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AIDS TO

PHYSIOLOGICAL

CHEMISTRY

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AIDS

TO

PHYSIOLOGICAL CHEMISTRY.

BY

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PHYSIOLOGICAL CHEMISTRY.

GENERAL CONSIDERATIONS OF THE CHEMICAL CONSTITUTION AND PROPERTIES OF PROTOPLASM.

THE earliest formative nucleus which can be distinguished in the multiplication or increase of living beings by growth, and which acts as a circumscribed seat of organized power, has been termed *protoplasm*. Some observers have not inappropriately termed this formation *bioplasm*, and there is no objection to the concurrent use of both names, provided that they are symbols of one and the same definition. This must be borne in mind the more distinctly as the term protoplasm was formerly, and up to 1850, applied to a shapeless organic liquid or paste, not rarely identified with serum and lymph, from which the formed parts of living bodies were supposed to take their origin by a kind of spontaneous generation. Since, however, it has been shown that all *cells* so-called are products of the subdivision of previously existing cells, and do not originate in clear organic liquids, these latter are no longer termed protoplasmatic. Protoplasm is always a shaped material, consisting of solid and liquid matters at the same time; these are held together by a peculiar kind of chemical combination, which may be termed *colloidation*. Protoplasm is always differentiated into several parts, which are

chemically heterogeneous, but stand in organic relation to each other. Of these two at least are common to all kinds of protoplasm, namely, the matter forming the *nucleus*, which is highly phosphorized, and has been termed *nuclein* or cyto-phosphatide, and the matter forming the bulk of the protoplastic particle around the nucleus, and which has been termed *plastin*, and is in the main an albuminous substance become insoluble under the influence of vital action. The colloid particle of protoplasm, including the nucleus, is permeable to, and actually and constantly permeated by, a great number of organic and inorganic, *i.e.* mineral, chemical principles. These enter the protoplasm partly in obedience to what are called mere *physical forces*, such as osmosis, partly in obedience to *specific chemical attraction*, partly in obedience to attractions which are more complicated than either of the previous ones, and which have been termed *vital forces*. The entrance of the principles into the bioplastic laboratory affords the opportunity and material for the accomplishment of three kinds of action, which are the results of the fact that protoplasm is *living matter*, and which it cannot perform any longer after it is dead. These kinds of action are firstly *increase* and *maintenance* by coaptation of homogeneous matter; secondly, *production of force*, by the expenditure of matter already assimilated; thirdly, production of specific materials, such as secretion and excretion; and fourthly, the *storing of materials* for the contingent production of materials, or of force. Whether the chemical synthesis which results in the formation of organic bodies takes place within the colloid particle of the bioplasm itself only, or also in the juices which circulate within cavities formed by the bioplasm, or around it in particular channels, cannot at present be definitively decided. It is not impossible that the more simple compounds can originate outside the bioplastic particle, while the more complicated ones are exclusively formed within its mysterious

spongy hold. The increase or growth of the bioplasm is a function of its own, which it performs readily under given external conditions, particularly the influence of light and heat, in the presence, of course, of the necessary materials. The production of force is also a function of bioplasm itself, and as it can transfer the result of its growth by *division*, so it can part with its force by com-mutation or transfer to accumulators, or consumers, *i.e.*, converters of force. The processes of the changes of pro-toplasm, or of matters in contact with it, which result in the production of force, have been termed their *metabole ;* their tendency to change has been termed *metabolism.* Applicable as the terms are to synthetical as well as analytical transitions, it must be pointed out that in medical physiological nomenclature they are not rarely confined to the analytical or retrogressive, more specifically animal metamorphoses, which terminate in the production of relatively simple excretory matters. But there is no reason why the chemical changes which result in the production of bioplasm, in the production of force and the storing of materials, should not all be termed *meta-boles.* °

We have already compared bioplasm to a sponge filled with water, and in continuing this comparison we may liken that part of the sponge which remains when all water which can be pressed out by mechanical means is re-moved, to the residue of bioplasm which remains when it

* Some readers may think, as others have thought before, that the use of so many terms derived from an ancient, particularly the Greek language, was a needless call upon their power of comprehension and memory ; it is therefore well to inform such, firstly, that such terms are current in physiological science ; secondly, that they are convenient symbols of ideas, actions or things ; and thirdly, that with-out their use an expeditious application of the results of modern science to purposes of life would be almost impossible. We therefore advise our readers to make themselves well acquainted with all the technical terms in this guide ; they will find them the greatest aid to memory in the appreciation of facts which can be practically obtained.

is subjected to the utmost pressure. This residue, which is still combined with much water of colloidation, is termed the *stroma*, while the liquid removed by pressure is termed *enchylema*. Thus in red blood corpuscles the colouring matter or hemochrom forms the enchylema, while the stroma is colourless ; the hemochrom is soluble in or miscible with water, while the stroma is insoluble in water. If the blood corpuscles could be isolated, their red enchylema could no doubt be pressed out mechanically ; an approach to this demonstration is obtained by freezing the blood, in which case the stroma is so much contracted as to squeeze out its own enchylema, which then on thawing dissolves in the surrounding serum. The enchylema can be isolated from the stroma by pressure in the case of vegetable tissues more easily than in the case of animal ones ; but of the latter the bioplasm of glands and of muscles will admit of the easy demonstration of this separation ; some kind of cancerous and medullary tumours, which consist of bioplasm mainly, yield much enchylema, while the bioplasm of polypoid growths on mucous surfaces yields abundance. The pressure required to free a given bioplasm from all separable enchylema is not less than four thousand kilograms acting on a surface of one hundred square centimetres.

Bioplasm mostly contains, deposited in its meshes in a granular and therefore solid state, certain more simple chemical matters, such as *glycogen*, or *pigments*. Both can be seen in the liver-cells ; pigments in the ganglionic cells, and particularly distinctly in the cells forming the bioplasm of the corpora lutea of the ovary. *Fat* is also frequently contained in bioplasm in the form of minute oily drops. Some of these mechanical deposits are so finely divided that on the separation of the enchylema by pressure they pass in part through the filter and are found mixed with the enchylema ; for this reason the liquid is mostly somewhat turbid and opaque, with a white

yellowish or reddish tinge. These granular movable masses, whether solid or oily particles, contained in protoplasm are termed *microsomata ;* a single particle is a *microsoma.* These particles are distinct from the nuclei and nucleoli ; they not rarely congregate in zones, or, as in the cells of the choroid, cover the whole of one side of the bioplastic aggregate.

We can here consider the structural details of bioplasm only in so far as they aid us in finding out the places which particular chemical principles occupy in this organization. The questions such as whether the bioplasm effects the contraction which it exhibits by means of particular fibres crossing the element in various directions, or by a diffuse contractility inherent in it as a mass, we must leave to be discussed by physiology. Bioplasm is an *entity, an organism*, which admits of an anatomical and morphological, but not of a chemical definition. Its ingredients and products, however, and the nature of its morphoses, as apart from their shapes, can be studied and understood by the aid of chemistry alone. From a physical point of view bioplasm has been defined as *a material system having a specific configuration and specific motion.* From the chemical point of view it has been defined as *a mixture of numerous combustible and incombustible compounds.* But it is just the word 'mixture' which does not define the fact that the inter-penetration of the ingredients is not uniform, that some are fixed to distinct spots, while others can move freely, and that this distribution is determined by a specific structure. Moreover, the chemical composition of bioplasm is subject to ceaseless change : its ingredients are never in a state of equilibrium; the specific motions, though partly mechanical, are mainly chemical, and of such intensity that they have been termed ' vortices propelled by molecular tornadoes and atomic cyclones.'

Bioplasm possesses *irritability,* or a power to react in

answer to external influences by change of shape, contraction, by chemical action, or by the production of effects which, when perceived by consciousness, are termed sensations, but which also influence the body without the participation of consciousness. These effects are in all cases conveyed and distributed by the highest form which bioplasm is capable of assuming, namely *nerve-tissue*.

As the typical protoplasma we must consider the *contents of the ovum*, from which all other forms of bioplasm are derived. These derived forms develop specific properties, varieties of shape and of function, all of which are accompanied with chemical specificities of the most marked kind. Irritability is most developed in the nerve-bioplasm, contractility in the muscle-bioplasm; chemical metamorphosis is most developed in the bioplasm of glands. To each of these specific developments corresponds a specific chemical constitution of the more permanent elements of the bioplastic organisms. As it were, each kind of bioplasm undergoes a process of evolution, whereby it becomes fit for its specific function. There can be no greater contrast than that between the chemical constitution of nerves and that of muscles; but the contrasting features being deducted, those which remain are characteristic of mere general bioplasm. They are its *generally necessary constituents*. These constituents are identical in all protoplastic centres of animals and plants. The constituents which are found exclusively in certain kinds of bioplasm, and not in others, or in much greater quantity than in others, are the *specifically necessary constituents*. Those ingredients which may vary in every kind of bioplasm may be termed *the accessory constituents*. The specificity of chemical constitution involves a corresponding specificity of function. Whenever this function is the production of a force, the resulting chemical products are probably not specific, but when the function is the production of a matter, then it is mostly specific.

All bioplasm possesses the power of *chemical synthesis,* as well as *lysis.* The bioplasm of flowering plants has a wider power than that of animals in this, that under the influence of peculiar organs, which convert solar into chemical energy, namely, *the chlorophyll balls,* it can transform primary compounds, carbonic acid, water, ammonia, nitric acid, sulphuric acid, etc., into secondary and all higher compounds necessary for the entire organization of these plants. The bioplasm of animals, on the other hand, although possessed of great synthetic powers, as evidenced by the formation of hemochrom, the colouring matter of blood, does not form compounds from the same simple materials as plants do, but requires for its processes compounds of a certain complexity. On the whole, however, the animal bioplasm is formed out of vegetable bioplasm by a process of digestion and assimilation in which synthesis forms but a subordinate incident. Hence it may be said that the metabolism of flowering plants in sunlight is mainly *progressive, synthetical,* whereas the metabolism of animals, which is not influenced by sunlight in any direct way, is mainly *regressive* or *lytical.* The metabolism of flowering plants in darkness also becomes *regressive.*

By various analytical processes it has been shown that bioplasm contains the following essential ingredients :

1. A colloid albuminous matter, containing, besides the elements of albuminoids, some phosphorus ; this is termed *plastin.* 2. A matter constituting the nucleus principally, indigestible in artificial gastric juice, and containing much phosphorus, *cyto-phosphatide* or *nuclein.* 3. Several soluble albuminous substances, designated as *myosin, vitellin,* and *pepsin.* 4. Several substances possibly derived from albuminous ones, having alkaloidal properties, *pepton* and *peptonoid.* 5. Phosphorized matters (not being nuclein), being bodies of the *phosphatide* group ; *para-myelin,* in which phosphorus stands to nitrogen in the

proportion of 1 : 1, and *amido-myelin*, in which phosphorus to nitrogen = 1 : 2. (Phosphatides of the blood corpuscles of the ox ; these seem to be the only bodies of this rubric which have ever been analyzed.) 6. *Cholesterin, para-cholesterin*, or *phytosterin*, isomeric alcohols, or perhaps homologues. 7. Amides and amido-acids, in vegetable bioplasm particularly *asparagin*. 8. *Alkaloids*, of complicated structures ; mixed with these *hypoxanthin*, and simpler ones. 9. *Ammonia*, as carbonate. 10. *Fats* and *fatty acids*, from stearic down to formic. 11. *Starch, glycogen, sugar*. 12. *Resins, pigments*, and unascertained organic ingredients. 13. Mineral substances, *alkalies, alkaline earths, iron, manganese*, partly combined with organic substances, partly with *inorganic acids* or *halogens*. 14. *Water*. The amount of the latter varies between 70 and 80 per cent. of the bioplasm ; so that from 30 to 20 per cent. is the amount of the solid constituents. 15. *Carbonic acid, oxygen, nitrogen*. For the purposes of this calculation, and of the foregoing enumeration of constituents, stroma and enchylema have not been separated but considered together.

No kind of bioplasm can endure a temperature below 0°, or above 65°, without perishing. Animal bioplasm invariably dies when it is exposed to a temperature of 45°. The bioplasm of warm-blooded animals is more sensitive to heat as well as cold ; the human body cannot be cooled down many degrees below its normal temperature without perishing. This is well seen in *cholera*, of which disease all those affected die in whom the systemic temperature remains for a certain time below the average of normal temperature. On the other hand, the fatal effects of high febrile temperature are seen (*e.g.*), in enteric fever or in tetanus, of which disease all those affected die whose systemic temperature rises to between 42° and 45°.

Bioplasm requires for its existence the constant presence of *oxygen*. Plants develop oxygen by the reduction of

carbonic acid and water in sunlight, but animals require the oxygen to be brought to their bioplasm ready for use. In this respect the wants of bioplasm are the greater the higher is the animal of which it forms part.

Bioplasm shortly after death undergoes a change, which manifests itself as a kind of curdling or setting, whereby it loses its suppleness and becomes more dense and hard : this change in muscles is termed *rigor mortis*. In nerve matter the change is accompanied with a visible separation of the naturally homogeneous contents of the nerve-tube into a central unequally contracted cylinder and a matter filling the space between this cylinder and the tube-membrane. A similar process ensues in all bioplastic centres, or cells, and liver, spleen, and kidneys have their rigor mortis no less than muscles and brain.

During the specific evolution which bioplasm undergoes when adapting itself to the several formative ideas of the organism, it is structurally, chemically, and functionally modified in various ways. The earliest bioplasmatic entity is a little lump of gelatinous matter without any surrounding wall or membrane, and without any cavity. Many bioplasmatic formations, such as the cells of the liver and other glands, remain permanently without a limiting membrane. Others form a limiting membrane, particularly when, like ova, they are called upon to become centres of new action in new places. Others form limiting membranes for protection from the mechanical and chemical influences of the outer world. This protection involves in high and larger beings the conservation of a complicated shape. This shape, in every species of being, is entirely preserved, under the forcing direction of the organizing idea, by the mechanism of the encrustation of bioplasmatic particles by specific principles. By this incrustation the bioplasmatic organism becomes a *cell*. In plants the encrusting material is a *carbohydrate*, termed *cellulin* or *cellulose*. In animals the encrusting or cell-

covering material is mostly a *nitrogenized albuminous substance*. Some of the lower animals, such as the *tunicata*, contain yet cellulin in their tissues ; in the *articulates* the encrusting or limiting material becomes *nitrogenized, chitin ;* this body is a cellulin in which a few hydroxyls are replaced, one by *amide*, another by *acetyl*, and perhaps another by *formyl*. The cellulin base is still recognisable chemically in some of the limiting membranes of *reptiles*. By continued evolution the carbo-hydrate cellulin assumes such a complicated form, that its existence in the higher animals can only be assumed hypothetically as the basal radicle of organoplastic substances. As *starch* (*amylon*) is probably the product of the synthetic action of bioplasm immediately preceding the formation of cellulin, this and all similar and all more complicated principles from chitin upwards have been termed *amylonides*, and as far as they take part in the construction of organs, *organoplastic amylonides.**

While bioplasm possesses no limiting membrane, it can expand and contract according to its wants and accidents ; but when, by the formation of a limiting membrane, it is transformed into a *cell*, it becomes more or less rigid and incapable of expansion. But contraction or diminution of its bulk can and must still take place, and in that case are formed empty spaces, termed *vacuoles*. These spaces are not materially empty, but contain gas or liquid, not being protoplasm. By a development of the cell, which the student should follow through all its phases in his microscopical exercises, it is at last raised to an organism of marvellous complication. This the student should carefully and deeply study on an active segment of the *vallis-*

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* The reader will find the arguments and data for this consideration in an article in vol. i., p. 1, of the 'Annals of Chemical Medicine,' entitled : 'The Chemical Constitution of the Organoplastic Substances considered with the Aid of the Hypothesis of their Amylonide Nature.'

neria under the microscope. He will there see the limiting membrane of cellulin, the inner encrusting layers of nitrogenized and mineral matter and the nuclei, the balls of protoplasm carrying chlorophyll, the enchylema with and in which these balls ceaselessly rotate, the outer enchylema, which moves in a direction opposite to the inner, and at a much slower rate, without being separated from it by a membrane, and without mixing with it. He can see here conditions which no doubt obtain in all kinds of bioplasm, though owing to the absence of rapid motion they are not visible to the eye.

If the student then reflects on the beginnings and final results of the metabolism of life, he will perceive that bioplasm must at one time or another or in succession contain all the chemical principles which are the result of progressive and retrogressive biomorphosis. These principles are more numerous in plants than in animals. Some are identical in plants and animals ; some occur exclusively in plants, like chlorophyll ; some exclusively in animals, like hemochrom. Some, which occur in plants, though analogous or nearly related to those which occur in animals, are not identical with them. Of this latter kind are the albuminous substances of plants, which are so similar in their chemical properties to those occurring in animals, that they were formerly believed to be identical with them.

Bioplasm possesses the power of *storing materials as reserves* for future material development or production of power. Animal bioplasm possesses this power mainly with regard to *fats*, and in a much lesser degree with regard to *carbohydrates*. But vegetable bioplasm possesses the power of storing reserves in an eminent degree. These reserves consist of *albuminous matters*, *fats*, and *carbohydrates*, besides sundry other *organic and mineral matters*. They are deposited inside of the substance or cell of the bioplasm in a solid state, and when wanted for growth or

nutrition are fluidified and carried to the places where they are consumed.

When bioplasm constitutes organs in function it may be said to have completed its specific evolution. After that it is only capable of organic changes under the influence of morbific causes which arrive from without. Such changes are atrophy, hypertrophy by increase or deposition of useless reserve materials, deposition of useless products of regressive metabole, such as uric acid in combination, pigments in granules, and pernicious neoplastic growths, such as cancers.

CHEMICAL CONSTITUTION OF NEUROPLASM, OR BRAIN AND NERVE-MATTER.

THE brain as a whole may be considered as an aggregated mass of bioplasm, which derives its peculiarity mainly from specific chemical additions. The specifically developed bioplasm, which may conveniently be termed *neuroplasm*, is deposited in the form of *cells* and *fibres*, the cells being termed *ganglionic*, because they were first observed in nerve-ganglia, anatomically so-called. Those parts of the brain and spinal cord and nerves which contain such ganglionic cells are, as a rule, coloured by *pigments—black*, *red*, and *yellow*, single or mixed—which give to the whole tissue a pale reddish or grey appearance. These pigments are normally deposited within the cells as microsomata, and are the principal means by which *cellular neuroplasm* can be visually distinguished from *fibrillar neuroplasm*, or grey from white tissue. The chemical ingredients of grey tissue have preserved a greater resemblance to those of ordinary bioplasm, while those of white tissue differ most widely from it, as will be more fully shown below. For general purposes, the brain may be examined as a whole. It will then be found that it is *the most complicated chemical laboratory of the animal body*, and yields a great

number and variety of chemical educts, which are present in neuroplasm as *immediate principles*, and, therefore, not produced by the chemical processes and reagents. Their enumeration and summary description alone will require the utmost attention of the student; the functions of these bodies are still more difficult to comprehend, and will, therefore, only be alluded to in a summary manner. The ingredients of neuroplasm may be conveniently divided into several groups and subgroups, of which the most important are the following :

GROUP OF PHOSPHORIZED PRINCIPLES OR PHOSPHA-TIDES.

Subgroup of Mononitrogenized Monophosphatides:
$$N : P = 1 : 1.$$

Lecithins.
Kephalins.
Paramyelins.
Myelins.
(Sphingomyelic Acid, a product.)

Subgroup of Dinitrogenized Monophosphatides:
$$N : P = 2 : 1.$$

Amidomyelins.
Amidokephalins.
Sphingomyelins (Apomyelins).

Subgroup of Dinitrogenized Diphosphatides:
$$N : P = 2 : 2.$$

Assurin.

