cheese which is poor in fat and in salts, are less



easily digested than soft-boiled or fresh white of egg, meat steeped in vinegar, or slightly coagulated moist and rich cheese; starch is much more rapidly converted into sugar when boiled than in its raw form, when, as we have already seen, it frequently and principally passes off in an unchanged state, whilst another carbo-hydrate, namely cellulose, is only employed as food by certain animals under special relations. Notwithstanding their identity of constitution, the members of the same group frequently exhibit very great differences, depending upon their greater or lesser accessibility to the agents of digestion. An article of food may, therefore, owing to the indigestibility of its constituents frequently possess a far less nutritive value than we should expect from the mixture and composition of its elements of nutrition. It must not, therefore, be wholly forgotten, that the digestibility of a substance constitutes one of the factors of its nutritive value. As, however, this subject closely corresponds with all that has already been stated in reference to the digestibility of the different nutrient matters, we will now revert to the main questions already noticed, the former of which considered the proper admixture of the individual elements of nutrition in the nutrient substance. Before we proceed to decide the question of what are the most favorable proportions of these four fundamental nutrient matters in any one article of food (and, therefore, how the normal nutrient matter must be constituted in order, under the common relations, to yield to the animal organism the materials necessary for the fulfilment of all its functions as well as for the renovation of effete matters), it will not be out of place to consider from this point of view the composition of the ordinary articles of food.

As the nitrogenous constituents of the nutrient matters, that is to say the albuminates, are principally employed in the reproduction of the tissues, and of the actual organs of the animal organism, investigators, amongst whom Boussingault ranks foremost,<sup>1</sup> have more especially directed their attention to the amount of these matters contained in the food. As vegetable food commonly contains only very small quantities of other nitrogenous matters besides the albuminates, it was thought that the nitrogen they contained would afford a proximate measure of the value of these matters in reference to the reproduction of the tissues, and therefore, to one of the most important parts of the metamorphosis of matter. Besides Boussingault, Thomson,<sup>2</sup> and more especially Schlossberger<sup>3</sup> and Horsford,<sup>4</sup> in part under the direction of Liebig, have made tolerably extended investigations in relation to this subject. Liebig has, moreover, suggested the institution of very complete investigations in reference to the other classes of nutrient matters, with a view of determining the quantity of the carbo-hydrates or starch and of salts contained in a number of different articles of food; Horsford and Krockers<sup>5</sup> have made the most admirable observations in respect to this point. As the numbers obtained in these inquiries are of the highest importance to nutrition in more than one point of view, although it is not possible to give a comprehensive list of them, we are induced, contrary to our usual custom, to give

<sup>1</sup> *Economie rurale*. Paris, 1844, p. 483.

<sup>2</sup> *Phil. Mag.* 1843. Vol. 23, p. 323.

<sup>3</sup> *Ann. d. Ch. u. Pharm.* Bd. 52, S. 106-120, and *Arch. f. physiol. Heilk.* Bd. 5, S. 17-28.

<sup>4</sup> *Ann. d. Ch. u. Pharm.* Bd. 58, S. 166-212.

<sup>5</sup> *Ibid.* p. 212-227.



the fundamental values found by these different observers. 100 parts of the thoroughly dried substances yielded the following results:

BOUSSINGAULT found	
	Nitrogen.
In rice, . . . . .	1.39
" potatoes, . . . . .	1.5
" turnips, . . . . .	1.7
" carrots, . . . . .	2.4
" rye, . . . . .	1.7
" maize, . . . . .	2.0
" barley, . . . . .	2.0
" wheat, . . . . .	2.2
" oats, . . . . .	2.2
" peas, . . . . .	3.8
" lentils, . . . . .	4.4
" beans, . . . . .	5.1
" haricots, . . . . .	4.5

THOMSON found	
	Nitrogen.
In white bread, . . . . .	2.27
" brown bread, . . . . .	2.63
" Glasgow unfermented bread, . . . . .	2.17
" Essex flour, . . . . .	2.17
" Canada flour, . . . . .	2.21

SCHLOSSBERGER and DÖPPING found

In Agaricus deliciosus, . . . . .	4.6
" " russula, . . . . .	4.2
" " cantharellus, . . . . .	3.2

SCHLOSSBERGER and KEMP found

	Nitrogen.
In cows' milk, . . . . .	3.78
" woman's milk, . . . . .	1.59
" Dunlop cheese, . . . . .	6.03
" Dutch Gouda do., . . . . .	7.11
" Cheshire do., . . . . .	6.75
" double Gloucester do., . . . . .	6.98
" old Gloucester do., . . . . .	5.27
" yolk of egg, . . . . .	13.44
" oyster, . . . . .	5.25
" liver and bile of crab, . . . . .	7.52
" raw Mussel ( <i>Mytilus edulis</i> ), . . . . .	8.41
" boiled do., . . . . .	10.51
" liver of the ox, . . . . .	10.66
" pigeons' liver, . . . . .	11.80
" portable soup, . . . . .	12.16
" raw eel, . . . . .	6.91
" boiled do., . . . . .	6.82
" eel extracted with boiling } alcohol, . . . . . }	14.45
" raw salmon ( <i>Salmo fario</i> ), . . . . .	12.35
" boiled do., . . . . .	9.70
" salmon extracted with alcohol, . . . . .	15.62
" raw herring, . . . . .	14.48
" boiled do., . . . . .	12.85
" herring extracted with alcohol, . . . . .	14.54

	Nitrogen.
In the milt of herring, . . . . .	14.69
" raw haddock ( <i>Æglefinus</i> } communis), . . . . . }	14.64
" boiled do., . . . . .	12.98
" haddock extracted with al- } cohol, . . . . . }	15.72
" raw flounder, . . . . .	14.18
" boiled do., . . . . .	15.18
" flounder extracted with al- } cohol, . . . . . }	15.71
" raw skate ( <i>Raja batis</i> ), . . . . .	13.66
" skate extracted with alcohol, . . . . .	15.22
" crab, . . . . .	13.66
" raw pigeon, . . . . .	12.10
" boiled do., . . . . .	12.33
" pigeon extracted with alcohol, . . . . .	13.15
" raw lamb, . . . . .	13.26
" lamb extracted with alcohol, . . . . .	14.56
" raw mutton, . . . . .	11.30
" boiled do., . . . . .	13.55
" mutton extracted with alcohol, . . . . .	14.76
" raw beef, . . . . .	13.87
" beef extracted with alcohol, . . . . .	14.88
" raw ham, . . . . .	8.57
" boiled do., . . . . .	12.48
" ham extracted with alcohol, . . . . .	14.21
" the white of hens' eggs, . . . . .	13.44

Among the interesting conclusions which may be drawn from these investigations, we will simply refer to the observation which had earlier been made by Schlossberger, *that the amount of nitrogen in muscular fibre does not essentially differ throughout the whole animal kingdom.* The *flesh of fish* contains the same absolute amount of nutrient matter as that of the higher animals; *oysters*, on the contrary, in opposition to the general view, contain far less, and hence the difference between the absolute amount of nutrient matter and the amount of easily digestible matter is most clearly shown.

We need, however, scarcely observe, that we cannot judge directly from the amount of nitrogen contained in animal nutrient matters regarding their direct value in the reproduction of the blood and tissues. For the nitrogen, which is found, depends in part upon the gelatigenous



matters of the animal nutrient substances; it is, however, still very doubtful whether the gelatinous substances can contribute anything towards the reproduction of the tissues, although it may at least be seen with certainty from their composition that they cannot fulfil the same objects as the true albuminous substances.

The following table gives the results of those investigations of Horsford which were at the same time directed to the elucidation of the amount of ash and sulphur contained in vegetable food:

FOOD.	Percentage of Nitrogen.	Percentage of Sulphur.	Percentage of Ash.	Percentage of calculated albuminous Substance.	Percentage of calculated Non-nitrogenous Substance.	Percentage of Water in the fresh food.
Wheat flour from Vienna, No. 1, . . . .	3.00	0.23	0.70	19.16	79.77	13.85
“ “ “ No. 2, . . . .	2.12	0.15	0.66	13.54	85.37	13.65
“ “ “ No. 3, . . . .	3.44	0.25	1.10	21.97	78.03	12.73
Talavera wheat from Hohenheim, . . . .	2.59	0.18	2.80	16.54	80.78	15.43
Whittington wheat from do., . . . .	2.68	0.19	3.13	17.11	78.58	13.93
Sandomier wheat from do., . . . .	2.69	0.19	2.40	17.18	78.89	15.48
Rye flour from Vienna, No. 1, . . . .	1.87	0.13	1.33	11.94	85.65	13.78
“ “ “ No. 2, . . . .	2.93	0.21	1.07	18.71	78.97	14.68
Rye (Staudenroggen) from Hohenheim, . .	2.78	0.15	0.86	17.75	80.86	13.94
Rye (Schilfroggen) from do., . . . .	2.47	0.18	2.37	15.77	82.67	13.82
Polenta-meal from Vienna, . . . .	2.14	0.15	0.86	13.66	84.90	13.36
Indian corn from Hohenheim, . . . .	2.30	0.16	1.92	14.68	84.52	14.96
One-grained wheat from Giessen, . . . .	2.07	0.15	2.01	13.22	84.52	14.40
Barley from Hohenheim, . . . .	2.31	0.16	2.84	14.74	84.80	16.79
Common winter barley from do., . . . .	2.79	0.20	5.52	17.81	80.64	13.80
Kamschatka oats from do., . . . .	2.39	0.17	3.26	15.26	86.05	12.71
Early white oats from do., . . . .	2.82	0.20	4.14	18.00	83.08	12.94
Common rice, . . . .	1.16	0.08	0.36	7.40	91.60	15.14
Buckwheat flour from Vienna, . . . .	1.08	0.07	1.09	6.89	91.52	15.12
Tartar buckwheat from Hohenheim, . . .	1.56	0.11	2.30	9.96	90.38	14.19
Green peas from Vienna, . . . .	4.42	0.14	3.18	28.02	67.31	13.43
Field peas from Giessen, . . . .	4.57	0.14	2.79	29.18	66.23	19.50
Table beans from Vienna, . . . .	4.47	0.14	4.38	28.54	66.70	13.41
Large white beans from do., . . . .	4.59	0.14	4.01	29.31	66.17	15.80
Lentils from do., . . . .	4.77	0.15	2.60	30.46	65.06	13.01
White potatoes from Giessen, . . . .	1.56	0.11	3.61	9.96	86.36	74.95
Blue potatoes, do. . . . .	1.20	0.08	3.36	7.66	88.20	68.94
Carrots, do. . . . .	1.67	0.12	5.77	10.66	84.59	86.10
Beet-root, do. . . . .	2.43	0.17	6.43	15.50	73.18	81.61
Radishes, do. . . . .	1.81	0.13	5.02	11.56	78.49	82.25
Yellow turnips, do. . . . .	1.45	0.10	4.01	9.25	90.32	83.28
Turnip-rooted cabbage, do. . . . .	1.98	0.14	7.02	12.64	81.33	87.78
Onions, . . . .	1.18	—	8.53	7.53	—	93.78

The numbers of the non-nitrogenous substances, given in the fifth column, refer not only to the starch, but include, in addition to this, the cellulose, wax, or fat, &c.; and hence it was important to determine directly the starch contained in these substances. Krockner made determinations of this kind, which yielded the following numbers for every 100 parts of the dried substance:

	Parts of starch.			Parts of starch.	
Pure starch from beans, . . . .	99.96	—	Kamschatka oats, . . . .	39.55	40.17
Wheat-flour, No. 1, . . . .	65.21	66.16	Barley meal, . . . .	64.63	64.18
“ “ No. 2, . . . .	66.93	67.42	Barley, . . . .	38.62	37.99
“ “ No. 3, . . . .	57.70	57.21	Jerusalem barley, . . . .	42.66	42.03
Talavera wheat, . . . .	55.92	56.59	Buckwheat flour, . . . .	65.05	—
Whittington wheat, . . . .	53.06	51.84	Buckwheat, . . . .	43.80	44.45
Sandomier wheat, . . . .	53.83	52.92	Indian meal, . . . .	77.74	—
Rye meal, No. 1, . . . .	61.26	60.56	Indian corn, . . . .	65.88	66.80
“ “ No. 2, . . . .	54.84	54.12	One-eared corn, . . . .	55.51	53.76
“ “ No. 3, . . . .	57.07	57.77	Rice, . . . .	85.76	86.63
Rye (Staudenroggen), . . . .	44.39	44.80	Beans, . . . .	37.71	37.79
“ (Schilfroggen), . . . .	47.71	47.13	Peas, . . . .	38.81	38.70
Meadow oats, . . . .	37.93	36.90	Lentils, . . . .	39.62	40.08



From these and several similar determinations Liebig<sup>1</sup> has constructed a table, which affords a general view of the proportion between albuminates and non-nitrogenous nutrient substances in the most common articles of food for man (taking the albuminates as the unit). As Liebig here considers the non-nitrogenous matters mainly as promoters of animal heat, and as these bodies, namely the fats and carbo-hydrates, exercise a different influence on the generation of heat, according to the amount of oxygen which they contain, it is necessary for the simplification of the proportion to take their amounts of oxygen as the measures of comparison between the fats and carbo-hydrates; ten parts of fat must thus in reference to the generation of heat correspond to about 24 parts of starch; sugar of milk and glucose are thus naturally reduced to the corresponding value of starch by the deduction of the water. On this supposition *the relation of weight between the plastic and the non-nitrogenous constituents of the food* is as follows:

	Plastic.	Non-nitrogenous.	
In cows' milk, . . . . .	10	30	= { 8.8 fat. 10.4 milk-sugar.
" woman's milk, . . . . .	10	40	
" lentils, . . . . .	10	21	
" horse beans, . . . . .	10	22	
" peas, . . . . .	10	23	
" fat mutton, . . . . .	10	27	= 11.25 fat.
" fat pork, . . . . .	10	30	= 12.50 "
" beef, . . . . .	10	17	= 7.08 "
" hare, . . . . .	10	2	= 0.83 "
" veal, . . . . .	10	1	= 0.41 "
" wheat flour, . . . . .	10	46	
" oatmeal, . . . . .	10	50	
" rye meal, . . . . .	10	57	
" barley, . . . . .	10	57	
" white potatoes, . . . . .	10	86	
" blue do. . . . .	10	115	
" rice, . . . . .	10	123	
" buckwheat meal, . . . . .	10	130	

Anderson<sup>2</sup> has recently made very extended analyses in reference to the nutrient qualities of different kinds of fodder for cattle.

If we refer to what has already been stated in the general consideration of the metamorphosis of animal matter regarding the physiological importance of the separate groups of nutrient substances generally, and of that of the fats and carbo-hydrates specially, we shall be induced to distinguish articles of food according to the quantity of fat and carbo-hydrates which they contain; that is to say, the relatively best kinds of food must contain fat as well as carbo-hydrates; under favorable relations the animal body is certainly able to elaborate from the carbo-hydrates the fat which it requires; but independently of the fact, that this production of fat would appear from all our positive experiments to be tolerably limited, the production of sugar in the animal organism shows, that fat and sugar have very different and not unimportant objects to fulfil in it (see p. 347). If it be true that the dictates of animal instinct ought in general to be followed, this is more especially the case in reference to the selection of food. The general disposition

<sup>1</sup> Chem. Briefe. 3 Aufl. 1851, S. 463 [or Letters on Chemistry. London, 1851, p. 361].

<sup>2</sup> Journal of Agriculture, 1853, p. 508-518.



to combine highly amylaceous food with fats, and fatty matters with amylaceous substances, and the undoubted greater digestibility of such mixtures, prove no less than the simultaneous occurrence of fat and sugar in the milk of animals, which is generally recognized as a normal type of food, that both substances are necessary to the completion of an article of nourishment which perfectly satisfies the requirements of the animal organism. If, therefore, any one of these substances may serve in certain general relations as a substitute for another, especially in reference to the development of heat, this does not in any way militate against the special utility of either. But when Liebig included such different substances as fats and carbo-hydrates under the general designation of respiratory elements, he was far from holding the opinion that, independently of the differences in their capacity for generating heat or their so-called respiratory value, they were of equal importance in the metamorphosis of animal matters—a fact of which we might readily convince ourselves by an attentive study of his most recent deductions regarding the forms of metamorphosis which the fats and sugar undergo. Although Liebig compares animals to “moving furnaces” in respect to the development of heat and its causes in the animal body, it requires a strong faith to interpret this expression in the broadest sense of the words, or to regard his somewhat overstrained physical view as calling for serious refutation. Liebig ranks the fats with the carbo-hydrates in his consideration of the different articles of food, on the one hand, because both serve to compensate for the carbon and hydrogen which are lost through the lungs, and on the other hand, because however much might be advanced in favor of a systematic separation of these groups, their specific functions in the metamorphosis of animal matter have not been determined with sufficient strictness either by decided experiments or direct observation. The time, however, will come, and is assuredly not far distant, when we shall be able, by establishing the relations of the most favorable admixture of different articles of food, to keep the fats and carbo-hydrates sufficiently separate, and to attempt to ascertain the proportion between each individual element of nutrition and all the others. For the present we must take the normal food which nature itself has prepared for the infant organism as the standard by which to judge of the most favorable proportions in the mixture of nutrient substances. If we assume the mean constitution of woman’s milk to be that mixture of the four groups of substances which is best adapted for the nourishment of the human organism, we should find that the most nutritious food exhibits the proportion of 10 parts of plastic matter, 10 parts of fat, 20 parts of sugar, and 0.6 of a part of salts.

In our investigation of the most favorable mixture of the different nutritive matters, we must not forget that these relations change in accordance with the condition of the organism, for the requirements of the body equally demand variations in the composition of the food and in its absolute quantity. Even in the consideration of milk, we are struck by the fact, that nature has been careful to vary its composition in accordance with different circumstances, whilst its proportions remain invariably the same under perfectly similar circumstances. The propor-



tion of the constituents of this nutrient fluid, which nature provides for the suckling which has just begun to breathe, is the same in every case, but is quite different from that which is supplied to young animals after they have breathed the air for a longer time. The proportions in which the constituents of the milk occur are moreover different for the different classes of animals; cows' milk contains relatively less sugar and more fat and casein than woman's milk; while asses' milk contains very little casein, but, on the other hand, much sugar and far more fat. It cannot be denied that (as we have already noticed in vol. ii. p. 61) the food which the mother may happen to take exerts a certain influence on the proportion of the constituents of the milk; but it may be readily shown by a comparison of the investigations made in relation to this subject, that there is for every species of animal a certain fixed proportion between the constituents of this primary food. It would appear obvious from these indications, that the requirements of the animal organism, which are influenced by various more or less preponderating agencies, must present differences in the admixture of the necessary nutrient matters. The effect of different influences of the external world, the higher or lower excitation of the individual animal functions, mental excitement, &c., necessarily call for a restoration of the material parts lost in the different processes. This is so clear that there can scarcely be a doubt on the subject; but we are still entirely in the dark in reference to the more exact determinations of the proportions which are required to enable us to calculate the composition of the food, which is best adapted for each special organism. The physiologist should, however, attempt to calculate for a given organism under certain definite conditions, the proportion in which the special nutrient matters ought to be mixed in order that the persistent well-being of the organism may be secured; and in this respect physiology has the best prospect of attaining to determinate numerical values; from these we may then construct general formulæ, by means of which we may be enabled to predict with mathematical certainty the result of any definite action upon the animal organism. The functions which must be considered in a formula of this kind are certainly very numerous, and very many investigations have still to be made before this object can be attained. But if this be an extensive field whose cultivation is still beset with great difficulties, it yet promises the richest results, which may not only influence theory, but which will also make a marked impression upon practical life. Dietetics would then be based upon a firmer foundation, and it will no longer remain a mere illusive idea that the healing art may be made accessible to exact inquiry.

A more important question than the determination of the relations of mixture in different articles of nutrition is that of the absolute quantities of food which are requisite for the maintenance of life, and for the energetic accomplishment of all its functions. A very great number of observations which contribute towards the solution of this question have been made on man as well as on animals. These investigations have, however, been conducted rather with the view of comparing together the excreta of the animal organism generally, and of finding some standard for the amount of the metamorphosis of animal matter, than with special reference to the question of the quantities of favorably mixed food, which



the organism requires for its natural well-being. If for the present we put these investigations entirely out of the question, and consider the methods by which we may determine the amount of food which is necessary to the organism, we find that there are two modes of determination which especially present themselves to our notice. The first method consists in experimenting upon oneself or upon animals with the smallest possible quantities of differently mixed food, until we have been able to find the suitable amount and the most correct proportion for each individual case; but this mode of testing could only be adopted at the expense of trouble and time, and would throw little or no light on the question. We must, therefore, look about us for some guide in this method of inquiry, and this we shall find in the investigation and quantitative determination of the excretions of the animal body. If the latter actually afford a standard for the metamorphosis of animal matter, and if we are able, from their quantity and composition, to judge of the true loss which the animal body experiences during the activity of its organs, they ought also to give us the quantity and quality of those substances, which the organism requires for the restoration of its effete matters. This last method of inquiry, which is based upon the proposition that the requirements of nutrition are regulated by the amount of the loss in the body, appears at first sight to be so simple that one might almost wonder why, after such labors as those of Boussingault, Liebig, Valentin, Barral and other distinguished investigators, this problem has not yet been completely solved; but the inquiry is here met by numerous difficulties which have hitherto prevented any exact determination even for the simplest relations, partly on account of the constant fluctuations in vital activity and partly from those external influences which do not admit of calculation, but which materially affect inquiries of this nature. In order to simplify the observation, we should be especially careful to see that the organism which was made the object of investigation did not present any increase of weight in its organs, or that it was no longer at that period of growth, during which it required to consume more materials than could be again traced in the excretions; we must further avoid that kind of feeding to which the term "fattening" is applied in agriculture; in short, the organism should be maintained in all respects in its normal state, in order that a conclusive proof may be drawn from the excreta in reference to the necessary amount of food. The best method, therefore, of finding at least the minimum of the food necessary for the support of life, is after stopping all supplies from without, to determine the quantities of matters which the organism loses by the excretion of urine, fæces, and products of perspiration. The numerous experiments on inanition, which were formerly made on different animals, appeared to present a good basis for this mode of observation. But, however important it may be to know the minimum quantities needed for the continuance of the life of the organism, these kinds of experiments afford very slight indications of the quantities of food which are necessary to maintain the animal in perfect health and in the full use of its powers. When we deprive an animal of all food, all its functions become impaired, both in their intensity and extent; and abnormal symptoms frequently occur, such as diarrhœa, stases of blood in the different systems of capillaries, &c.; if, therefore, we wish to make the



excretions of such animals a measure by which to judge of the quantity of food indispensable to life, we must remember that this measure would scarcely suffice to afford the organism more than a scanty existence, for as we have already stated the functions of the organs, the manifestations of force, and the metamorphosis of matter connected with it, are totally different in a state of repletion and in inanition. Such experiments are nevertheless of high value to science.

But how can the smallest quantity be discovered for an amount of food which may give the organism the full use of its faculties? If the absorption of nutrient matters in the intestine, that is to say, the absorption of digested matters were limited to a greater extent than it really is, if no more nutrient matters entered the blood than were necessary for the reproduction of the tissues and of the various functions, we might, perhaps, notwithstanding some difficulties, calculate with tolerable exactness the amount of food required for the organism, from a comparison of the excretions and the food which had passed unchanged into the fæces. Now we know, from our previous considerations, that the organism is not able to convert an unlimited quantity of nutrient matter into blood; we always found that after partaking abundantly of any kind of nutrient substance, some portion of it remained unchanged. The exact determinations by weight, made by Boussingault in reference to fat, those of Bidder and Schmidt in reference to the albuminates, and those of von Becker in reference to the carbo-hydrates, prove that only definite quantities of these substances can be resorbed by the intestine within a certain period of time. But nature has also here given very wide limits to animal motions; thus, for instance, very many experiments show that the organism is able to absorb through the intestinal capillaries and the lymphatics a much larger amount of nutrient matter or chyle, than it requires for the restitution of the effete substances, or for the accomplishment of different purposes of life. In overfeeding the animal which is being experimented upon, a part of the food certainly passes unchanged into the excrements, but another portion enters as superfluous nutrient matter into the blood, where it is not employed either for the restoration of lost materials, or for the increase of mass in the body or its individual organs, or for the accomplishment of any other objects of life, but is again given to the external world, after having undergone certain alterations which render it more capable of being excreted. There is, therefore, an actual superfluous consumption (*Luxus-consumption*, to use C. Schmidt's expression), whenever there is this abundant supply of food. In such a case the organism takes up far more than it requires even for the most active accomplishment of all the vital functions. The difficulty consists, therefore, simply in this, that we are unable accurately to determine the mean which will give the organism neither too little nor too much nourishment for the maintenance in their normal equilibrium of all the movements of matter, and the manifestations of force depending upon them. Schmidt and Bidder have, therefore, designated as superfluous consumption (*Luxus-consumption*) whatever exceeded the amount of food which was shown in experiments upon fasting animals to be absolutely necessary to life; and hence they have taken the minimum value of the metamorphosis of matter, as the unit with which all further experiments on nutrition might be compared.



In determining the absolute quantities of the nutrient substances on which the metamorphosis of matter depends, there are three magnitudes which we are especially called upon to consider : the first is the quantity of food which will prevent the organism from sinking by starvation ; the second is that which affords the right supply of nourishment for the perfect accomplishment of the vital functions ; and the last is that which indicates the sum of nutrient matter which may under the most favorable circumstances be subjected to metamorphosis in the blood.

If we should succeed in ascertaining the mean amount of the metamorphosis of matter, and consequently of determining the corresponding quantity of food, it would be very readily seen, that like everything in the living organism, this amount will also vary excessively according to existing conditions. It appears almost self-evident that there should be a greater consumption when all the vital functions are in a state of unwonted energy, or during any considerable or continuous manifestation of force, than in a state of rest or vegetative passivity ; the previously noticed increase of the urinary constituents, and the more profuse perspiration after bodily exertion, have afforded the most positive proof of this fact. The necessity for nourishment is, therefore, increased with the increase of external activity (activity dependent on exertion) ; this proposition is so clear, and is proved by such numerous facts in our daily experience, that it would be superfluous to enter more fully into this subject ; we will only observe that in addition to the above-indicated standard, a special standard might also be established for the consumption required during a period of bodily labor, and that, in addition to these, many other relations involve differences in the requirements of nutrition.

In all these cases, we have proceeded on the assumption that we are considering an organism which has attained its full development,—in which, therefore, the absolute weight of the living object remains the same, so that the excreta can be accurately balanced by the ingesta. There is still greater difficulty in deciding the question regarding the absolute extent of the requirements of nutrition when growth, corpulence, or pregnancy, and similar relations in which there is an increase of weight, have to be considered ; in these cases the excreta fall below the ingesta, and hence the latter cannot furnish any conclusions regarding the quantity of the nutrient matters which are necessary for the due accomplishment of these physiological functions. Boussingault was here, as throughout the whole of this department of inquiry, the first to lead the way, and he instituted a numerous series of investigations which have already yielded the most brilliant results. Yet notwithstanding all these investigations we have hitherto failed in establishing any sharply defined determinations of the amount of food necessary to the organism under certain given relations. However much we may have learnt from the laborious researches of different inquirers, we are still entirely wanting in the exact normal determinations, to which we had hoped to attain in this department of science.

The sketch which we have here given of the experiments made to determine the necessary amount of food could only serve as an introduction to further considerations of the actual phenomena of nutrition ; while



at the same time it might indicate the direction by which we might most securely traverse the still mysterious labyrinth of ever varying phenomena. It might not be out of place if, before we passed to the special statistics of the metamorphosis of animal matter, we were once more to revert to the limit which the resorption of nutrient matters from the intestine cannot exceed, and which consequently appertain to nutrition and the metamorphosis of matter. Although this subject has frequently been touched upon in the course of this work, we have deferred to the present moment entering more fully into this question, as it has the most direct bearing upon the phenomena of nutrition, which we are about to consider, its elucidation being to a certain extent the first point from which we are able to obtain an insight into the quantitative relations of the metamorphosis of matter during nutrition. Unfortunately, however, we possess only very imperfect investigations on this subject, the most complete of which are those which were made by Boussingault<sup>1</sup> on ducks. These animals were left without food for 36 hours before the beginning of each experiment, although they were allowed to take water during this time; for the purpose of the actual experiment the food in question was introduced in the form of balls; the ducks were killed at different intervals of time, and the excrements, as well as the contents of the intestines were analyzed with special reference to the quantity of fat and nutrient matters still remaining unresorbed. It was of course necessary to determine before each series of experiments the quantity of fat and of other matters, which generally remained in the intestine even after 36 hours' fasting. However carefully these investigations may be conducted, we ought to exercise considerable caution in deducing any conclusions from the results thus obtained. For independently of the fact, that these results obtained from ducks do not admit of comparison with the corresponding relations of higher animals, the birds thus experimented upon not only obtained the articles of food given to them, unmixed with other substances, but also in a form to which they were entirely unaccustomed. We have already seen under the head of "Digestion," that individual articles of food, as for instance, the nitrogenous matters, when they are introduced into the intestinal canal independently of other substances, are less easily digested; there would, therefore, be less matter to be resorbed in these cases than usually occurs under the ordinary relations of nutrition in ducks. Nor can any one deny, that food differing so much from the ordinary kind, as rolled up pieces of dry cheese or gelatin, must be quite inadequate to afford any conclusive evidence of the normal relations of nutrition in ducks. If, however, all these objections were obviated, and the contents of the intestine and the excrements were not only weighed, but also analyzed, the circumstance that the intestinal excretion was different during digestion from what it was in a state of fasting, must essentially influence the accuracy of the results; for we know, and shall have still further occasion to see in the course of our considerations, that something more than the undigested and indigestible remains of the nutrient substances passes into the intestinal excrements, for although we have learnt that far less bile passes into the excrements than was formerly supposed to be the case, we have seen that the intes-

<sup>1</sup> Ann. de Chim. et de Phys. 3 Sér., T. 18, p. 444-478.



tinal excretion is by no means inconsiderable for certain substances. A far smaller quantity of bile and intestinal mucus is, however, secreted in a fasting state than in a condition of repletion. Yet notwithstanding these uncertainties, Boussingault's results retain their value, for if we were not possessed of these direct determinations, we should scarcely be able to obtain even an approximately correct idea of these relations. We have, therefore, simply given in the following table the results obtained by Boussingault's investigations, according to which the different substances pass in one hour, in the quantities indicated, from the intestinal canal into the blood of a duck.

	Grammes.	Grammes.	Grammes.
Dry rice (8·68% of albumen and 89·2% of starch), . . . . .	= 4·20	(= 0·34 of albumen and 3·86 of starch).	
Dry cheese (70·69% of fat), . . . . .	= 2·50	(= 1·93 of casein and 0·57 of fat).	
Bacon (96·3% of fat), . . . . .	= 0·88	(= 0·84 of fat).	
Cacao seed (48·4% of fat), . . . . .	= 1·77	(= 0·84 of fat).	
Starch, . . . . .	= 5·26		
Sugar, . . . . .	= 5·62		
Boiled white of egg, . . . . .	= 1·25		
Casein (anhydrous), . . . . .	= 1·37		
Gelatin (anhydrous), . . . . .	= 4·40		
Beef (boiled, free from fat), . . . . .	= 1·41		
Albumen and gelatin (649 : 3000), . . . . .	= 5·18	(= 0·92 of albumen and 4·26 of gelatin).	

In connection with these uncertain determinations, several highly interesting considerations here suggest themselves, to which we shall revert at a future page; contenting ourselves for the present with the observation, that the albuminous substances alone are totally insufficient for the restoration to the body of the carbon which is lost by respiration; according to Boussingault, a duck expires in one hour 1·25 grammes of carbon, whilst the albuminates which are resorbed within an hour contain at most only 1·0 gramme of carbon. Fats or carbo-hydrates must, therefore, necessarily be commingled with the albuminates, in order that there may be a due compensation in the body for the loss of carbon which normally occurs through the respiration. It is still more striking, that the quantity of fat which is resorbed in one hour should be wholly inadequate for this restitution of the carbon; 0·84 of a gramme of fat, which is all that is resorbed during one hour, contains about 0·7 of a gramme of carbon, and, therefore, scarcely half as much as is exhaled by the lungs in one hour. The carbo-hydrates are, however, resorbed by the intestine in sufficient quantities for the requirements of respiration, and it is moreover worthy of notice, that very nearly as much carbon is introduced into the body in equal periods of time by starch as by the absorbed sugar. (For 5·26 parts of starch and 5·62 parts of sugar which are resorbed in one hour, both contain about 2·37 of carbon.)

The very important question here presents itself, as to what changes are impressed upon the blood in consequence of the absorption of different nutrient matters; this being undoubtedly the first step we ought to take if we would enter upon the investigation of the nutrition of the animal body. Yet notwithstanding the efforts of numerous admirable investigators, we are still very imperfectly acquainted with the most important points of this inquiry. We have already referred to the influence which nutrition in general or digestion exerts on the physical and chemical



characters of the blood (see vol. i. p. 631). Very few special investigations, deserving of notice, were made in reference to the influence of different kinds of food on the constitution of the blood before those of H. Nasse,<sup>1</sup> with which we may associate an observation of Verdeil<sup>2</sup> on the ash of the blood of one and the same dog, which had been fed both on animal and vegetable diet. The relative quantity of chloride of sodium was in both cases nearly the same (50%); after the dog had been fed upon animal food the ash contained more sulphuric and phosphoric acids, and considerably more soda and oxide of iron, but somewhat less potash, and very much less magnesia than after a vegetable diet. Boussingault<sup>3</sup> was as little able as Bouchardat and Sandras to discover that fatty food had any decided influence on the amount of fat in the blood of dogs.

Notwithstanding the numerous experiments which have been made by Nasse, the number of constant results which they have yielded is relatively very small, in consequence of the great fluctuations which were observed in the constitution of the blood; these results reduce themselves to the following points: after a meat diet the blood-corpuscles in the dog exhibit a greater capacity for sinking; the blood itself presents a darker color, which becomes whitish after the abundant use of fat; the coagulation occurs somewhat more rapidly than on a vegetable diet; a continuous animal diet increases the amount of fibrin (as I have observed<sup>4</sup> in my own case,) after living exclusively on purely animal food, and augments the amount of the phosphates and of the salts generally. The quantity of fat in the blood increases even during the first hour after the use of food which is rich in fat; but it speedily falls again.

The blood of dogs is for the most part of a somewhat lighter shade of color when kept on vegetable than when kept on animal food, and the sinking capacity of the blood-corpuscles is somewhat smaller; the specific gravity of the blood, as well as that of the serum, is increased during the first five hours by a vegetable diet (especially if this be combined with the simultaneous use of sugar). The amount of fibrin is not altered; the fat, however, is somewhat diminished, whilst the amount of the salts including that of the phosphates is somewhat lessened.

Continuous deprivation of food renders the blood somewhat paler in color, retards its coagulation, and raises the specific gravity both of the blood and of the serum; the number of the blood-corpuscles is very fluctuating; the fibrin rises only slightly; while the amount of the salts is very considerably increased.

After the last meal the quantity of the solid constituents of the blood increases to the ninth hour, when it again begins to sink.

The few results which Nasse has been able to deduce from the careful labors which he prosecuted for years, show how unable we still are to trace the metamorphosis of the nutrient matters in nutrition through its individual phases. We have here a confirmation of the remarks which we made in our introduction, that our knowledge of the internal metamorphosis of matter is still extremely incomplete, and that it is only by a comparison of the chemical qualities of the different juices and tissues,

<sup>1</sup> Ueber den Einfluss der Nahrung auf das Blut. Leipzig, 1850.

<sup>2</sup> Ann. d. Ch. u. Pharm. Bd. 69, S. 89-99.

<sup>3</sup> Ann. de Chim. et de Phys. 3 Sér., T. 24, p. 460-464.

<sup>4</sup> Journ. f. pr. Ch. Bd. 27, S. 16.



and more especially by carefully conducted statistics of the final results of the metamorphosis of animal matter, that we can hope to form a correct judgment or arrive at anything like conclusive views. We cannot, therefore, trace in detail the final destinies to which the albuminates, the fats, the carbo-hydrates, and the salts are subjected in the animal body, nor can we venture to do more than indicate the facts that lead us to those considerations, which we have already given in relation to the metamorphosis of matter generally (see p. 337). It, therefore, only remains for us to notice, in reference to the chemical phenomena of nutrition, the facts and the conclusions to be deduced from them which have hitherto been obtained from statistical investigations.

The next question which must engage our attention in this respect, is to determine the amount of food which, under normal relations, is daily subjected to the metamorphosis of matter in an adult man, and the mode in which the products, into which the nutrient matters are decomposed during their stay in the body, are distributed in the excretions. The earliest exact investigations of this kind were made by Valentin<sup>1</sup> on his own person. His bodily weight being 53 kilogrammes, Valentin found that he consumed in the twenty-four hours on an average 2924.03 grammes of mixed food; of the products of metamorphosis which were excreted during that time 190.73 grammes were eliminated with the solid excrements, 2447.70 grammes with the urine, and 1246.93 grammes with the perspiration; the ratio of the solid and fluid to the gaseous excretions, is, therefore, on an average as 1 : 0.833. This estimate seems tolerably high for the perspiration; but it appears from Valentin's special investigations, that the main factor which raises the amount eliminated by the perspiration is especially the separation of water through the skin, on which account this proportion must be totally different in animals.

The experiments of Rawitz,<sup>2</sup> which were conducted with great patience and self-sacrifice, still leave much to be desired in reference to their exactness; the mean of twenty-two observations, in which he studied the effect of many of the most common articles of food, yielded on an average, for a consumption of 1875.4 grammes of mixed food, 1136.4 grammes of egesta through the intestine and kidneys, and 739.0 through the perspiration; the ratio given by Rawitz of the solid and fluid to the gaseous egesta differs, therefore, very considerably from that of Valentin, being as 1 : 0.650; the ratio in his individual observations was extremely fluctuating, as was also the case with Valentin.

Rigg<sup>3</sup> determined the ingesta and egesta of a strong man, in accordance with their elementary constituents; he obtained results which accorded tolerably well with those of other observers: it is however remarkable, that for 100 parts of the nitrogen which was absorbed in these experiments (which were prolonged for twelve days) only 50.8 parts passed into the urine.

The following observation, in reference to the excretion of nitrogen, was made by myself,<sup>4</sup> on my own person: during a purely animal diet

<sup>1</sup> Valentin's Repert. 8 Jahrg.; Handwörterbuch der Physiologie. Bd. 1, S. 367-470; and Physiol. d. Menschen. Bd. 1, S. 710-780.

<sup>2</sup> Ueber die einfachen Nahrungsmittel. Berlin, 1842.

<sup>3</sup> Medical Times, 1842, p. 278.

<sup>4</sup> Journ. f. pr. Ch. Bd. 27, S. 258.



(eggs), I took daily on an average 30·3 grammes of nitrogen, and discharged 24·4 grammes by the urine; hence five-sixths of the absorbed nitrogen were again given off through the kidneys.

The best investigation of the statistico-chemical relations of the quantitative metamorphosis of matter in the animal organism, which has as yet been made, is due to Barral,<sup>1</sup> who, however, has merely taken into account the elements of nutrition and of the excretions. He made five series of observations, two on himself (when at the age of twenty-nine years, the one in winter and the other in summer), one upon a boy aged six years, the fourth upon a man whose age was fifty-nine years, and the fifth upon a woman aged thirty-two years. The combined results of this investigation were as follows:

	Daily absolute quantity in grammes.						
	Ingesta.			Egesta.			
	Fluid and solid food.	Oxygen.	Sum.	Perspired water.	Carbonic acid.	Solid and fluid excretions	Other losses.
Man aged 29 years, in winter, . .	2755·0	1061·5	3816·5	1287·8	1230·9	1265·0	32·8
“ “ in summer, .	2386·0	777·3	3163·3	1141·6	888·4	1099·4	33·9
Boy, aged 6 years, . . . . .	1396·2	423·4	1819·6	694·7	514·0	604·6	6·3
Man, aged 59 years, . . . . .	2710·7	889·1	3599·8	522·6	1088·3	1962·8	26·1
Woman, aged 32 years, . . . . .	2339·6	886·7	3226·3	998·7	1006·9	1191·6	29·1

For a healthy adult man the egesta, corresponding to 100 grammes of ingesta (that is to say, 73·8 grammes of food, in which there were 18·56 parts of solid matters and 55·24 parts of water, and 26·2 parts of oxygen), would be distributed in the following manner, namely: 34·95 grammes of water and 30·55 grammes of carbonic acid would be eliminated by the lungs and skin, 33·95 grammes as urine and fæces, and 0·55 of a gramme through other channels.

If we calculate from Barral's experiments the distribution which 100 grammes of absorbed carbon undergo in its excretion after it has fulfilled its functions in the organism, we shall find that (in an adult man) 91·59 grammes pass into the products of perspiration, and only 4·58 grammes into the urine, and 3·83 grammes into the fæces. According to this estimate, more than nine-tenths of the carbon contained in the food are entirely consumed and converted into carbonic acid.

If we pursue a similar method of inquiry in reference to the mode of excretion of nitrogen, and follow the experiments which Barral instituted on his own person, we arrive at the following results: (the nitrogen in the food taken by Barral being to the carbon as 1 : 12·8;) for every 100 parts of absorbed nitrogen only 8·33 parts were again excreted with the fæces, while 42·07 parts were given off with the urine, and 49·6 parts through the skin and lungs. The relative amount of the nitrogen eliminated by the perspiration is here excessively large, and entirely at

<sup>1</sup> Compt. rend. T. 27, p. 361, and Ann. de Chim. et de Phys. 3 Sér., T. 25, p. 129-171.



variance with the experiments which many other investigators have made on animals.

It further appears from the above table, that for every three parts by weight of solid and fluid food (that is to say, such food as Barral used during the prosecution of his experiments, and which consisted on an average of 25.15% of solid substances), about one part by weight of oxygen entered into the metamorphosis of matter. The water which was separated through the lungs and skin amounted in all the cases (excepting that of the man aged fifty-nine years), to somewhat more than the quantity which was discharged by the sensible excretions. It follows, moreover, from these experiments, that an adult man oxidizes on an average 289.0 grammes of carbon, and 18.6 grammes of hydrogen, in the twenty-four hours.

However carefully these investigations may appear to have been conducted, they yet can only serve as examples of the manner in which the consumption of matter occurs under different relations in the human organism; but as very many conditions which exert an essential influence on vegetative life must be wholly disregarded, and as, moreover, the method of investigation does not exclude all doubt of the accuracy of the results even in special cases, these very meritorious labors can scarcely for these reasons, and in consequence of their isolated character, be of any great service to science, or furnish any fixed points of support for more extended conclusions. As was naturally to be expected, the comprehensive experiments on animals, conducted by Valentin and Bous-singault, and more recently, and to a still greater extent, by C. Schmidt and Bidder, possess far greater certainty, and afford us a deeper insight into the combined relations of nutrition in the animal organism.

Valentin<sup>1</sup> prosecuted very careful investigations on the balance of the metamorphosis of matter for three days consecutively on a four-year-old mare. The results of these experiments may be thus summed up. The quantity of the discharged fæces exceeded in this case, by three or four-fold, the quantity of the urine that was excreted; half of all the excreted matters was always carried off by the perspiration, and, consequently, half of the daily food was again eliminated by the lungs and skin during the twenty-four hours. A larger quantity of water was discharged with the fæces than with the urine, and less water was given off by the perspiration than through the urine and excrements. The quantity of water which was daily introduced into the system amounted to one-fourteenth of the mean weight of the body. A larger quantity of organic matter was removed with the fæces than with the urine. Upwards of twice, but considerably less than three times the amount of the organic elements was eliminated by the perspiration. The quantity of organic matter daily consumed amounted to from 1.42d to 1.43d of the mean weight of the body; the organic matters eliminated with the fæces ranged from 1.139th to 1.150th of the weight of the body, and those excreted with the urine from 1.208th to 1.209th; and those through the perspiration on an average to 1.62d of the weight of the body. By far the greater part of the fixed salts was eliminated with the fæces. About 3-10ths of the fixed salts taken up with the food are carried off by the perspiration. The sensible ex-

<sup>1</sup> Op. cit.



cretions consisted on an average of 84.11% of water, 13.76% of organic constituents, and 2.13% of ash; and the perspiration contained 64.28% of water, 34.67% of organic constituents, and 1.05% of ash: the food which was daily consumed contained on the other hand 74.75% of water, 23.63% of organic constituents, and 1.62% of ash. The percentage numbers obtained for the food stand between those yielded by the sensible excretions and the perspiration.

Boussingault<sup>1</sup> made a similar series of experiments on a horse and a cow. From these experiments of Boussingault, Valentin has drawn up the following table in which the total sum of the water, of the ash, and the individual elements of organic matter taken up with the food, is placed in juxtaposition with the mean numbers of the daily quantities of water, ash, and organic elements again eliminated through the urine, fæces, and perspiration.

Constituents.	Total sum of the food.	Fæces.	Urine.	Perspiration.
	Grammes.	Grammes.	Grammes.	Grammes.
Water, . . . .	17364.7	10725.0	1028.0	5611.7
Carbon, . . . .	3938.0	1864.4	108.7	2465.0
Hydrogen, . . . .	446.5	179.8	11.5	255.2
Oxygen, . . . .	3209.2	1328.9	34.1	1846.1
Nitrogen, . . . .	139.4	77.6	37.8	24.0
Ash, . . . .	672.2	574.6	109.9	12.3
Sum, . . . .	25770.0	14250.3	1330.0	10189.7

Hence the elements of the 100 parts of the food consumed by the horse are distributed in the following proportions in the excretions:

Of 100 parts of		The Fæces.	The Urine.	The Perspiration.
Water, . . . .	There are given off to	61.8 per cent.	5.9 per cent.	32.3 per cent.
Carbon, . . . .		34.6 "	2.7 "	62.7 "
Hydrogen, . . . .		40.3 "	2.5 "	57.2 "
Nitrogen, . . . .		55.7 "	27.1 "	17.2 "
Oxygen, . . . .		41.4 "	1.0 "	57.6 "
Ash, . . . .		85.5 "	16.2 "	—
The food generally,		55.3 "	5.2 "	39.5 "

An experiment which was continued for three whole days upon a milch cow yielded the following numbers:

Constituents.	Total amount of the food.	Milk.	Fæces.	Urine.	Perspiration.
	Grammes.	Grammes.	Grammes.	Grammes.	Grammes.
Water, . . . .	71965.0	7388.4	24413.0	7239.2	32924.4
Carbon, . . . .	4813.4	628.2	1712.0	261.4	2211.8
Hydrogen, . . . .	595.5	99.0	208.0	25.0	263.5
Oxygen, . . . .	4034.6	321.0	1508.0	253.7	1951.9
Nitrogen, . . . .	201.5	46.0	92.0	36.5	27.0
Ash, . . . .	890.0	56.4	480.0	384.2	30.6
Sum, . . . .	82500.0	8539.0	28413.0	8200.0	37348.0

<sup>1</sup> Ann. de Chim. et de Phys. T. 61, p. 128.



For the cow, therefore, every 100 parts of the elements of the food are distributed in the following proportions in the excreta :

Of 100 parts of		The Milk.	The Faeces.	The Urine.	The Per- spiration.
		Per cent.	Per cent.	Per cent.	Per cent.
Water, . . . . .	There pass into	10.2	34.4	10.0	45.8
Carbon, . . . . .		13.0	25.8	5.4	54.2
Hydrogen, . . . . .		16.6	34.9	4.2	55.7
Nitrogen, . . . . .		22.8	45.6	18.1	13.5
Oxygen, . . . . .		7.9	37.4	6.3	48.5
Ash, . . . . .		6.1	53.9	43.1	3.1
The food generally, .		10.3	34.4	9.9	45.4

It will be unnecessary to consider at the present time the conclusions to be drawn from these experiments ; partly because they are self-evident from a mere inspection of the table itself, and partly because we shall revert to them at a future page, when we shall enter upon the consideration of similar experiments.