Subgroup of Nitrogenized Phosphatide-Sulphatides:

Cerebro-sulphatide, body from group of cerebrinacides, containing Phosphorus, Nitrogen, and Sulphur.*

* This might perhaps be the place for the classification of a body present in protoplasm (and probably in the ganglionic cells), and repeatedly isolated, which has been termed 'nuclein.' (See below : Gangliocytin, under albuminous substances.) Some analyses showed the presence of about 6·2 per cent. of P, and 15·98 per cent. of N ;

Subgroup of Non-nitrogenized Monophosphatides :
Lipophosphoric acid.
Butophosphoric acid.
(Kephalo-phosphoric acid, a product.)

GROUP OF NITROGENIZED NON-PHOSPHORIZED
PRINCIPLES.

Subgroup of Cerebrosides :
Phrenosin.
Kerasin.

Subgroup of Cerebrinacides:
Cerebrinic acid.
Sphærocerebrin.
Other principles **not yet defined.**

Subgroup of Cerebrosulphatides :
Cerebrosulphatide, body containing sulphur.

Subgroup of Amidolipotides, or Nitrogenized Fats :
Bregenin.
Krinosin.

Subgroup of Alkaloids :
Hypoxanthin.
Gladiolin.
Tennysin.

Subgroup of Amidoacids, Imides, and Urea :
Leucin and homologous principles.
Tyrosin.
Urea.

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or $P : N = 1 : 5·7$. But *all* the later analyses of the same inquirer only yielded 3·604 per cent. of P, and the percentage of nitrogen or of other elements is not stated. The student may therefore accept the statement, that nuclein is a phosphorized and nitrogenized matter contained in protoplasm, commonly but not exclusively in its nuclei, which is insoluble in artificial gastric juice, soluble in alkalies, and precipitated by acids, but has not as yet been obtained in an approximately chemically pure state.

GROUP OF PRINCIPLES COMPOSED OF THREE ELEMENTS ONLY.

Subgroup of Alcohols (*non-nitrogenized*) :
   Cholesterin.
   Phenosterin (?).

Subgroup of Carbohydrates :
   Inosite.
   Glycogen (?).

Subgroup of Organic Acids (*non-nitrogenized*) :
   Formic Acid.
   Sarcolactic Acid.
   Succinic Acid.
   Oxyglyceric Acid.

GROUP OF ALBUMINOUS SUBSTANCES.

Subgroup of Nitrogenized Sulphatide Phosphatides :
   Plastin.
   Gangliocytin (Cytophosphatide, a nuclein).

Subgroup of Nitrogenized Sulphatides :
   Albumen.
   Collogen.

GROUP OF INORGANIC PRINCIPLES.

This includes acids and bases and salts, either free or in combination with many of the foregoing organic principles.
   Sulphuric Acid.
   Hydrochloric Acid, and Chlorine in Chlorides.
   Phosphoric Acid.
   Carbonic Acid.

Potash
Soda
Ammonia
Lime
Magnesia
Copper
Iron
Manganese

in combination with immediate principles forming their bases, or in combination with phosphoric acid, and attached to immediate principles as phosphates, or in combination with mineral acids, as free mineral salts in the juices and extracts, *i.e.*, the enchylema.
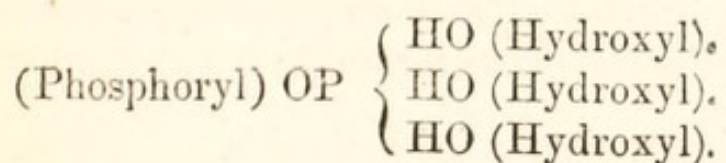
Alumina, Silica, Fluorine.

After this enumeration of the Groups, Subgroups, and Individual Principles constituting Neuroplasm, we proceed to a somewhat closer description of them, which will include their chemical definition and prominent properties. The student will find here a considerable amount of recently acquired information, and is, therefore, particularly invited to verify as many matters as he can by practical studies in the laboratory.

GROUP OF PHOSPHORIZED PRINCIPLES OR PHOSPHATIDES.

The group of the *phosphorized bodies* contains the phosphorus in the form of *phosphoric acid*, combined with from two to five *organic compound radicles*. As the earliest known body of this group, *lecithin*, yielded its phosphoric acid mainly in combination with *glycerol*, as *glycero-phosphoric acid*, it was supposed that the phosphorized bodies, of which a number were theoretically admitted to exist, were constituted, like the fats, by combination of compound organic radicles with the radicle of glycerol; in other words, that they were ethers of the alcohol glycerol, and contained the phosphoric acid as an inserted, and not as a fundamental radicle. But as we shall find in the following at least one phosphorized principle which does not contain any glycerol, and does, therefore, not yield, on chemolysis, any glycero-phosphoric acid, but phosphoric acid merely, without any attached organic
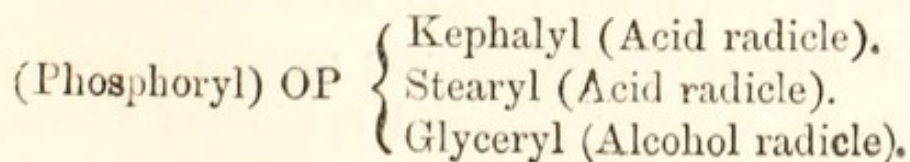
radicle, we thereby obtain a new insight into the chemical constitution of the phosphorized substances altogether, and are under the necessity of subjecting their theory to a revision. According to the result of this revision, the phosphorized substances are not glycerides at all, as commonly defined, and have nothing in common with fats considered as glycerides, except that some of them contain certain fatty acids, also present in fats, while they differ in physical and chemical properties widely from fats. In accordance with this new knowledge, we term the phosphorized substances *phosphatides,* that is to say, substances which are similar to (but not by any means identical with) phosphates, on the assumption that their basal, or principal joining radicle, is that of phosphoric acid, and that in this acid one, two, or three molecles of hydroxyl may be replaced by radicles of alcohols, acids, or bases ; and that to a molecle, formed by three such substitutions, there may yet be attached, either by substitution of an element in a radicle, itself already substituted (side-chain), or by addition with elimination of water from the added radicle, a fourth radicle, and that thus bodies of the following typical formulæ may be produced :

Phosphoric Acid.

(Phosphoryl) OP $\begin{cases} \text{HO (Hydroxyl).} \\ \text{HO (Hydroxyl).} \\ \text{HO (Hydroxyl).} \end{cases}$

Nonnitrogenized Phosphatide.

Example : *Kephalophosphoric Acid.*

(Phosphoryl) OP $\begin{cases} \text{Kephalyl (Acid radicle).} \\ \text{Stearyl (Acid radicle).} \\ \text{Glyceryl (Alcohol radicle).} \end{cases}$

Nitrogenized Phosphatide.

Example : *Lecithin.*

(Phosphoryl) OP $\begin{cases} \text{Oleyl (Acid radicle).} \\ \text{Margaryl (Acid radicle).} \\ \text{Glyceryl (Alcohol radicle).} \\ \text{Neuryl (Alkaloidal nitrogenized} \\ \quad \text{radicle).} \end{cases}$
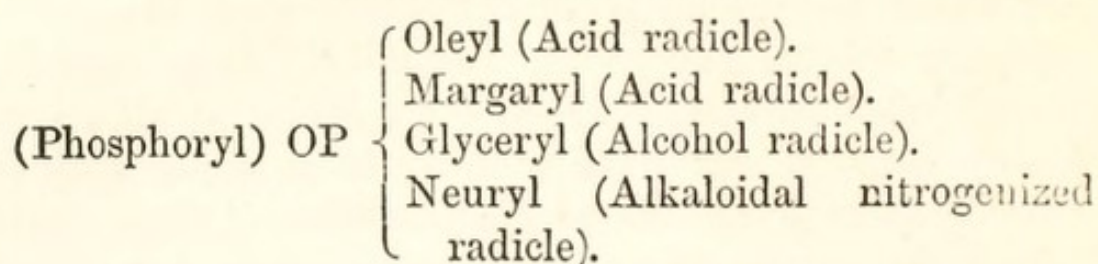
Dinitrogenized Phosphatide.

Example : *Amidomyelin.*

(Phosphoryl) OP $\begin{cases} \text{Acid radicle.} \\ \text{Alcohol radicle.} \\ \text{Alkaloidal nitrogenized radicle (sub-} \\ \quad \text{stituted).} \\ \text{Alkaloidal nitrogenized anhydride} \\ \quad \text{(attached as side-chain).} \end{cases}$
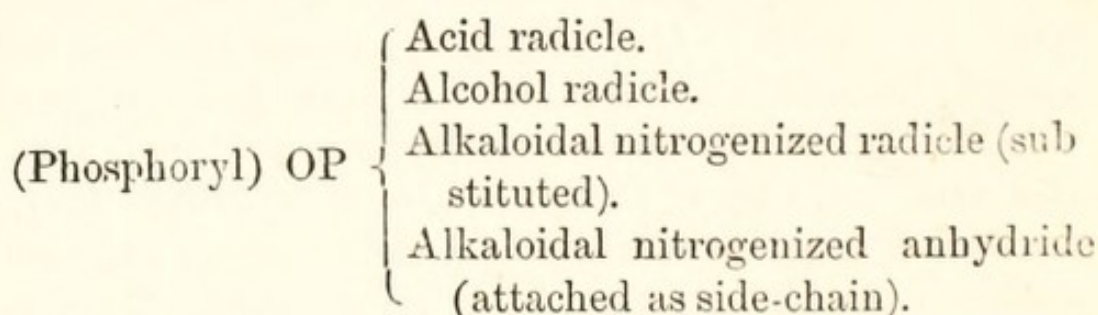
The bodies to which the foregoing formulæ may be applied contain the phosphorized radicle once, and may, therefore, be termed *monophosphatides ;* but there are present in the brain, and other protoplastic centres, bodies which contain the phosphorized radicle twice, and which may therefore be described as *diphosphatides ;* the immediate principle representing this subgroup contains about seven per cent. of phosphorus, and may perhaps be constituted according to the following formula :

Dinitrogenized Diphosphatide.

Example : *Assurin.*

$\left. \begin{array}{l} \text{Acid radicle} \\ \text{Alcohol radicle} \\ \text{Alkaloidal radicle} \end{array} \right\} \text{PO}-\text{OP} \left\{ \begin{array}{l} \text{Acid radicle.} \\ \text{Alcohol radicle.} \\ \text{Alkaloidal radicle.} \end{array} \right.$
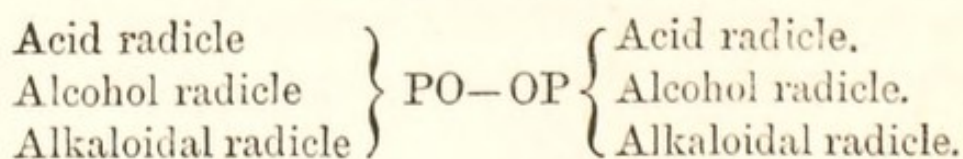
The subgroup of the Nitrogenized Phosphatide Sulphatides is not yet sufficiently studied to admit of a formula being given for any of its members.

After this definition of phosphatides, we proceed to the consideration of the several subgroups.

*Subgroup of Mononitrogenized Monophosphatides.*

In this subgroup nitrogen is to phosphorus in the proportion of one atom to one atom, a relation to be expressed by the formula, $N : P = 1 : 1$. Of the educts of the brain, four species, with all their varieties, belong to this subgroup, namely, the *lecithins, kephalins, paramyelins*, and *myelins;* a product also may be alluded to obtained from a dinitrogenized educt by the loss of a nitrogenized radicle, namely, *sphingomyelic acid.* This latter contains no glycerol; the lecithins and kephalins (and paramyelins probably) contain glycerol, and yield glycero-phosphoric acid; of the myelins, the constitution in this particular respect has yet to be ascertained.

Lecithin, originally obtained from and named after its occurrence in eggs, is only with difficulty evolved from the brain, on account not only of the many stages of the processes necessary for its isolation, but also on account of its readiness to decompose under certain conditions. This tendency is greatest in the presence of hydrochloric acid and platinic chloride, with which lecithin readily combines. It ceases almost entirely when lecithin is combined with cadmium chloride and the compound is dried. Lecithin crystallizes from concentrated solutions on long standing, but the crystals are only with difficulty freed from mother-liquid by pressure. Thus compressed, the crystals are wax-like. There are three lecithins known, all characterized by the presence of the radicle of oleic acid in their composition, namely :
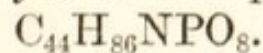
Oleo-palmito-glycero-neuro-phosphatide.

$$C_{42}H_{82}NPO_8.$$
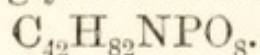
Oleo-margaro-glycero-neuro-phosphatide.
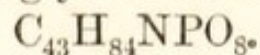
$$C_{43}H_{84}NPO_8.$$

Oleo-stearo-glycero-neuro-phosphatide.

$$C_{44}H_{86}NPO_8.$$

Of the second lecithin there have been analyzed the following salts :

Cadmium chloride salt : $C_{43}H_{84}NPO_8 + CdCl_2$.

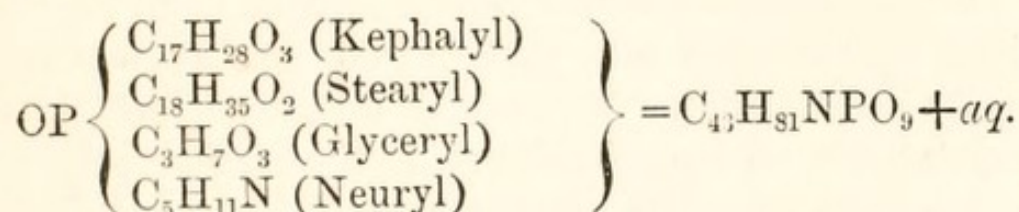Hydrochlorate : $C_{43}H_{84}NPO_8 + HCl$.

Platinic chloride hydrochlorate : $2(C_{43}H_{84}NPO_8 + HCl) + PtCl_4$.

In the chemolysis of lecithin, *oleic acid* is always obtained, and this is the acid which characterizes the phosphatide. It is by means of this radicle that it yields the purple reaction with sugar and oil of vitriol termed, after its discoverer, Raspail's reaction, and which, in its application to biliary acid, is termed Pettenkofer's test. Besides oleic, *margaric acid* is mostly obtained. The student should be aware that many chemists, after Heintz, maintain that margaric is identical with *palmitic acid*. But as regards this subject there is still some doubt, which has been strengthened by the discovery of the isomers of several known fatty acids, which make the diagnosis by melting points, upon which Heintz relied, very fallacious. The lecithins which yield palmitic and stearic acid occur in very small quantity only by the side of that which yields margaric acid. Besides these acids, the lecithins always yield glycero-phosphoric acid and neurin on chemolysis with baryta. The compound of lecithin with cadmium chloride is easily soluble in cold benzol, insoluble in ether.

Kephalin.—In the same manner as the lecithin species is characterized by the presence of the radicle of oleic acid, so the *kephalin* species is characterized by the presence of the radicle of a peculiar acid, to which I have given the name of *kephalic acid*. This acid is much more changeable than oleic, and imparts its quality to all the compounds in which it is present. The change in these cases seems to be either acquisitive, *e.g.*, by the accession of oxygen, or intra-molecular ; *e.g.*, by transposition of atoms, but does not lead to lysis into proximate nuclei so

easily as in the case of lecithin. The second fatty acid
radicle in the case of the principal kephalin, is *stearyl,*
other radicles in the place of stearyl occurring only in ex-
tremely small quantities. The members of this sub-group
vary in the amount of oxygen which they exhibit on
analysis, in a manner so as to be apparently sharply charac-
terized thereby as *oxykephalin* and *peroxykephalin.* But
this variability of the constituent oxygen may be transi-
tional. A kephalin may be defined as

Kephalo-stearo-glycero-neuro-phosphatide,

and represented by the formulæ—

$$\text{OP} \begin{cases} C_{17}H_{28}O_3 \text{ (Kephalyl)} \\ C_{18}H_{35}O_2 \text{ (Stearyl)} \\ C_3H_7O_3 \text{ (Glyceryl)} \\ C_5H_{11}N \text{ (Neuryl)} \end{cases} = C_{43}H_{81}NPO_9 + aq.$$

To be a kephalin a phosphatide must contain the radicle
kephalyl (or a homologue or isomer, whereby *kephaloidins*
result), which governs most of the properties of the com-
pound; its peculiar properties prevail over those of the
second acid.

Kephalin is easily soluble in ether, and precipitated from
this solution by alcohol, in which it is almost insoluble.
It combines with cadmium chloride, platinic chloride, lead,
and a number of acids and salts : all compounds are easily
soluble in ether ; the first three mentioned are insoluble in
alcohol ; the hydrochlorate is easily soluble in alcohol.

The first decomposition product of kephalin by chemo-
lysis is *kephalophosphoric acid,* which has already been
mentioned under the non-nitrogenized monophosphatides.
It may be considered as kephalin which has lost its neurin
and taken up a molecle of water. By further chemolysis
this acid yields the three others of which it is composed,
namely *kephalic, stearic,* and *glycerophosphoric acid.*

Kephalic acid is a fatty acid which changes rapidly in

the free state, and becomes brown. All its salts are soluble in ether, insoluble or little soluble in alcohol ; they are brown precipitates. It has not yet been possible to remove this brown colour from acids or salts by any process. It is for this reason that the formula of the free acid is most difficult to determine.

The *stearic acid* obtained from kephalin is the ordinary stearic acid of melting-point 69·5°, and yields the ordinary salts. It is necessary to bear this in mind, as we shall make the acquaintance of several *isomers* of stearic acid, which have melting points and properties by which they differ greatly from the acid just alluded to.

Glycerophosphoric acid can be isolated from kephalin as lead salt, calcium salt, $C_3H_7CaPO_6$, and as *acid calcium salt* $C_6H_{12}CaP_2O_{12}$; as barium salt, $C_3H_7BaPO_6$, which crystallizes on long standing, as the similar calcium salt crystallizes when its concentrated solution is boiled ; the acid barium salt, composed similarly to the acid calcium salt, when precipitated from its solution by alcohol, retains at least three molecles of alcohol and six of water, which cannot be removed by pressure ; the powdery compound is therefore an *alcoholo-hydrate*.

The nitrogenized radicle of kephalin by chemolysis appears as *neurin*.

Paramyelin.—The third subdivision of this subgroup is represented by *paramyelin*, a phosphatide which contains (probably) *glyceryl*, *neuryl*, and an *oleocholide radicle* (of a fatty acid) hitherto unknown. It strikes, with oil of vitriol and sugar syrup, an immediate deep purple colour ; the mixture of acids obtained by chemolysis does the same in a more intense manner. Paramyelin is a white, firm, solid body, crystallizing from boiling spirit in plates and needles. In the presence of lecithin it is much more soluble in ether and alcohol than by itself, and it can be separated from lecithin only partially by crystallization. But it combines with cadmium chloride, and the solubility

of this compound in hot benzol, and its insolubility in cold, afford facilities on the one hand for its separation from lecithin, the cadmium chloride compound of which is soluble in cold benzol ; on the other hand of its separation from amidomyelin cadmium chloride, to be described below, which is insoluble in both hot and cold benzol.

Paramyelin has probably a composition expressed by the formula $C_{40}H_{80}NPO_9$; the direct analyses give a little less carbon, and have to be controlled by chemolyses. Besides the cadmium chloride salt, paramyelin gives a hydrochlorate platinic chloride compound.

Myelin.—While lecithin and paramyelin exhibit mainly alkaloidal functions, and kephalin shows alkaloidal and acid functions, the fourth species of the non-nitrogenized monophosphatides, the *myelins*, exhibit mainly acid properties. The representative *myelin* is a firm compound, and combines with lead like a dibasic acid, that is to say, admits a didynamic atom of lead in place of two atoms of hydrogen. On the other hand, it does not combine with cadmium chloride as do lecithin, kephalin, paramyelin, amidomyelin, and sphingomyelin. This peculiarity seems to indicate a peculiar constitution, of which, without exhaustive chemolyses, no account can be given, but which may be such as to necessitate the separation of myelin from the other three members of this subgroup, and its allocation to a subgroup of which it would be the peculiar representative. The most probable formula of *myelin* is $C_{40}H_{75}NPO_{10}$; that of its lead salt $C_{40}H_{73}PbNPO_{10}$. As there are several varieties of lecithin and kephalin, so there may possibly be varieties of paramyelin and myelin varying in carbon from 38 to 44 atoms.

Subgroup of Dinitrogenized Monophosphatides.

In this subgroup nitrogen is to phosphorus in the proportion of two atoms to one atom, a relation to be expressed by the formula N : P = 2 : 1. Of the educts of the brain three species, with all their varieties, belong to this sub-

group, namely, *amidomyelin*, *apomyelin*, and *sphingo-myelin*.

Amidomyelin.—This principle is analogous to apomyelin and sphingomyelin by this, that the two atoms of nitrogen are disposed in two different radicles, and influence the character of the compound so that it presents itself as a diacidic base or a dipolar alkaloid. In the latter quality it combines with cadmic chloride in two ratios, the fully saturated compound, which is that most commonly obtained, containing a little more than 30 per cent. of cadmium chloride.

Amidomyelin has been proved to exist in five forms, one of isolation, four of combination.

Amidomyelin - - -	$C_{44}H_{88}N_2PO_9$
Amidomyelin hydrochlorate	$C_{44}H_{88}N_2PO_9 + HCl$
Amidomyelin monocadmium chloride - - - -	$C_{44}H_{83}N_2PO_9 + CdCl_2$
Amidomyelin dicadmium chloride - - - -	$C_{44}H_{88}N_2PO_9 + 2(CdCl_2)$
Amidomyelin hydrochlorate platinic chloride -	$2(C_{44}H_{88}N_2PO_9 + HCl) + PtCl_4$

Amidomyelin crystallizes in white needles and plates. It is little soluble in ether and cold alcohol, very soluble in hot alcohol. It is isolated by the insolubility of its saturated cadmium chloride compound in benzol. Its cleavage products by chemolysis have not yet been examined.

Sphingomyelin.—This is the most complicated body of this sub-group ; in the course of its isolation and study conditions of the utmost difficulty and complexity are met with, arising mainly from *homology* and *isomerism*. Thus one product of its chemolysis is a fatty acid of the composition expressed by the formula $C_{18}H_{36}O_2$, being the *third isomer of stearic acid*, termed *sphingostearic acid*, fusing at 57°, therefore at almost the same interval below, as the second isomer of stearic acid, namely, *neurostearic acid*, fusing point 84°, fuses above the fusing point of

ordinary stearic acid, which latter melts at 69·5°. It is evident from this that henceforth a fatty acid from the brain can be diagnosed neither by its elementary composition alone, nor by its melting-point alone, but that a knowledge of both is required to approximately fix its nature ; an accurate diagnosis requires the knowledge of all physical and chemical properties and of reactions.

How wonderfully the phenomenon of isomerism complicates brain chemistry and biological chemistry in general will become still more apparent by the following. Another product of the chemolysis of sphingomyelin is an alcohol, *sphingol*, of the empirical formula $C_9H_{18}O$, or $C_{18}H_{36}O_2$, which, on the supposition that the latter formula expressed its atomic weight, would be *the fourth isomer* of stearic acid.

A third product of the chemolysis of sphingomyelin is *an alkaloid* closely resembling the *sphingosin* of the cerebrosides, to be described below, $C_{17}H_{35}NO_2$, but showing a little more carbon and hydrogen. To these three radicles a molecle of *neuryl*, $C_5H_{11}O$ is yet attached.

The typical sphingomyelin crystallizes well in microscopical plates, combines with cadmium chloride in two ratios, the compounds being crystalline, and gives up one nitrogenized radicle on limited chemolysis, namely, the loosely bound neuryl, as neurin, $C_5H_{13}NO$, leaving an acid which contains all the phosphorus of the sphingomyelin together with half the original nitrogen, and in which therefore $N : P = 1 : 1$. The formula of the acid, a produced mononitrogenized monophosphatide, from the C_{53} sphingomyelin, is $C_{48}H_{95}NPO_{12}$, and its name *sphingomyelic acid*.

The direct analyses of sphingomyelin lead to the formula $C_{52}H_{104}N_2PO_9 + H_2O$, but its fully saturated cadmium chloride compound showed formula $C_{51}H_{99}N_2PO_{10} + 2(CdCl_2)$. The theory derived from chemolysis leads to a somewhat higher formula with 58 carbon. Seeing that

apomyelin possesses 54 carbon, it is not impossible that there are several sphingomyelins, differing in their carbon, just as the other phosphatides do, owing to their containing different fatty acids.

Sphingomyelin does not yield glycerophosphoric acid on chemolysis, but *phosphoric acid* only by the side of the organic radicles indicated. It is therefore the main support of the theory of the phosphatides which has been given above.

Apomyelin.—This body has the formula $C_{54}H_{109}N_2PO_9$, and forms a hydrochlorate platinic chloride compound.

The diamidated phosphatides all yield *hydrochlorates*, which crystallize from appropriate solvents in the absence of water, and in presence of excess of hydrochloric acid, in exquisite form and purity; but they are not stable in the presence of watery reagents, and yield hydrochloric acid to solvents at every recrystallization, so as to become almost free from the acid by mere repetition of the process.

Subgroup of Dinitrogenized Diphosphatides.

Of this subgroup only one representative is at present known, namely, *assurin*, which in its platinum chloride compound has the formula $C_{46}H_{94}N_2P_2O_9$. It is at present the most *phosphorized body* of this entire group known, its precentage of that element being higher than the percentage in some kinds of nuclein according to the best analyses. Assurin is not precipitated by either lead salts or cadmium chloride, but is precipitated by platinum chloride.

The Subgroup of Nitrogenized Phosphatide Sulphatides is at present not sufficiently studied to admit of definition by formulæ. The representative body, *cerebrosulphatide*, is isolated from the group of *cerebrinacides*, to be described below. Like these, it combines with lead and baryta, and is therefore *an acid*.

The Subgroup of Nonnitrogenized Monophosphatides

is illustrated by a product from kephalin already alluded to, namely, *kephalophosphoric acid*. To this group belong two acids which are found in brain extracts, and which are respectively termed *lipophosphoric* and *butophosphoric acid*. They combine with lead, and can be easily isolated, but are not sufficiently studied to admit of further description.

It is clear from the foregoing that the phosphorized bodies of neuroplasm are many in number, of greatly varying chemical constitution and function, and it will be shown hereafter that they are specifically concerned in the most intimate parts and processes of protoplastic life. Their general properties are very remarkable. Thus, the presence of water diminishes the number or avidity of affinities in all phosphatides ; it combines itself with these bodies in a peculiar manner, by which they show their character as *colloids*, and it afterwards dissolves them, some like amidomyelin in a perfect, others like lecithin in a peculiar and imperfect manner. Some are made insoluble in water by heat, like amidomyelin, the clear watery solution of which begins to curdle at a temperature below that of the highest fever heat, and at a temperature from 42° to 45° becomes entirely gelatinized. Some are made more dense by heat, and swell and diffuse again on cooling. Some are so sensitive that they can be made to exhibit the change to the eye, and may then be said to be eminently *thermoscopic*.

The phosphatides easily combine with acids, alkalies, and salts, and these combinations are as easily destroyed by the influence of water. The phosphatides therefore possess alkaline affinities (for acids), acid affinities (for alkalies), and alkaloid affinities (for salts) ; all these affinities are overcome by water in quantity, but the affinities for water of some of them are overcome by some metallic oxides, such as of lead, copper, manganese, iron, and even to a slight extent by lime and potash ; these latter compounds

are dissociated only by strong mineral acids, and the compounds can then be dialysed out. All other combinants separated by water alone can be completely removed from the phosphatides by dialysis on vegetable parchment. By their physical properties the phosphatides are principally instrumental in maintaining the mechanical structure of neuroplasm, and by their chemical qualities they are the principal agents for the atomic changes which result in the production of power.
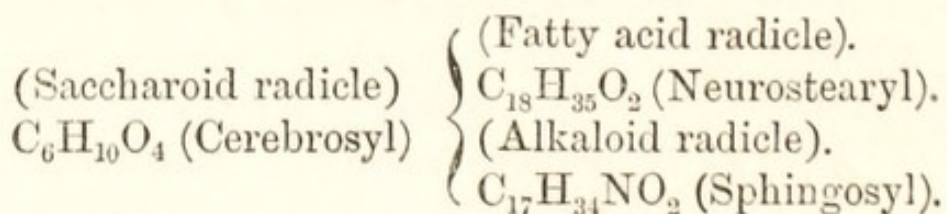
GROUP OF NITROGENIZED NONPHOSPHORIZED PRINCIPLES.

This group includes six great subgroups, of which the first four have a greater number of features in common, while the two last subgroups are dissimilar to the former, and much more simple as regards chemical constitution.

Subgroup of Cerebrosides.

The *cerebrosides* are characterized by containing a peculiar sugar, *cerebrose*, in which different radicles of acids and alkaloids (it is not known whether of alcohols also in some cases) are inserted. Thus of *phrenosin*, $C_{41}H_{79}NO_8$, the definition and formula of constitution are the following :

Neurostearo-Sphingoso-Cerebroside.

(Saccharoid radicle) $C_6H_{10}O_4$ (Cerebrosyl)
$\left\{\begin{array}{l}\text{(Fatty acid radicle).}\\ C_{18}H_{35}O_2 \text{ (Neurostearyl).}\\ \text{(Alkaloid radicle).}\\ C_{17}H_{34}NO_2 \text{ (Sphingosyl).}\end{array}\right.$

The derivates of phrenosin by chemolysis and synthesis of products are the following : *Cerebrose*, a crystallized sugar, isomer of glucose, and like this dextro-rotatory, reducing copper solution, and tasting sweet, of formula $C_6H_{12}O_6$; *Neurostearic acid*, an isomer of stearic acid, fusing at 84°, of formula $C_{18}H_{36}O_2$; *Neurostearic ether*,

$C_{20}H_{40}O_2$, or $(C_2H_5)C_{18}H_{35}O_2$, produced during chemolysis of phrenosin in alcohol by sulphuric acid ; can be distilled unchanged in vacuo ; *Sphingosin*, an alkaloid, $C_{17}H_{35}NO_2$, gives the purple oleocholide reaction with canesugar, or cerebrose, and oil of vitriol ; as *sulphate*, $2(C_{17}H_{35}NO_2)$ H_2SO_4, insoluble in absolute alcohol ; as *hydrochlorate*, $C_{17}H_{35}NO_2,HCl$, soluble in water ; *Psychosin*, $C_{23}H_{45}NO_7$, being the *cerebroside of sphingosin*, a body having alkaloidal properties, but less pronounced than those of sphingosin ; *Æsthesin*, a compound of sphingosin and neurostearic acid, less water, $C_{35}H_{69}NO_3$. Under the influence of heat *phrenosin* yields a *caramel*, $C_{41}H_{71}NO_4$, by the loss of four molecles of water ; by a similar reaction *psychosin* also yields a *caramel*, of the formula $C_{23}H_{37}NO_3$; these caramels are brown, insoluble in spirit, soluble in ether.

Kerasin.—Accompanying phrenosin is a cerebroside, which has been termed *kerasin ;* it may possibly comprise a number of analogously constituted bodies, of which the most probable formulæ are, $C_{42}H_{83}NO_8$, $C_{44}H_{89}NO_8$, and $C_{46}H_{92}NO_9$. It has yielded by chemolysis *cerebrose*, *psychosin* as sulphate, and fatty acids of the general formula $C_nH_{2n}O_2$, which latter have not yet been reduced to simple forms. Both phrenosin and kerasin are neutral bodies, and do not combine with acids, alkalies, or salts in stoichiometric proportions. While phrenosin crystallizes in characteristic rosettes, kerasin crystallizes from hot spirit in microscopic filamentous needles, which are very voluminous, and enclose mechanically great volumes of spirit. While phrenosin is deposited from alcohol above 28°, kerasin, when its solution does not exceed a certain degree of concentration, remains in solution at 28°, and is only deposited gradually below that temperature. This bearing affords a means for the separation of these bodies.

Subgroup of Cerebrinacides.

The *cerebrinacides*, or cerebrin bodies which combine with lead and other bases, are as yet little known, not only because they are numerous and difficult to separate from each other, but also because they occur mixed with the *sulphurized bodies*, to be placed in the next subgroup. It is probable that the first cerebrinacide to be considered, namely, *cerebrinic acid*, may be a cerebroside in which three hydroxyls are replaced (in phrenosin and kerasin only two hydroxyls are replaced), two by fatty acid radicles, one by an alkaloid radicle. Whether others of the cerebrinacides are cerebrosides can at present be neither asserted nor denied. Several of the cerebrinacides, which have been isolated, such as *spherocerebrin* and the (according to quantity) *principal cerebrinacide*, are distinguished from the cerebrosides and cerebrinic acid by their containing a much larger proportion of oxygen than these bodies. The following is a synopsis of these bodies as far as they are isolated, together with their preliminary empirical formulæ :

Cerebrinic acid - - -	$C_{59}H_{113}NO_9.$
Caramel of Cerebrinic acid -	$C_{59}H_{105}NO_5.$
Spherocerebrin - - -	$C_{53}H_{123}NO_{17}.$
Cerebrinacide, principal - -	$C_{55}H_{113}NO_{21}.$

There are a number of subordinate cerebrinacides waiting for closer investigation.

Subgroup of Cerebrosulphatides.

Of this group hardly more than the existence is demonstrated. The most concentrated preparation of *cerebrosulphatide* which could be produced contained 4 per cent. of sulphur. It combines with lead and baryta.

Subgroup of Amidolipotides, or Nitrogenized Fats.

The members of this sub-group are so constituted, and exhibit such properties, that they may be described as

nitrogenized fats, or amidolipotides. Although they occur mixed with the cerebrosides, nevertheless they are at once demonstrated not to be such by the low amount of oxygen which they contain. Of these the first is *bregenin* (from the Low German word ' bregen,' head or brain), which is easily soluble in cold ether, crystallizes, and has the formula $C_{40}H_{81}NO_5$. The second one is *krinosin* (from the Greek word for hair, the wavy crystals resembling a mass of tangled long hair), $C_{38}H_{75}NO_5$, insoluble in cold, easily soluble in boiling ether. Homology of these bodies, which is suggested by a comparison of the formulæ,

Bregenin $C_{40}H_{81}NO_5$,
Krinosin $C_{38}H_{77}NO_5$,
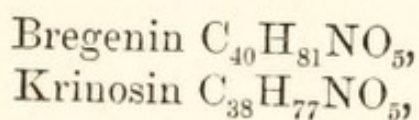
may not be assumed, as the one with the higher number of carbon atoms fuses at a much lower temperature than the one with the lesser number of carbon atoms.

Subgroup of Alkaloids.

Of the bodies belonging to this subgroup, *hypoxanthin,* $C_5H_4N_4O$, is isolated with the greatest precision. It yields the well-known compounds with hydrochloric acid and platinic chloride, with nitric acid, silver nitrate, and silver. Whether it is produced in the brain as a free principle dissolved in the enchylema, or becomes detached from principles with which it is also found combined, cannot at present be ascertained.

The other alkaloids contained in the brain are either much more complicated or more simple than hypoxanthin ; The second alkaloid is *gladiolin,* and exhibits a composition expressed by the formula $C_{15}H_{20}N_6O_5$, while its gold compound is $C_{15}H_{20}N_6O_5,HCl,AuCl_3$, or a hydrochlorate gold chloride. The third alkaloid, *tennysin,* has the formula C_3H_5NO.

Subgroup of Amidoacids, Imides, and Urea.

The *amidoacids* and *imides*, represented by *leucin*, $C_6H_{13}NO_2$, *tyrosin*, $C_9H_{11}NO_3$, and related principles, are isolated from brain in extremely small quantities only. *Urea*, CH_4N_2O, is found in the brain and cerebro-spinal fluid, particularly in disease. In cases of *cholera*, the cerebrospinal fluid has been found to contain as much urea as healthy human urine—namely, about 2 per cent.

GROUP OF PRINCIPLES COMPOSED OF THREE ELEMENTS ONLY.

Subgroup of Alcohols (Nonnitrogenized).

The alcohols have very slight combining power. The most prominent of them, as regards both quantity and appearance, is *cholesterin*, $C_{26}H_{44}O$. As an alcohol it is monodynamic, and if it did combine with acid radicles naturally, would therefore give rise to one class of ethers only.

Some data seem to point to the existence of a second alcohol by the side of cholesterin and isomeric with or homologous to it. A cholesterin is sometimes found fusing at 137°, the point at which some earlier writers supposed all cholesterin to fuse. But since the fusing-point of the principal cholesterin is certainly 145° the lower fusing-point may belong to the supposed isomer or homologue, and this latter may be termed *phrenosterin*.

A third kind of cholesterin occurs in plants, *e.g.*, seeds, and is termed *phytosterin*.

Subgroup of Carbohydrates.

The bodies which may conveniently be considered under this subgroup are *inosite*, $C_6H_{12}O_6$, an isomer of dextroglucose, originally discovered in, and bearing its name from muscle, and *glycogen*, of which the three varieties have the formulæ $C_6H_{10}O_5$, $C_6H_{12}O_6$, and $C_6H_{14}O_7$. The

inosite from the human brain seems to be somewhat different from that of the ox brain ; for the latter easily gives a compound with cupric oxide of the formula $C_6H_{12}O_6 + 3CuO + 3H_2O$, while human inosite gives no such precise combination, and reacts with cupric acetate in a peculiar manner. Some have supposed inosite to be the material from which, by a post-mortem change, the lactic acid of the brain takes its origin. But since it has been shown that inosite by ferments yields ordinary zymolactic acid, whereas the lactic acid of the brain is always and exclusively the optically active paralactic or sarkolactic acid originally discovered in flesh, this hypothesis has become obsolete.

Glycogen occurs in the neuroplasm of young animals.

Subgroup of Organic Acids (Nonnitrogenized).

The subgroup of *Nonnitrogenized Organic Acids* is represented by at least four different principles—*formic acid*, CH_2O_2 ; *sarkolactic acid*, $C_3H_6O_3$; *succinic acid*, $C_4H_6O_4$; and *oxyglyceric acid*, $C_3H_8O_4$. Formic acid is present in such small quantity only that it can just be recognised. But sarkolactic acid occurs in quantities up to 1 per mille of the fresh brain substance.

GROUP OF ALBUMINOUS SUBSTANCES.

Subgroup of Nitrogenized Sulphatide Phosphatides.

The albuminous ingredients of neuroplasm are of two kinds—soluble and insoluble. The subgroup here to be considered consists of the insoluble principles, which remain when all soluble ones are extracted. *Plastin* is the material of which the stroma of neuroplasm is principally constructed. It is mechanically mixed with the *cytophosphatide* which has been variously named *nuclein* or *gangliocytin*. Of plastin little is known, except that it is the least soluble of the matters of this subgroup.

Gangliocytin is soluble in alkali and precipitated by acid. It contains phosphoric acid, and the elements of an albuminous substance in such proportions that some have considered it to be an albuminous phosphatide.

Subgroup of Nitrogenized Sulphatides.

Albumen is present in neuroplasm in a soluble state in small quantity. *Collogen* is present as the companion of the blood-vessels which pervade the brain ; but it is not proved that collogen is a constituent of pure neuroplasm. These matters yield many or all of the cleavage products which are obtained from albuminous substances by chemolysis.

GROUP OF INORGANIC PRINCIPLES.

The *inorganic ingredients* or *mineral substances* of the brain are distributed amongst its juices and solid ingredients in a very remarkable manner. These bodies were formerly studied by means of analyses made on materials obtained by combustion of the brain as a whole. This proceeding had two sources of fallacy connected with it, which greatly diminished the value of its results. In the first place, the phosphoric acid produced by the destruction of the phosphatides (in which, of course, phosphoric acid is in *organic* combination) was calculated as *mineral* phosphoric acid, it being found partly in combination with bases, partly free. Owing to its being in excess over the whole saturating power of the bases, it expelled all volatile acids, such as carbonic, and sulphuric, and chlorine, and was not even itself entirely preserved from the reducing influence of the glowing charcoal, which volatilized a portion of it as phosphorus. This inconvenience was only partially avoided by the use during combustion of caustic baryta or barium nitrate. In fact, by no method as yet proposed could *the sulphur* or *phosphorus in organic combination* be kept separate from that in *inorganic combination.*

Some progress has, however, been made by the separation of the soluble educts from the insoluble ones, and from the interstitial juices or enchylema; and as each of these complex substances retains mineral matter peculiar to itself, while the phosphatides can be almost completely excluded by precipitation with acid from their solution or suspension in water, it is feasible to obtain by a minimum of three sets of analyses some insight into the nature and distribution of the mineral ingredients of the brain. The elements which enter into their composition are :—

Metals.—Sodium, Potassium (Ammonium), Calcium, Magnesium, Iron, Manganese, Copper.