Valentin has also directed his attention to the distribution of the *salts* in the metamorphosis of matter, for which purpose he instituted a comprehensive series of experiments on a horse. These experiments yielded several interesting results in regard to the resorption of certain mineral substances in the intestine : it was found that lime, phosphoric acid, and the alkaline salts were present in great abundance in the urine (having been absorbed during digestion); but that the magnesia occurred only in very small quantities. In the ash of the excrement the phosphate of magnesia was to the phosphate of lime in an inverse ratio to that which occurred in the food, because 60.23% of the magnesia, which had been absorbed, was again eliminated with the solid excrements, whilst only about 25% of the absorbed lime was again given off with the faeces. (Hence arise the frequent intestinal concretions observed in herbivorous animals.)

A mare whose weight was 935 lbs., and her age four years, consumed daily for nutrition and growth, and for other excretions than the faeces and urine, 2.025 ounces of lime, 0.125 of an ounce of magnesia, 0.74 of an ounce of silica, 0.035 of an ounce of chlorine, 0.64 of an ounce of sulphuric acid, 19.25 ounces of phosphoric acid, and 0.76 of an ounce of alkalies. Thus, too, a tolerably large proportion of the silica, which had been contained in the food, could not be again found in the excrements and the urine. Of the 0.3796 of a lb. of the silica which was taken in the food, 0.0464 of a lb. did not reappear in the excretions ; their application to the formation of the epidermis and hair seems, however, to be proved by the amount of silica which was shown to be present in these parts by Brunner and Valentin as well as by Gorup-Besanez.

Boussingault<sup>1</sup> made a series of experiments with a view of settling the question whether nitrogen was or was not exhaled through the lungs. These experiments, which were made on turtle-doves fed upon millet, gave the following result for the distribution, through the excrements and the perspiration, of the elements taken with the food. We have cal-



culated the mean of the results of two observations, the one of which extended over five, and the other over seven days.

Of 100 parts of		To the Fæces.	Perspiration.
Carbon, . . .	There are given off	20.3 per cent.	79.7 per cent.
Hydrogen, . . .		18.7 "	81.3 "
Nitrogen, . . .		64.96 "	35.04 "
Oxygen, . . .		19.19 "	80.81 "

Sacc<sup>1</sup> made a perfectly similar series of experiments on fowls which had been fed on barley, at the same time that they had swallowed chalk and sand. These animals (a cock and a hen) had increased 19.18 grammes in weight during the seven days of the experiment; this increase depended upon the assimilation of 12.436 grammes of organic matter and 6.744 grammes of mineral substances; if these are abstracted from the food, we find from Sacc's experiments, that the elements are distributed as follows in the fæces and the perspiration:

Of 100 parts of		To the Fæces.	Perspiration.
Carbon, . . .	There are given off	24.5 per cent.	75.5 per cent.
Hydrogen, . . .		23.0 "	77.0 "
Nitrogen, . . .		42.2 "	57.8 "
Oxygen, . . .		23.9 "	76.1 "

C. Schmidt<sup>2</sup> has recently, in conjunction with Bidder, prosecuted an inquiry into the relations of nutrition, and these inquiries are distinguished from all previous investigations of this nature by the exactness of the methods employed, the comprehensive determination of all determinable amounts, and the copiousness of the results. These experiments were made on cats and dogs, some of which were abundantly, others sparingly supplied with meat, and others again left for a prolonged time without any food. The nutrient matters and the excretions generally were carefully investigated in reference to their proximate constituents, as well as to the elements which they contained.

We subjoin a table of the distribution of the elements of nutrition in the organism of one of the carnivora, that we may be able to add the results of Schmidt's investigation to the above experiments of other observers; the first series of experiments were made on a full-grown cat, weighing 3228 grammes, which had as much meat for a week as it could eat.

Of 100 parts of		To the Fæces.	To the Urine.	To the Perspiration.
Water, . . .	There were given off	1.2 per cent.	82.9 per cent.	15.9 per cent.
Carbon, . . .		1.2 "	9.5 "	89.4 "
Hydrogen, . . .		1.1 "	23.2 "	75.6 "
Nitrogen, . . .		0.2 "	99.1 "	0.7 "
Oxygen, . . .		0.2 "	4.1 "	95.7 "
Sulphur, . . .		50.0 "	50.0 "	
Salts, . . .		92.9 "	7.1 "	

<sup>1</sup> Ann. d. Ch. u. Pharm. Bd. 52, S. 77.

<sup>2</sup> Verdauungssäfte und Stoffwechsel. S. 289-413.



A comparison between this table and the previous tables, calculated from experiments on herbivorous animals, exhibits very considerable differences in reference to the distribution of the elements in the carnivora and the herbivora; but the most striking feature of this experiment vanishes when we consider that carbon and hydrogen are for the most part conveyed to the latter animals in an indigestible form, and that to a certain extent this is also the case with the nitrogen, which is enclosed in the shape of albuminates in the cells forming the husks of the grain, which are extremely inaccessible to the passage of the digestive fluids.

We at once see that the water is absorbed in much smaller quantity from the intestine in the herbivora than in the carnivora; the difference here is extremely great; in horses and cows, on an average only half of the water which entered the intestine was absorbed, but in the carnivora, as was shown by Schmidt's other experiments, the quantity amounted only to 1%, or at most 4%. If we disregard the quantities of the other elements which remain in the intestine, we find that in the herbivora, a very small portion, from 15% to 20% only of the water, which is either absorbed or formed, is eliminated through the kidneys, whilst in the herbivora as much as 4-5ths of the absorbed water passes into the urine. The fact that the absorbed carbon is excreted in far larger quantities through the lungs in the herbivora than the carnivora (the relation of the carbon in the urine being as 1:19 in the former, and as 1:9.5 in the latter) possibly depends solely upon the nature of the food, and not upon any special relations of the organism; for the non-nitrogenous matters become almost completely decomposed into carbonic acid and water, and hence they yield absolutely nothing, or only a very small amount to the urine, whilst the products of decomposition which are produced from the albuminates yield their nitrogen to the urine, although always in combination with certain quantities of carbon. We thus obtain a kind of check for our calculations of the urine and respiration. In the same manner we find in reference to the hydrogen that relatively much less is eliminated through the kidneys in the herbivora than in the carnivora. (The ratio of the hydrogen excreted through the urine is to that eliminated through the lungs as 1:23.0 in the herbivora, and as 1:3.3 in the carnivora.) The case differs in respect to the nitrogen; for the herbivora frequently excrete by perspiration as much as 40% of the nitrogen they had absorbed, whilst the carnivora scarcely eliminate as much as 1%. Earlier investigations have taught us that the urine of the herbivora is poorer in nitrogen and in urea, the substance in which it is carried off, than that of the carnivora, which (as Schmidt has also observed) is very often scarcely anything more than a saline solution of urea. It would, therefore, almost appear as if the process of oxidation were so far more abundant in the herbivora than the carnivora, that in the organism of the former the albuminates were decomposed even beyond what was necessary for the formation of urea; and on this account, the urine of the herbivora is entirely deficient in the earlier product of the disintegration of the albuminates, namely uric acid.

When the metamorphosis of matter is effected in the organism without



any compensation from without, the proportions of the elements of the urine to those of the perspiration are almost exactly the same as in feeding with fat meat, and hence, for the sake of brevity, we shall omit all further details.

If we pause for a moment in our consideration of the excretion of the elements, we shall find the most decisive confirmation, in two interesting series of experiments by Schmidt, of the proposition first enounced by Liebig, that the bile is not only resorbed in the intestine, but is also consumed, and for the most part separated through the lungs. Thus, for instance, we find from the statistical observations made by Schmidt on two dogs having biliary fistulæ, that whether the animals had had a very abundant or only a scanty flesh diet, from 10% to 12% of the absorbed carbon, and from 11% to 13% of the absorbed hydrogen were excreted by the bile, and that this loss was not uniformly distributed through the excretions, but was exclusively limited to the products of respiration. Only 3% or 3.2% of the absorbed nitrogen passes into the bile, and this is as nearly as possible the quantity which is missing from the urine.

We regret that we are compelled to deviate from our general rule in respect to this comprehensive inquiry, by omitting to confirm by numerical data the facts and conclusions that have been advanced; but had we done otherwise we should have been obliged to transcribe the whole of Schmidt's observations, as he has merely given the most necessary empirical results. We must, therefore, content ourselves with giving the most important conclusions deduced from his inquiries, more especially as many points referring to the individual factors of the metamorphosis of matter would have been introduced in the proper place, had we been earlier acquainted with the special details of these admirable labors.

We learn from the experiments on cats, that for 1000 grammes' weight of these animals there are required in the twenty-four hours at least as much as 44.118 grammes of flesh to maintain the original bodily weight, and that in addition to this, 18.632 grammes of oxygen must be absorbed in order to apply this nutrient matter to the wants of the organism; and, consequently, that the minimum of food for the carnivorous animals experimented upon averages, according to this observation, about 1.23d, and the necessary oxygen about 1.55th of the whole weight of the body. On the other hand, when the animals are kept without food, only, 22.118 grammes are lost in the course of twenty-four hours from the whole weight of the body by the excretions (between the third and the ninth day), to the metamorphosis of which 15.749 grammes of oxygen are applied; the body loses, therefore, during the first eight days of inanition only about 1.46th part of its weight in the twenty-four hours. But when cats are supplied with as much flesh as they will eat, they are able to absorb such excessively large quantities of it in the metamorphosis of matter, that the flesh they consume amounts to 1.19th, and the oxygen absorbed with it to almost 1.24th part of their bodily weight.

When we compare the products of excretion yielded during a scanty and an abundant supply of flesh, we find that the quantities of the excretions stand in a direct relation to the amount of nourishment,



and that, consequently, the increase or diminution of the food exerts no influence whatever on the proportions between the different excreta, or on their quality; the ratio of the absorbed oxygen to that in the exhaled carbonic acid, is in all cases the same, namely, as 100:79.3. The ratio between the expired carbonic acid and the expired water becomes, however, changed when a larger amount of animal food is taken; thus, for instance, in one case it was found that on a scanty flesh-diet 75.6 parts of aqueous vapor were expired for 100 of carbonic acid, while on an abundant flesh-diet there were only 42.15 parts of water to 100 of carbonic acid; hence in the latter case a relatively larger quantity of water must be separated by the kidneys, as indeed Schmidt's determinations have also shown; for the ratio of the perspired aqueous vapor to the water excreted by the kidneys and fæces is 23.3:76.7 in the former, and 17.84:82.16 in the latter case. On a scanty flesh-diet, water being at the same time withheld from the animals, the ratio of the carbonic acid to the expired aqueous vapor became so far changed that for 100 parts of carbonic acid 80 parts of water were exhaled by the skin and lungs, and hence in this case there was relatively less water separated by the kidneys than on a scanty flesh-diet without the deprivation of water. These proportions are best seen in the following comparative table which we have calculated from Schmidt's results. We take the flesh that was consumed (that is to say, its dry residue) as the unit, and calculate the amount of solid matters which pass away in the urine and fæces, the perspired carbonic acid and aqueous vapor, but exclude the quantity of water that has been taken and that is separated by the solid and fluid excretions. I. has reference to the metamorphosis of tissue when the minimum quantity of food was taken, there being at the same time free access to water. II. The greatest possible quantity of food and unimpeded access to water. III. A normal flesh diet (that is to say, one with which the weight of the body remains constant) without water. These three experiments were made on the same animal, an adult male cat weighing 3200 grammes.<sup>1</sup> IV. has reference to a young cat weighing 1170 grammes which was allowed an excess of flesh and water *ad libitum*.

	I.	II.	III.	IV.
Dried flesh, . . . . .	100.0	100.0	100.0	100.0
Absorbed oxygen, . . . . .	167.0	166.0	167.3	166.2
Solid residue of the urine, . . . . .	31.3	30.4	30.6	31.4
“ the fæces, . . . . .	1.7	2.5	1.7	2.0
Expired carbonic acid, . . . . .	182.0	181.4	182.6	181.4
“ aqueous vapor, . . . . .	137.6	76.4	152.6	128.7

It is sufficiently obvious from this review that the elementary analysis which flesh taken as food may be regarded as undergoing in the living body, gives in the normal state as accurately defined values as if it

<sup>1</sup> [A memoir has just appeared by Drs. Falck<sup>a</sup> and Scheffer, “On the metamorphosis of matter during the deprivation of water,” which I have not had an opportunity of consulting. An abstract of it is given by Dr. Weber, in his “Annals of Physiology,” in the British and Foreign Medico-Chirurgical Review, vol. 14, p. 253.—G. E. D.]

<sup>a</sup> Arch. für physiol. Heilk. Bd. 13, S. 61.



underwent a mere process of fermentation or combustion; hence under all conditions, as the above table shows, 1 part of dry flesh is decomposed in the living body with the co-operation of 1.67 parts of oxygen into 0.31 of urinary substances, 0.02 of faecal matter, and 1.82 of carbonic acid. The conclusions which may be hence drawn regarding the general metamorphosis of matter in the animal body and especially in the carnivora, are too self-evident to require notice.

Since the lean flesh which Schmidt supplied to the cats employed in these experiments, contained 19.56% of albuminates and gelatigenous substances, 4.74% of fat, 1.00% of inorganic matters, and 74.70% of water, while there are contained in the solid residue of the urine, on an average, 85.5% of urea, and 14.5% of salts (containing 2.3% of sulphuric acid), and in the dry solid excrements, on an average 63% of biliary residue, we obtain the following comparative results for 1000 grammes' weight of a carnivorous animal (cats having been employed), if we assume that an animal consumes 50 grammes of fresh lean flesh in twenty-four hours for every kilogramme's weight.

A cat, for every kilogramme's weight, takes in 24 hours,	Water.	Albuminates and gelatigenous matters.	Fat.	Salts.
50.000 grammes of flesh, . . . .	37.350	9.728	2.370	0.510
21.125 " of oxygen, . . . .				
71.125 grammes.				

A cat, for every kilogramme's weight, gives off, in 24 hours,	Water.	Carbonic acid.	Urea.	Salts.	Fæces.	Bile.
39.468 grammes of perspiration,	16.445	23.023				
30.761 " of urine, .	26.839	. . .	3.53	0.569		
0.806 " of fæces, .	0.681	. . .	. .	0.041		
71.125 grammes.	43.965			0.610	0.039	0.135

We need scarcely observe that the excess of water in the excretions, amounting to 6.615, corresponds to the water which is formed by the process of respiration; the augmentation of the salts is due to the oxidation of sulphur.

While our preceding observations have had reference to the metamorphosis of tissue in full-grown animals, which are undergoing neither an augmentation nor a diminution of their bodily weight, we now proceed to the determination of those relations of nutrition in which either the food is not sufficient to maintain the normal weight of the organism and the energy of its functions, or when an augmentation of the weight of the body, growth or fattening, is going on.

We can here include in a few words all that need be said regarding the conditions which seem to render the nutriment *insufficient* for a given organism, since the consideration of this point necessarily arises from our previous remarks. The nutriment may be insufficient either



in its quantity or its composition. We have already attempted, in so far as the present state of our knowledge allows us, to answer somewhat in detail the question regarding the quantity of food that is requisite to retain the organism in its normal state; but we have not entered so fully into the question regarding the quality of the food requisite to keep the body in a thriving condition. Although the subject has been already noticed in the preceding pages, and it might be concluded *à priori* from the facts there laid down, that only such a nutriment could permanently support the integrity of the organism, as contains all the essential elements of food, namely albuminates, fats, carbo-hydrates, and certain salts, it yet remains for us to mention the experiments made by Boussingault, which yield a positive proof of the correctness of these views. Even in what are now considered the older works on physiology, we find a description of the experiments of Tiedemann and Gmelin, who failed in keeping geese alive on an abundant diet of white of egg. The experiments made under the direct observation of the Paris Academy on the questionable nutrient power of bone-gelatin and of gelatigenous tissue, afford us sufficient evidence that this nutrient power cannot be concentrated into a single chemical compound, even if it be of a somewhat complex nature.

Accurate quantitative determinations regarding the influence upon the animal organism of food which is insufficient in quality were first instituted by Boussingault, and were especially conducted in reference to certain agricultural points. We have previously alluded to those experiments of this chemist,<sup>1</sup> by which he demonstrated the importance of salt for the well-being of the organism—a fact which has been subsequently confirmed by the researches of Plouviez<sup>2</sup> and Dupasquier.<sup>3</sup> The most decisive conclusions in reference to this subject are however afforded by the investigations which have been carried on by Boussingault,<sup>4</sup> Playfair,<sup>5</sup> Thomson,<sup>6</sup> Payen and Gasparin,<sup>7</sup> Persoz<sup>8</sup> and others, in reference to the fattening of animals with various kinds of fodder. Since we shall subsequently revert to the influences which most essentially affect the augmentation of the weight (during growth or the process of fattening) we shall here merely give the results (by way of illustration) which Boussingault obtained in his experiments on cows. Potatoes and beet-root alone were insufficient to nourish a cow (that is to say, to retain it at the same bodily weight), even when these kinds of food were supplied to the animal in very great excess. It follows from these, as well as from certain earlier investigations, that every kind of food is insufficient, (1) if it cannot be taken in such large quantities that its nitrogenous matters may serve to replace the organic particles rendered effete by the metamorphosis of tissue, (2) if its digestible constituents do not contain sufficient carbon to supply the carbon which is lost by the respiration and other excretions, (3) if it does not contain sufficient salts, especially phosphates, and, (4) consequently we find that a certain quantity

<sup>1</sup> Ann. de Chim. et de Phys. 3me Sér. T. 19, pp. 117-123.

<sup>2</sup> Bullet. de l'Acad. de Méd. T. 14, pp. 1077-1085.

<sup>3</sup> Journ. de Pharm. 3me Sér. T. 9, pp. 309-344.

<sup>4</sup> Ann. de Chim. et de Phys. T. 12, p. 153. <sup>5</sup> Philosoph. Magaz. Vol. 22, p. 280.

<sup>6</sup> Trans. Med. Chir. Soc. Vol. 29, pp. 327-340.

<sup>7</sup> Compt. rend. T. 18, p. 797.

<sup>8</sup> Ibid. p. 245.



of fat in the food, notwithstanding the simultaneous presence of carbohydrates, if not positively necessary, is yet very desirable in order to retain the organism in a healthy condition.

It seems placed almost beyond doubt, by these experiments, that the proportions in which these factors of nutrition are mixed in the food exert the most decided influence on the welfare of the organism, and that the intermixture of the different factors of nutrition is essential for the metamorphosis of matter. Great as are the fluctuations which nature allows in these proportions, an undue preponderance of one or other of the factors always acts injuriously upon the due course of the process of nutrition: no single section of this process can go on without the concurrence of all these factors; thus, for instance, all these experiments teach us that the carbo-hydrates alone are not sufficient for the formation of fat in the animal body; in order that fat may be formed, protein-bodies as well as salts must co-operate in the metamorphosis; and it is only by the mutual action of these substances that a formation of fat can possibly take place. Had the results of the above-described experiments been duly considered, such a series of observations as that instituted by Letellier,<sup>1</sup> who fed turtle-doves on sugar, would hardly have been necessary. Letellier having determined the quantity of fat in doves of equal age, weight, &c., fed similar animals for a long time with sugar; the birds, several of which died after eight days, lost on an average 5.1 grammes, or 3.4% of their bodily weight daily; when a little pure albumen was added to the sugar as food, they died at a somewhat later date, having lost daily 2.3 grammes, or 1.53% of their weight. While the amount of fat in the healthy birds before the commencement of the experiments was 20.88 grammes, or 15%, the amount after death, in those which had been fed on pure sugar, was only 11.3 grammes or 7.36%, and in the case of those which had simultaneously received albumen (and when life was therefore somewhat prolonged) it was only 1.57 grammes or 3.15%. Indeed even after feeding them with butter, the birds sunk, and there was a considerable loss not only in their bodily weight, but even in their fat. (The daily loss of bodily weight was 3.25 grammes or 2.82%, and altogether more than half the original quantity of fat disappeared, there being only 7% after death.) The animals, therefore, sunk in this, as in the other cases, with all the symptoms of inanition, while the process, whose most essential requirements were present, not only failed, but could scarcely be said to have commenced. Hence this proposition, which we previously regarded as resting on many inferences, may be considered to be definitely proved by these experiments.

This consideration directly leads us to the quantitative relations of the metamorphosis of tissue, when *all solid food is withheld*. In reference to this point we will first mention a series of observations made by Boussingault, which are closely connected with those of Letellier, which we have just described. Boussingault's experiments were also made on turtle-doves, which were kept for seven days without any solid food; they lost daily 4.12% of their bodily weight, and 2.696% (of their weight) of carbon by the respiration, having exhaled daily 3.722% when fed upon millet. The green, bilious-looking, slimy excrements, with which only

<sup>1</sup> Ann. de Chim. et de Phys. T. 11, p. 433.



a few detached white patches of uric acid were mixed, averaged daily, when dried, 0.210% of the weight of the body. The excrements contained 31.95% of carbon, 4.35% of hydrogen, 24.74% of nitrogen, 28.32% of oxygen, and 16.40% of ash. A bird weighing 187 grammes lost, therefore, daily during its starvation 0.1257 of a gramme of carbon, 0.0171 of a gramme of hydrogen, 0.0974 of a gramme of nitrogen, and 0.1114 of a gramme of oxygen. Now if we assume with Boussingault, that dry blood (after the deduction of the ash) contains 54.4% of carbon, 7.5% of hydrogen, 15.9% of nitrogen, and 22.2% of oxygen, and that the amount of nitrogen exhaled by the lungs is equal to half of that which is contained in the excrements, it follows that the bird experiences a daily loss of 0.1455 of a gramme of nitrogen, which is equivalent to 0.915 of a gramme of dry blood. In this 0.915 of a gramme of blood there is, however, only 0.498 of a gramme of carbon; and since the bird discharged 2.532 grammes of carbon daily in carbonic acid and the excrements, it obviously follows that 2.034 grammes of the consumed carbon must have been yielded by fat.

No experiments on the subject of inanition are so worthy of notice as those of Chossat,<sup>1</sup> whose careful observations were continued for years, and embraced mammals, birds, and amphibia. In twenty-four cases, in which Chossat caused turtle-doves to die from starvation, the greatest daily loss of weight was manifested on twenty-two occasions at about the middle of the experiment, and twice on the day in which death occurred (excluding in this calculation the first day in which food was withheld, as some nutrient matter might then be taken up by the body from the contents of the intestinal canal). For some hours before death the body underwent no additional loss of weight. Taking the entire loss of weight which the animals suffered from the commencement of the experiment to their death as 1, it appeared that during the first third the loss was 0.393, during the second third it was nearly 0.260, and during the last third 0.347.

The entire loss of weight which the starving animal undergoes previously to its death varies very considerably with the species; thus Chossat found that rabbits (taking the mean of five experiments) died when they had lost 37.4% of their weight; guinea-pigs (five experiments) when they had lost 33.0%; turtle-doves (fifteen experiments) when they had lost 37.9%; domestic pigeons (twenty experiments) when they had lost 41.6%; hens (two experiments) when they had lost 52.7%; and crows (one experiment only being made) when they had lost 31.1%. As an average of all the forty-eight experiments 39.7% seems to be about the loss of weight which the body undergoes previously to death by starvation. Hence in the higher animals the organism loses from 1-3d to 2-5ths of its weight before it succumbs to starvation.

Taking the averages in Chossat's experiments, it was found that the mammals, during the process of starvation, lost daily 4.0% of their weight, and the birds 4.4%, the mean of all the observations on both classes being 4.2%. We find, therefore, that the animal body loses daily about 1-24th of its mass by the metamorphosis of its tissues; a result which is in the most complete accordance with the result which had been already ob-

<sup>1</sup> *Recherches expérimentales sur l'inanition.* Paris, 1843.



tained by a different method (see p. 504), namely, that the daily quantity of properly selected food which an animal requires must amount to at least 1·23d of its bodily weight.

Chossat has ascertained and compared in pigeons the relative losses of weight which each individual organ undergoes in cases of starvation—an investigation of the highest importance in relation to general physiology. We must here confine ourselves to the mere enumeration of the following results: the greatest amount of loss was experienced by the fat, 93·3% of this substance disappearing during the process of starvation; the blood suffered next in proportion, its loss amounting to 75·0%; of the muscles there disappeared 42·3%; of the bones only 16·7%; and of the nerves the least of all, namely 1·9%. If we compare, as Chossat has done, the total loss of bodily weight with the absolute amount of loss of the individual organs or tissues, it follows that the daily diminution of bodily weight may be thus subdivided: half may be referred to the muscular tissue, a quarter to the fat, and the remaining quarter to all the other organs. Hence it is chiefly the products of decomposition of the muscular tissue and of the fat which are represented in the excretions.

Two very carefully conducted series of observations on inanition have been made by Bidder and Schmidt on cats. In one case the animal only sometimes obtained a little water; in the other case water was artificially injected into the stomach. The first series of experiments was made upon a cat weighing 2,572 grammes, which had been previously employed in a series of experiments on nutrition. The animal died on the eighteenth day of starvation; the loss of weight was tolerably constant from the third day to the period of its death; on the whole it lost 1330·8 grammes or 51·7% of its weight, the average daily loss consequently being 73·9 grammes or 2·87%; these numbers, as we perceive, far exceed those found by Chossat. During the whole duration of the experiment, the loss of weight was tolerably steady; from the first to the eighth day it corresponded to the quantity of carbon that was expired (0·56% to 0·58% of the weight of the body); subsequently the amount of carbonic acid which was excreted sunk less than the bodily weight: it was only during the last two days that the excreted carbon sunk very considerably as compared with the loss of bodily weight.

The secretion of urine at first diminished in a far more rapid proportion than the bodily weight, but afterwards, till the sixteenth day, the loss proceeded in each in almost the same proportion; the urine, like the carbonic acid, diminished considerably during the last two days. The urine was richer than usual in phosphoric and sulphuric acids; the chlorides disappeared after the first few days. The ratio between the sulphuric and phosphoric acids in the urine remained constant during the whole period of inanition.

From the tenth day of inanition all the bile that was secreted passed into the fæces. (Schmidt had calculated the quantity of bile which this animal should secrete from observations on cats in which biliary fistulæ had been formed; see vol. i. p. 474.) The ingestion of water was found at every period of inanition to increase the urinary secretion and all its constituents, but it did not affect the exhalation of carbonic acid gas; hence we must conclude, with Schmidt, that the augmentation of the



urinary secretion does not in any way depend upon a greater intensity of the process of inanition, but that it is solely dependent upon the circumstance that the urinary constituents, accumulated in the blood, are more rapidly eliminated by the agency of the water.

Since the muscular substance (with the connective tissue), when freed from fat, contains, according to Schmidt's analysis, 50.0% of carbon, 6.57% of hydrogen, 15.07% of nitrogen, 21.43% of oxygen, 1.06% of sulphur, and 5.86% of mineral substances, we may calculate the amount of muscular tissue which is destroyed during the process of inanition by the amount of nitrogen contained in the excretions. Since during the whole process of inanition 30.807 grammes of nitrogen are given off externally, it follows that 200.43 grammes of muscular substance, free from water and fat, must have been consumed during these eighteen days. Since, further, 205.96 grammes of carbon were given off during the whole process, while only 102.24 grammes of this substance were contained in the 200.43 grammes of muscle, the remaining portion of the excreted carbon, amounting to 103.72 grammes, must arise from the oxidation of the fat. As fat contains on an average 78.132% of carbon, 132.76 grammes of this substance must have been oxidized. The animal has therefore lost, during the eighteen days' starvation, 200.43 grammes of muscle, and 132.75 grammes of fat; but the whole loss of weight being, as has been already mentioned, 1264.8 grammes, it follows that, with this loss of muscle and fat, there must have been a separation of 927.62 grammes of water. This amount of water is more considerable than it would have been if it had been merely the water pertaining to the lost muscular tissue which had been excreted; according to Schmidt, only 204.43 grammes of water pertain to that quantity of muscle; hence 653.5 grammes were abstracted from the remaining organs, which, moreover, on dissection, exhibited the appearance of being very poor in water.

Moreover, according to Schmidt's calculation, 76.5 parts of carbon are, on an average, given off for every 100 parts of oxygen that are absorbed during inanition. Of every 100 parts of water that were separated, 41.72 parts were given off in the perspiration, and 58.28 parts by the urine and fæces. With every 100 parts of carbonic acid, there were 75.15 grammes of water perspired. Schmidt has, moreover, determined the loss of weight of the muscle and fat for each individual day, from the amount of the excretions, in the same manner as we have calculated the loss which those tissues undergo during the whole process of inanition. It follows from these calculations that the quantity of muscular substance which undergoes decomposition sinks very considerably in the first two days (almost 50%), then to the ninth day it remains nearly stationary, from the ninth to the sixteenth day it again sinks very slightly, but on the last two days rapidly and very considerably. On the other hand, the quantity of the fat which is daily oxidized remains nearly the same from the beginning of the inanition to its termination. On an average the loss of muscle which an animal experienced in 24 hours was 0.611% of its weight at the time, while the corresponding loss of fat was 0.422%; and they yielded 2.16% of carbonic acid, 1.6% of (perspired) aqueous vapor, 0.20% of urea, 0.008% of sulphuric acid, 0.011% of phosphoric acid, 0.029% of inorganic urinary constituents,



0.080% of dry fæces (in which was 0.02% of biliary residue), and 2.24% of fluid water separated with the urine and fæces.

In the second series of experiments Schmidt employed an adult cat, weighing 3047.8 grammes, into whose stomach 150 grammes of water were daily injected from the commencement of the process of inanition. The observations were only continued for one week, during which time the animal had lost 438.0 grammes in weight, and therefore 62.57 grammes daily. The daily excretion of nitrogen was 0.578, and that of carbon 4.740 for 1000 parts (by weight) of the animal; consequently, for 100 parts of the bodily substance 0.3835 of a part of muscle, and 0.3613 of fat were disintegrated, and together with 1.4670 parts of water were daily removed from the animal through the agency of 1.5749 parts of oxygen. It is obvious, from these numerical results, that the metamorphosis which occurs during inanition is considerably diminished by the abundant use of water; that is to say, that the body, during the process of starvation, experiences far less loss in albuminates and fat when water is freely allowed, than when (as was in part the case in the first set of experiments), there is a deprivation of this fluid.

Like Chossat, Bidder and Schmidt have attempted to determine the amount of loss of each individual organ during inanition. The body of the animal, which was employed in the first series of experiments, was used for this determination of the different weights. It appeared that, during the eighteen days' inanition, the blood experienced the greatest loss, namely, 93.7% of its original weight; next in order to the blood was the pancreas, which lost 85.4%; the loss of the adipose tissue with the mesentery was 80.7%; that of the muscles and tendons, 66.9%; that of the brain and spinal cord, 37.6; and of the bones, 14.3%: the loss experienced by the kidneys was the least, being only 6.2%. It is apparent from these determinations that the loss of weight in the body is mainly owing to the destruction of the muscular tissue, the blood, and the fat.

We must here mention certain experiments of J. Scherer's,<sup>1</sup> which, although they only have reference to the urinary excretion, are of especial interest, as having been instituted in the human subject. He found that an adult man, for every kilogramme's weight of his body, discharged in twenty-four hours 29.5 grammes of urine, in which there were contained 28.4 grammes of water, 0.420 of a gramme of urea, 0.335 of a gramme of salts, and 0.346 of a gramme of extractive matters; while an insane patient (a man aged 50 years), who had resolved on starving himself to death, discharged, in a similar time, and for the same amount of weight, only 11.07 grammes of urine, in which were 0.176 of a gramme of urea, 0.167 of a gramme of salts, and 0.198 of a gramme of extractive matters.

Hence the amount of urine in the starving man stands to that in the man living on an ordinary diet in the ratio of 1 : 2.6, while the solid constituents are as 1 : 2.4, the urea as 1 : 2.3, the salts as 1 : 5, and the extractive matters as 1 : 1.7. It is a very striking fact in these experiments, that at the very time when no nutrient matter is supplied to the organism, and when there is no excess of combustible materials for the process of oxidation, relatively more extractive matters were excreted than by the man living on his ordinary diet.

<sup>1</sup> Verhandl. d. phys.-med. Ges. z. Würzburg. Bd. 3, S. 187-190.



We now pass to the consideration of those relations of nutrition which are accompanied by an *increase of bodily weight*. This increase may possibly depend upon the typical augmentation of the individual organs within the limits of the highest development to which the organism can attain—consequently, upon *growth*. Although all the organs do not progress uniformly in this typical development, they yet simultaneously participate to a greater or less extent in this general increase and evolution,—the increase of one or other organ preponderating at the different periods of life. These are well-known facts, derived from anatomy and general physiology; but they draw our attention to the difficulties which oppose our endeavors to determine the metamorphosis of matter and the conditions of nutrition at this period of life.

An increase of bodily weight is, however, quite possible after the terminations of growth; and daily experience shows us that this augmentation manifests itself more especially in two directions, namely, by a true *hypertrophy* of the most vitally active organs, as, for instance, the muscles, or by a more abundant deposition of adipose tissue in the panniculus adiposus of the skin, in the mesentery, &c.; but although this increase may be regarded as a normal condition of the human organism at a certain period of life, it very frequently, however, assumes an abnormal or pathological character at this age. A similar remark refers equally to the fattening of agricultural stock,—a process which consists essentially in an augmentation of the fat in the organism, and very often assumes a course very different from that of normal nutrition; for we cannot regard the development of a fatty liver in geese, or the frequently observed partial disappearance of the nitrogenous constituents of organs, as, for instance, the muscles, in certain modes of fattening, as normal processes. Unfortunately, however, we are not entirely in possession of the conditions necessary to give any one special direction to the process of nutrition, by which we might be enabled to determine the relations already indicated. The difficulties which the unequal development of heterogeneous organs oppose to the determination of the metamorphosis of matter during the period of growth, depend upon the circumstance that we are not able to make nutrition assume any special form, either by means of food or any other external relations. The ingenious combinations of Liebig have sufficiently shown us the conditions under which, independently of proper food, a more abundant deposition of fat may be formed in the animal organism; and many of the investigations prosecuted by Boussingault and his pupils have confirmed this by the most striking proofs. Daily experience has further taught us that increased exercise of the organ gives rise to an increase of volume and weight exceeding the normal growth, whilst the deposition of fat is at all events very greatly favored by the opposite relations. But although we have actually arrived at many general and clear ideas of these relations by means of laborious investigations and ingenious deductions, we cannot boast of being in possession of clear ideas based upon thoroughly exact inquiries. In accordance with the object of the present work, we abstain from all diffuse disquisitions and involved deductions, and limit ourselves to the facts yielded by exact inquiry.



Boussingault<sup>1</sup> has instituted some experiments on pigs, with a view of ascertaining the development of the *osseous system*, and with special reference to the mineral constituents.

I. A newly born pig weighed 650 grammes; its dried skeleton 48.25 grammes; the ash 20.73 grammes.

II. A pig aged 8 months weighed 60055.0 grammes; its dried skeleton 2901.0 grammes; the ash 1349.5 grammes.

III. A pig aged 11½ months weighed 67240.0 grammes; its dried skeleton 3407.0 grammes; the ash 1686.0 grammes.

The ash of these three skeletons, when burned perfectly white, contained:

	I.	II.	III.
Phosphate of lime, . . . . .	84.1	91.3	92.4
Phosphate of magnesia, . . . .	11.0	3.6	3.8
Carbonate of lime, . . . . .	4.5	3.6	3.4
Alkaline salts, . . . . .	0.4	1.5	0.4

According to this result, the pig aged 8 months, which was kept on ordinary food, gained on an average daily 11.7 grammes in the weight of the osseous system, 5.5 grammes of ash, 2.4 grammes of phosphoric acid, and 2.8 grammes of lime. The other pig, which lived 93 days longer, and was fed on potatoes only during that time, gained daily 6 grammes in the weight of the dry skeleton, 2.6 grammes of ash, about 1.4 grammes of phosphoric acid, and about 1.6 grammes of lime.

In the 544 kilogrammes of potatoes which the pig consumed during the last period of 93 days, there were 5440 grammes of mineral substances, including 615 grammes of phosphoric acid and 98 grammes of lime, whilst its skeleton had taken up during the same period of time 129 grammes of phosphoric acid and 150 grammes of lime. Consequently, 52 grammes more of lime were taken up than were contained in the potato ash. Besides this, there were 216 grammes of lime discharged with the excrements; consequently, 170 grammes of lime must have been supplied to the animal from some other source. Boussingault shows that this lime must be derived from the water in which the potatoes had been boiled.

We are entirely deficient in investigations instituted in a similar manner in relation to the development of other tissue or organs, when compared with the amount of food. But it would scarcely be out of place were we, before we enter upon the consideration of the increase in muscle and fat, to notice the experiments of Prevost and Morin, which connect themselves with the observations made by Baudrimont and St. Ange (see p. 461) on the respiration of the incubated egg. The results of these labors may be thus set down:

100 parts of the contents of the *un-incubated* egg consist of—

10.72 parts of fat.

16.53 “ matters free from fat, namely 8.19 in the albumen, and 8.36 in the yolk.

72.53 “ water.

<sup>1</sup> Ann. de Chim. et de Phys. 3me Sér. T. 16, p. 486-493.



After *seven days' incubation* 100 parts of the inner portion of the egg contained—

9.32	parts of ether-extract.
13.94	“ dry matter, free from fat, of which 8.00 were albumen.
76.74	“ water.

The albumen itself contained 34.9 per cent. of dry matter, free from fat.				
The thick yolk	“	16.5	“	“
The liquid yolk	“	4.4	“	“
The membranes	“	2.0	“	“
The embryo	“	7.7	“	“
The liquor amnii	“	1.3	“	“

Consequently, during this period, the fat and the solid substances generally have diminished, while the water has been relatively augmented.

After *fourteen days' incubation* the inner membrane of the shell, the interior parts of the embryo, and, in one case also, the liquor amnii, exhibited an acid reaction. 100 parts of the inner portion of the egg contained—

9.46	parts of ether-extract.
16.09	“ dry matter, free from fat, in which there were 7.7 parts of albumen.
74.43	“ water.

100	parts of albumen contained	3.3	parts of dry matter, free from fat.
“	the yolk	“	19.3
“	membranes	“	9.1
“	embryo	“	7.2
“	liquor amnii	“	1.4

After *twenty-one days' incubation*—

100	parts of the interior of the egg contained	5.68	parts of fat.
“	“	“	15.44 parts of dry matter, free from fat, of which one-sixth consisted of yolk, one-sixth of yolk-membrane, and two-thirds of the embryo.
“	“	“	78.88 parts of water.
100	parts of the yolk contained	29.0	parts of dry substance.
“	membrane	20.6	“
“	embryo	14.6	“

The *weight of the egg-shell* remained almost constantly the same. The *fat in the egg* is of a uniform yellow color before incubation, although it undergoes various alterations during the development of the embryo. On the seventh day a yellow oil was extracted by ether from the thick yolk, while the fluid yolk yielded first a yellow and subsequently a colorless fat. The membranes and the albumen yielded a transparent white oil, the liquor amnii a thick white fat, and the embryo a white fat like lard. On the fourteenth day the oil of the yolk became yellow and thick; the same was the case with the oil of the membranes; that of the albumen was colorless and thick; that of the embryo reddish and solid. On the twenty-first day the fat of the yolk became thick and of a pale yellow color, and that of the membranes dark yellow and partially solid; ether extracted from the embryo a fat which at first was solid and yellow, but at a later stage was white and soft.



We will now simply subjoin the results of the *ash-determinations*.

Un-incubated eggs contained in—

	Dry substance free from fat.	Ash.	Insoluble Phosphates.	Soluble Salts.
The white, . . . .	15.090	0.85	0.13	0.68
The yolk, . . . .	15.166	0.90	0.90	0.00
	30.156	1.74	1.03	0.68

Eggs after twenty-one days' incubation contained in—

The yolk, . . . . .	5.51	0.150	0.145	0.005
The yolk-membrane, . . . .	4.80	0.205	0.205	0.000
Putamen, chorion, and amnios,	0.42	0.040	0.015	0.025
The embryo, . . . . .	16.87	1.825	1.095	0.730
	27.30	2.220	1.460	0.760

According to Baudrimont and St. Ange, the absorbed oxygen is to the oxygen exhaled in the carbonic acid as 100 : 54.9 during the period of the development of the hen's egg from the 9th to the 12th day, and as 100 : 81.0 from the 16th to the 19th day,—a fact which is entirely in accordance with the circumstance that it is in the last third period of incubation that the greatest quantity of the fat of the egg is consumed. The remaining results are readily obtained from the above numerical data.

Schmidt and Bidder have instituted a very admirable observation on a nearly full-grown cat, in reference to the assimilation of muscle and fat. This animal gained 337 grammes in weight in the course of eight days, when fed on flesh containing fat; the question therefore arose, whether the muscular substance only, or the fat, or both together, had contributed to this increase of weight. The animal had consumed during this experiment 1866.7 grammes of flesh, with 27.4 grammes of fatty tissue, and had eliminated 62.36 grammes of nitrogen. Now, since, according to Schmidt's analysis, the flesh consists of 70.26% of water, 5.71% of fat, 22.83% of muscular substance, and 1.2% of mineral matters, (the muscular substance, when free from water and salts, containing 53.01% of carbon and 16.11% of nitrogen), we may easily perceive that these 62.36 grammes of nitrogen must have been derived from the decomposition of 387.09 grammes of muscular substance, or of 1695.5 grammes of flesh. As 1866.7 grammes of flesh were consumed, the difference between the two quantities gives us 171.2 grammes as the quantity of flesh retained in the body. As, however, the increased weight of the body amounts to 337 grammes, the question arises, how far the remaining portion of the assimilated materials (155.8 grammes) is derived from assimilated fat or from the water retained in the body. These 387.09 grammes of decomposed dry muscular substance contain 205.20 grammes of carbon; but in addition to this nitrogen (62.36 grammes), 194.02



grammes of carbon were eliminated, and consequently 18.11 grammes remained in the body. Since, therefore, the muscular substance is more than sufficient to compensate for the carbon which has been excreted during the metamorphosis of matter, it is not conceivable that the fats, together with the muscular substance, can have participated largely in the oxidation; from hence Schmidt further concluded, and no doubt correctly, that the urea produced by the decomposition of the muscular substance must be separated through the kidneys before the remaining carbon and hydrogen of the muscular substance are exhaled in a state of oxidation through the lungs and skin. As only 1.98 grammes of fat are eliminated with the *fæces* in the form of saponified lime and magnesia, and as, according to Schmidt's analysis of the fatty tissue, 129.25 grammes of fat are taken up within the eight days, 127.27 grammes of fat are assimilated and remain in the body, in addition to the above 171.2 grammes of flesh and the 138.4 grammes of water. After the subjection of this calculation to the corrections required in consequence of various causes, and especially of the partial oxidation of the sulphur, Schmidt reckoned that 40.16 grammes of muscular substance and connective tissue, 143.42 grammes of fat, 1.78 grammes of salts with sulphur, and 134.15 grammes of water, were assimilated in eight days by this animal, weighing 2177 grammes, and that in the case referred to, the cat for every kilogramme, daily assimilated 18.346 grammes of muscular substance and fat.

However indispensable such conclusions and the calculations based upon them may be for the purpose of obtaining a deeper insight into the metamorphosis of animal matter, we ought not to disguise the fact, that they only lead us to a very slight degree of relative certainty.

Independently of the circumstance that slight deviations in the observation often lead to very different results, or justify very different conclusions, we must be conscious that in our inability to determine all these causes with exactness, or to represent them in an arithmetical form, we very often employ for our equations certain postulates, several of which may in the existing circumstances be equally probable, although they essentially modify our calculations. We must therefore here be cautious in dealing with illusive equations, which, although perfectly correct in an arithmetical point of view, may lead us into the most flagrant errors.

By feeding cats alternately with flesh and pure fat, Schmidt has moreover given probability to the view, that the albuminates are always more readily decomposed in the body than the fats, and that a diet consisting exclusively of fat (or of an insufficient amount of albuminates with an abundance of fat) causes the nitrogenous matters of the body to be subjected to metamorphosis, whilst the fats which are taken up are, on the contrary, at first either entirely or for the most part deposited in the body, being oxidized at a later period, and probably only by degrees.

It is from this and a previously indicated point of view, that we must consider the results of those numerous experiments which have been instituted in reference to relations of nutrition during the fattening of animals generally, or of cows with a view of obtaining a more abundant supply of milk. In association with Schmidt's experiment, we have to



notice an observation made by Persoz,<sup>1</sup> who fattened geese on maize; the blood of the geese which had been thus fed was very rich in fat, but poor in albuminates; the quantity of the muscular substance diminished perceptibly, and where the fattening had been rapid the geese exhibited an absolute loss of bodily weight.

We do not here enter more fully into the individual series of experiments which have been instituted on animals in connection with the process of feeding stock or of augmenting the quantity of milk; they were for the most part instituted solely in reference to what was formerly regarded as a very doubtful question (see pp. 340-344), whether food deficient in fat sufficed for the feeding or fattening of animals, and whether fat could be produced in the animal organism from the amylacea. They are consequently only of interest to us in relation to the latter point. Although Liebig at an early period demonstrated, partly by exact experiments, and partly by the most ingenious application of various facts which bore upon the point, that fat is formed in the animal body from carbo-hydrates, this proposition was yet for a long time denied by Dumas and Boussingault, and numerous experiments were made, some of which appeared to favor and others to oppose Liebig's view. As, however, we have already discussed this subject somewhat in detail (in vol. i. p. 228) we need here only mention two series of experiments by which the correctness of Liebig's opinion was placed beyond all further question. Dumas,<sup>2</sup> in conjunction with Milne Edwards, repeated Gundelach's experiment of feeding bees with honey freed from wax (at all events the honey employed as their food only contained one-ten-thousandth part of wax). Of four swarms which were employed in the experiment, only a single one began to secrete wax and to build with it. The numerical results of this investigation may be most easily seen in the following manner:

Fat which was found in the body of each bee at the beginning of the experiment, . . . . .	0.0018 of a gramme.
Wax which, on an average, each bee consumed with the honey during the whole of the experiment, did not exceed, . . . . .	0.0003    "
The whole amount of fatty matter whose origin might possibly be derived from the food, averaged for each bee at most, . . . . .	0.0022    "
During the whole length of the experiment the wax secreted by each bee averaged, . . . . .	0.0064    "
At the termination of the experiment the wax or ordinary fat in the body of each bee averaged, . . . . .	0.0042    "

Finally, Boussingault<sup>3</sup> found by experiments on pigs that (to take an example) eight-months' pigs contained far more fat than had existed in their food, but that when they are fed solely on potatoes there was no more fat accumulated in them in the course of six months than corresponded to the amount of fat contained in the potatoes, which they consumed; and that such kinds of food as potatoes, which could not of themselves be applied to the formation of fat within the body, acquired this property by a slight addition of fat or of albuminous matters.

In our previous notice of the quantitative metamorphosis of matter we have not done more than draw the balance between the ingesta and the

<sup>1</sup> Compt. rend. T. 18, pp. 245-254.

<sup>2</sup> Journ. de Pharm. et de Chim. 3 Sér. T. 9, p. 339-344.