Metalloids.—Chlorine, Sulphur, Phosphorus, Carbon, Oxygen, Hydrogen, Fluorine.

CHEMICAL CONSTITUTION OF MYOPLASM, THE SUB-STANCE CONSTITUTING STRIPED AND SMOOTH MUSCULAR FIBRES.

IN the chemical consideration of muscle, the student has to bear in mind that each muscular fibre is a morphological as well as a chemical unit, or a bioplastic individuality in the sense which has been defined in the general consideration of protoplasm. Although, therefore, the ingredients must be separated, and defined, and considered separately, it is necessary to supply by thought the power of cohesion and coaction by which they remain and perform together as if they were one substance in the chemical sense. We proceed, in the first instance, to consider the striped muscular fibre. It is necessary for us to avoid all discussion of intricate microscopical structure, beyond that which is supported by microchemical reactions.

The muscular fibre, then, consists of a homogeneous membranous bag, or sheath, termed *sarkolemma,* and of *contractile matter* arranged in thin layers inside the sarkolemma, the *flesh-discs.*

The sarkolemma is composed of a material which has elastic properties, unlike connective tissue, which, like that of the tendons, is particularly inelastic. The substance of the sarkolemma is insoluble in dilute acids, such as acetic and hydrochloric, insoluble in dilute alkalies, and is not dissolved or transformed into gelatin by boiling water. For these, mainly negative, and other reasons, it has been supposed to be nearly related to, though not quite identical with, the principle which constitutes the elastic tissue of elastic bands, such as the *ligamentum nuchæ*, and the elastic coat of arteries, namely, *elastin*. This hypothesis, though not proved, may be admitted as probable. According to some histologists the substance of the sarkolemma also extends through the space between every two layers of contractile matter, as the boards of a bookshelf do between the books, but this hypothesis is not probable.

The *contractile matter, myoplasm,* filling the sarkolemma, is, like the nerve-fibre, morphologically a compound of many bioplastic individuals, which are arranged longitudinally, *i.e.*, parallel to the long axis of the fibre. This is evidenced by the shape, position and surroundings of the *nuclei*, which are distributed through the contractile matter, and also by the faculty which the contractile matter possesses, of arranging itself, under the influence of certain reagents, into parallel longitudinal layers or threads, termed *fibrillæ*. These latter, therefore, although they are not, as some histologists have believed, expressions of an actually existing arrangement of matter, have a morphological origin ; that is to say, they reproduce the position of the sarkous matter which it had before it coalesced to form the striped elements ; they reproduce it under the influence of an attraction emanating from the bioplastic nucleolar centres, which survives the fusion, and which becomes active as soon as the attractions which result in the formation of flesh-discs either cease, *e.g.*, by the cessa-

tion of innervation, or are overcome, *e.g.*, by the influence of chemical reagents or, what is practically the same, disease-products.

In myoplasm stroma and enchylema are so intimately mixed, that only little of the latter can be pressed out of the former by mechanical means. To effect the separation of these two components of myoplasm it is necessary to finely mince the muscle and exhaust it with water. The enchylema thus dissolves in the water, and the stroma remains insoluble, mixed with the sarkolemma.

Constituents of the Stroma of Myoplasm.—The principal constituent of the stroma is the substance which the older chemists termed *muscle-fibrin*, but which Liebig, in 1849, when he had discovered some features by which it differed from fibrin, termed *musculin*. At a later period again he exchanged this name for *syntonin*, thereby indicating that he believed it to be the *contractile matter*. This substance was isolated by macerating the stroma, previously freed from enchylema by water, in water containing hydrochloric acid. Denis extracted the same matter from stroma by a solution of common salt in water, and, besides this, a second one, which was insoluble in the dilute hydrochloric acid, in which syntonin dissolved. In accordance with his nomenclature he termed it *globulin*, thereby declaring it to be identical with the matter which constitutes the stroma of the blood-corpuscles. It is supposed that this body, which presents the properties of globulin after extraction, is present in living myoplasm, not in the solid, but in the liquid state, mixed with the other ingredients of the enchylema, and coagulates shortly after death, thereby producing the phenomena of the rigor mortis. The adherents of that hypothesis term the body *myosin*. Some microscopists maintain further that Liebig's syntonin, is a mixture of three different principles, namely : firstly, of a longitudinal cementing medium, which is said to unite the fibrillæ, and to yield the earliest to the solvent action

of hydrochloric acid ; secondly of the sarkous elements ; and thirdly, of a transverse cementing substance interspersed in the muscular fibres between the sarkous elements or flesh-discs. Supposing these cementing media to exist and to differ in composition from the sarkous elements, they would probably constitute only a mere small percentage of syntonin. Essentially, therefore, *we have in syntonin the contractile matter*, even though it may be a little impure by the presence of the two cementing materials ; and we can therefore summarise what is known of the constitution of the stroma of the muscular fibre as follows : Mainly *syntonin*, with little *globulin* (or *myosin*), *myocyto phosphatide* (muscle nuclein), and *microsomata* of *fats* and *pigments*, and *inorganic salts*. As obtained after extraction by water of all matters soluble therein, the stroma is mixed with the sarkolemma, the nerve-tubes and their attachment plates, and the capillary bloodvessels and the connective tissue by which they are accompanied. The blood-vessels and connective tissue are present to such an amount, that when their fibres are transformed into *glutin* by boiling with water, and the glutin is dried, it will amount to from 0·6 to 2·0 per cent. of the fresh muscle.

The syntonin and globulin and cyto-phosphatide of the stroma amount to from 13 to 16 per cent. of the fresh muscle ; the enchylema, soluble in cold water, makes up 6 per cent. of the fresh muscle ; of this latter quantity, from one-third to one-half, *i.e.*, 2 to 3 per cent. of the fresh muscle consists of *soluble albumen* and *hemochrom* (*myochrom*). Altogether the muscular tissue of the higher vertebrates contains from 20 to 25 per cent. of solids, and from 80 to 75 per cent. of water.

The enchylema of myoplasm, which is alkaline during life and rest, after death and the loss of the myosin becomes quickly acid, as can be observed on all ordinary meat when it is kept exposed to air ; the acid dissolves an albuminous substance, *acid-albumen*, which is deposited on

neutralization of the acid. If to this neutral liquid a greater amount of acid is now added than it did contain previously and as long as a precipitate is produced, another albuminous substance is precipitated, which was in combination with potash, and this is termed *potash-albumen.* This precipitation also occurs in meat naturally by formation of paralactic acid, which at first shares the potassium of the phosphate, and transforms it into acid phosphate. To this latter salt is mainly to be ascribed the reaction of kept meat. Only when excess of paralactic acid in its free state is present does the albumen separate from the potash-albuminate. Both acid-albumen and potash-albumen may be modifications of the principal albumen contained in the muscle-enchylema, namely, *serum-albumen.* This latter begins under some circumstances to curdle at 45°, and precipitates obtained at this low temperature have been supposed to represent a particular modification of albumen. But as the coagulation of albumen depends on so many factors besides heat, particularly the concentration of the solution (in the case of flesh, therefore, particularly on the amount of water taken for its extraction), much importance cannot be attributed to this point. The *serum-albumen* of the watery solution of the enchylema begins to curdle at temperatures lower than that at which it is entirely precipitated, namely, 65° ; the mixture may be heated a few degrees above this point, and then filtered ; the white coagulated serum-albumen remains in the filter, while a red solution passes through. When this is placed before the spectroscope, it is seen to present the same absorptive phenomena as a solution of blood in water of equal intensity of colour. This red matter, which has been termed *myochrom*, is apparently identical with *hemochrom*, the red colouring matter of the enchylema of blood corpuscles. When the red solution is heated to 90°, the hemochrom is precipitated in the curdled or insoluble state. When this is filtered off, the solution represents a

faintly yellow broth, which retains in a remarkable degree the specific odour of the meat from which it is made. This broth, when made from mutton, retains that name, but when made from beef, is popularly termed beef-tea. One thousand parts of flesh of one of the higher vertebrates, *e.g.*, the ox, yield, after exhaustion with cold water, and removal of the albumens and of myochrom by boiling, a watery extract, which contains twelve parts of organic matter in solution, besides the salts to be enumerated. Of these twelve parts, little more than two parts are at present known as to their chemical quality, and these are relatively simple crystalloids. Consequently five-sixths of the organic part of the extract of meat are at present unknown to us.

When this watery extract of the flesh of animals, oxen and sheep, is evaporated to an almost solid consistency, it is technically termed 'extract of meat,' and as such has become an article of wholesale manufacture and of trade. It contains about 18 per cent. of salts, of which nearly half the weight is potash ; less than 18 per cent. of water ; and of its dry residue, 60 per cent. is soluble in alcohol of 80 per cent. strength. This extract was first made and recommended by the French chemist, Proust ; but its dietetic and economic advantages were not appreciated until Liebig made them widely known by his writings.

By far the greater portion of the organic substances of the extract of meat, other than the crystalloids to be described below, exhibit the reactions which are *characteristic of alkaloids*. At the same time, they possess *the collateral character of acids*, just like the second alkaloid from brain, described above, namely *gladiolin*. Some have termed these alkaloids *peptones*, but this name contains no information either regarding their origin, which is unknown, or their nature. They can be precipitated by phosphomolybdic or phosphotungstic acid ; when these

precipitates are decomposed by baryta in the ordinary way, the product retains barium in strong combination, so that it cannot be removed by carbonic acid. These barium compounds are little soluble in alcohol, and can thereby be fractionally precipitated from their watery solutions. One of these bodies has more the properties of an acid than a base, and has been termed *kreatylic acid*; its lead-salt has the formula $C_9H_{12}PbN_2O_5$; the acid is therefore somewhat similar to cryptophanic acid of the urine, but contains only about half the amount of the oxygen of the latter. These important substances were by the older chemists termed *osmazome* (meaning that which smells in broth, from *osme*, smell, and *zomos*, broth), on account of the agreeable savoury smell which they emit when they are heated, particularly when they are dehydrated by being heated a little above the boiling point of water. The older chemists, *e.g.*, Berzelius, paid to these '*extractive substances*' much more attention than do the modern ones, some of whom omit them altogether from consideration.

The *lower crystalloids* contained in muscular enchylema, some of which are also normal ingredients of the urinary secretion, are the following : *Kreatin*, $C_4H_9N_3O_2$, a neutral body, and easily transformable into the next, namely, *kreatinin*, $C_4H_7N_3O$, a powerful organic base ; it is believed that kreatin is a product of the reaction of kreatinin with water ; for whenever a solution of kreatinin, made from definite compounds, by the aid of which alone it can be separated, is evaporated, it is to a large extent transformed into kreatin; *uric acid*, $C_5H_4N_4O_3$; *xanthin*, $C_5H_4N_4O_2$; *hypoxanthin*, or *sarkin*, $C_5H_4N_4O$; *guanin*, $C_5H_5N_5O$, all of which appear in the urine of man or the lower animals ; *carnin*, $C_7H_8N_4O_3$, which on oxidation yields hypoxanthin ; *taurin*, $C_2H_7NSO_3$, the body obtainable from taurocholic bile-acid, and which may therefore, perhaps, be formed in the muscles, and carried

to the liver, or be formed in the liver and carried to the muscles, or be formed in both in different ways; *inosinic acid*, $C_5H_6N_2O_5$, and acids of analogous composition; further, bodies free from nitrogen, as *paralactic*, or as it is also termed, *sarkolactic acid*, $C_3H_6O_3$, the optically active isomer of the optically inactive lactic acid of fermentation; *formic acid*, CH_2O_2; *acetic acid*, $C_2H_4O_2$; *butyric acid*, $C_4H_8O_2$; *glykogen*, $C_6H_{12}O_6$, and its two varieties, one with an atom of water less, another with an atom of water more; *dextrin*, occasionally, supposed by some to be derived from glycogen; *dextroglucose*, of the same hypothetical origin; and *inosite*, $C_6H_{12}O_6$, crystallizing with $1H_2O$, the same as present in brain.

The inorganic salts of the entire myoplasm consist to the extent of above 86 per cent. of *potassium phosphate*, with some *ferric phosphate*, of bases *soda, magnesia, lime,* some *sulphuric acid*, and little *sodium chloride*. In some cases from 10 to 14 per cent. of KCl has been found in the ash. If particular precautions are not employed, any phosphoric acid formed by the combustion of the phosphatides will drive out hydrochloric and sulphuric acid, as from brain ash. Four parts of mineral salts are contained in 100 of dry substance, or 1 per cent. in natural muscle. Only the greater part of these salts passes into the enchylema on extraction with water; a part, consisting of potassium and calcium phosphate, and some sulphate, remains combined with the stroma (and its admixtures), but this latter contains no chloride.

The muscle is a machine for the transformation of chemical and nerve-force into mechanical force, and for the storing and exercise of that force. The exercise, consisting in contraction and relaxation, is partly constant and involuntary, partly intermittent and subject to the will. The loaded muscle is alkaline, full of disposable oxidizable matter, and of oxidant, namely oxygen. The nerves of

motor influence effect chemical contact and immediate contraction of the various elements. The muscle becomes acid during work, and gives off large quantities of carbonic acid. The disintegration of its albuminous matter seems hardly to be increased immediately, but that of the carbonaceous substances is evident. Muscular exercise does not increase the quantity of secreted urea, but it augments that of the carbonic acid exhaled to perhaps tenfold the amount excreted in rest during equal times. The muscle participates in all febrile diseases of the body, and is frequently the seat of idiopathic processes. In *typhoid* and *typhus fever* it becomes disorganized in a high degree, losing structure, and assuming a yellow appearance. In *fatty degeneration* it loses its contractility, and shows fat in a free state amongst changed structure elements. In *green pigment degeneration* microsomata of green colour are deposited in long strings at both ends of the nuclei; microsomata consisting of calcium phosphate are deposited in similar places in other degenerations. In *death from carbonic oxide* the muscle has a red florid colour, due to the combination of the poisonous gas with its myochrom. In *tetanus* the muscle is spasmodically contracted, changed, and frequently torn; in *hydrophobia* it is similarly torn and injured; in *trichiniasis* it is the specific seat of the parasite, the trichina spiralis, which does not grow and develop in any other tissue. Most important are the chemical changes which muscle undergoes in *cholera;* under the influence of the disease cause, myoplasm in part loses its state of colloidation, and the liquefied albuminous matter passes into the blood, and is thence secreted into the intestinal canal; while thus liquefying, myoplasm absorbs heat, which becomes latent; the direct consequences are the great fall in the temperature of the body (of which the muscles form almost one third in weight), and the production of spasms in many parts of the muscular system, particularly the extremities. The

changes of myoplasm in disease have only just begun to be studied, and cannot fail to be found of the utmost importance in the appreciation of morbid function. As the muscle during life takes up oxygen from the blood, besides nutriment of the most varied kind, and renders back to the venous blood carbonic acid, water, and a number of other crystalloid refuse matters, so does the dead muscle, its partly coagulated enchylema notwithstanding, continue to breathe for some time, to take up oxygen and give out carbonic acid. At last its atoms take a new direction, and physiolysis or putrefaction commences. The muscle then yields the products of putrefaction common to all albuminous substances, such as we shall describe them below. The same, or similar, products are obtained by chemolysis ; leucin was first discovered (by Braconnot) in muscular stroma decomposed by sulphuric acid. By continuing the study of these chemolyses we shall probably be able to learn more about the changes of the muscles in disease, as well as about the ingredients of flesh extracts which are at present unexplained.

When myoplasm on the one, and blood of the same animal on the other hand are dried and subjected to elementary combustion, almost the same figures are obtained for the organic substances. This shows that blood and muscle, considered as organs, preserve in the aggregate of their constituents, however much some are specifically developed, the unity of the chemical idea of bioplasm ; probably other kinds of bioplasm observe the same bearing. In the mineral ingredients muscle and blood differ greatly, the former containing mainly potash salts, the latter mainly soda salts.

Urea does not occur in the muscles of the higher vertebrates, but is present in appreciable quantities in those of plagiostomi (*i.e.*, rays and sharks). These also contain a peculiar sugar, which has been termed *scyllite*.

The *smooth* or *organic involuntary muscular fibres* are

single bioplastic elements, long so-called cells, each with a nucleus situated about the middle. They contain micro-somata, and in disease deposits of degeneration resembling those of the striated muscle. This normal stroma and enchylema is similar to that of striped muscle. The former yields *syntonin,* the latter *serum albumen,* and of lower crystalloids *kreatin* and *hypoxanthin,* as well as *lactic, formic, acetic,* and *butyric acid, glycogen,* and *inosite.* In the ash also the potash salts prevail over the soda salts. The smooth muscular fibres require yet to be studied more closely, which is a matter of some difficulty, as they cannot easily be isolated.

CHEMICAL CONSTITUTION OF THE BLOOD
(HEMOPLASM).

THE blood, like the brain and muscles, must be considered as a great aggregate of bioplastic centres, *the corpuscles,* and of bioplastic matter, *the living serum ;* as such it is an organ, but unlike other organs, which are fixed, it is in a state of constant movement. Morphologically the walls of the blood-vessels are the limiting membrane of this aggregate hemoplasm, though when fully developed for their ubiquitous function they do not any longer stand in any chemical or histological relation to their contents. The living serum may therefore be considered only in a morphological sense as the enchylema of the blood-vessels considered as stroma. But the corpuscles fully preserve their bioplastic structure, such as we have defined it in the first chapter.

The blood-corpuscles, then, consist of a stroma and an enchylema, which can be separated from each other. While the stroma can be obtained free from enchylema, the latter can at present not be obtained in a state free from some admixed serum. The stroma is isolated from blood by the

process of Denis, which consists in the addition of salt water of defined strength, in measured quantity, to defibrinated blood, and in the treatment of the macerated mixture with large quantities of pure water. On standing, the stromata of the corpuscles, previously separate, now coherent, settle as a membranous or filamentous mass. This has been termed *globulin*, and believed to be a unitary chemical compound. It contains, however, besides the colloid albuminous body to which we leave the name globulin, at least two, possibly three, *phosphorized bodies*, which, in the case of corpuscles from the ox, are obtained as *paramyelin and amidomyelin ;* in the case, however, of *nucleated* blood-cells, a *cytophosphatide (i.e.,* a nuclein) may also be present. Globulin is characterized by forming viscous solutions with salt water, which are precipitated by a large amount of water ; it is purified by the use of these processes. To separate the phosphatides it has to be boiled with alcohol, whereby it undergoes a change. Its separation from any nuclein has not yet been effected.

The enchylema, which dissolves in water, has for its principal constituent the red colouring matter, *hemochrom* (also termed hematocrystallin, hematoglobulin, and hemoglobin). This body can be isolated and obtained in a crystallized state. It contains carbon, hydrogen, nitrogen, iron, sulphur and oxygen in the proportions indicated by the formula $C_{600}H_{960}N_{154}FeS_3O_{177}$. This leads to an atomic weight of 13,280, or if it be determined by the quantity of the iron contained in it, an atomic weight of about 13,000. Hemochrom crystallizes in a variety of forms, tetrahedra, octahedra, with and without prisms, or in prisms only, mostly belonging to the rhombohedric system. They always contain four-tenths per cent. of iron, and should be free from phosphorus. Their watery properly diluted solution, when examined before the spectroscope, shows two characteristic bands of absorption in orange and green, and obscuration of the blue and violet end of the

spectrum. As the blood of all vertebrate animals, when viewed within the living blood-vessels, shows the same bands, we can assume that hemochrom is present in the living blood in the same condition as in the crystals, and is not formed by the process of preparing the crystals—in other words, that it is an educt and not a product. Hemochrom can be deprived of its loosely bound oxygen, and then its spectrum changes so as to present only one absorption band; this is characteristic of the so-called *deoxydized* or *reduced hemochrom*. Shaking of this solution with oxygen restores the double-banded spectrum. It is owing to this reaction of hemochrom that arterial blood shows two bands, while venous blood exhibits only one. Hemochrom contains, as proximate constituents, *an albuminous body*, which after separation remains amorphous and colourless, and *hematin*, which retains the colouring power, the influence upon the spectrum, and the iron of the original substance, though all varied in kind, proportion, and quantity. Hematin has the composition expressed by the formula $C_{32}H_{32}FeN_4O_6$, which leads to 432 as the atomic weight; the amount of iron contained in it is 9·08 per cent. It occurs together with hemochrom in the urine in some forms of *cruenturesis* (paroxysmal hematuria). It yields many remarkable products of decomposition. Its spectra in various solvents, and in the reduced state, and the spectra of the new derivates, are very characteristic. The optical and chemical phenomena of hemochrom and hematin are applicable to medico-legal research, as affording the most certain diagnosis of blood upon the smallest quantity of material. A diminution of hemochrom in the blood constitutes the disease termed *chlorosis*; in this the serum of the blood is not diminished *pari passu* with the hemochrom; but in *anæmia* or *spanæmia* both serum and hemochrom are diminished below the normal. 1000 parts of human blood contain on an average 125 parts of hemochrom; **ox** blood contains 114·5; duck's blood 78·12

parts in 1000 ; the pig and the ass attain the highest percentage of hemochrom met with amongst mammals, namely, from 150 to 155 g. in a litre of blood.*

The blood-corpuscles carry oxygen, which has great affinity for hemochrom, from the lungs to the most distant or hidden and internal parts of the body. There they yield it up to the bioplasm of every kind, to the tissues, principally the muscles or the oxidizable matters contained in their enchylema, and the tissues, thus oxidized, return the carbonic acid, water, urea, and other products into the blood. The muscles may either become oxidized immediately, or store the oxygen in large quantity, particularly during sleep, by means of their myochrom. Although the carbonic acid affects the colour and condition of the blood-corpuscles, nevertheless the latter are not carriers of carbonic acid. This gas is dissolved in the serum. It is there partly dissolved in the same manner as it may be dissolved in pure water, but to a great extent it is combined with alkaline bases, particularly sodium. It is believed by some chemists that when the blood-corpuscles of the venous blood arrive in the lungs, they have undergone a change which consists in the partial oxidation of a small quantity of their hemochrom, and this is transformed into an acid, which may be termed *hematic acid*. This blood-acid contains nitrogen, and is not volatile but fixed ; it is evolved from the blood-corpuscles, and passes into the serum at the very moment when the former arrive in the small breathing cells of the lungs. There the blood-acid combines with the sodium, and the carbonic acid is set free and is left to take its course, with water vapour, through the lung-tissue into the respiratory passages. The student should know that this theory of the evolution of carbonic by hematic acid is not admitted as proved by

* For a collection of data concerning the quantities of hemochrom in the blood in health and disease, see Article XX. of 'Annals of Chemical Medicine,' vol. ii., p. 231, *et seq.*

some physiologists, who, however, at the same time admit that it *may* be true.

In a number of acute and chronic diseases the blood-corpuscles, or many of them, become altered so as to be unable to perform their functions as oxygen carriers. Thus, in *cholera*, the composition of the serum is greatly altered by the alvine flux, and the mixing with the serum of liquefied muscular protoplasm. Water and other matters are thereby abstracted from the corpuscles, and their oxygen-carrying power is diminished. This increases the fall of temperature which is engendered primarily by the fluidification of colloid matter of the muscles, and helps to bring the algid condition and collapse of cholera to its extreme development.

In *yellow fever*, the hemochrom of a portion of the blood-corpuscles leaves them, dissolves in the blood, decomposes, and colours the skin yellow. A similar decomposition takes place in some cases of *pyæmia*, and in *poisoning by arseniuretted hydrogen*, and by the bite of venomous serpents. In *paroxysmal cruenturesis*, a number of blood-corpuscles are also decomposed, and the hemochrom thereof appears in the urine, either as such, or altered as *peroxyhemochrom*, or decomposed as *hematin*. Several poisons, such as *hydrothion* (sulphuretted hydrogen), *carbonic oxyde*, *hydrocyanic* or *prussic acid*, kill or injure by decomposing the hemochrom, and keeping the oxygen out. Thus it is clear that the study of many morbid conditions requires an intimate knowledge of the constitution of the blood-corpuscles. The value of this we have only just begun to appreciate, and the chemical and optical methods of investigation applied with rigorous accuracy will bring us not only the explanation of normal phenomena at present remaining obscure, but also useful practical information on the nature of diseases, processes of poisoning, and their treatment by antidotes.

Coagulation of the Blood.—One of the most remarkable

properties of the blood is its power of coagulating or setting shortly after it has left the body. Of this phenomenon many ingenious theories have been given, but none has yet satisfied the demand of exact chemical science. The latest one is that of A. Schmidt, according to which the serum contains three substances, of which two have the power of combining with each other under the influence of the third, which is *a ferment*, and is not supposed to enter into the combination. The result of the alleged combination is the formation of *fibrin*. As the data on which this theory, and other hypotheses concerning the coagulation of the blood which are prevalent in the present day, are founded are mainly the results of the labours of the French inquirer P. S. Denis, it is very useful to the student to make himself well acquainted with the facts and views of that author before he considers the use which has been made of them by later writers.

The terms *liquor sanguinis, serum of circulating blood, living serum,* or *plasma,* are used to signify the entire liquid part of the blood containing, yet in solution, the matter or matters which on coagulation form fibrin, with the exclusion, however, of all blood-corpuscles, coloured as well as colourless. By the term *plasmin* (not to be confounded with *plastin,* the colloid constituent of bioplastic formations) Denis indicated the coagulable lymph dissolved in the plasma, which is the antecedent of fibrin, and which he says might be termed 'fibrinogen,' if such a term were admissible. Denis isolated the plasmin by precipitating from fresh blood the corpuscles, by sulphate of sodium ; he thus obtained a mixture of plasma and sulphate of sodium solution, which he filtered from white corpuscles and fat. On adding to this solution sodium chloride in fine powder, the plasmin was precipitated. This plasmin dissolves in about twenty parts of water. The solution is coagulable by heat, alcohol, acids and alkalies. But its most remarkable property is that it coagulates spon-

taneously, and in doing so *gives rise to new albuminous substances which have no longer the properties of plasmin.* For although the plasmin solution in salt water sets into a firm coagulum, nevertheless the plasmin does not become insoluble to the extent of its whole amount; a portion of its bulk remains in solution and possesses no power of coagulating by itself. The coagulated portion also has properties which differ from those of the plasmin precipitated by salt in powder, in this : that it is not affected by either salt solution or water. The coagulum is separated from the non-coagulated part by pressure in a linen bag ; the coagulum is termed by Denis ' *concrete modified fibrin,*' the non-coagulated part in solution is termed ' *pure dissolved fibrin.*' The proportion of coagulated to soluble matter is as 2 : 1.

The ' concrete modified fibrin,' differs from fibrin commonly so called, obtained from venous blood by whipping, and termed by Denis ' concrete pure fibrin,' in this more particularly, that while, as stated, the former is insoluble in 10 per cent. chloride of sodium solution, the latter is entirely soluble therein if three parts of it are added to one part of the fresh moist fibrin, and the mixture is triturated and warmed to between 40° and 50°.

The ' concrete pure fibrin ' dissolved in sodium chloride solution is precipitated from this solution by the addition to it of large volumes of water ; the precipitated ' pure fibrin ' can be collected on a filter and washed with water ; it retains its solubility in 10 per cent. sodium chloride solution, and the solution presents the reaction of the first solution. On account of this persistent solubility Denis terms this fibrin ' soluble pure fibrin,' or ' soluble fibrin ' simply.

The ' " DISSOLVED " pure fibrin,' obtained in the course of the coagulation of isolated plasmin (which coagulation appears at first sight more like a decomposition or dissociation than like a synthesis) is not stated by Denis to be

identical with the 'SOLUBLE pure fibrin' just described. The student must therefore maintain the distinction implied by the difference of the names. For there is no proof as yet that the dissolved pure fibrin from plasmin was ever in the state of concrete fibrin, or could be brought into it, so as to present the characteristic properties of fibrin ordinarily so-called. We may regret that Denis should have given the name of fibrin at all to this dissolved product of the coagulated plasmin, but in order not to produce confusion in the consideration of so complicated and difficult a matter, we have not meddled with the terms employed by Denis while describing his experiments.

A third variety of solid fibrin, the fourth of the bodies termed fibrin by Denis, is obtained by allowing venous blood to coagulate without whipping it, and pressing and washing with water the coagulated clot enclosed in a cloth. If this fibrin is placed with three times its weight of 10 per cent. of sodium chloride solution, it does not dissolve and become filterable like the fibrin obtained from venous blood by whipping, but forms a bulky viscous mass, which can be drawn into threads but not filtered, and is in fact not a solution, but merely a matter in a state of swelling by imbibition. When this viscous matter is placed in water it immediately resumes the appearance of the fibrin from which it came. This fibrin resembles so much the *globulin*, the body forming the stroma of blood-corpuscles above described, that Denis termed it *globulin* also. It contains, however, a small proportion of 'concrete pure fibrin,' as can be shown by treating the viscous matter obtained with salt solution with absolute alcohol, and digesting it cold for an hour. After that all the globulin has been modified so as to be no longer swelled up by salt water; but this salt water extracts some 'pure fibrin,' which is not very quickly altered by alcohol, and can from the salt water solution be entirely precipitated by saturation with powdered magnesium sulphate.

It would therefore seem that in this process the globulin, which is undoubtedly present, so alters the fibrin with which it is admixed or combined as to prevent it from dissolving in the salt solution ; the fibrin by itself, when freed from the influence of the globulin, resumes its solubility in salt solution. This substance should therefore not be termed globulin, but should have a name indicating its character as a compound or mixture of globulin and fibrin.

We have now to consider what becomes of that part of coagulated plasmin which remains dissolved, and has been termed 'dissolved pure fibrin,' in the process of the spontaneous coagulation of the blood. Whether this fibrin be removed by whipping, or be allowed to combine or mix with globulin, in both cases the 'dissolved pure fibrin' can be isolated from the serum by saturation with powdered magnesium sulphate.

It is thus clear that plasmin (which, whether obtained from venous or arterial blood by the sodium sulphate and sodium chloride process, always splits up or dissociates into 'concrete modified fibrin' and 'dissolved pure fibrin') when it dissociates or changes in venous blood, which is being whipped, produces 'concrete pure fibrin' together with 'dissolved pure fibrin.' When plasmin is dissociating in venous blood which is coagulating without being whipped, or subjected to any other commotion, it produces the so-called globulin containing fibrin. Plasmin in arterial blood, whether the blood be whipped during coagulation, or be allowed to set while in repose, and also in the case when it has been received in sodium sulphate, and the plasma has been poured into water, there to coagulate, always yields 'concrete modified fibrin' only, besides 'dissolved pure fibrin.' Venous blood received in sodium sulphate yields a plasma which, when poured in water, gives the same products as arterial blood just described.

A. Schmidt formed the hypothesis that the plasmin of

Denis was not a unitary body, but a mixture of two bodies, each of which was precipitable by sodium chloride in powder added to the solution until it was saturated. He further argued that the formation of fibrin depended upon the interaction of the two bodies constituting Denis's plasmin. The nature of this action, whether it consisted in cleavage of one or the other, or in combination of one with the other, was not ascertained. At first it was believed that these two bodies only were the agents in the production of fibrin, but it was soon shown that a third body was necessary, namely, the *fibrin ferment*. There are then three bodies required for the formation of fibrin : firstly, '*fibrinogenous matter*,' which is supposed to furnish the principal material substratum of the fibrin ; of this apparently the whole is always removed from solutions of plasmin during their coagulation. The second body required Schmidt termed '*fibrinoplastic matter*,' which is supposed to give more impulse than material for the formation of fibrin ; of this, which is identical with the 'dissolved pure fibrin,' a quantity is always left uncombined in the coagulation of plasmin, as well as other fibrin-forming liquids : the third body required is the *ferment*.

Fibrinogenous matter, or *fibrinogen*, is not easily isolated in a state of approximate purity ; it is contained in the precipitated plasmin of Denis, and bears no other synonym.

Fibrinoplastic matter, or *fibrinoplasmin*, on the other hand, which can be isolated by a variety of methods, has received a number of different names, amongst which are the following : — Serum-casein (Panum), paraglobulin (Kühne), insoluble albumen of serum, and 'dissolved pure fibrin' (Denis).

The fibrin ferment is soluble in water. It is isolated by precipitation with alcohol and extraction with water. Some authors maintain that the ferment is derived from the red, others that it comes from the white blood-corpuscles ; others,

again, maintain that it forms in serum which is quite free from white corpuscles. Others, again, maintain that the ferment is formed only after the blood has left the blood-vessels, and is not present in circulating blood.

As there is much that is uncertain or even contradictory in the above data concerning the formation of fibrin, so there is much difference in the statements of the authors concerning *fibrin*. Some say that there is only one kind of fibrin, and that this is insoluble in salt solution. The author has repeated the experiment of Denis, and found fibrin from beaten ox-blood (mixed arterial and venous) almost entirely soluble in sodium chloride, and yielding the products and reactions which Denis describes with the greatest accuracy. The student may therefore take it as proved that there are two kinds of *concrete fibrin*, such as are described above in the account of Denis's experiment—namely, one which is soluble in 10 per cent. sodium chloride solution, and another which is insoluble therein.

The Serum.—The yellowish liquid which remains when the fibrin has been allowed to set in the blood, and to enclose and retain in its contracting meshes the blood-corpuscles, is termed the serum. It contains a quantity of *fibrinoplasmin* in solution; indeed, if fibrinoplasmin does not enter into the constitution of fibrin, the serum must contain the whole of the fibrinoplasmin as contained in the blood itself. Formerly only a small quantity of this body was obtained from serum by dilution with water, and treatment of the solution with a current of carbonic acid; a little more by cautious neutralization with acetic acid; all the matter which remained dissolved in the serum after this treatment was supposed to be *serum albumen*, amounting to from 7·9 to 9·8 per cent. of the serum. But latterly it has been made probable that there is much more fibrinoplasmin in the serum than can be precipitated by carbonic or acetic acid, and that this is precipitated by magnesium sulphate. From serum

of horse-blood from 3 to 5 per cent. of fibrinoplasmin were obtained by saturation with magnesium sulphate. *The serum albumen* present in serum would thus be lowered to about half, or even less than the previously estimated amount. It is precipitated by boiling the solution in the presence of a little acid. If no acetic acid is present when the serum is boiled, sodium albumen, formed during the process of coagulation, remains in solution. *Serum albumen*, termed *serin* by Denis, coagulates at 75°, and its solution rotates the ray of polarized light to the left about 60°, while albumen of eggs exhibits a rotation of only about 36°. The serum contains *neutral fats* and *soaps*, or *salts* of *fatty acids* in solution, or suspension; in the latter case it is rendered milky or turbid thereby. In certain diseases the serum also contains *free fatty acids*. These acids are emulged with the phosphate of sodium of the serum, and after extraction by ether, in which they are easily soluble, are again emulged by boiling with a solution of common sodium phosphate in water. A similar emulsion occurs in so-called *chylous urine*, and in certain effusions in the scrotum, termed *milky hydrocele*, or *lactocele*, or better *liporocele*. The serum further contains *cholesterin*, $C_{26}H_{44}O$, *kreatinin*, $C_4H_7N_3O$, *urea*, CH_4N_2O, hippuric acid, $C_9H_9NO_3$, *lactic acid*, $C_3H_6O_3$, in small quantities, and at least one yellow colouring matter, *serolutein*. In *gout*, uric acid as urate of sodium and calcium is found in it; in *diabetes*, sugar; in *jaundice*, biliary colouring matter; and in *leukocythæmia, formic acid, xanthin*, and other matters.

Of inorganic salts the serum contains *sodium chloride, sodium dicarbonate*, and *calcium phosphate*, small quantities of *magnesium phosphate*, still smaller ones of *potassium salt*. In the chemical operations of the serum (and blood on the whole) sodium salts are mainly employed, while in those of the muscles potassium salts are mainly used. The liver of higher animals also employs sodium as the

principal metallic base for its peculiar acids. But in the bile of sea-fish, which live in a medium abounding with sodium salts, the prevailing mineral base is potassium.

Gases in Serum.—The serum carries nearly the whole of the carbonic acid contained in the blood, particularly when it becomes venous. This is present in two forms, the one dissolved and removable by the vacuum, the other combined with soda as carbonate and dicarbonate, and dislodged only by acids and boiling. It is also possible that the sodium phosphate attracts a portion of carbonic acid, and holds it in peculiar loose combination. The physiology of the gases of the blood, of the oxygen, nitrogen, and carbonic acid contained in its modifications of arterial and venous character, we must leave to works on general physiology. The methods for the investigation of the relations of oxygen in diseases have lately been greatly improved.

The total quantity of blood contained and circulating in a living man has for many years been greatly overestimated, owing to fallacious conclusions derived from the practice of blood-letting. The best methods available about thirty years ago reduced the quantity to 7·7 per cent. of the weight of the body. In these processes, in which the quantity of the blood was estimated colorimetrically from the hemochrom, no allowance was made for the myochrom. If for this 0·7 is deducted, then 7 per cent. of the weight of the body will be a more correct estimate of the quantity of the blood in man than any other hitherto made. This method must be applied with circumspection to different classes of animals, as they contain different quantities of hemochrom in equal quantities of blood, a subject already alluded to above.

The colourless, or white corpuscles of the blood, which are identical with those of *lymph*, and of *pus*, can hardly be isolated from healthy blood, but from blood in *leukocythemia*, and from lymph and pus they can be obtained

sometimes in a state fit for the demonstration of their principal chemical ingredients. They contain the usual constituents of bioplasm, namely a stroma of *plastin*, with a *phosphatide* nucleus, and an *enchylema*. The stroma is peculiarly contractile, and shows movements which have some very distant resemblance to the movements of a semi-asphyxiated *amœba*, and have therefore been termed *amœboid*.

The blood in *leukocythemia* is characterized by a great excess of these white corpuscles. The serum contains a variety of acids in abnormal quantity, such as *formic*, *acetic*, and *lactic*, also *hypoxanthin*, and a substance resembling *glutin*. It is also said to contain *glycero-phosphoric acid*, but this is not proved.

The white blood-corpuscles possess a peculiar attraction towards the walls of capillaries, and frequently travel slower than the red corpuscles in a serous layer of the blood, from which red blood-corpuscles are absent. This phenomenon resembles the double current in the cell of the vallisneria, in which the outer slower one containing microsomata keeps to the cell-wall, while the inner quicker one with the chlorophyll balls revolves in the central space. But, while in the capillaries both currents, though travelling at different rates, go in the same direction, in the vallisneria these currents go in opposite directions, as has already been shown in the first chapter. In inflammation this attraction of the white blood-corpuscles to the walls of the capillaries is increased, and they then by the aid of their amœboid movements penetrate the walls of the capillaries, and become the ingredients of exudations of a lymphatic kind, or, by further changes, of *pus*.

CHEMICAL CONSTITUTION OF THE SALIVARY GLANDS (PTYALOPLASM) AND OF THEIR SECRETION, SALIVA.

The salivary glands are aggregations of specifically developed bioplastic centres or nucleated cells, which are so arranged anatomically that (1) they receive an abundant supply of arterial blood, and after having supplied their wants, send it away as venous blood and lymph; (2) that they receive innervation by nerves and ganglionic cells, of which fibres run directly into and fuse with at least some of the bioplastic centres; (3) that they can send their specific product—namely, saliva—into open channels, which unite to form ducts. These ducts send the saliva to surfaces in cavities of the body, where it is used for the various effects of lubrication and of preparation of the food for the purposes of digestion.