<sup>3</sup> Compt. rend. T. 20, p. 1726.



egesta which we have observed in the living animal organism under various physiological conditions. It has been objected against this method, that it affords us no light whatever in reference to the interchange of the organic elements within the body in the process of nutrition; but independently of the fact that this is the only path we are able to pursue in order to obtain a general view, it has also led us to a number of facts which enable us to gain an insight into the intermediate stages of molecular motions in the body. It cannot, however, be denied that, notwithstanding many of the conclusions yielded by this method, we are still so ignorant of the *intermediate metamorphosis of matter*, that we can only adduce the facts known in reference to this subject as mere appendages to our previous remarks. While we have endeavored throughout the whole course of this work to notice all the important relations of each substance—substratum, fluid, and tissue—in reference to the metamorphosis of matter, we have always directed our fullest attention to this subject, which we regard as the crowning point of physiological chemistry, and the advance made in science during the last few years has indeed yielded the most extraordinary results in this respect. Notwithstanding many obvious deficiencies and numerous imperfections, we see revealed before our eyes the image of a life rich in internal relations and external forms, and alike inexhaustible in the multiplicity of its phenomena and the incentives to future investigations. But still it is only a mere picture, in which many results of vegetative life are undoubtedly represented in too ideal a form; for whilst all phenomena are only parts of a motion regulated by definite laws, many portions of this sketch are drawn in false perspective. To find the correct perspective, we require to make a certain number of direct measurements, since it will be impossible properly to introduce the different distances in the picture until the quantitative relations have been established and the points of sight mathematically determined. The present would seem a fitting place, in which to embrace the entire metamorphosis of matter in one grand comprehensive picture, which being sketched in accordance with mathematical rules, may represent all the individual parts in their natural and real connection with one another. But unfortunately in physiological chemistry we are sadly deficient in these mathematical rules, by which alone we can ascertain the correct perspective of the individual parts of this picture of vegetative life.

There are very different methods by which we may obtain these geometrical points of sight; thus, for instance, in my investigations regarding the function of the liver and the formation of bile, I have adopted those points of sight which refer to the quantitative relations of the juices flowing to and from the liver; the results of these experiments, which certainly exceeded the very limited expectations I had formed of them, induced me in the case of other organs also to compare the ingesta with the egesta, and indeed far more important quantitative facts have already been obtained than one could have anticipated from the difficulty of procuring these egesta and ingesta in sufficient quantity, or in a condition adapted for examination, and from the very great deficiency of the means necessary for analysis. We have the more readily abstained from giving the fragmentary results of these yet unfinished labors, as



they have already appeared in another place<sup>1</sup> with all the necessary details, and would seem to be better adapted to some of the earlier sections of this work.

C. Schmidt<sup>1</sup> has endeavored to determine the intermediate metamorphosis of tissue in another way, namely, by a network of mathematical lines; he simultaneously compared the constitution of the different transudations and of the blood, and attempted to establish the quantitative relations between the two, and to determine the laws which influence the elimination of matters from the blood through certain tissues into definite organs. We have incorporated the most essential conclusions of this work in this volume; but notwithstanding many brilliant facts and conclusions, it soon became apparent that this method of investigation also failed in affording us correct answers to many questions.

In association with Bidder,<sup>2</sup> Schmidt has tried a third method, by which probably the greatest advances have been made; it consists in the attempt to determine the amount of that motion which impels a very considerable fraction of the animal juices towards the intestinal canal. From the statements which have been previously made regarding the quantitative relations of the digestive fluids it appears that according to Bidder and Schmidt's investigations and calculations, an adult man weighing about 64 kilogrammes [or 10 stone] secretes in twenty-four hours about 1600 grammes of saliva, in which are 15 grammes of solid matters, 1600 grammes of bile containing 80 grammes of solid matters, 6400 grammes of gastric juice with 192 grammes of solid matters, 200 grammes of pancreatic fluid with 20 grammes of solid constituents, and 200 grammes of intestinal juice with 3 grammes of non-volatile matters; consequently there are in twenty-four hours 10,000 grammes of juices, containing 9690 grammes of water and 310 of solid substances, which pass from the blood into the intestinal canal, from which they are again for the most part resorbed. Since the body of a man weighing 64 kilogrammes contains about 20 kilogrammes [or 44 lbs.] of solid matters, and 44 kilogrammes [nearly 97 lbs.] of water, it follows that from 1-5th to 1-4th of the latter would be brought into the intestinal canal, in the course of twenty-four hours, but only from 1-70th to 1-60th of the former. The coincidence between the amount of solid constituents in this collective sum of the digestive fluids and in the lymph (according to Marchand's determination), namely 3.1%, is a point of much interest. Since very careful analyses of the digestive fluids, as well as determinations of their amounts, were instituted by Schmidt, it is easy to see that we may obtain the most decisive conclusions from these numerically-established points, regarding the relative amount of this metamorphosis of matter within the body, as well in reference to the individual organic matters as to the elements in general. We may notice, as especially important in this point of view, the relations which have been established by these investigations between the biliary secretion and the respiration, and between the former and the urinary secretion. Thus, for instance, a dog for each kilogramme's weight consumes in twenty-four hours 8.6 grammes of carbon, while in the same time it excretes 1 gramme of biliary matter; 0.5 of a gramme of carbon of this biliary matter returns from the intestine into the blood,

<sup>1</sup> Ber. der k. sächs. Ges. d. Wiss. zu Leipzig. 1853.

<sup>2</sup> Charakteristik der Cholera, u. s. w.



hence it follows, that from 5% to 6% of the expired carbon has to go through the stage of bile-formation. This proportion is not essentially affected during a flesh-diet; but is altered by the use of highly amylaceous food, when the amount of respired carbon considerably exceeds the quantity passing through the bile. When the mineral constituents of the food are much increased, the biliary secretion is relatively more increased than the respiration; but during starvation the former is more diminished than the latter. Of every 100 grammes of nitrogen which are separated by the kidneys, at most not more than 3 grammes pass through the bile (as taurine and glycine), while of 100 parts of sulphur from 54 to 86 parts take that course; under no conditions, however, does the whole of the sulphur pass through the stage of bile. In herbivorous animals scarcely 2-3ds of the glycine separated with the urine in the hippuric acid are contained in the glyco-cholic acid. During starvation we may put down the average typical relation as follows: for every 100 parts of expired carbon there are given off 15.4 parts of carbon, under the form of urea, by the kidneys. While in fasting animals (the calculations being made for equal bodily weight) the same daily quantities of carbonic acid and urea were secreted, the biliary secretion sunk to such an extent that on the tenth day of inanition only 2.5ths of the quantity of bile were obtained, which was secreted on the third day.

There are other interesting points of view which present themselves when we contrast, in relation to quantity, the elements of the intermediate metamorphoses of matter and those of the final excretions with the corresponding elements of the organism or of the blood; as for instance, when we compare the quantities of the carbon separated by the bile or by the saliva, with that which is separated by the kidneys or lungs, and reduce the numbers of both to 100 parts of the carbon contained in the organism or in the blood. As a standard of comparison Bidder and Schmidt employed results which they had obtained from a cat, and which, as they stand at present isolated to science, we must on no account omit. They found that each kilogramme's weight of the animal (which was a young cat weighing 1505 grammes) contained—

Muscles and tendons, . . . . .	450.36 grammes, or when dry	107.64 grammes.
Bones, . . . . .	147.45 “ “	80.36 “
Skin, . . . . .	120.86 “ “	57.05 “
Intestinal tract, . . . . .	64.91 “ “	14.60 “
Brain and spinal cord, . . . . .	19.40 “ “	4.29 “
Liver, . . . . .	47.51 “ “	12.78 “
Lungs, . . . . .	10.78 “ “	2.24 “
Kidneys, . . . . .	9.00 “ “	1.85 “
Spleen, . . . . .	3.16 “ “	0.67 “
Pancreas, . . . . .	3.00 “ “	0.66 “
Salivary glands, . . . . .	1.13 “ “	0.23 “
Heart, . . . . .	4.22 “ “	0.94 “
Aorta and Venæ cavæ, . . . . .	1.34 “ “	0.31 “
Mesentery, with its fat, . . . . .	38.16 “ “	21.60 “
Eyes (including muscles and fat), . . . . .	14.70 “ “	4.50 “
Larynx and trachea, . . . . .	2.28 “ “	0.75 “
Bladder, . . . . .	0.97 “ “	0.23 “
Testicles, . . . . .	0.41 “ “	0.09 “
Blood (which escaped during dis- section), . . . . .	60.36 “ “	9.60 “
	<hr/> 1000.00	<hr/> 320.39



Hence in 100 parts of this animal there were contained 32.039 of solid materials. Schmidt employs these determinations in order to calculate the amount of the different elements of the water, and of the salts in the body of the cat, and it follows from his calculations that in every kilogramme's weight of the cat there are contained about 679.61 grammes of water, 148.72 grammes of carbon, 20.19 grammes of hydrogen, 35.45 grammes of nitrogen, 54.78 grammes of oxygen, 2.43 grammes of sulphur, 1.88 grammes of sodium, 1.51 grammes of chlorine, 51.02 grammes of earthy phosphates, including about 0.4 of a gramme of iron, and 4.41 grammes of other salts, including 2.12 grammes of phosphoric acid.

This calculation gains additional support from the circumstance that, as follows from the data formerly given, a dog fed with flesh gives off 2.25 grammes of water by perspiration, and respiration, and 5.97 grammes by the urine and fæces (and, therefore, on the whole 8.22 parts) for every 100 grammes of water which it contains, while 23.25 grammes are effused into the intestine with the intestinal juice. Hence the intermediate circulation of the water towards the intestine is far more considerable than its final excretion, and amounts to almost the fourth part of the whole quantity of water in the body. If, on the other hand, we compare the aqueous excretions with the amount of water in the blood, and fix the latter at 100, 27.9 parts are entirely removed from the body in twenty-four hours, while 79.0 parts are effused into the intestinal canal. Of every 100 parts of salts in a dog fed with flesh there are in twenty-four hours 5.3 parts given off to the external world, while 8.5 parts are effused with the digestive fluids over the surface of the intestinal canal; while of 100 parts of blood-salts 21.2 parts are completely excreted in twenty four hours, and, 34.1 parts conveyed into the intestine. Of every 100 parts of carbon in the body 4.26 parts are separated by the respiration and urine, while only 1.31 parts pass into the intestine (of which 0.376 passes through the bile); and a similar ratio holds good with regard to the hydrogen. Of every 100 parts of nitrogen in the animal body, 3.89 parts are completely separated, and only 1.28 parts pass into the intestine (of which not more than 0.101 passes through the bile). Of every 100 parts of sulphur contained in the animal 3.3 parts are daily excreted by the kidneys, while 2.6 parts enter the intestine (1.7 of which passes through the bile). Of 100 parts of phosphoric acid of the soluble phosphates of the animal body there are daily eliminated 7.27 parts, while 2.9 parts complete the circulation through the intestine.

These are only a few instances of results to which such statistico-chemical investigations of the intermediate metamorphosis of matter lead us, when they are conducted with that accuracy and circumspection which are indispensably requisite in such cases. As yet we unfortunately possess no other investigations of this nature than those of Bidder and Schmidt, of which we have made mention. But whatever ingenuity may be discernible in these inquiries, and however brilliant may be the results to which they have already led, it must be admitted that they have merely indicated the path by which more numerous investigations may enable us to reach the aim towards which we are striving. Since we are conscious of the deficiency of our knowledge, and the uncertainty of most of the facts in our possession, we likewise omit a mathe-



matical, or rather arithmetical, sketch of all the movements of matter in the living body considered in accordance with all their relations and value.

As it is our firm conviction, that it is only by the above indicated mathematical determination of the limits of the metamorphosis of matter that the general propositions of our science can be completely established, we are the more ready to leave to future chemists the bold attempt of classifying vital phenomena according to number, mass, and weight, and thus securing to their theories an amount of relative truth which might at all events equal that to which the other empirical sciences have long since attained.

In drawing towards the close of this work, we cannot forbear reverting once more to that department of our science, known as pathological chemistry; and the present would seem to be the fitting place for entering more minutely into the consideration of *pathological processes*; and this we had fully purposed doing, for our original intention was to investigate the pathological metamorphosis of matter after we had considered the same process in its normal character. Although we had occasion in almost every section on the juices and tissues to deplore our defective knowledge of their pathological relations, we yet endeavored to collect all the scattered materials in our possession, and to combine them as far as possible into one comprehensive whole, in order to obtain a basis for at least some few of the more tenable hypotheses and views; but it soon became obvious that it would have been necessary to deviate from the general plan of this work, if we had attempted to compensate for the absence of real facts by ideal combinations from amidst the confused mass of scanty, unconnected, and often careless observations. If we were not satisfied with mere speculations, we were driven to the necessity of ruminating once more over the observations and facts which had already been casually noticed in the course of this work; for we are deficient in the points of departure necessary to a scientific mode of treatment, while our explanations are wanting in certainty. Phenomenological data are indispensable to an ideal interpretation, although they can scarcely justify us in undertaking anything beyond a causal investigation. But can we be said to possess anything approaching a phenomenology of pathologico-chemical processes in the science known as pathological chemistry? Are we even in possession of investigations capable of exhibiting the causal connections of these pathologico-chemical phenomena? or are those which we do possess conducted with sufficient exactness to justify us in drawing from them any more general conclusions? What has been, or can as yet be done in pathological chemistry? Some few factors or resultants of the metamorphosis of animal matter have been investigated in a number of diseases, and in the most favorable cases the results have been compared together, although they very frequently did not admit of comparison. And even if the observations made on one and the same object in different conditions, did actually admit of comparison, we might indeed derive from them proofs or counter-proofs in reference to some popular view in humoral pathology, but they could never afford us any insight into the pathological process in the disease in question. It has only seldom been considered that it is indispensably necessary to the comprehension of a pathological process, that we should



simultaneously investigate, if not all, at least many of the factors and resultants of one and the same object, and that we should endeavor to ascertain the mutual relations of the different parts of the group of phenomena. Instead of instituting accurate analyses of the urine, the blood, the solid excrements, and the expired air, in one and the same disease, in one and the same individual, and making careful determinations of the quantities of the egesta when compared with the ingesta or the weight of the body, infinite pains have been taken to compare the composition of the blood in different diseases, without a suspicion of the insufficiency of our analytical methods, and their inability to afford us any insight into the internal metamorphosis of matter. We believe that we have already sufficiently characterized the deplorable nature of most of the analyses of morbid urine. Diabetic urine has frequently been examined, the other juices have also been analyzed in diabetes, and sugar has everywhere been found. Yet this much-discussed disease has never been investigated with reference to the general metamorphosis of matter; on no occasion has any attempt been made to determine the ingesta and egesta of the body during its continuance; and even those experiments which have been made to determine the relation of nutrition to the formation of sugar, have either been left incomplete, or have utterly failed in their object, while the relations of respiration, which are so important in this disease, are still shrouded in complete obscurity. A comprehensive examination of the kind to which we refer is essentially needed in the case of inflammatory fever, or the inflammatory process accompanied by fever, which constitutes one of the main processes of most diseases. It would have served as the first point of attachment for a systematic inquiry, as the keystone to a true system of pathological chemistry; a more favorable opportunity could scarcely be found for establishing and examining from a physical point of view these complicated relations in the deviations from the normal course of the metamorphosis of matter. But the ground before us is still unbroken, and the fruitful soil has as yet yielded little more than weeds.

In reverting once more to the points of view which afford a prospect of a successful elaboration of pathological chemistry, in thus endeavoring to justify our silence in reference to pathologico-chemical processes, we in no way intend to animadvert upon those true inquirers who have exercised their powers on this uncultivated department; for the deficiencies in their labors were owing less to those who prosecuted them, than to the extraordinary difficulties of the pursuit, which will still require many years of labor to overcome; indeed, we have already endeavored, throughout the whole course of this work, to place these difficulties in their true light, and to caution our readers against attaching too high a value to the results yielded by this branch of science. We have often observed that pure chemistry, and more especially physiological chemistry, is still too incomplete to admit of the successful prosecution of such investigations, and hence the cause why so few chemists of celebrity have devoted themselves to pathological chemistry.

The cultivation of this department of science has therefore for the most part been left to beginners or mere chemical dilettanti, who too often were ignorant of even the first principles of physiology. It is to



the anxiety of physicians to obtain chemical elucidations, to the imperfect training in the true method of physical inquiry manifested by these investigators, to their ignorance of scientific processes, and to their misconception of the true objects of pathological chemistry, that we owe those confused works, which, instead of enriching pathological chemistry, have done nothing more than encumber and complicate it. In the hasty anxiety to turn all things to account, these carelessly and hurriedly collected materials have been indiscriminately applied to every possible diagnostic, prognostic, and other practical purpose. Such a method of proceeding, when carried to its extreme length, degenerates into mere purposeless uroscopy and other similar follies, which are not a whit better than the practices of the old water doctors. The labors of such medical handicraftsmen have at most only served to foster the flights of fancy of ready-writing journalists and ingenious physicians, who were not endowed with the mind requisite for earnest natural inquiry, and who, from the barren symbolization of sensuous perceptions and of confused hallucinations, have interwoven a complicated network of facts, which has been dignified with the title of humoral pathology.

Let us not, however, be discouraged by these drawbacks, which are inseparable from all newly developed sciences; but let us rather trustfully and hopefully look forward to a brighter future.

"THOUGH IT BE WINTER NOW, THE SPRING MUST COME AGAIN."<sup>1</sup>

<sup>1</sup> "Es muss doch Frühling werden."







APPENDIX OF PLATES.



# APPENDIX OF PLATES

## PLATE I

1. Lobes of Tarsal Gland.
2. Salivary Gland.
3. Nervous Cells of Thoracic Ganglion.
4. Section of a Tarsus of the House Fly.
5. Portion of the Gaster with light marked.
6. Connection of the Lobes of the Liver with the Hepatic Vein.
7. Arrangement of the Cellular Tissue of the House Fly.

## PLATE II

# APPENDIX OF PLATES

8. Hepatic Cells.
9. Liver of the House Fly.
10. Transverse section of the liver and the surrounding cellular tissue.
11. Effect of oxygen in various phases.
12. Water vapour of the blood.
13. Water vapour of the blood separated 100 diameters.
14. Portion of the human trachea.
15. Red blood corpuscles.

## PLATE III

16. Blood corpuscles collapsed.
17. Red in blood.
18. Blood in laboratory condition.
19. Healthy blood with blood.
20. A lymphatic gland.
21. Portion of the lymphatic system.
22. Lymphatics of the human membrane of the stomach.
23. Section of lymphatic gland.

## PLATE IV

24. Transverse section of the liver.
25. Transverse section of the membrane of the stomach.
26. Human Milk.
27. Milk of the cow.
28. Columnar epithelium.
29. Squamous cells, and their development.
30. Squamous cells in the interior of the vessels of the liver.
31. Human corpuscles.



## APPENDIX OF PLATES.

### PLATE I.

FIG.

1. Lobule of Parotid Gland.
2. Salivary Calculus.
3. Secreting Cells of Human Liver.
4. Section of a Lobule of the Human Liver.
5. Portion of the Same more highly magnified.
6. Connection of the Lobules of the Liver with the Hepatic Vein.
7. Arrangement of the Cellular Parenchyma of the Human Liver.

### PLATE II.

8. Hepatic Cells gorged with Fat.
9. Gall Stones.
10. Development of Lymph and Chyle-Corpuscles into Blood-Corpuscles.
11. Chyle-Corpuscles in various phases.
12. White Corpuscles of the Blood.
13. White Corpuscles of the Blood magnified 400 diameters.
14. Phases of the Human Corpuscles.
15. Red Blood-Corpuscles.

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16. Blood-Corpuscles collapsed.
17. Fat in Blood.
18. Blood in Inflammatory condition.
19. Healthy Fibrin with Blood.
20. A Lymphatic Gland.
21. Portion of Intra-Glandular Lymphatic.
22. Lymphatics of the Mucous Membrane of the Stomach.
23. Section of Lymphatic Gland.

### PLATE IV.

24. Termination of Milk Duct.
25. Ultimate Follicles of Mammary Gland.
26. Human Milk.
27. Milk-Globules.
28. Colostrum-Corpuscles.
29. Spermatozoa from Man, and their development.
30. Spermatozoid in the interior of the vesicle of development.
31. Mucus-Corpuscles.



## PLATE V.

FIG.

- 32. Mucus and Pus-Corpuscles, Epithelial Particles and Blood Disks.
- 33. Sweat Gland.
- 34. Cortical Substance of the Human Kidney.
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- 36. Distribution of the Renal Vessels.
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- 38. Crystals of Chloride of Sodium.
- 39. Chloride of Sodium from Urine.
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- 41-46. Uric Acid Crystals.
- 47. Illustration of the origin of one of its forms.
- 48. Uric Acid developed under the Microscope.
- 49. Uric Acid Crystals.

## PLATE VIII.

- 50-52. Uric Acid Crystals.
- 53. Uric Acid Calculus.
- 54. Section of the same.
- 55. Urate of Ammonia.
- 56. Urate of Ammonia from Fever or Gout.
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## PLATE IX.

- 58-59. Cystine Crystals.
- 60-65. Oxalate of Lime Crystals.

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- 66. Oxalate of Lime or Mulberry Calculus.
- 67. Internal structure of the same.
- 68. Oxalate of Lime Calculus.
- 69. Alternating Calculus.
- 70. Mixed Phosphates.
- 71. Phosphate of Lime Calculus.
- 72, 73. Crystalline forms of the Phosphate of Magnesia and Ammonia.

## PLATE XI.

- 74, 75. Crystalline forms of the Phosphate of Magnesia and Ammonia.
- 76. Phosphate of Magnesia and Ammonia Calculus.
- 77, 78. Fusible Calculus.
- 79. Internal structure of the same.

## PLATE XII.

- 80, 81. Urinary Sediment of Carbonate of Lime.
- 82. Ultimate Granules of Bone.
- 83. Cartilage at Seat of Ossification.
- 84. Transverse Section of a part of the Bone surrounding an Haversian Canal.



## PLATE XIII.

FIG.

- 85. Transverse Section of Bone.
- 86. Vertical Section of the Enamel of Human Molar Tooth.
- 87. Transverse Section of Enamel.
- 88. Transverse Section of Tubules of Dentine.

## PLATE XIV.

- 89. Formation of Enamel.
- 90. Formation of Cementum.
- 91. Section of Branchial Cartilage of Tadpole.

## PLATE XV.

- 92. Section of Fibro-Cartilage.
- 93. The Two Elements of Areolar Tissue.
- 94. White Fibrous Tissue.
- 95. Yellow Fibrous Tissue.

## PLATE XVI.

- 96. Cells of Adipose Tissue.
- 97. Fat-Vesicles.
- 98. Bloodvessels of Fat.
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- 101. Fat-Cells, &c., from Steatomatous Tumor.
- 102. Structure of a Fatty Tumor.
- 103. Vertical Section of the Skin of the Thumb.
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## PLATE XVIII.

- 105. Cells of Smooth Muscular Fibre.
- 106. Fibres of Unstriated Muscle.
- 107. Development of Striped Muscular Fibre.
- 108. Striated Muscular Fibre.

## PLATE XIX.

- 109. Structure of Tubular Nerve-Fibres.
- 110. Primitive Fibres and Ganglionic Globules of Human Brain.
- 111. Yellow Tubercle.
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- 113. Tubercle-Corpuscles from the Peritoneum.

## PLATE XX.

- 114. Tubercle-Corpuscles, Granules, and Molecules from Lung.
- 115. Tubercle-Corpuscles from a Mesenteric Gland.
- 116. Isolated Tubercle-Corpuscles.
- 117. Pus-corpuscles, natural appearance.



FIG.

- 118. Pus-Corpuscles, magnified 400 diameters.
- 119. Healthy Pus-cells.
- 120. Pus-Corpuscles of Cancer.
- 121. The same after the application of Acetic Acid.
- 122. Scrofulous Pus.
- 123. Scrofulous Pus from a Lymphatic Gland.

## PLATE XXI.

- 124. Peptic Gastric Gland.
- 125. Section through a Cluster of Gastric Cæca.
- 126. Mucous Gastric Gland.
- 127. Horizontal Section of a Stomach-cell.
- 128. Capillary network of the lining Membrane of the Stomach.
- 129. A portion of Mucous Membrane of the Stomach, magnified 75 times.

## PLATE XXII.

- 130. One of the Tubular Follicles of the Pig's Stomach.
- 131. Section of Mucous Membrane of Small Intestine in the Dog.
- 132. One of the Intestinal Villi, with the commencement of a Lacteal.
- 133. Portion of Mucous Membrane of the Large Intestine.
- 134. Transverse Section of Lieberkühn's Tubes or Follicles.

## PLATE XXIII.

- 135. Distribution of Capillaries in the Villi of the Intestine.
- 136. Solitary Gland of Small Intestine.
- 137. Part of a patch of Peyer's Glands magnified.
- 138. Bloodvessels of an Intestinal Villus.
- 139. Air-cells of Human Lung.

## PLATE XXIV.

- 140. Section through a Bronchial Tube.
- 141. Arrangement of Capillaries of the Air-cells of the Human Lung.
- 142. Epithelium-cells.
- 143. Epithelium of Serous Membrane.
- 144. Epithelium detached and free in the Cavity of the Duodenum of a Dog.
- 145. Epithelial Cells in Urine.
- 146. Primary Organic Cell.



FIG. 1.

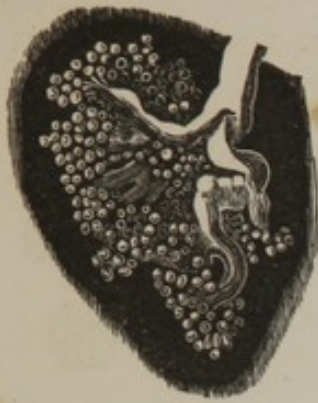


FIG. 2.



FIG. 3.



FIG. 4.

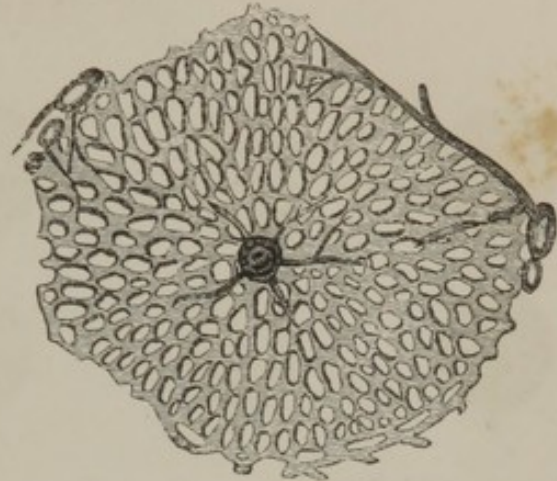


FIG. 5.

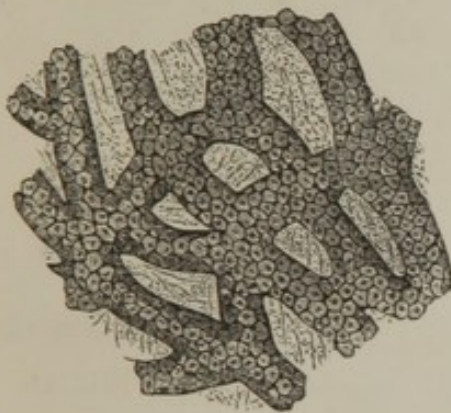


FIG. 7.

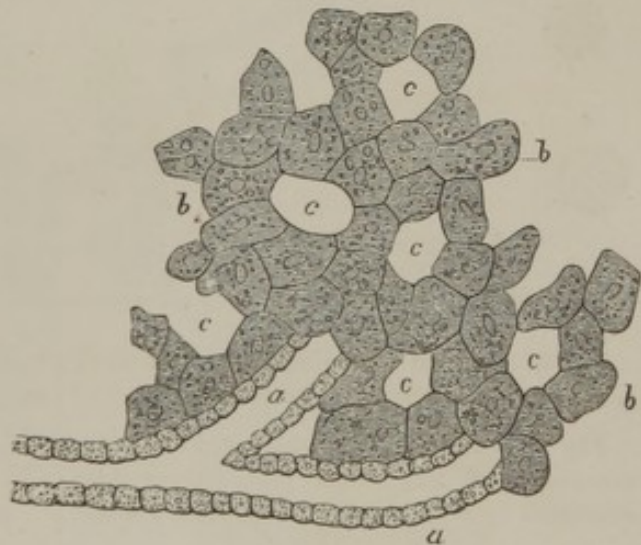


FIG. 6.



Fig. 1. LOBULE OF PAROTID GLAND of a newborn Infant, injected with mercury. Magnified 50 diameters.

Fig. 2. SALIVARY CALCULUS of considerable size; removed by operation.

Fig. 3. SECRETING CELLS OF HUMAN LIVER *a*, nucleus; *b*, nucleolus; *c*, oil-particles.

Fig. 4. TRANSVERSE SECTION OF A LOBULE OF THE HUMAN LIVER, showing the reticular arrangement of the Bile-ducts, with some of the branches of the Hepatic Vein in the centre, and those of the Portal System at the periphery.

Fig. 5. A small portion of this section more

highly magnified, showing the secreting cells within the tubes.

Fig. 6. CONNECTION OF THE LOBULES OF THE LIVER WITH THE HEPATIC VEIN: 1, trunk of the vein; 2, 2, lobules depending from its branches, like leaves on a tree; the centre of each being occupied by a venous twig, the Intralobular Vein.

Fig. 7. Diagram of the arrangement of the CELLULAR PARENCHYMA (*bb*) OF THE HUMAN LIVER, with reference to the radicals of the interlobular ducts (*aa*), and the vascular spaces (*cc*).



# PLATE II.

FIG. 8.



FIG. 9.



FIG. 11.



FIG. 10.



FIG. 13.

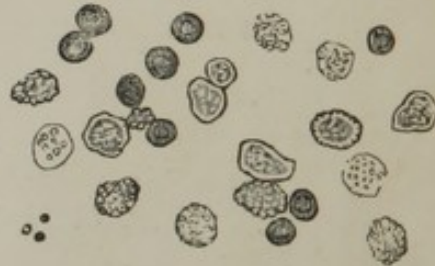


FIG. 14.



FIG. 15.

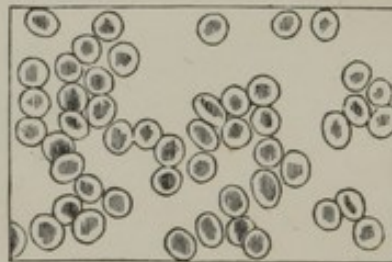


FIG. 12.

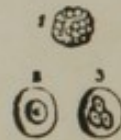


Fig. 8. HEPATIC CELLS GORGED WITH FAT; *a*, atrophied nucleus; *b*, adipose globules.

Fig. 9. SMALL, IRREGULAR GALL-STONES, composed of inspissated and altered bile cemented by mucus.—From Dr. Budd's work.

Fig. 10. DEVELOPMENT OF HUMAN LYMPH-AND CHYLE-CORPUSCLES INTO BLOOD-CORPUSCLES. A. A lymph or white blood-corpuscle. B. The same in process of conversion into a red corpuscle. C. A lymph-corpuscle with the cell-wall raised up round it by the action of water. D. A lymph-corpuscle from which the granules have almost all disappeared. E. A lymph-corpuscle acquiring color; a single granule, like a nucleus, remains. F. A red corpuscle fully developed.

Fig. 11. CHYLE-CORPUSCLES IN VARIOUS PHASES;—*a* *a*, stellate form occasionally seen after escape of their contents; *b* *b*, free nuclei; *c*, a nucleus surrounded by a few granules; *d*,

*e*, small cells, some with distinct nucleus; *f*, *g*, larger cells, one with a visible nucleus; *h*, similar cell after addition of water; *i*, similar cell after addition of acetic acid.

Fig. 12. WHITE CORPUSCLES OF THE BLOOD. 1. A corpuscle in its natural condition. 2 and 3. Different appearances produced by the action of diluted acetic acid.

Fig. 13. WHITE CORPUSCLES OF THE BLOOD. Magnified 400 diameters.

Fig. 14. PHASES OF THE HUMAN BLOOD-CORPUSCLE (after Wharton Jones). *a* and *b*. Colorless corpuscles or Granule-cells in the coarsely and finely granular state. *c* and *d*. Nucleated cells, *c* without color, *d* with color. *e*. Free cellæform nucleus, or perfect red corpuscle.

Fig 15. RED BLOOD-CORPUSCLES. Magnified 400 diameters.



FIG. 16.

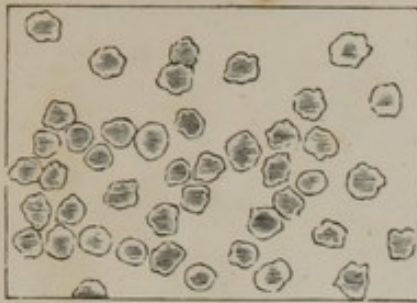


FIG. 17.

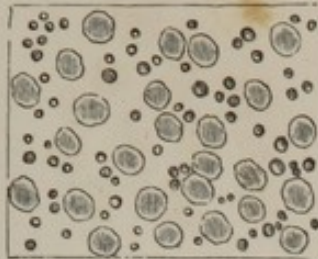


FIG. 21.

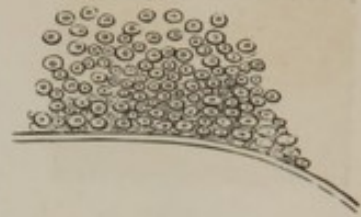


FIG. 18.



FIG. 19.



FIG. 20.

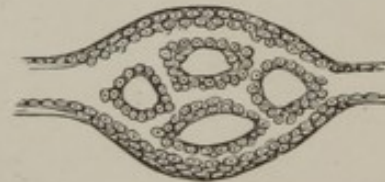


FIG. 22.



FIG. 23.



Fig. 16. BLOOD-CORPUSCLES COLLAPSED, magnified 400 diameters.

Fig. 17. FAT IN BLOOD.

Fig. 18. The Microscopic Appearance of a Drop of Blood in the Inflammatory condition. The red corpuscles lose their circular form, and adhere together; the white corpuscles remain apart, and are often more abundant than usual.

Fig. 19. FIBRILS OF HEALTHY FIBRIN, entangling red and white blood-corpuscles (three of the latter are figured separately), and a few fibrinous fibrils.

Fig. 20. DIAGRAM OF A LYMPHATIC GLAND, showing the intra-glandular network, and the transition from the scale-like epithelia of the

extra-glandular lymphatics, to the nucleated cells of the intra-glandular.

Fig. 21. PORTION OF INTRA-GLANDULAR LYMPHATIC showing along the lower edge the thickness of the germinal membrane, and upon it the thick layer of glandular epithelial cells.

Fig. 22. LYMPHATICS OF THE MUCOUS MEMBRANE OF THE STOMACH, after Breschet. *a*. Superficial layer; *b*, deep layer.

Fig. 23. SECTION OF LYMPHATIC GLAND, showing *a a*, the fibrous tissue which forms its exterior; *b b*, superficial vasa inferentia; *c c*, larger alveoli near the surface; *d d*, smaller alveoli of the interior; *e e*, fibrous walls of the alveoli.



# PLATE IV.

FIG. 24.



FIG. 25.

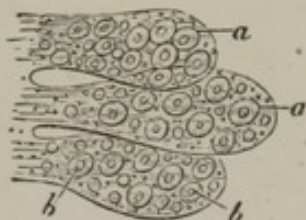


FIG. 26.

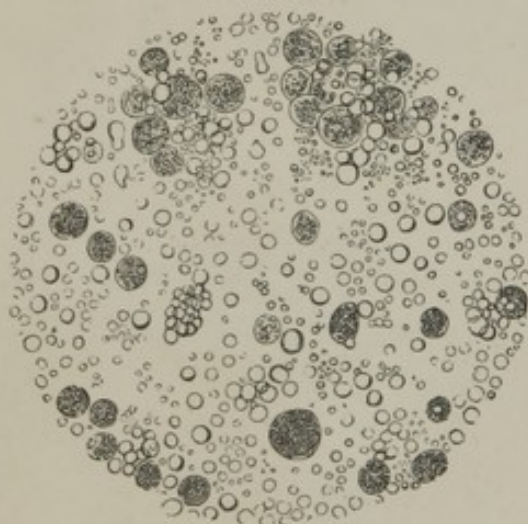


FIG. 27.

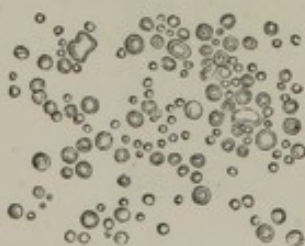


FIG. 31.



FIG. 29.

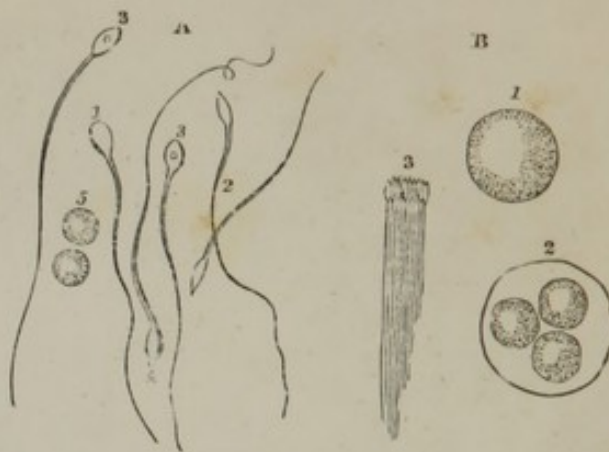


FIG. 30.



FIG. 28.

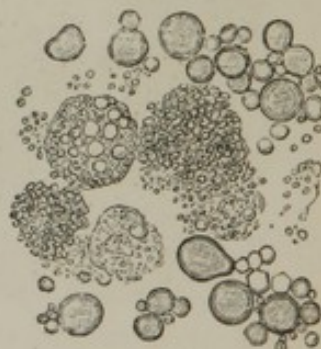


Fig. 24. TERMINATION OF PORTION OF MILK-DUCT IN FOLLICLES; from a mercurial injection, by Sir A. Cooper; enlarged four times.

Fig. 25. ULTIMATE FOLLICLES OF MAMMARY GLAND, with their secreting cells *a, a*, and nuclei, *b, b*.

Fig. 26. MICROSCOPIC APPEARANCE OF HUMAN MILK, with an intermixture of Colostric corpuscles at *a, a*, and elsewhere.

Fig. 27. MILK-GLOBULES.

Fig. 28. COLOSTRUM-CORPUSCLES.

Fig. 29. SPERMATOOA FROM MAN, and their development. (Wagner.) A. Spermatozoa from the semen of the vas deferens. 1 to 4. Show their variety of character. 5. Seminal granules.—B. Contents of the semen of the testis. 1. Large round corpuscle or cell. 2. A cell containing three roundish granular bodies, from which the spermatozoa, are developed. 3. A fasciculus of spermatozoa, as they are seen grouped together in the testis.

Fig. 30. SPERMATOOID OF THE DOG in the interior of the vesicle of development.

Fig. 31. MUCUS-CORPUSCLES.



FIG. 32.



FIG. 33.

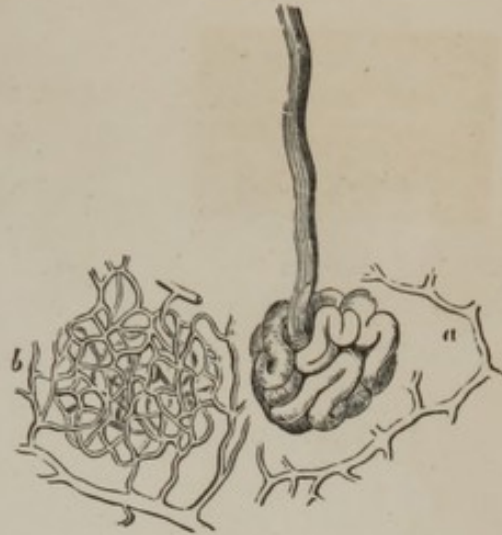


FIG. 34.



FIG. 35.



Fig. 32. Mucus- and pus-corpuscles, epithelial particles, and blood-disks, from mucous or cervical leucorrhœa. 220 diameters.

Fig. 33. SWEAT-GLAND AND THE COMMENCEMENT OF ITS DUCT. *a*. Venous radicles on the wall of the cell in which the gland rests. This vein anastomoses with others in the vicinity. *b*. Capillaries of the gland separately represented, arising from their arteries, which also anastomose. The bloodvessels are all situated on the outside or deep surface of the tube, in contact with the basement membrane. —Magn. 35 diam.

Fig. 34. SECTION OF THE CORTICAL SUBSTANCE OF THE HUMAN KIDNEY:—*A A*, tubuli uriniferi divided transversely, showing the spheroidal epithelium in their interior; *B*, Malpighian Capsule; *a*, its afferent branch of the renal artery; *b*, its glomerulus of capillaries; *c c*, secreting plexus, formed by its efferent vessels; *d d*, fibrous stroma.

Fig. 35. Portion of one of the TUBULI URINIFERI, from the kidney of an adult; showing its tessellated epithelium.



# PLATE VI.

FIG. 36.

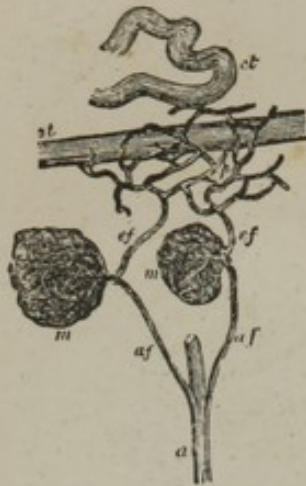


FIG. 38.

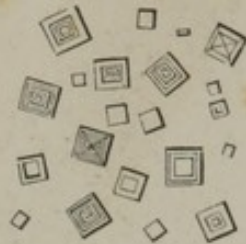


FIG. 37.



FIG. 39.



FIG. 40.

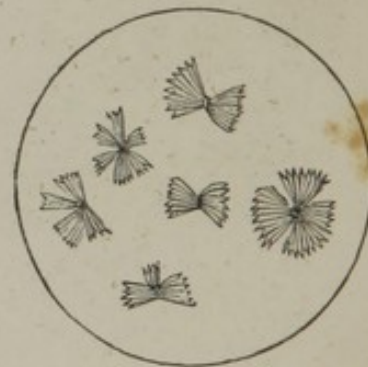


Fig. 36. DISTRIBUTION OF THE RENAL VESSELS, FROM KIDNEY OF HORSE: *a*, branch of Renal artery; *af*, afferent vessel; *m*, *m*, Malpighian tufts; *ef*, *ef*, efferent vessels; *p*, vascular plexus surrounding the tubes; *st*, straight tube; *ct*, convoluted tube. Magnified about 30 diameters.

Fig. 37. A, Portion of a secreting canal from the cortical substance of the kidney. B, The epithelium or gland-cells, more highly magnified (700 times). C, Portion of a canal from the medullary substance of the kidney. At

one part the basement-membrane has no epithelium lining it.

Fig. 38. CHLORIDE OF SODIUM. Obtained by treating urate of soda with hydrochloric acid and slowly evaporating.

Fig. 39. CHLORIDE OF SODIUM resulting from slow evaporation of healthy urine.

Fig. 40 Triple Compound of CHLORIDE OF ZINC and CREATININE with creatine, from concentrated urine treated with fused chloride of zinc.



# PLATE VII.

FIG. 41.



FIG. 42.



FIG. 43.

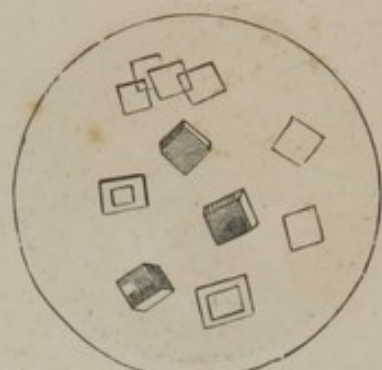


FIG. 44.



FIG. 45.



FIG. 46.



FIG. 47.



FIG. 48.



FIG. 49.



Figs. 41-43. DIFFERENT FORMS OF URIC ACID CRYSTALS.

Fig. 41. Uric Acid Crystals which result from the slow introduction of a warm solution of Urate of Soda into warm dilute Hydrochloric acid.

Fig. 42. Uric Acid Crystals from Human Urine.

Fig. 43. Uric Acid Crystals in which, when the deposit is of long continuance, the rhomboidal form is replaced by a square one.

Fig. 44. Uric Acid. Accidental Varieties of the rhomboid and square forms.

Fig. 45. Uric Acid. Thick lozenges, often

found mixed with urate of ammonia and oxalate of lime.

Fig. 46. Uric Acid of human urine.

Fig. 47. Illustration of the mode in which the crystalline form of (Fig. 46) is produced; viz., by the union of two rhomboidal crystals with their apices approximated.

Fig. 48. Uric Acid as artificially developed from urate of soda, and observed under the microscope. A, B, C, and D, are its successive changes when the urate is treated with strong acetic acid. E, F, and G, when the urate is concentrated and treated hot with an excess of acetic acid and cooled.

Fig. 49. Uric Acid of human urine.



# PLATE VIII.

FIG. 50.



FIG. 51.



FIG. 52.



FIG. 53.

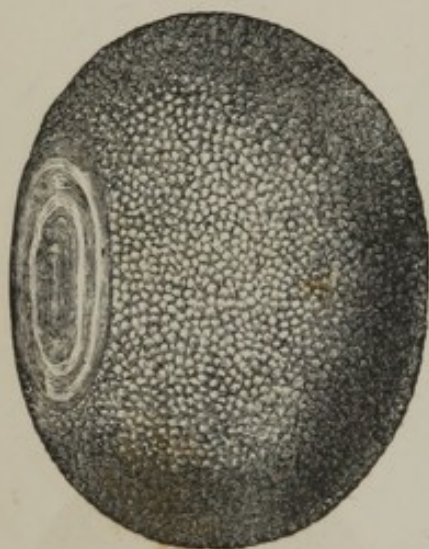


FIG. 54.



FIG. 55.



FIG. 56.



FIG. 57.



Fig. 50. Uric Acid of human urine, as sometimes found crystallized on a hair.

Fig. 51. Uric Acid in irregular masses, resulting from sudden cooling of the urine, or by the addition to it of a strong acid.

Fig. 52. Uric Acid crystallized on a fibrinous cast of a uriniferous tube.

Fig. 53. URIC ACID CALCULUS.

Fig. 54. SECTION OF A URIC ACID CALCULUS, showing the internal concentric layers.

Fig. 55. URATE OF AMMONIA, from urine.

Fig. 56. URATE OF AMMONIA from the urine of patients laboring under gout or fever.

Fig. 57. URATE OF AMMONIA CALCULUS.



FIG. 58.

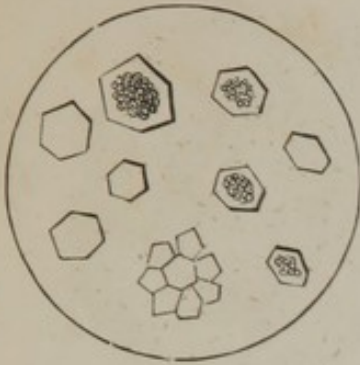


FIG. 59.



FIG. 60.

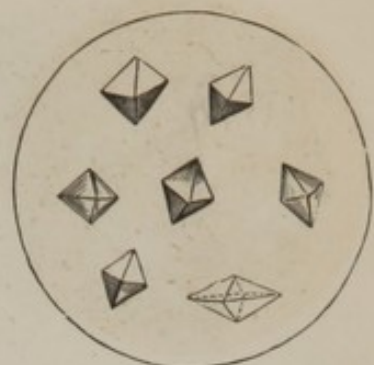


FIG. 61.

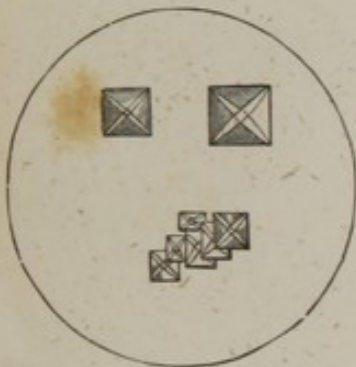


FIG. 62.

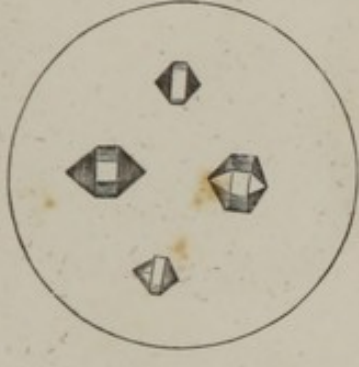


FIG. 63.