The bioplastic constituents of the salivary glands have not yet been chemically examined. The analytical operations concerning the salivary glands have been confined to the extraction of two specific colloid ingredients, which also pass out with the secreted saliva—namely, *mucin*, and *ptyalin*, and of some simple crystalloids, such as *leucin*, and *xanthinlike* bodies. Of the organic colloid ingredients ptyalin is *a ferment*.

Saliva, as it collects in the cavity of the mouth to be used for lubrication or insalivation of food, is a mixture of varying components. These are secreted by four different groups of glands, and the secretion of one and the same set of glands may vary according to the agencies which call them into action.

Underneath the forepart of the tongue is secreted from one and the same duct the saliva of a gland which lies under the tongue, *the sublingual*, and that of two other glands which lie farther back on both sides of the tongue within or underneath the lower jaw, the *submaxillary* glands.

To collect the secretion of either of these sets of glands, little tubes have to be introduced into the respective ducts. As this mechanical operation is a matter of some difficulty, the chemical composition of the secretions of the separate glands is very imperfectly known. Experiments upon animals made by different observers have shown that these glands can give four different kinds of secretion, according to the nerves which are irritated for the purpose. One nerve—a branch of the facial, and a continuation of the chord of the tympanum—on irritation causes a clear, slightly ropy secretion from *the submaxillary glands.* This 'chordal' saliva contains about 4 per cent. of solid matter, of which 1·5 is mucin, coagulable albumen, and a third albuminous matter; 2·5 is mineral, mainly alkaline chlorides and lime salts; of these latter the carbonate, dissolved in excess of carbonic acid, frequently decomposes in the mouth, and deposits crusts of *calcium carbonate* upon the teeth, which are popularly termed tartar. (In some analyses, these crusts have also been found to contain *calcium phosphate,* and in quantity outweighing the carbonate.) On irritation of the sympathetic nerve, the submaxillary glands secrete an opaque, very tough saliva. This contains from 15 to 28 per mille of solids, amongst which is *mucin,* granules or roundish lumps of an albuminous matter supposed to be brokendown bioplasm, and much free alkali. The third kind of saliva is that which flows when the submaxillary ganglion is made the centre of a reflex action which works by way of the lingual nerve. This is stated to be the only secretory act which takes place without the intervention of cerebro-spinal influence that is known at present. The fourth kind of saliva is the 'paralytic,' or thin watery fluid, which is secreted under the influence of paralysis of the secretory nerves, caused either by degeneration, or poisoning, or wounds, and the composition of which is not yet ascertained.

The mixture of sublingual and submaxillary saliva in man (not in animals) contains rhodanate or sulphocyanate (also termed rhodanide or sulphocyanide) of potassium and sodium, CNKS, and CNNaS, recognised by the red colour which iron chloride imparts to saliva, or to the distillate obtained from it with acids. This phenomenon admits at present of no particular theory.

The saliva which is secreted by the parotid glands can easily be collected by the introduction of canulæ into the ducts. It is an alkaline, hardly viscous fluid, which contains the particular ferment *ptyalin*, a *little albumen*, and other albuminous substances, but no mucin. It contains much rhodanate, and is the most suitable material for preparing the distillate of rhodanic acid. It contains: water, 995·3; solids, 4·7; of these are organic, 1·4; mineral, 3·3; of the latter, there is lime carbonate, 1·2. The parotid saliva transforms boiled starch into a kind of sugar by means of the ferment termed *ptyalin*. This is the only agent in saliva which has that power. Some authors * maintain or assume the identity of ptyalin with the *diastase* of malt, as also the identity of the sugar which ptyalin forms out of boiled starch and glycogen with dextrose sugar: they are, however, refuted by the fact that diastase of malt does not form dextroglucose, but *maltose* out of starch; others, however, believe the sugar formed by ptyalin from these carbohydrates to be a particular kind of glucose, and term it *ptyalose*. The truth seems to be that ptyalin is closely related to diastase in this, that it transforms boiled starch into *maltose* and *dextrin*, but differs from it by a lesser intensity. *Ptyalin* does not possess the faculty of converting cane-sugar, or transforming it into the mixture of dextrose

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* The reader may consult an exhaustive article, entitled 'On the Action and Products of the Starch-Transforming Ferments, Diästas, Ptyalin, Pancreatin, Acids, and various matters derived from Albuminous Substances,' in 'Annals of Chemical Medicine,' etc., vol. i., p. 45.

and levulose sugar termed invert sugar. Diastas acts best at 66°, while ptyalin is destroyed at 60°. Diastas can beneficially supplement ptyalin. Thus an interesting and important application has been made of diastas by Liebig for the production of food for infants, which supplies efficiently the want of alkali and ptyalin in the digestive juices of children who are being brought up without mothers' milk, or with such as is not in a healthy state.

The secretion of the salivary glands mixed with the mucus secreted by small simple glands, so-called follicles (baglets), situated in the membranes of the cavity of the mouth (buccal glands) constitutes *mixed saliva*. This can be collected in quantity by irritating the fauces with a feather, and producing vomiturition. It does not reduce alkaline copper solution, but retains a little copper oxide in solution, when cupric salt and alkali only are added. It transforms starch into maltose and dextrin, so that chewed pap, after some standing, with cupric sulphate and caustic potash, at 70°, yields red copper suboxide. It does not change canesugar into invert sugar. The quantity of mixed saliva secreted by a man in twenty-four hours varies between 300 and 1500 g. ; it may be greatly increased by excitants, and irritating medicines and poisons.

Little is known of saliva in disease. During the excessive discharge of saliva, under the influence of mercury, termed salivation, rhodanates disappear from the saliva, while *mercury* is contained in it. Many medicinal salts pass easily into the saliva from the blood, such as *iodide* and *chlorate of potassium*, and when used long in quantity produce slight salivation. In *diabetes*, the saliva contains *lactates*, but no sugar. In the paralytic saliva of hysteric persons *leucin* has been found. Acid saliva seems to contain *lactic acid*, and its occurrence is anomalous. The occasional presence of *urea* has been alleged, but not proved with certainty. In hydrophobia the saliva is the bearer of the contagion, or contact poison, by which the disease is propagated to other individuals.

CHEMICAL CONSTITUTION OF PEPTOPLASM, AND OF ITS PRODUCT, THE GASTRIC JUICE.

THE bioplasm which produces the digestive liquid of the stomach is arranged in the mucous membrane of that organ in the shape of cells, which line the inside of little bags, and leave central canals between them. These tubular organs are the *peptic glands.* Interspersed with them are glands of a somewhat different structure, which secrete mucus, and are termed *gastric mucous glands.* It has not yet been possible to separate the bioplasm of both kinds of glands for analysis. It is probable that each kind of bioplasm forms and contains within its substance the materials of the secretion which it pours into the cavity of the stomach during digestion. For when the mucous membrane of a stomach in process of digestion is wiped clean and isolated by scraping it off the underlying connective and muscular tissue, a considerable amount of the digestive ferment, *pepsin,* can be extracted from it. At the same time *mucin* can be extracted from the mucous glands. But the acids which are freely thrown out by the glands during digestion, namely, *hydrochloric* and *lactic,* are only obtained in traces, if at all, by extraction of the peptoplasm. The pepsin-powders which are sold in trade for medical purposes, are mostly produced from, and not rarely consist only, as regards active ingredients, of, peptoplasm—that is, scraped, dried, and powdered mucous membranes of the stomachs of pigs. During digestion, the peptic cells swell, and become filled with microsomata, so as to present a cloudy appearance. They are also contractile, and, during contraction, the nuclei, which lie near the surface, project over and out of it. In the state of repose, the peptic cells are transparent and of much smaller size than during action.

These peptic or rennet glands secrete a liquid termed *gastric juice,* which in man contains about 994·6 per mille

of water, and 5·39 of solid and permanently fluid in-
gredients other than water. Of these 3·0 are *pepsin*, 0·2
hydrochloric acid, with which, perhaps, a small quantity
of lactic acid is mixed, and chlorides of the alkalies with
some phosphates of earths. There is also some calcium
chloride in the juice. The gastric juice has been examined
mainly as obtained from persons who, by accident, had
fistulous openings in their stomachs, and upon dogs upon
whom such fistulous openings had been formed by skilled
operations. When the composition of the natural juice
had thus been ascertained, artificial juice, so-called, was
made after its pattern ; the latter, however, required the
addition of pepsin obtained from an active gastric mucous
membrane, and was therefore only in part artificial. It
served, however, for the purpose of studying the processes
and results of stomach digestion upon many kinds of food,
and of supplying a kind of remedy in diseased conditions
in which the natural juice is supposed to be deficient.

The natural, as well as the so-called artificial, gastric
juice possesses the power of dissolving or reducing to a
liquid state albuminous substances, which are either by
nature, or by preparation, such as boiling, insoluble in
water. Albumen, casein, fibrin, syntonin, the albuminous
substances of vegetables, gluten, and the collogenetic
tissues, or gristle, are under the influence of the gastric
juice, or of a mixture of pepsin and hydrochloric acid, dis-
solved to thickish, somewhat turbid matters, to which the
name of *peptons* is given. Pepsin may be isolated by
the processes described under its name in the special part.
It is not itself destroyed during digestion, but is capable
of transforming great quantities of solids into fluids by its
mysterious influence. When the juice is saturated with
peptone it ceases to act, but an addition of dilute acid
fluid enables digestion of newly introduced albuminous
matters to be effected.

Insalivation and gastric digestion of food.—The food of most vertebrate animals is comminuted in the mouth by chewing. At the same time it is mixed with the saliva secreted by the several glands described. This mainly serves a mechanical object, but predisposes a part of the food to a change. *Ptyalin* acts upon starch as a ferment. *Starch* consists of two bodies, which in the little granules are disposed in alternate layers. The first is *amylo-granulose*, and has the property of being coloured blue at once by free iodine. The second is *amylo-cellulose*, not coloured blue by iodine at once, but only after sulphuric acid or zinc chloride has been allowed to act upon it. When unboiled starch is mixed and digested with saliva for days, the amylo-granulose is dissolved out of the corpuscles and transformed into *dextrin* and *maltose*, and the amylo-cellulose only is left. At higher temperatures this also is changed. Boiled starch is more easily transformed, as the granules are burst and admit the altering juices between their layers with facility. The first symptom of the addition of saliva to boiled starch, or flour pap, cooled to 40°, is increased fluidity, indicating the formation of soluble starch and dextrin. At a later period maltose only is formed.[*] This process may take place according to the equation

$$C_{18}H_{30}O_{15} + H_2O = C_{12}H_{22}O_{11} + C_6H_{10}O_5$$

Starch.   Maltose.   Dextrin.
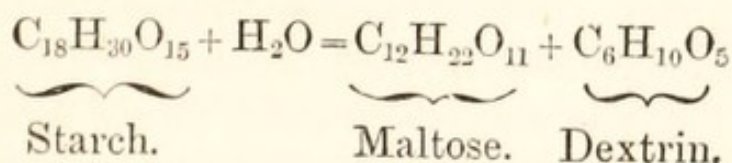
While the saliva influences starch as indicated, and does not lose its activity by the admixture of acid or the concentration of the gastric juice, it certainly, under ordinary circumstances, does not transform the whole of the starch into dextrin and maltose. The gastric juice has no influence upon starch ; the pancreatic juice has a trifling

[*] *Cf.* 'Zymolysis of Starch by Saliva.' 'Ann. Chem. Med.' i. 62.

influence upon amylo-granulose, a somewhat greater one on amylo-cellulose ; indeed, in herbivorous animals, it seems to have great digestive power over the cellulose in general, which these creatures have to devour in large quantities. All the maltose, dextrin, and lactic acid formed during the digestion of a given quantity of starch are insufficient to account for it, and it is necessary to assume that other products are formed which as yet elude analysis. It is not impossible that some of these products find their way into the liver and are there transformed into glykogen. Of this latter body more will be said under the paragraph which treats of hepatoplasm, the bioplasm of the liver.

The various kinds of sugar occurring in food are not influenced by saliva, nor are the fats or albuminous substances. The latter are mainly changed by the gastric juice. Those which are by nature, or by preparation, such as boiling, insoluble in water, are reduced to a liquid state. Albumen, casein, fibrin, syntonin, and all the various bioplastic substances, the plastins ; further, the albuminous substances of vegetables, gluten, and the collogene tissues or gristle, are under the influence of gastric juice, or of a mixture of pepsin and hydrochloric acid, dissolved to thickish, somewhat turbid matters, to which the name of *peptons* is given. It is at present impossible to say what these albuminous matters are. Some physiologists maintain that there is only one pepton, others that there are five or more peptons, and the statements as well as the experiments upon which they are based are not easily harmonised with each other. None of these researches have as yet been carried out by means of the quantitative chemical method, excepting the comparison of the composition of the peptons with the original matters.

This comparison showed that the peptons had almost the same elementary composition as the original albuminous substances out of which they were produced, so

that some observers believed them to be isomeric substances, while others believed peptons to be mere hydrates of albumens considered as anhydrides. The pepton solutions are not coagulated by boiling, but are precipitated by absolute alcohol, most easily in the concentrated state. They give Millon's reaction with nitrate and nitrite of mercury, that is, a red precipitate in a red solution. They diffuse only little through parchment-paper, and can, like albumen, be purified from acids, alkalies, and salts, or crystalloids in general, by dialysis; with the crystalloids, however, a certain amount of peptons passes into the diffusate. They are optically characterised by turning the ray of polarised light to the left. They possess some reaction of alkaloids in this, that they are precipitated from acid solutions by phosphomolybdic and phosphotungstic acid, and can by this means be separated rapidly from a great number of substances with which they may be mixed.

The student should also remember that it is maintained that some of the so-called insectivorous plants secrete a pepsin-like ferment, and an acid, and effect a solution and absorption of albuminous matter like the stomach and intestine of animals. It is certain that ferments having powers like pepsin, ptyalin, and others, can be extracted from the protoplasm of a number of plants, and are probably contained in the flour of many cereals.

The coagulation of milk in the stomach, or by rennet out of it, is supposed by some not to be due to pepsin, but to another ferment which transforms sugar of milk or lactose into lactic acid, and precipitates casein, considered as soda-albumen, by neutralisation of its alkali. But casein is more than soda-albumen, and therefore this view is problematical.

The quantity of gastric juice secreted daily in the human stomach has been estimated at 10 per cent. of the body-weight, or 16 lb.; other also direct observations lead to 30 lb. These estimates are probably excessive.

During digestion, some gases, consisting of carbonic acid, hydrogen, marsh gas, and nitrogen, are not rarely formed from the digesting food. This may become a distressing symptom in disease. Thus, a man who suffered from widening of the stomach, and consequent lactic and butyric acid fermentation, one day would bring up combustible marsh gas by eructation—another, he would vomit liquids containing an excess of the acids mentioned. He described his stomach as alternating in function between those of vinegar-works and those of gas-works.

The albuminous substances, such as casein, more particularly tissues, meat, gristle, etc., are not entirely digested by pepsin and acid in the stomach, but a certain portion of them passes with the peptons, etc., as chyme, into the duodenum. They are here subjected to another kind of digestion, by the aid of metabolic ferments acting *in alkaline solution*. But of these ferments and alkalies we must first consider the secreting bioplasms—those of the liver, the pancreas, the villi of the intestinal canal, the Brunner's and Peyer's patches—before proceeding to the chemistry, firstly, of the secretions ; and secondly, of the results of the action of these secretions upon the various contents of the intestinal canal.

CHEMICAL CONSTITUTION OF THE PANCREAS (PANCREOPLASM), AND OF ITS SECRETION, THE PANCREATIC JUICE.

THE pancreas has been examined frequently with regard to the lower crystalloids which it contains, but of its main albuminous and phosphatide constituents hardly any notice has been taken. It contains, of course, blood-vessels, lymphatics, nerves, and connective tissue, and efferent canals, but its main bulk is composed of bioplasm in the shape of nucleated cells. Of these bodies a good many can be isolated by tearing, triturating, and levigating

the organ. The water employed in the latter process contains *soluble albumen* of the usual properties. When the insoluble bioplasm is now macerated during twenty-four hours, in twice its weight of concentrated salt water, it swells and becomes a viscous mass; when this matter is now suitably diluted with water, the *previously insoluble albuminous matter dissolves*, and the solution can be filtered from the insoluble parts. In this solution alcohol and heat produce copious precipitates. It has, moreover, many interesting properties, by which it shows itself related to fibrin. The cells may also be subjected to pepsin digestion, when the nuclei remain undissolved, and show the properties of *cytophosphatides*. The water-extract of the pancreas, which contains the soluble albumen, yields, after coagulation of the latter, between 1 and 2 per cent. of *leucin*, as also *xanthin, hypoxanthin, guanin,* and *inorganic salts*. The most remarkable ingredients, however, of the water-extract are several peculiar ferments, of which one is a *diastas*, transforming starch into maltose and dextrin, like ptyalin; another has a solvent effect upon certain kinds of tender or young cellulin; a third ferment decomposes neutral fats, setting free fatty acids and glycerol; and a fourth ferment, which acts mainly in alkaline solution, digests or transforms into soluble modifications albuminous substances, particularly such as have been for some time influenced and partially digested by pepsin in acid solution. The latter albumen digesting ferment is probably not present in the perfectly fresh pancreas, but forms in it when it is left to itself for a few hours. The matter, itself inert, from which the active ferment is supposed to be formed, is termed *zymogen;* the ferment has been termed *pancreatin*, or *trypsin*. When it acts upon pepton, it transforms a portion of it into a substance which has been termed *antipepton*.

The pancreatic juice is the product of the action of the

bioplasm of the pancreas, and is effused through the gland-duct into the duodenum. It contains the ferments already mentioned as present, or capable of being formed, in the gland, one *pancreatin* (syn. trypsin) the function of which is the completion of the solution of pieces of meat and albumen, which issue from the stomach with the chyme ; another which decomposes fats into glycerol and fatty acids ; and a third which has the power of emulging neutral fats, and transforming them into a subdivided condition, in which they may pass as microsomata into the bioplasm of the villi and thence into the chyle-ducts ; the fourth ferment transforms a small quantity of starch into maltose and dextrin ; the same, or a fifth, transforms cellulin into products similar, probably, to those from starch. These ferments in their full power are present only in juice which is emitted, or abstracted, from the pancreatic duct of an animal during full digestion. Juice thus procured is tough or viscid, and contains 10 to 11 per cent. of solids, while juice obtained from a permanent fistula has only 5 per cent. of solids, and lacks the power of digesting albuminous fragments. It is probable that this deficiency is caused by a degeneration of the gland, consequent upon the operative interference. The juice contains an albuminous matter at present undefined, possibly some *mucin*, and generally *leucin*, of which we have already noticed the presence in the parenchyma of the gland ; it has always an alkaline reaction, which may be more or less strongly developed.

The action of the pancreatic juice when effused into the intestinal canal is sufficiently clear from the nature of its ferments.

The pancreas has been observed in diseases to be degenerated and cancerous ; and as in these cases lumps of fat are stated to have been observed in the fæces, this appearance of fat has been ascribed to the failure in the supply of pancreas-juice. In lientery the pancreas as

well as the stomach and pylorus are probably at fault, perhaps in consequence of some ganglionic paralysis, which may progress to more general forms of paralysis in chronic cases.

CHEMICAL CONSTITUTION OF THE LIVER (HEPATO-PLASM), AND OF ITS SECRETION, THE BILE.