FIG. 64.



FIG. 65.



Fig. 58. CYSTINE crystallized from ammoniacal solution by spontaneous evaporation.

Fig. 59. CYSTINE CRYSTALS in groups.

Figs. 60, 61, 62. OXALATE OF LIME.

Fig. 63. The OCTOHEDRAL CRYSTALS of oxalate of lime, as seen when allowed to dry.

Figs. 64, 65. DUMB-BELL CRYSTALS of oxalate of lime from urine.



PLATE X.

FIG. 66.



FIG. 67.



FIG. 68.



FIG. 69.



FIG. 70.



FIG. 71.



FIG. 72.

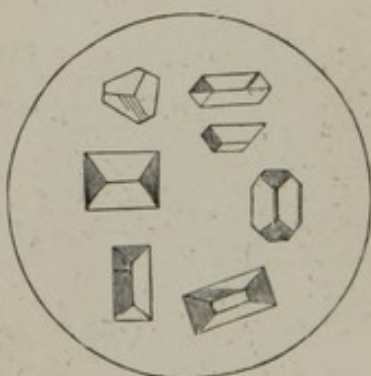


FIG. 73.

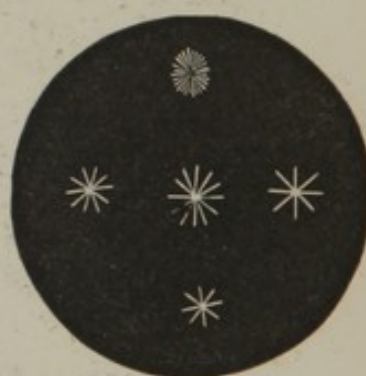


Fig. 66. OXALATE OF LIME or mulberry calculus.

Fig. 67. Internal structure of the same.

Fig. 68. OXALATE-OF-LIME CALCULUS.

Fig. 69. ALTERNATING CALCULUS of uric acid and oxalate of lime.

Fig. 70. MIXED PHOSPHATES. The minute dots represent the amorphous particles of phosphate of lime.

Fig. 71. PHOSPHATE-OF-LIME CALCULUS.

Figs. 72, 73. VARIETIES OF CRYSTALLINE FORMS. The triple or neutral phosphate of magnesia and ammonia.



PLATE XL

FIG. 74.



FIG. 75.



FIG. 76.



FIG. 77.



FIG. 78.



FIG. 79.



Figs. 74, 75. VARIETIES OF CRYSTALLINE FORMS. The triple or neutral phosphate of magnesia and ammonia.

Fig. 76. PHOSPHATE OF MAGNESIA AND AMMONIA CALCULUS.

Fig. 77. FUSIBLE CALCULUS.

Fig. 78. FUSIBLE CALCULUS.

Fig. 79. Internal structure of the same.



# PLATE XII.

FIG. 80.

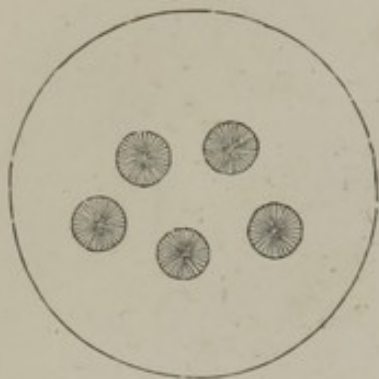


FIG. 81.

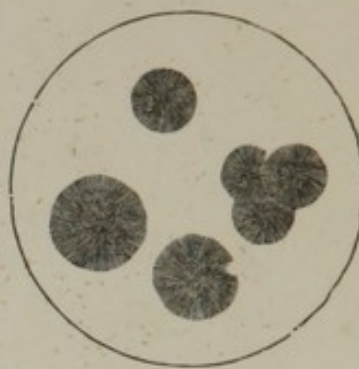


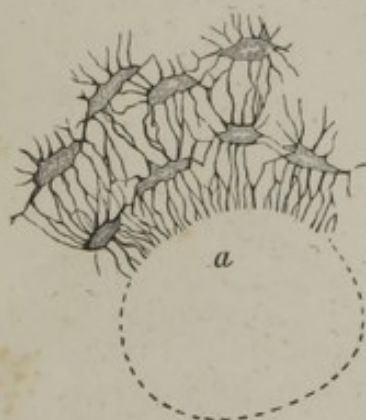
FIG. 82.



FIG. 83.



FIG. 84.



Figs. 80, 81. CARBONATE OF LIME, a rare form met with in alkaline urine. It is most usual as an amorphous powder.

Fig. 82. ULTIMATE GRANULES OF BONE, isolated and in small masses, from the femur.—(From a preparation of Mr. Tomes.) Magnified 320 diameters. Prepared by prolonged boiling in a Papin's digester. Also may be obtained by calcination or digestion in hydrochloric acid.

Fig. 83. Vertical section of CARTILAGE AT THE SEAT OF OSSIFICATION; the clusters of cells are arranged in columns, the intercellular spaces between them being 1-3250ths of an

inch in breadth. At the lower end of the figure, osseous fibres are seen occupying the intercellular spaces, at first bounding the clusters laterally, then splitting them longitudinally and encircling each separate cell. The greater opacity of this portion is due to a threefold cause; the increase of osseous fibres, the opacity of the contents of the cells, and the multiplication of oil-globules.

Fig. 84. TRANSVERSE SECTION of a part of the bone surrounding an Haversian canal, showing the pores commencing at the surface. *a*, anastomosing and passing from cavity to cavity.—Magnified about 300 diameters. From a preparation made by Mr. Tomes.



FIG. 85.



FIG. 86.



FIG. 87.

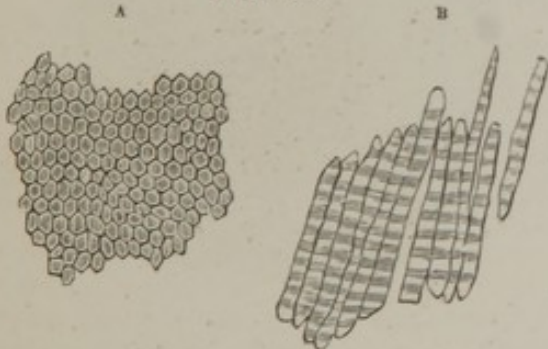


FIG. 88.

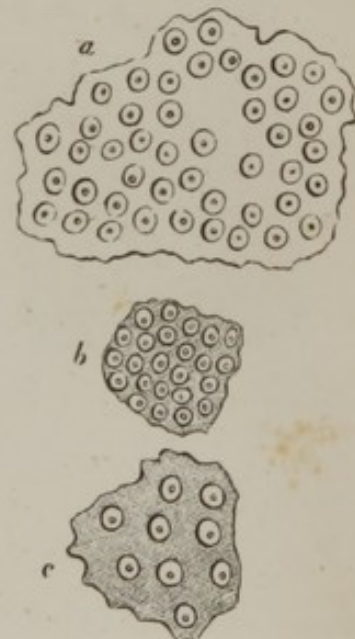


Fig. 85. TRANSVERSE SECTION of compact tissue (of humerus) magnified about 150 diameters. Three of the Haversian canals are seen, with their concentric rings; also the corpuscles or lacunæ, with the canaliculi extending from them across the direction of the lamellæ. The Haversian apertures had got filled with debris in grinding down the section, and therefore appear black in the figure, which represents the object as viewed with transmitted light.

Fig. 86. Vertical section of the ENAMEL of the human molar tooth.

Fig. 87. A, Transverse section of ENAMEL, showing the hexagonal form of its prisms; B, separated prisms.

Fig 88. TRANSVERSE SECTIONS OF TUBULES OF DENTINE, showing their cavities, walls, and the intertubular tissue. *a*. Ordinary distance apart *b*. More crowded. *c*. Another view. Human molar.—Magnified 400 diameters.



FIG. 89.

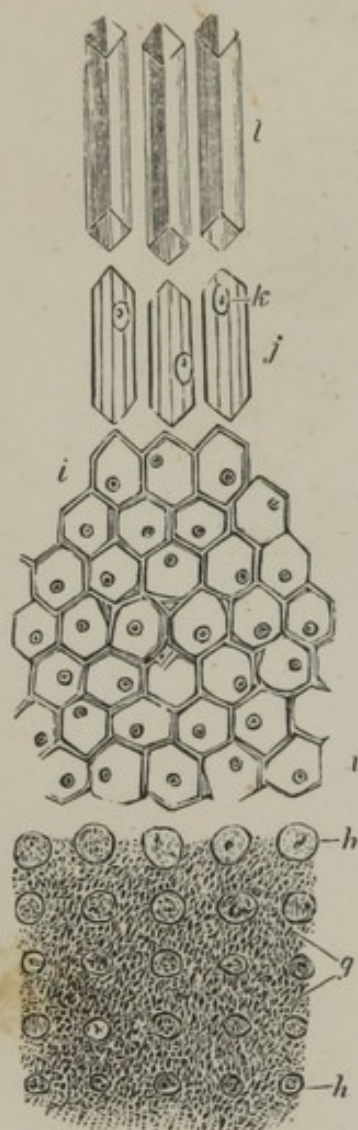


Fig. 89. FORMATION OF ENAMEL; *h*, primary cells suspended in fluid blastema *g*; *i*, the same more fully developed and become angular; *j*, the same becoming prismatic; *k*, the nucleus disappearing; *l*, the modified prismatic cells, filled with calcareous salts, forming the fibres of enamel.

Fig. 90. FORMATION OF THE CEMENTUM: *m*, primary cells; *p*, their granular nuclei; *n*,

FIG. 90.

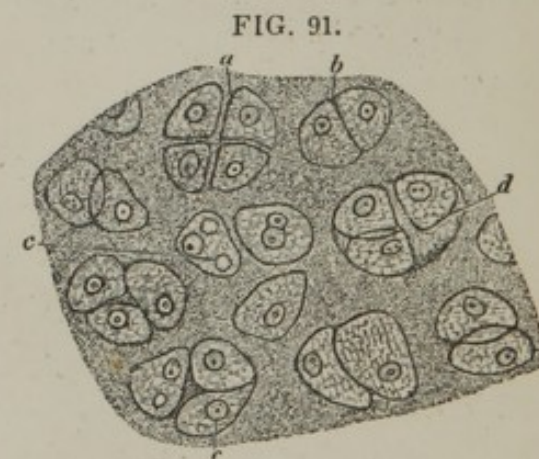
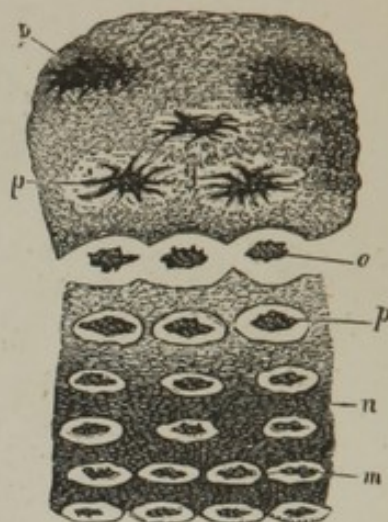


FIG. 91.

more minutely granular blastema; *o*, the primary cell enlarged, and receiving the hardening salts; *n'*, calcified blastema; *p*, *p'*, stellate nuclei of fully formed cemental cells.

Fig. 91. SECTION OF THE BRANCHIAL CARTILAGE OF TADPOLE; *a*, group of four cells, separating from each other; *b*, pair of cells in apposition; *c*, *c*, nuclei of cartilage cells; *d*, cavity containing three cells.



FIG. 92.



FIG. 93.



Fig. 92. SECTION OF FIBRO-CARTILAGE; showing disposition of cartilage cells, in areolæ of fibrous tissue.

Fig. 93. THE TWO ELEMENTS OF AREOLAR TISSUE, in their natural relations to one another:—1. The white fibrous element, with cell-nuclei, 9, sparingly visible in it. 2. The yellow fibrous element, showing the branching or anastomosing character of its fibrillæ. 3. Fibrillæ of the yellow element, far finer than the rest, but having a similar curly character. 8. Nucleolated cell-nuclei, often seen apparently loose.—From the areolar tissue

FIG. 94.



FIG. 95.



under the pectoral muscle, magnified 320 diameters.

Fig. 94. WHITE FIBROUS TISSUE:—2. Straight appearance of the tissue when stretched. 1, 3, 4, 5 Various wavy appearances which the tissue exhibits when not stretched. Magnified 320 diameters.

Fig. 95. YELLOW FIBROUS TISSUE, showing the curly and branched disposition of its fibrillæ, their definite outline, and abrupt mode of fracture. At 1, the structure is not disturbed, as in the rest of the specimen.—Magnified 320 diameters.



FIG. 96.

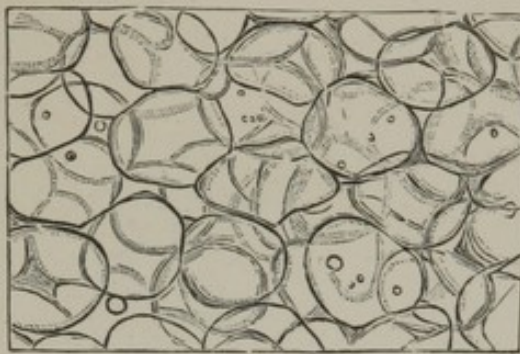


FIG. 97.

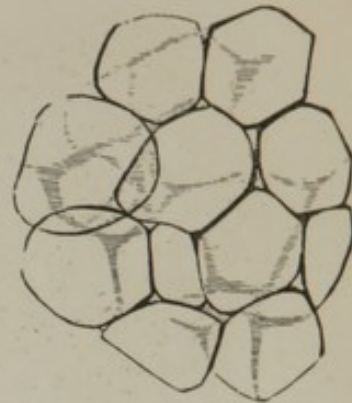


FIG. 98.



FIG. 99.



FIG. 100.



Fig. 96. CELLS OF ADIPOSE TISSUE. Magnified 135 diameters.

Fig. 97. FAT-VESICLES assuming the polyhedral form, from pressure against one another. The capillary vessels are not represented. From the omentum; magnified about 300 diameters.

Fig. 98. BLOODVESSELS OF FAT:—1. Minute flattened fat lobule, in which the vessels only are represented. 3. The terminal artery. 4. The primitive vein. 5. The fat-vesicles of

one border of the lobule, separately represented. Magnified 100 diameters.—2. Plan of the arrangement of the capillaries on the exterior of the vesicles: more highly magnified.

Fig. 99. FAT-GLOBULES.

Fig. 100. FAT-VESICLES from an emaciated subject:—1, 1. The cell-membrane. 2, 2, 2. The solid portion collected as a star-like mass, with the elaine in connection with it, but not filling the cell.



FIG. 101.



FIG. 102.



FIG. 103.

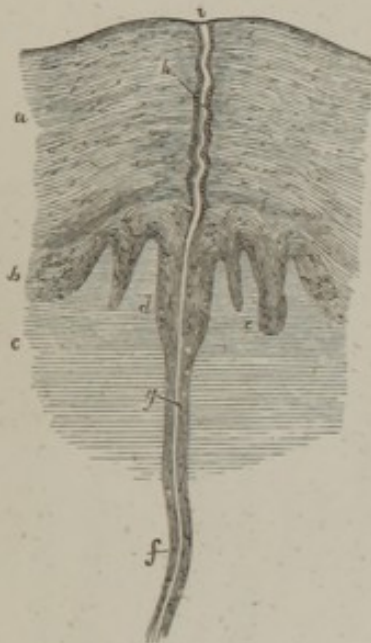


FIG. 104.

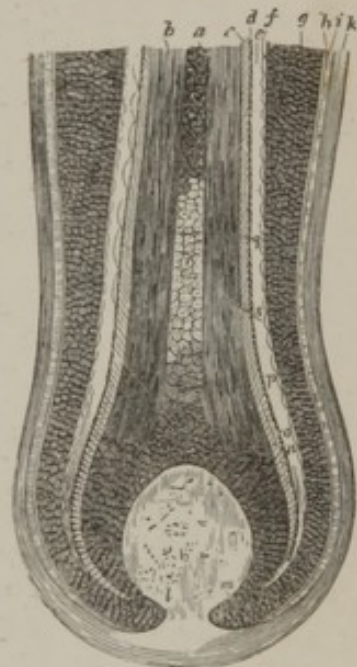


Fig. 101. FAT-CELLS AND GRANULAR MATTER, from a steatomatous tumor of the ovary.—Bennett.

Fig. 102. STRUCTURE OF A FATTY TUMOR removed from the back. Lipome. *a*. Isolated cells showing the crystalline nucleus of margaric acid.—Bennett.

Fig. 103. VERTICAL SECTION OF THE SKIN OF THE THUMB, showing the Epidermis and outer layer of the Corium; treated with acetic acid: *a*, horny layer of Epidermis; *b*, mucous layer; *c*, cutis vera; *d*, single papilla; *e*, composite papilla; *f*, epithelium of the perspiratory duct, continuous with the mucous layer of the epidermis; *g*, canal of the same through the cutis; *h*, its passage through the horny portion; *i*, perspiratory pore.

Fig. 104. HAIR-BULB OF A WELL-DEVELOPED HUMAN HAIR, with its follicle: *a*, medullary

substance, containing air-spaces, with indistinct cells; *b*, fibrous cortical substance; *c, d*, inner and outer layers of the scaly envelope; *e, f*, inner and outer layers of the internal root-sheath; *g*, external root-sheath; *h*, structureless membrane; *i*, transverse fibre-stratum; *k*, longitudinal fibre-stratum; *l*, hair-papilla; *m*, lowest cells of the hair-bulb, continuous with those of the external root-sheath; *n*, perpendicularly-arranged nucleated cells, which, near *q*, become non-nucleated, and are continuous with the inner layer of the scaly envelope; *o*, small perpendicularly-arranged cells, likewise nucleated, passing into the outer layer of the same; *p*, lowest portion of the inner root-sheath; *r*, commencement of the medullary substance in the condition of colorless cells; *s*, part where the cells of the bulb begin visibly to lengthen themselves, to form the fusiform cells of the shaft.



# PLATE XVIII.

FIG. 105.

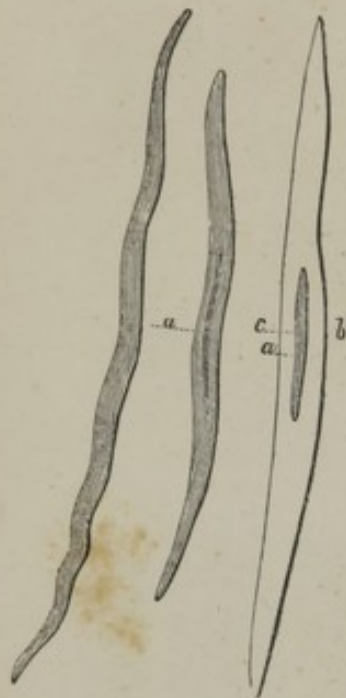


FIG. 107.

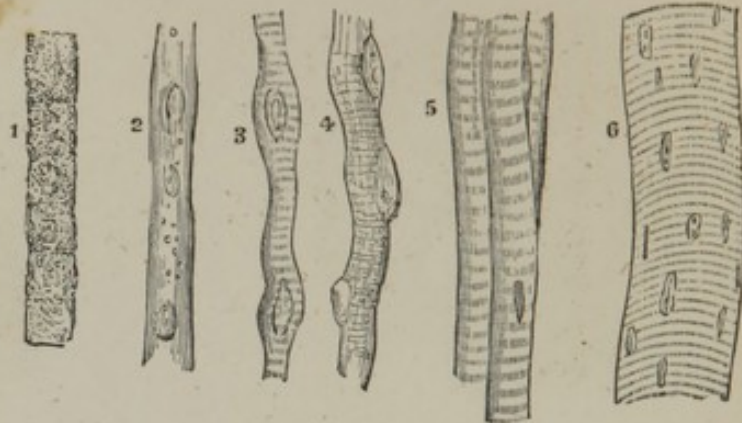


FIG. 106.



FIG. 108.



Fig. 105. FUSIFORM CELLS OF SMOOTH MUSCULAR FIBRE, from the renal vein of Man; *a*, two cells in their natural state, one of them showing the staff-shaped nucleus; *b*, a cell treated with acetic acid, with its nucleus *c* brought strongly into view.

Fig. 106. FIBRES OF UNSTRIPED MUSCLE: *c*. In their natural state. *a*. Treated with acetic acid, showing the corpuscles. *b*. Corpuscles, or nuclei, detached, showing their various appearances.

Fig. 107. STAGES OF THE DEVELOPMENT OF STRIPED MUSCULAR FIBRE: 1. Arrangement of the primitive cells in a linear series.—After

Schwann. 2. The cells united. The nuclei separated, and some broken up; longitudinal lines becoming apparent.—From a foetal calf three inches long. 3, 4 Transverse stripes apparent. In 3, the nuclei are internal, and bulge the fibre. In 4, they are prominent on the surface.—From a foetal calf of two months old. 5. Transverse stripes, fully formed and dark; nuclei disappearing from view.—From the human infant at birth. 6. Elementary fibre from the adult, treated with acid; showing the nuclei.—Magnified about 300 diam.

Fig. 108. PORTION OF STRIATED MUSCULAR FIBRE separating into disks, by cleavage in direction of transverse striæ.



FIG. 109.



FIG. 110.

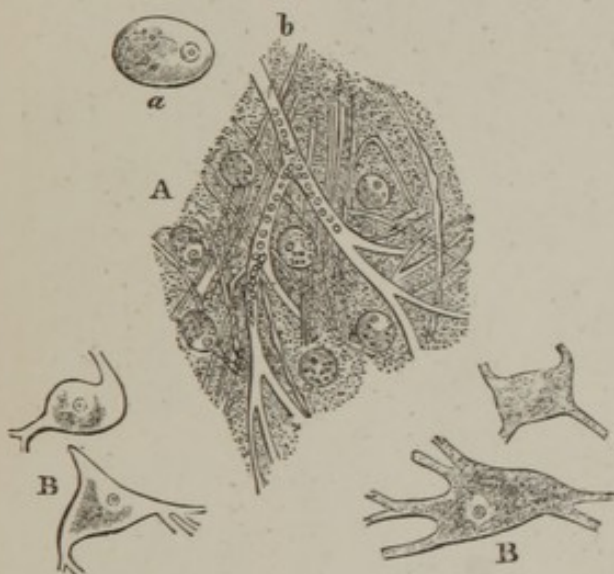


FIG. 111.



FIG. 112.

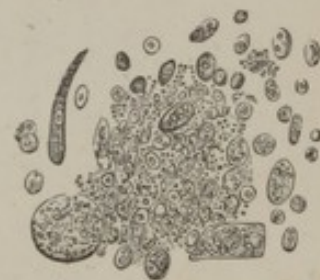


FIG. 113.

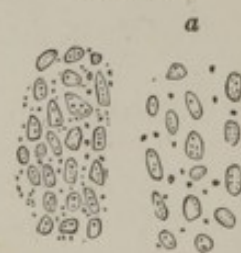


Fig. 109. STRUCTURE OF TUBULAR NERVE-FIBRES, magnified 350 diameters: A, cylindrical tubuli from nerve; B, varicose tubuli from brain; C, nerve-tubes, of which one exhibits the remains of nuclei in its walls.

Fig. 110: PRIMITIVE FIBRES and GANGLIONIC GLOBULES of human Brain, after Purkinje. A, ganglionic globules lying amongst varicose nerve-tubes, and bloodvessels, in substance of optic thalamus; a, globule, more enlarged; b,

small vascular trunk. B, B, globules, with variously-formed peduncles, from dark portion of crus cerebri. 350 diam.

Fig. 111. YELLOW TUBERCLE; crude mass.

Fig. 112. GRAY TUBERCLE; miliary granulation.

Fig. 113. TUBERCLE-CORPUSCLES from the peritoneum. a, the same, after the addition of acetic acid.



# PLATE XX.

FIG. 114.



FIG. 115.



FIG. 116.

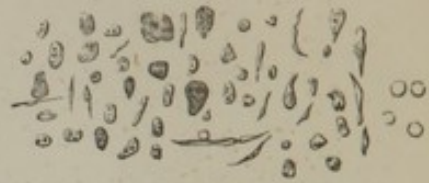


FIG. 117.



FIG. 118.



FIG. 120.



FIG. 119.



FIG. 121.



FIG. 122.

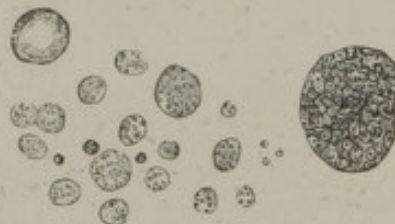


FIG. 123.



Fig. 114. TUBERCLE-CORPUSCLES, granules, and molecules, from a soft tubercular mass in the lung. 250 diameters linear.

Fig. 115. TUBERCLE-CORPUSCLES, from a mesenteric gland.

Fig. 116. ISOLATED TUBERCLE-CORPUSCLES. On the right are four blood-globules.

Fig. 117. *a*. Natural appearance of PUS-CORPUSCLES. *b*. Appearance after application of acetic acid.

Fig. 118. PUS-CORPUSCLES, magnified 400 diameters.

Fig. 119. HEALTHY PUS-CELLS.

Fig. 120. PUS-CORPUSCLES OF CANCER, mag-

nified 833 diameters. *q*. Type form before the addition of any reactive. *r*. Outline of nucleus seen surrounded by thick granulations.

Fig. 121. The same, after the application of acetic acid. *s*. The irregular contour of the corpuscle freed from the granulations, leaving the nuclei clear. *t*. Characteristic nucleus without any nucleolus. *u*. Free nuclei, the walls having been destroyed. Diameter of pus-corpuscle varies from 1-100th to 1-80th millimetre, that of the nucleus 1-333d. *v*. Remnant of contour.

Fig. 122. SCROFULOUS PUS: a large glomerulus is shown, and some oil drops.

Fig. 123. SCROFULOUS PUS from a lymphatic gland. 250 diameters linear.



FIG. 124.

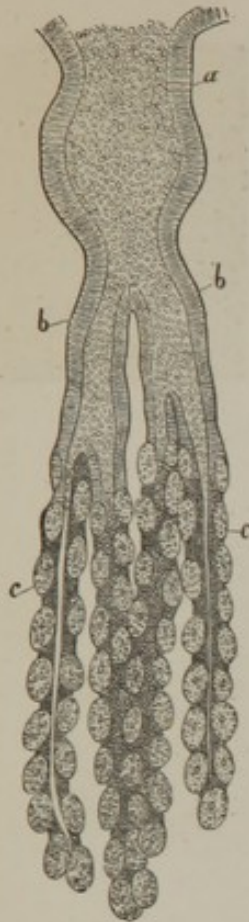


FIG. 128.



FIG. 126.

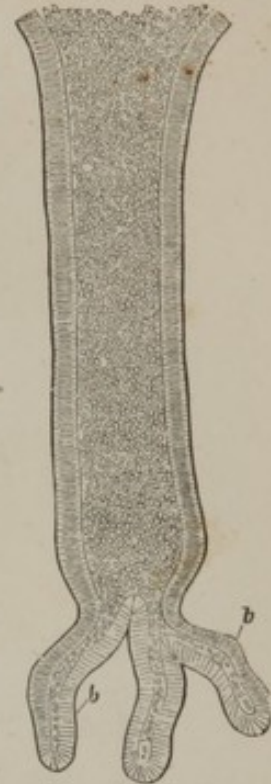


FIG. 125.



FIG. 127.



FIG. 129.

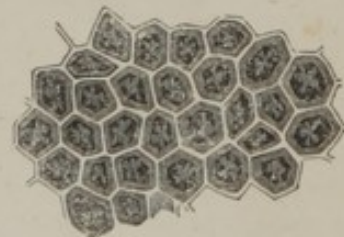


Fig. 124. PEPTIC GASTRIC GLAND: *a*, common trunk; *b, b*, its chief branches; *c, c*, terminal caeca with spheroidal gland-cells.

Fig. 125. Transverse Section passing through a cluster of GASTRIC CAECA, separated and surrounded by fibrous tissue; *a, a*, orifices of divided capillaries.

Fig. 126. MUCOUS GASTRIC GLAND, with cylinder-epithelium; *a*, wide trunk; *b, b*, its caecal appendages.

Fig. 127. Horizontal Section of a STOMACH-CELL, a little way within its orifice. *a*. Basement membrane. *b*. Columnar epithelium. All but the centre of the cavity of the cell is occupied by transparent mucus, which seems to have oozed from the open extremities of the epithelial particles. *c*. Fibrous matrix sur-

rounding and supporting the basement membrane. *d*. Small bloodvessel.

Fig. 128. CAPILLARY NETWORK of the lining membrane of the Stomach, with the orifices of the gastric follicles.

Fig. 129. A portion of the MUCOUS MEMBRANE OF THE STOMACH, magnified seventy-five times. The alveoli measured 1-200th of an inch in length, by 1-250th in breadth; the width of the septa being 1-1000th of an inch. The smaller alveoli measured 1-250th of an inch in length, and 1-300th in breadth. The trifid or quadrifid division of a small artery is seen at the bottom of each alveolus, and in the depressions between the divisions of the artery, the apertures of the gastric follicles; two, three, or four in each depression.



# PLATE XXII.

FIG. 130.



FIG. 131.

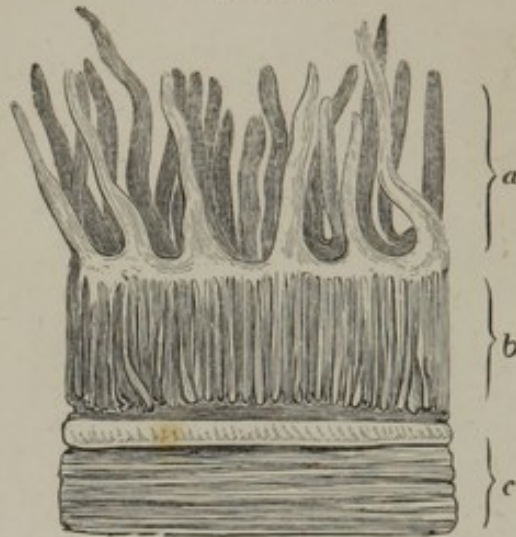


FIG. 132.



FIG. 133.



FIG. 134.



Fig. 130. One of the **TUBULAR FOLLICLES** of the **PIG'S STOMACH**, after Wasmann, cut obliquely so as to display the upper part of its cavity, with the cylindrical epithelium forming its walls. At the lower part of the follicle, the external nucleated extremities of the cylinders of epithelium are seen.

Fig. 131. Section of the **MUCOUS MEMBRANE** of the **SMALL INTESTINE** in the **DOG**, showing Lieberkühn's follicles and villi. *a.* Villi. *b.* Lieberkühn's follicles. *c.* Other coats of the intestine.

Fig. 132. One of the **INTESTINAL VILLI** with the commencement of a **LACTEAL**.

Fig. 133. A portion of the **MUCOUS MEMBRANE** of the **LARGE INTESTINE**, magnified seventy-five times. The alveoli measured 1-250th of an inch in length, by 1-450th in breadth; the septa between the alveoli measur-

ing 1-600th of an inch in width. The alveoli are less regular in form and shallower than those of the stomach; and in the bottom of each is a gland with a central excretory aperture. In some of the larger alveoli there are two glands.

Fig. 134. *A.* Transverse section of **LIEBERKUHN'S TUBES** or **FOLLICLES**, showing the basement-membrane and subcolumnar epithelium of their walls, with the areolar tissue which connects the tubes. *a.* Basement-membrane and epithelium, constituting the wall of the tube. *b.* Cavity or lumen of the tube. Magnified 200 diameters.—*B.* A single Lieberkühn's tube, highly magnified. A happy accidental section in the oblique direction has served to display very distinctly the form and mode of packing of the epithelial particles, the cavity of the tube, and the mosaic pavement of its exterior. *a.* Basement-membrane. *c.* Internal surface of the wall of the tube. Magnified 200 diameters.



FIG. 135.



FIG. 136.



FIG. 138.



Fig. 135. DISTRIBUTION of CAPILLARIES in the Villi of the Intestine.

Fig. 136. SOLITARY GLAND of SMALL INTESTINE. After Boehm.

Fig. 137. PART of a PATCH of the so-called PEYER'S GLANDS magnified, showing the various forms of the sacculi, with their zone of foramina. The rest of the membrane marked

FIG. 137.



FIG. 139.



with Lieberkühn's follicles and sprinkled with villi. After Boehm.

Fig. 138. BLOODVESSELS of an INTESTINAL VILLUS, representing the arrangement of capillaries between the ultimate venous and arterial branches; 1, 1, the arteries; 2, the vein.

Fig. 139. AIR-CELLS of HUMAN LUNG, with intervening tissues: *a*, epithelium; *b*, elastic trabeculae; *c*, membranous wall, with fine elastic fibres.



FIG. 140.

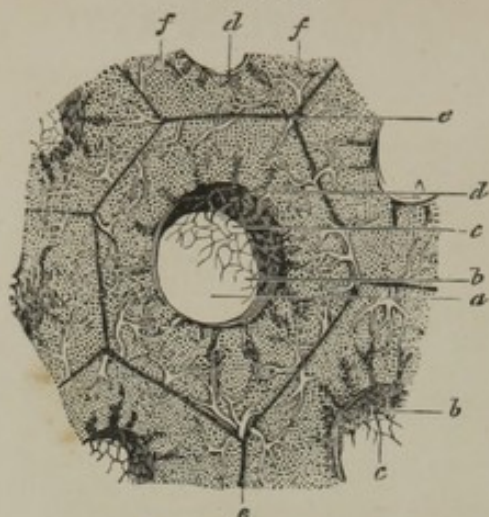


FIG. 143.

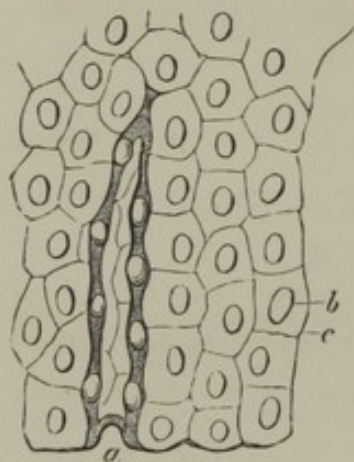


FIG. 144.



Fig. 140 Slightly oblique section through a BRONCHIAL TUBE, showing at *a* the cavity of the tube. *b* Its lining membrane, containing bloodvessels with large areolæ. *c, c*. Perforations in this membrane, where it ceases at the orifices of the lobular passages, *d, d*. *e, e*. Spaces between contiguous lobules, containing the terminal pulmonary arteries and veins supplying the capillary plexus, *f, f*, to the meshes of which the air gains access by the lobular passages.

Fig. 141. ARRANGEMENT of the CAPILLARIES of the AIR-CELLS of the HUMAN LUNG.

Fig. 142. A. SEPARATED EPITHELIUM-CELLS, *a*, with nuclei, *b*, and nucleoli, *c*, from mucous membrane of the mouth. B. Pavement epithelium of the mucous membrane of the smaller bronchial tubes: *a*, nuclei with double nucleoli.

Fig. 143. EPITHELIUM OF SEROUS MEM-

FIG. 141.



FIG. 142.

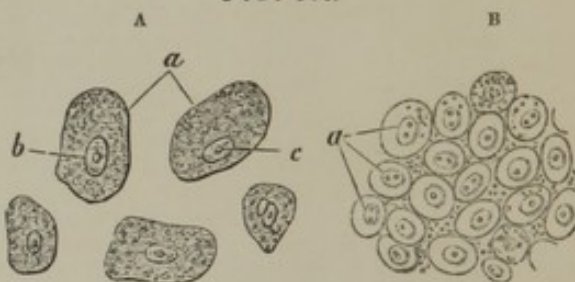


FIG. 145.



FIG. 146.



BRANE. At *a*, an accidental fold is represented, the two dark edges of which exhibit the thickness of the particles, and of their nuclei. *b*. One of the oval nuclei. *c*. Line of junction between two particles.—Magnified 300 diameters.

Fig. 144. A. EPITHELIUM detached, and free in the cavity of the duodenum, taken, immediately after death, from a dog fed 24 hours before. Each cell is filled with apparently fatty matter, partly granular and partly in globules. Magnified 600 diameters. B. The same, suffered to stay an hour or two under the microscope, showing the fatty material aggregated into larger globules, the rest of the cell-structure having become indistinct.

Fig. 145 EPITHELIAL CELLS IN URINE.

Fig. 146. PRIMARY ORGANIC CELL, showing the cell-membrane, the nucleus, and the nucleolus.



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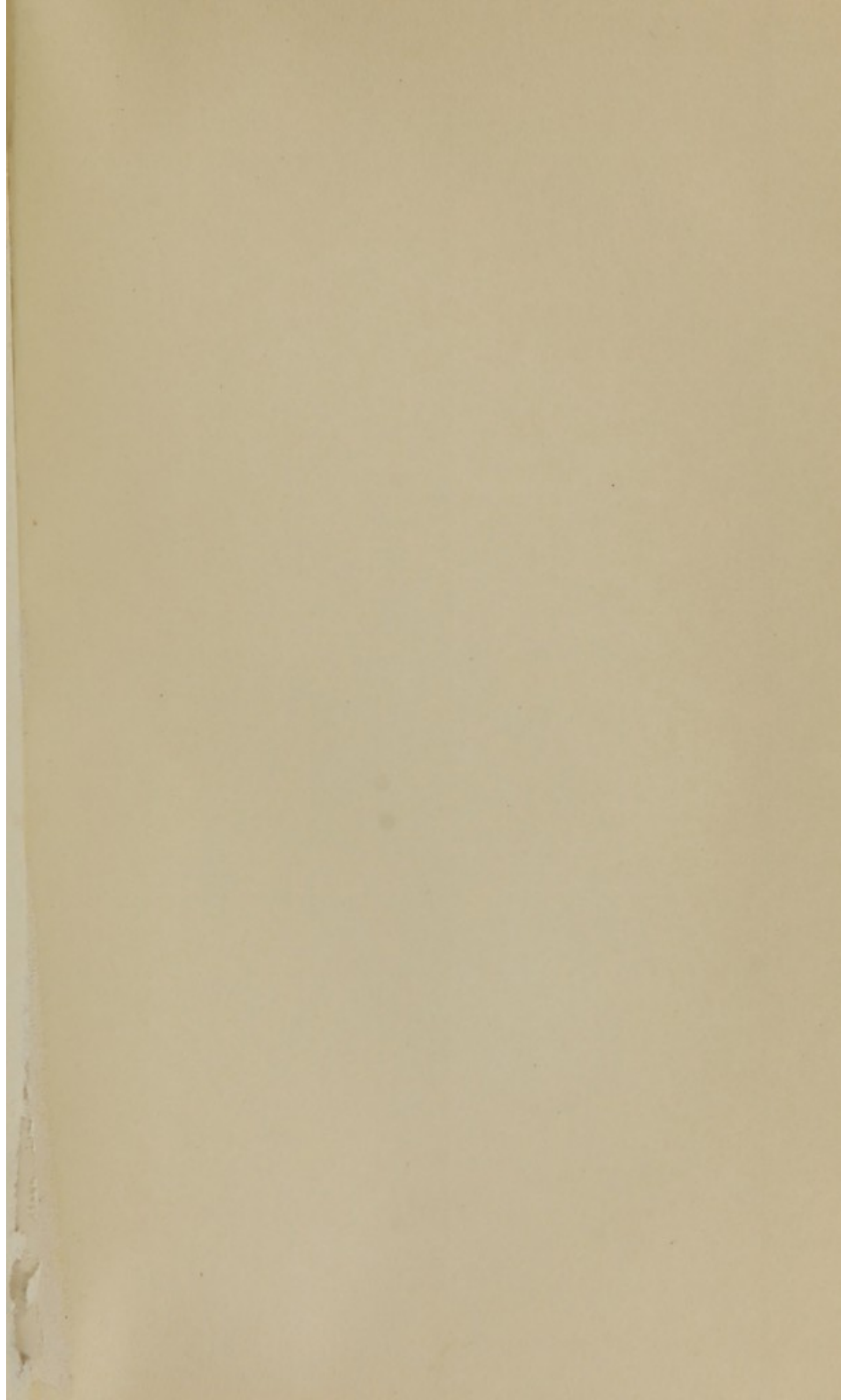
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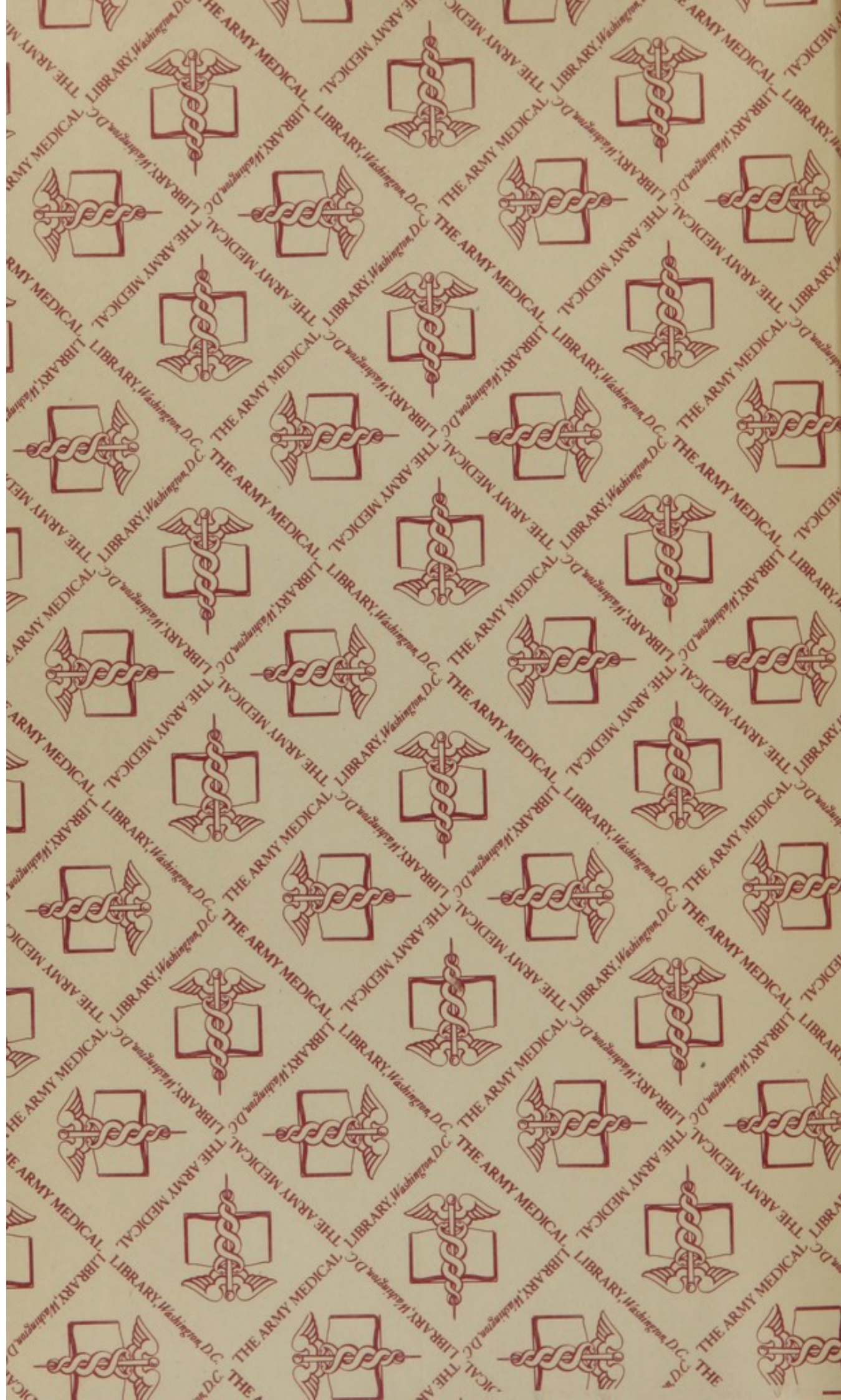
Dear Sir,  
I have the honor to acknowledge the receipt of your letter of the 10th inst. in relation to the matter of the  
and in reply to inform you that the same has been forwarded to the proper authorities for their consideration.  
I am, Sir, very respectfully,  
Your obedient servant,  
J. H. [Signature]

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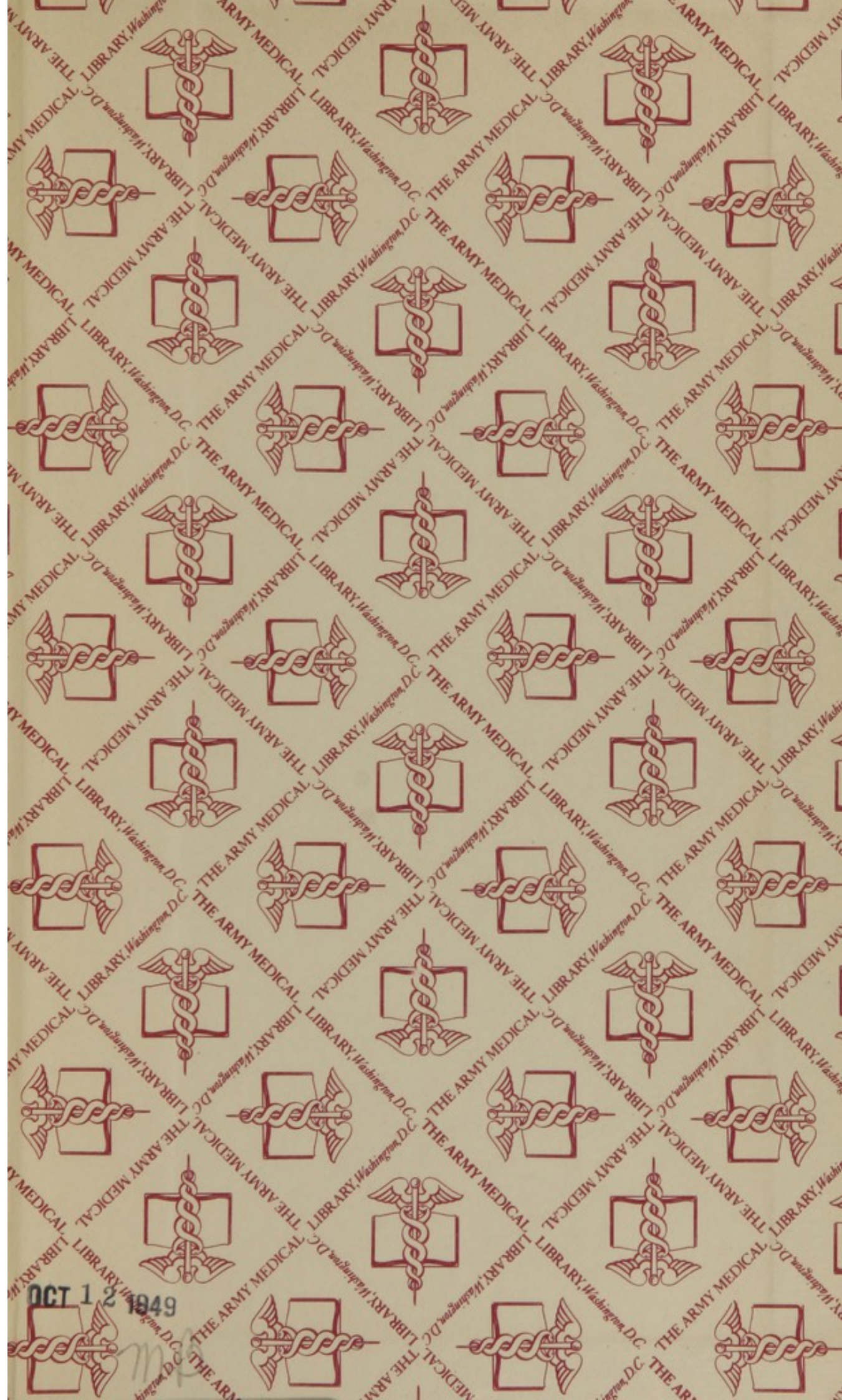












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