THE liver consists of a framework of connective tissue, in which the blood-vessels, lymphatics, nerves, and efferent ducts, and lastly the hepatoplasm, or liver-cells, are distributed. The tissue of the liver contains 70 per cent. of water, and 30 per cent. of dry solids, of which 1 per cent. are mineral. The cells are lumps of bioplastic material, containing mostly one nucleus, sometimes two nuclei. They were first examined by Braconnot, who found *soluble albumen*, later by Denis, who extracted from them by means of salt water an albuminous substance which he termed *globulin*, like all the similar bodies similarly extracted from other organs. The body may be identified as *hepatoplastin*. The last observer also extracted *fibrin*. The cells, moreover, contain *glycogen*, and *fat*, visible as microsomata, also *cholesterin*; in disease, some microsomata are coloured brown, or red, and consist of colouring matters; in the human subject, this colouring matter is a mixture of *bilifuscin* and *bilirubin*, in the ox, the latter only. The *sugar* found in the liver is derived from the glycogen by decomposition, which takes place rapidly; *inosite* and *lactic acid* have also been extracted from the liver of the ox. *Hypoxanthin* and *xanthin* are also contained in hepatoplasm, and some authors mention *urea*. *Leucin* and *tyrosin* are not present in the healthy cells, but occur in the parenchyma in disease; under pathological conditions *cystin* has also been found. There are also present in the extract from the cells matters which have the properties of *alkaloids* of

the class of so-called *extractives*, and which require further study. In diseases of the kidneys these extractives increase very much in quantity. Amongst the mineral ingredients the *phosphates* predominate ; of the *phosphates* of alkalies the *potassium* salts prevail over the *sodium salt*, as in muscle ; chlorides and sulphates are present in small amount, calcium and magnesium as phosphates ; iron, manganese, and copper are always present in liver-tissue. It will thus be seen that in some of its peculiarities hepatoplasm resembles myoplasm and neuroplasm. The latter it resembles still more by the presence not only of a *cytophosphatide*, contained in the nuclei, but also by that of a *phosphatide* similar to those which are specific to the brain. Of this latter phosphatide more will be said under the description of bile. *Biliary acids* are believed not to occur in the cells, but it is evidently difficult to prove their absence and distinguish between any contained in the ducts and any contained in the cells.

The secretion of the liver, *bile*, or gall, which in some animals is temporarily, at least in part, collected in a special receptacle, the gall-bladder, in others is effused directly into the intestinal canal, consists of specific acids and their salts, of peculiar coloured ingredients, of phosphatide bodies, of cholesterin, salts and water.

Group of Specific Biliary Acids.

Taurocholic acid, $C_{26}H_{45}NO_7S$, contains all the *sulphur* which is in organic combination in bile. It yields on chemolysis an acid free from nitrogen and sulphur, *cholic acid*, $C_{24}H_{40}O_5$, and a body containing all the sulphur and nitrogen of the original acid, namely *taurin*, $C_2H_7NO_3$, considered to be dehydrated isaethionate of ammonium, and producible from such.

Glykocholic acid, $C_{26}H_{43}NO_6$, is nitrogenous, but free from sulphur. It yields cholic acid by decomposition,

and as the second product *glykocin*, or amido-acetic acid, $C_2H_5NO_2$. The chemical constitution of the smaller nuclei is thus shown to be well known, but the same could not be said of cholic acid. Glykocin appears in the urine, coupled with benzoic acid, as hippuric acid ; but it is at present uncertain whether excreted glykocin has previously taken any share in the composition of the bile or not. Taurin, however, is consumed in the body, and its sulphur appears in the excretion as *sulphuric acid*. The acids just described occur in **ox-bile**, the bile of some fishes, and of dogs.

Human bile yields both *taurin* and *glykocin* when it is decomposed, but the acid combined with them is supposed to be a peculiar acid, and to have the composition expressed by the formula $C_{18}H_{28}O_4$; it has been termed *anthropocholic acid*. This matter is at present in the stage of a probable hypothesis, supported by some data, opposed by others.

Pig's bile contains *hyoglykocholic acid*, $C_{27}H_{43}NO_5$, as alkaline salt, and splits up into *hyocholic acid*, $C_{25}H_{38}O_3$, and *glykocin*, $C_2H_5NO_2$.

Goose bile contains *chenotaurocholic acid*, $C_{29}H_{49}NSO_6$, also as alkaline salts, and splits **up** into *chenocholic acid*, $C_{27}H_{44}O_4$, and *taurin*.

The chemical relations of the several cholic acids to each other are not yet known. Hyoglykocholic acid is pseudo-homologous to *glykocholonic acid*, an acid obtained from glykocholic by the influence of concentrated mineral acid. But cholic and hyocholic acid are not homologous. Chenocholic acid is, however, perhaps homologous with hyocholic. Thus :

Hyocholic acid, $C_{25}H_{40}O_4$.
Chenocholic acid, $C_{27}H_{44}O_4$.

All the natural biliary acids enumerated in the foregoing, as well as all the cholic acids obtained from them, give

with oil of vitriol and cane-sugar syrup a deep violet-coloured mass; this reaction was first discovered by Raspail, further elaborated by Pettenkofer, and is known either as Raspail's or Pettenkofer's test. It is also yielded by oleic acid, and olein, and several of the phosphatides of the brain, as also by the cerebrins; it is expedient to allude to it as the *oleocholiae reaction.* The products are not identical, as the several purple-coloured matters show different spectra.

Group of specific biliary colouring matters, Cholochroms.

Human bile is mostly brown, owing to the presence in it of a brown pigment, *bilifuscin*, which probably has the composition $C_9H_{11}NO_3$. This pigment prevails in quantity over others in human gallstones, where it occurs as calcium salt. Bilifuscin is easily soluble in alcohol, and is thereby distinguished and separated from the next pigment.

Bilirubin, $C_9H_9NO_2$, occurs in human bile, and in larger quantities in ox bile; only little of it is present in human gallstones, but ox gallstones consist principally of a *calcium-salt* of bilirubin. By oxidation and loss of carbonic acid, bilirubin easily passes into *biliverdin*, $C_8H_9NO_2$, according to the formula $C_9H_9NO_2 + 2O = C_8H_9NO_2 + CO_2$.

These pigments yield a colour-test with nitric acid which contains nitrous, which after its discoverer is termed Gmelin's reaction.

Hyoflavin is the yellow colouring matter peculiar to pig's bile; it differs in properties and reactions from the pigments contained in human and bovine bile. It also occurs in the very rare gallstones of the pig.

It is very probable that a great variety of bile acids and bile pigments will be met with in different classes, families, and species of animals.

The student must be particularly cautioned against the assumption so frequently made, that every green colouring matter of bile, or every green product obtained by reaction,

is biliverdin ; there are met with many natural and artificial *green* bodies, all differing greatly from biliverdin, some being products of substitution, some of combination.*

As regards the hypothesis that the biliary pigments are derived from the colouring matter of the blood, it must be borne in mind that there is as yet no evidence for that proposition.

Group of Nitrogenized Phosphatides.

All varieties of bile hitherto examined have yielded evidence of the presence of *phosphorus* in organic combination. Ox bile by chemolysis gave a base, *cholin*, to which the formula $C_5H_{15}NO_2$ was attributed ; it was supposed to be closely related to *neurin*, a base obtained from *lecithin*, to which the formula $C_5H_{13}N$ was given. It is probable that the base from bile is identical with the base from brain, and that the true formula of both is $C_5H_{13}NO$. These data, together with the discovery of *fatty acids* in the products of chemolysis, led to the hypothesis that the bile contained lecithin. This assumption has, however, been shown to be erroneous as regards ox bile. From the latter a *tetranitrogenized phosphatide* has been isolated as a crystallized hydrochlorate platinic chloride salt, of the formula $C_{82}H_{164}N_4PO_{36}+HCl+2PtCl_4$.

Group of Alcohols.

Cholesterin, $C_{26}H_{44}O$, is always present in bile in very small quantity. It is a monodynamic alcohol, capable of forming ether, but no such ether has as yet been discovered in the body. It is the principal ingredient of the commonest form of human gallstones, but does probably not occur in those of the ox except in traces. In a degeneration of the

* The reader who is desirous of full information on the subject of the Chemistry of Bile will find it in several articles in the ' Annals of Chemical Medicine,' vols. i. and ii.

liver called bacony, considerable quantities of cholesterin remain stagnant in the hepatoplasm.

Group of Mineral Salts.

The salts of the bile are contained in it in two forms— in solution and in combination with the organic acids. The biliary acids are held in solution by alkalies ; in human and bovine bile, sodium salts prevail ; in fish bile, potassium salts. Sodium chloride, carbonate and phosphate, calcium and magnesium phosphates, and traces of iron, copper, and manganese, are also found in bile ash. Sulphates are not naturally present, but are produced by the combustion of taurocholic acid.

The bile always contains small quantities of *gases,* oxygen, nitrogen, and carbonic acid.

Quantities of ingredients and of bile secreted in time.

Human bile is not easily obtained in a state fit for physiological analysis. The solids contained in it have been found to vary between 9 and 17 per cent. Ox bile contains from 7 to 11 per cent. of solids ; the bile of sheep and pigs, about 5 per cent. ; dogs and cats the same. In most varieties of bile the mineral matters amount to from 6 to 7 per cent. of the dry residue.

The quantity of bile secreted in the human body in a day has been estimated at 1,200 grammes, or the bulk which would fill a wine-bottle and a half. Conclusions from quantities observed in animals can only be used with caution, as some animals, *e.g.,* guinea-pigs, produce enormous quantities of bile relatively to their body-weight, while dogs and sheep produce relatively small quantities. The production is more likely to stand in proportion to the size and weight of the liver (hitherto neglected as a physiological factor) than to the weight of the body, to which hitherto quantities were almost exclusively referred.

Function of the Liver and Bile.—The main function of the liver is one of considerable intricacy, and is essentially connected with the great features of the process of digestion. The liver elaborates its products probably mainly out of venous blood, coming from the villi of the intestine. The products take different courses, one, amongst others, glykogen, passing into the blood; while the ingredients of bile pass into the intestinal canal. Here they meet, together with the pancreatic juice, the products of digestion coming from the stomach, and enter upon a complicated reaction with them, to explain which we may usefully recapitulate the main points of the doctrine of gastric digestion. .

Digestion in the stomach is produced by a process in which, of chemical ingredients, hydrochloric acid takes a main part. In the dog and the hyæna this hydrochloric acid is so strong that the hardest bones are absolutely dissolved. In man such a solution of bones cannot easily take place, but they are certainly corroded when introduced into the stomach. The acid which dissolves them in the dog is hydrochloric acid only; in man it is probably a mixture of hydrochloric and lactic acid. But although we find in the economy chlorides everywhere, and lactates constantly in the chyle, yet we do not meet with these acids in the free state. It is therefore assumed that in the bioplasm of the glands of the stomach, the peptoplasm, a chemical process is constantly taking place by which hydrochloric and lactic acids are formed. This process consists in the separation of the chlorine from sodium chloride (common salt), and the combination with this chlorine of a certain quantity of hydrogen derived from water. What takes place in the glands of the stomach may therefore be stated to be a splitting up of water and sodium chloride, and a cross-combination of the elements of hydrochloric acid on the one side, and sodium hydroxide on the other. $NaCl + H_2O = HCl + NaHO$. The lactic acid

is produced from lactates in a similar manner, and in the formula of its formation the place of chlorine in the foregoing formula would be occupied by the formula of the radicle *lactyl*, $C_3H_5O_3$. That the soda formed in this process is present in the peptoplasm, probably as carbonate, is made probable by the alkaline reaction of the peptic glands. But of course it cannot remain there long, but must be removed by the blood-current. Before, however, it is carried away by the blood, a part of this soda, or sodium carbonate, has an important function to perform, namely, to protect the stomach against the corrosive action of its own secretion. It keeps the blood and tissues more alkaline, and prevents the acids and pepsin, which has become more energetic after secretion and mixture with the peptones, from corroding the texture of the stomach. (Such corrosion immediately takes place in cases in which the supply of blood to a part of the stomach is interrupted, or where food remains in the stomach undigested after the secretory energy has passed away ; gastric ulcer, hematemesis, chronic dyspepsia, or painful digestion, with follicular erosion, and other pathological conditions, are produced in this way.) The soda is soon transformed into carbonate in the blood, and passes through the gastric veins into the portal vein, and thus into the liver. Here it is combined with the biliary acids and pigments formed by the hepatoplasm, gives out its carbonic acid, which passes towards the lung, and appears in the bile. If now bile is treated with hydrochloric acid, and the liquid separated from the precipitated acids is evaporated, sodium chloride is again obtained. $NaHO + HCl = NaCl + H_2O$. The same process takes place in duodenal digestion ; the acid of the chyme meets the alkali of the bile, and they unite, while water and bile acids are set free. They are, however, not precipitated, as the more soluble taurocholic acid holds the glykocholic in solution. A precipitate of peptones is, however, produced in the mixture

of chyme and bile. This, mixed with the bile acids and the biliary colouring matter, passes along the intestine as a pasty solution, to be altered and made absorbable by the many influences of intestinal reaction. It is soluble in alkali, and as much of the intestinal secretion besides pancreatic juice is alkaline, the transformation is favoured thereby. The pepton then may pass into the bioplasm of the villi of the intestinal canal, the *enteroplasm*, and be there transformed into the ingredients of blood and chyle, but the bile is not so easily accounted for. The acids certainly split up, taurin and glykocin returning into the circulation ; but the cholic acid mainly disappears, without leaving any trace in the blood or chyle ; neither contains a trace of biliary matter. In the fæces only occurs a small proportion of the cholic acid, amounting in man to from two to three grammes, being, perhaps, one-eighth or one-twelfth of the entire amount secreted. The cholochrom has been also changed and become insoluble in chloroform. We must assume that the cholic acid is already split up or chemolysed in the intestine, and reaches the circulation in the more simple form of products of its decomposition. The bile influences fats and fatty acids in the manner of a soap.

Bile, then, has been considered to represent the accomplishment of a purpose, which we may term the metabolism of albumen in the direction of a *specific* chemolysis. It is assumed by some physiologists that in this process glykogen and fats, and perhaps other matters, are formed, as well as bile acids from albumen. The sulphur of taurocholic acid is supposed to be that contained in the original albumen. However probable this explanation may be, it wants yet further support from quantitative physiology.

But the further uses of the bile are numerous and important ; by its aid cholesterin is thrown into the intestinal canal, either to be used further, or to be excreted ; the use of the phosphatide is at present entirely obscure.

The pigment seems to be excreted. Bile precipitates pepsin, and when it regurgitates into the stomach, arrests digestion completely. It therefore puts an end to pepsin digestion in the duodenum and favours the alkaline pancreas digestion.

In disease the bile may be retained and cause jaundice and slowness of the pulse ; or it may be decomposed in a peculiar manner and produce concretions ; in man these consist most commonly of cholesterin and a little modified bile acid, and bilifuscin, with bilirubin, and earths ; in oxen, bilirubin calcium predominates, and modified bile acid with lime soaps are present in lesser amount. In pigs these calculi contain a peculiar lime salt, which assumes a voluminous crystalline form when the powder is digested with cold alcohol.

CHEMICAL CONSTITUTION OF THE BIOPLASM OF THE INTESTINAL CANAL, ENTEROPLASM.

Enteroplasm is the aggregate mass of nucleated cylindrical, or columnar, epithelium, which covers the inner surface of the intestine from the pylorus to the vent. The reader is supposed to know the construction of the villi, and of the other organs of the surface, the Peyer's, Brunner's, and Lieberkühn's glands. These glands, though closely interspersed with villi, cannot be considered as possessing the same chemical function as enteroplasm ; for they have secreting faculties, while enteroplasm has probably absorbing and compounding qualities mainly.

In the columnar epithelium we have again to distinguish the cytophosphatide of the nuclei, and the stroma and enchylema of the colloid plasma. The general constitution of these cells is not unlike that of the liver-cells, but owing to the great difficulties of their isolation, it has not yet been sufficiently examined. These bodies possess the

power of taking into their substance, out of the contents of the intestinal canal, all kinds of albuminous and collogenous peptons, fats and fatty acids, starches, dextrins, sugars, alcohols, acids, salts, extractive and mineral substances, and large quantities of water, preparing them in a certain manner, and then giving them up to the lymphatic or chyle-vessels, and to the blood-vessels, to be carried into the blood, and serve the purposes of general nutrition. In addition to the natural ingredients of food, enteroplasm also takes up and transfers to chyle and blood substances which are of no use to the body, such as a number of inert metallic salts ; or which are hurtful to it, such as poisons ; or which benefit it, such as medicines. The secreting power of enteroplasm is supposed to be shown by the effects of purgation or diarrhœa from natural disease causes. But by other pathologists it is held that the liquid discharges, however produced, only indicate diminished absorption, and more rapid peristaltic propulsion of the contents of the intestines introduced by the mouth, or effused into it by the glands. On the whole, we are inclined to support this latter view, although there is no doubt that when large tracts of the enteroplasm are lost, *e.g.*, in cholera, an effusion of serous matter into the intestinal canal takes place. Serous lymphatic effusions also take place in diseases of the kidneys, but whether the enteroplasm is lost in such cases is not yet certain.

It is obvious from the foregoing that the chemical constitution of enteroplasm is rather guessed by analogy than found by analysis. The same may be said of the chemical changes which the chyme undergoes in its course through the intestinal canal and in contact with enteroplasm. Between the time at which an ingredient of chyme has been fully prepared by the ferments, and that at which the prepared matter is absorbed, so short a period elapses, that the prepared matters are never collected in any appreciable quantity in the intestine. This makes it very difficult to

appreciate the changes of chyme before absorption. In addition to the changes by endogenous ferments, many ingredients of the chyme, particularly the albuminous ones, are liable to suffer from septic bacteria, *i.e.*, to putrify under circumstances unfavourable to healthy digestion. These few considerations will show to the student the great difficulty of accounting chemically for the changes which food undergoes in digestion : there are all the ferments of all the secretions, the biliary products, the particles of unchanged and unabsorbed or unabsorbable food, the particles of food changed by the ferments, the particles of food changed by bacteria, and possibly some matters excreted by minor glands, and like the unabsorbable matters intended for excretion. Out of this mass of natural material enteroplasm selects what is serviceable for the economy of the body, and transfers it to blood and chyle.

CHEMICAL CONSTITUTION OF LYMPH AND CHYLE.

THE principal products of the activity of enteroplasm are *lymph* and *chyle* ; both these liquids are, as regards their essential constitution, identical with *serum* of the blood ; it is practically possible to obtain serum which cannot be distinguished from chyle, and on the other hand to obtain chyle and lymph which are identical with serum, both considered in the living state, viz., with the coagulable matters yielding fibrin yet dissolved in them. Chyle is certainly in great part the direct product of enteroplasm, but a portion might be lymph exuded as serum from the blood or from various kinds of bioplasm into the lymph spaces, and thence transferred into the chyle-vessels. By this consideration we are brought face to face with the question concerning the origin of serum, chyle, and lymph, and whether in fact they have not all the same origin and are identical. We see from the early development of the blood in the

fœtus, that bioplasm can produce serum long before it produces chyle. We can therefore have no difficulty in hypothetically ascribing to enteroplasm the power of producing serum. Now as serum penetrates into all parts of bioplasmatic formations, to yield to them the materials for their life, and as far as it has not been used returns from them, carrying also a part of the waste products of the life of the tissues, as lymph, it is necessary to assume that lymph is slightly modified serum. Chyle, on the other hand, might be the new product of enteroplasm only, or a mixture of serum brought as such into contact with enteroplasm, and of chyle newly made within the enteroplasm from chyme. We incline to the latter opinion. Most probably, therefore, enteroplasm produces serum, which it adds to the serum of the blood and transmits to the liver, and also produces serum, which it adds to lymph, and transmits to the lymphatic glands, and through them to the thoracic duct, and through that to the venous blood and the systemic circulation. Thus we arrive at the result that serum, lymph and chyle are products of the life-action of enteroplasm, and that lymph and chyle become serum only after having undergone the modifying influence of three other kinds of bioplasm, namely, the bioplasm of the liver, hepatoplasm, the bioplasm of the lymphatic glands, lymphoplasm, and the bioplasm of the corpuscles of the blood, hematoplasm. The student will thus arrive at the conclusion that the name of enteroplasm is far preferable to that of intestinal epithelium ; because enteroplasm is a powerful chemical and mechanical machine, and not a mere lining material, such as the word epithelium implies.

Lymph is an alkaline liquid which may be more or less clear according to the number of lymph-corpuscles or white blood-corpuscles which are suspended in it. It does not coagulate so quickly as blood, and from ten minutes to an hour may elapse before it forms fibrin after having been withdrawn from the body ; the coagulum has been

observed to assume a rose-red colour on exposure to air, a phenomenon which some have interpreted as the beginning of a generation of the pigmentary principles of the blood, through the influence of the atmospheric oxygen, others as the effect of an admixture of red blood-corpuscles. But neither hypothesis is very probable, and the pink colour of lymphatic fibrin should be studied on its own merits. Lymph also contains so-called extractives in considerable quantity, but the nature of these alkaloidal derivata of the albuminous substances is yet obscure. Some inquirers have discovered dextrose and urea in the lymph. Chlorides, phosphates, and carbonates of alkalies and earth are present in small quantity; 1,000 parts of lymph may yield 45 parts of pressed coagulated fibrin and corpuscles; the coagulum contains more than 90 per cent. of water, and about 5 per cent. of fibrin; $3\frac{1}{2}$ per cent. are corpuscles and fats, 1 per cent salts. The serum contains above 3 per cent. of albumen, more than 3 per cent. of fats, fatty acids, and other organic matters, and above 7 per cent. of salts. It must be borne in mind that such lymph is liable to great variation in the quantity of its solid constituents, and that it may in given cases be much more concentrated.

Chyle is in all respects similar to lymph, but contains a larger proportion of solid matters, not only of those which are in solution, but also those which, like fats, are mainly in suspension. In animals which are herbivorous, the chyle will be much less fatty than in those which feed on milk and flesh and oily seeds. 1,000 parts of chyle may yield 33 parts of moist coagulum; the latter may contain about 4 per cent. of fibrin, besides some free fat fatty acids, corpuscles, red-coloured matter, and mineral constituents. The serum of the chyle may contain about 4 per cent. of albumen, quantities of fats and fatty acids varying between 0·08 and 4 per cent., sugar, lactates, and extractives, and almost 1 per cent. of mineral ingredients.

In the foregoing description of lymph and chyle, the term albumen includes all albuminous matters precipitated by boiling ; much of these is serin, but the other modifications have not yet been satisfactorily determined.

As regards the fats and fatty acids occurring in the chyle, the student should bear in mind that fats are ethers of the tridynamic alcohol *glycerol*, $C_3H_8O_3$ (formerly termed glycerin), in which an atom, or two or three atoms, of hydrogen may be replaced by a fatty acid radicle each. In most of the common fats three radicles are thus substituted ; and in this manner *tripalmitin* $3(C_{16}H_{31}O)$ $C_3H_5O_3 = C_{57}H_{98}O_6$, *tristearin*, $C_{57}H_{110}O_6$, and *triolein* are formed. But in cow's butter there are glycerides which contain only two fatty acid radicles substituted in glycerol, particularly *butyryl*. Glycerol occurs, as we have seen, in the phosphatides of the brain and nerves ; in these, also, a great number of peculiar acids are in combination, which are partly isomeric with those of ordinary fats. Now, in ordinary digestion the chyme would contain a variety of fats, and of phosphatides ; these might be partly decomposed by the gastric juice, partly, as is strongly maintained by some physiologists, by the pancreatic juice ; the free fatty acids are now supposed to be transformed into soaps by the free alkali of the intestine juice ; but another action also takes place—namely, the fatty acids are emulged by phosphates of sodium, and in this finely divided state are transferred by the enteroplasm into the chyle. By far the greater part of the neutral fats, however, is transferred in a finely divided state, and without any previous chemical decomposition. Oleic acid is not emulged by sodium phosphate, neither are any of the neutral fats.

It is thus clear that chyle mostly contains, besides some neutral fat, a quantity of fatty acid which dissolves in ether directly with the fats, and another quantity of fatty acid which must be freed from alkali before it can dissolve in ether. And it is also clear that the neutral fats may

be *tripalmitin, tristearin, triolein,* or *tributyrin,* or *di-butyrin,* and several other glycerides in small quantity, while the fatty acids may not only be *palmitic, stearic, oleic, butyric,* but also any of the fatty acids resulting from the decomposition of phosphatides contained in the food or in the bile. This explains the great difficulty of analyzing the fatty substances of the chyle and serum; and if it is considered that sometimes they seem to contain also *undecomposed phosphatides,* it cannot be doubted that the analysis of small quantities of material is impossible.

CHEMICAL INGREDIENTS OF THE FÆCES.

THE fæces contain all insoluble residues of the food, some decomposed and altered bile acid, changed cholochrom, myochrom, cholesterin possibly changed into *excretin,* $C_{20}H_{36}O$, some peculiar fatty matters, *skatol,* a yellow coloured matter, and phosphate of magnesium and calcium. The fæces of most animals contain a much greater quantity of insoluble matter than those of man; the fæces of carnivora are the most simple in chemical constitution, and the smallest in bulk. The fæces of animals which devour bones, like hyænas, wolves and dogs, contain generally much calcium phosphate, which becomes dissolved in the stomach and reprecipitated in the lower intestine. Human fæces vary with the diet, being dark, semi-fluid, and of small bulk after meat diet, but of larger bulk, paler and more solid, after bread diet.

The fæces of children at the breast contain *cholesterin,* some casein in flakes, a quantity of matter not yet defined, and a yellow matter, soluble in alcohol, *enterolutein.* This is spectroscopically characterized by an absorption band in the blue.

The anomalies of fæces are still less known than their normal composition. The evacuations in cholera are

similar to water in which rice has been boiled, and are therefore termed rice-water evacuations ; they contain products of the decomposition of albuminous substances, and are in a state of fermentation, probably of bacterial or microzymotic origin. They yield sometimes the spectrum of the *indol* reaction, with nitric and nitrous acid.

Iron preparations taken into the stomach colour the fæces black, mercurial ones green. This latter fact gave rise to a prevalent belief, now shown to be erroneous, namely, that mercury was a cholagogue, and increased the excretion of bile. Bile (not decomposed) has never as yet been found in any fæces.

Most remarkable and suggestive is the discovery by Liebig of *alloxan*, $C_4H_2N_2O_4$, a product of the oxydation and cleavage of uric acid, in the mucous evacuations from a case of intestinal catarrh. Possibly, therefore, functions of biolysis are allotted to the intestine, which at present we localize in other organs, or know not where to place. Gout might find an explanation in the failure of this biolytic action, for uric acid once in the blood seems as far out of the reach of oxygen as sugar is in the blood in diabetes.

Imperfect digestion further causes the production of gases, of which *carbonic* and *hydrogen*, and *marsh-gas*, CH_4, are the principal ingredients in varying proportions. Marsh-gas mostly prevails, and is most easily produced by the fermentation in the large intestine of cellulin of the food. But there are several sources for these gases ; the development of them in diseases is sometimes very copious, and in typhus, *e.g.*, they collect sometimes in large masses in the intestine, causing the condition known as tympanites or meteorismus.

CHEMICAL CONSTITUTION OF THE KIDNEYS, RENOPLASM, AND OF THEIR SECRETION, URINE.

THE kidneys contain many blood-vessels, lymphatics, a little connective tissue and tubes of homogeneous membrane, inside of which the *renoplasm*, or cells of the tubules, renal epithelium, are deposited. When a kidney is comminuted, some *soluble albumen* may be obtained, but it is difficult to separate that which belongs to the true enchylema of renoplasm from serum and lymph. When kidney-pulp is levigated with water, a turbid liquid may be obtained, which contains nothing but renoplasm, *i.e.*, cells of the tubules in suspension. They can be collected by deposition or filtration. To salt water they yield *plastin* (globulin of Denis), and after digestion with pepsin and acid they leave *cytophosphatide*, the material of the nuclei. The water extract of renoplasm after removal of albumen contains *chlorrhodinic acid*, uric acid, and bodies resembling hypoxanthin and xanthin, but urea is scarcely to be found in it. Cystin and inosite have on some rare occasions been met with. The chemical changes of the kidneys in diseases have not yet been sufficiently examined.

The *urine* is the secretion of the kidneys. It is the lixiviated refuse from the chemical processes of the body. Besides water, it contains mainly crystalloid substances, and a few matters only observing the bearing of colloids. They can be arranged in groups, and although such an arrangement is not free from objection (such as that an alkaloid is classed under the ureides), yet it offers practical advantages which the student will appreciate.

GROUP OF UREIDES.

The ingredient which occurs in the urine in the largest quantity, amounting on an average to 2 per cent., is *urea*,

CH_4N_2O ; of this a man secretes about 30 grammes in twenty-four hours. Then there is *kreatinin*, $C_4H_7N_3O$, the same as that which occurs in the muscles. It is partly changed into kreatin, $C_4H_9N_3O_2$, by taking up a molecle of water during the process of preparation. Kreatin is a ureide, as it splits up into *sarkosin*, $C_3H_7NO_2$, and urea. There is further contained in urine *uric acid*, $C_5H_4N_4O_3$, which contains the elements of two molecles of urea and of oxalic acid and carbonic anhydride. It may form calculi in the bladder, or gouty deposits in and around joints, in the latter case mainly in combination with calcium. To this group further belongs a series of bodies which are less oxidized than uric acid, and differently constituted, and occur only rarely or abnormally in human urine, namely *guanin*, $C_5H_5N_5O$, *hypoxanthin*, $C_5H_4N_4O$, *xanthin*, $C_5H_4N_4O_2$, and *allantoin*, $C_4H_6N_4O_3$.

GROUP OF AROMATIC PRINCIPLES.

The principal member of this group is an acid which, from having been first discovered in horses' urine, is termed hippuric, $C_9H_9NO_3$, remarkable by its consisting of a combination of *glykocin*, $C_2H_5NO_2$, and *benzoic acid*, $C_7H_6O_2$, less a molecle of water. It is present in the urine of herbivorous animals, particularly when they are fed upon grass, and is found in the human body in considerable quantity when benzoic acid or articles of food containing benzoyl compounds, such as greengages, are taken. To this group belong, further, *indol-sulphuric acid*, which by oxydation yields *indigo*; further, *phenol-sulphuric acid*, $C_6H_6SO_4$, and *cresol-sulphuric acid*, which give the relative products of decomposition, and thus furnish the sulphuric acid, which while in organic combination is not precipitated by barium salts. Another member of this group is *urrhodinogen*, which under the influence of acids yields *urrhodin*.

GROUP OF PIGMENTARY OR COLOURING PRINCIPLES.

To this group belongs the yellow pigment of urine, *urochrom*, which, however, has many properties of an alkaloid, and therefore might also be treated of in the next group. This, by the influence of sulphuric acid, yields various remarkable products of decomposition or condensation ; the first of these latter is uromelanin, $C_{36}H_{43}N_7O_{10}$, with an atomic weight of 733. The next product is *uropittin*, not as yet sufficiently studied ; then there is *omicholin*, empirical formula $C_{22}H_{38}NO_5$, also an organic base with fluorescent properties and a peculiar spectrum ; and *omicholic acid*, $C_{15}H_{22}NO_4$, also fluorescent, but slightly differing in its spectrum, and more in its composition, from omicholin ; these bodies are the bearers of the radicles which yield the powerful odour when urine is burnt. During their decomposition much *acetic* and *formic acid* are also formed. *Uromelanin* may represent the nucleus of hematin. *Urerythrin* is a fiery reddish-yellow pigment, which has a characteristic spectrum in alcoholic solution ; in the dry solid state, treated with caustic lye, it strikes a *green colour*.

GROUP OF ALKALOIDS.

To this group belong some substances already placed in other groups, such as *hypoxanthin*, *kreatinin*, and *urochrom*. In addition to these, there can be isolated by the phosphomolybdic process *reducin*, a body which quickly blackens silver salts, and has for nearest empirical formula $C_6H_{11}N_3O_4$. A *second* new crystalline *alkaloid* has formula $C_7H_8N_4O_2$, and is similar to, but not identical with, theobromin. A *third alkaloid* has formula $C_6H_9N_3O$, when combined with zinc oxide ; its formula is therefore that of reducin minus two atoms of oxygen. A *fourth alkaloid* combines with platinic chloride, and this com-

pound, on combustion, gives out vapours smelling like burning tyrosin.

GROUP OF EXTRACTIVE ACIDS.

These extractive acids are remarkable by this, that they contain nitrogen, and can be precipitated from urine by ferric chloride, but not by phosphomolybdic acid. Urochrom, however, is precipitated by both; if this and the other alkaloids are therefore removed first by the phosphomolybdic process, the extractive acids may be precipitated free from urochrom by ferric chloride. The extractive acids are at least three in number; first *kryptophanic* acid, which, when considered as dibasic, has the formula $C_5H_9NO_5$, but which must perhaps be considered as tetrabasic, and then has the formula $C_{10}H_{18}N_2O_{10}$; in that case its metallic salts will have the general formula $C_{10}H_{14}M_4N_2O_{10}$. Another extractive acid is *paraphanic* acid, $C_{11}H_{18}N_2O_6$, dibasic.

GROUP OF INORGANIC SALTS.

Of inorganic salts, the phosphates of the alkalies and the alkaline earths and potassium chloride are present in considerable quantity, but most prevalent in human urine is sodium chloride, or common salt. In the urine of herbivora, alkaline potash salts are found to prevail.

GROUP OF ACCIDENTAL AND MORBID INGREDIENTS.

Of some matters minute traces appear in the urine; thus, of sugar and alcohol, after these bodies have been taken by deglutition. In diseases there may appear blood, hemochrom, peroxyhemochrom, hematin, albumen, fibrin, fatty acids and fats, large quantities of sugar, as in diabetes; leucin and tyrosin, as in yellow atrophy of the liver; oxalic acid and calcium oxalate, as in the disease termed oxaluria which frequently ends in the formation of calculi.

Much as the urine as been studied, its chemistry is by no means accomplished ; and on the causes of some of the most troublesome diseases showing themselves by symptoms in the urine—gout, uric acid calculus, oxalic diathesis, diabetes, chylous urine—our knowledge is as yet very incomplete. Under all circumstances, however, the analysis of the urine is an indispensable aid to clinical diagnosis, and furnishes most valuable positive and negative information on acute as well as chronic diseases.

CHEMICAL CONSTITUTION OF THE LUNGS AND BREATH.

THE bioplasm of the lungs, which is their specific active part, may perhaps be termed *pneumoplasm*. The elements or cells in the shape of which it is disposed in the ultimate ramifications of the air-passages are perhaps the thinnest of any epithelia, forming rather structureless thin plates with nuclei in their centre, than bodies of three dimensions. They have not been isolated, but their plastin can be extracted, and their cytophosphatide be isolated by pepsin digestion.

In the process of respiration, the oxygen of the air, inhaled together with its nitrogen, is absorbed by the blood, and in exchange carbonic acid and water are given out. The expired air therefore contains less oxygen than the inspired, and a quantity of carbonic acid instead. But the whole of the oxygen does not return as carbonic acid and water : a portion is otherwise combined, and leaves the body in the urinary products of oxidation, particularly urea. A healthy, strong man exhales in twenty-four hours upwards of 400 litres of carbonic acid, and inhales upwards of 500 litres of oxygen. The expired air during rest contains about 4 volumes per cent. of carbonic acid. During activity, the expiration of carbonic acid becomes much more rapid, and in extreme cases may sometimes rise to tenfold

its normal quantity in the same time. Activity or muscular work, on the other hand, hardly increases the quantity of urea excreted by a man.

The breath in disease may contain carburetted hydrogen (of which a trace is also excreted in health) and volatile matters at present unknown, ammonia being perhaps amongst them. These investigations have been made possible by the invention of an apparatus, which permits living beings to be observed for days in glass chambers, and their excretions to be accurately analyzed and estimated as to quantity. By means of this method it has now been found that man, during sleep, stores up a quantity of oxygen in his body, particularly his muscles, which is then ready for the production of force the moment it is wanted. This explains some of the phenomena of activity and rest much better than they could hitherto be defined.

THE SECRETIONS OF THE SKIN.

THE secreting organs of the skin composed of active bioplasm are of two kinds mainly, *sweat glands* and *fat glands*. It would be affectation to speak of the chemical constitution of these glands, as they can probably never be isolated. But their chemical peculiarities may be guessed by the aid of the analogy in composition presented by many bioplasms which are different in action.

The *sweat*, discharged ordinarily in small quantity and evaporated immediately from the surface, is discharged in large amount under the influence of muscular exertion or a heated atmosphere. It must be filtered from surface epithelium cells, which make it turbid. Of chemical ingredients there are observed *lactic* and *sudoric acid*, the latter peculiar to sweat, and not found elsewhere, and *urea*. There is much sodium chloride, little or no phosphate. Sometimes volatile fatty acids, *e.g.*, *valerianic*, are found in small quantity, but it is possible that they are

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formed after the sweat has been excreted from some material as yet unknown.

CHEMICAL CONSTITUTION OF CONNECTIVE TISSUE.

THE connective tissue forms tendons, fasciæ, or envelopes of muscles and limbs, ligaments of joints and capsules, and binds all organs of the body together. It consists of fibres, of which each is a bioplastic individual, with nucleus, stroma, and enchylema. The latter is albuminous, and small in quantity; the stroma consists of *collogen*—that is to say, a substance which, under the influence of acetic acid, or of prolonged boiling in water, is transformed into *colla, glutin,* or *glue.* This collogen like its product, glue, by chemolysis yields most of the products of the albuminous matters, tyrosin, leucin, volatile acids, and alkalies, ammonia, carbonic and oxalic acid, and glykocin, the latter formerly termed glykocoll, from the fact of this sweet-tasting substance having been discovered in chemolyzed glue.* In the stroma of the connective tissue cells, microsomata are frequently deposited—normally, or as results of disease processes, as in the choroid, the rete Malpighii of the negro, bronzed skin (suprarenal glands) disease, freckles, melanotic cancers, and others. The chemical constitution of *isinglass* and *ossein,* the organic part of bone, are identical with that of collogen, but *chondrin,* similar in some respects, deviates in others. The fibres of the connective tissue are united to each other not only by being interwoven, but also by a particular *cement,* which is soluble in caustic lime and barita, and precipitated from these solutions by acetic acid; this cement seems to be *mucin,* identical with that of the salivary glands and embryonic tissues, *e.g.,* the umbilical

* See 'Chemolysis of the Collogenous Substances by Barita-hydrate.' 'Annals of Chemical Medicine,' vol. i., p. 38.

cord. The connective tissue is mostly interspersed with *elastic fibres*, which are not changed by boiling water as the *collogen fibres* are.

CHEMICAL CONSTITUTION OF FATTY TISSUES.

THE fatty tissue is composed of cells, containing a nucleus, stroma, and enchylema, in the interior of which fat is deposited, at first in the shape of microsomata, later on in large masses, frequently surmounting in size that of the original cell. Interspersed with these specifically developed cells are cells of connective tissue, which are probably able to deposit some fat within this structure under certain circumstances. Some fat tissue remains permanently in the body, always filled with fat ; some may lose its fat during starvation, or disease, and regain it afterwards. The fats in the human fat-tissue are mostly those described in the paragraph on digestion, namely, *tristearin*, $3(C_{18}H_{35}O_2)C_3H_5$; *tripalmitin*, $3(C_{16}H_{31}O_2)C_3H_5$; *triolein*, $3(C_{18}H_{33}O_2)C_3H_5$; it is also probable that a fat exists of which *margaric acid* is the characteristic constituent, *margarin*, $3(C_{17}H_{33}O_2)C_3H_5$; those who deny the individuality of this highly crystalline fat declare it to be a mixture of tristearin and tripalmitin. The fatty tissue is subject to hypertrophy, or excessive infiltration ; there are also peculiar colorations observed in natural fats, some of which are white, while others have a yellowish tinge. This tinge increases and becomes orange, even red, in wasting diseases. The colour is due to the presence of a pigment, *lipolutein*, which is spectroscopically distinguished by three absorption bands in the blue. The increase of colour is due to the accumulation of lipolutein after the absorption of fat free from pigment. Newly formed fat tissue is observed in the fatty tumours of *lipomata*. It is believed that fat in tissue may originate in several ways ; it may have been eaten with the food, being originally of vegetable or animal origin, and after

absorption have only been carried to the cells ; or it may be formed from sugar, dextrin, and glykogen; or, lastly, it may owe its existence to the decomposition of albumen. Thus, the cholic acid of bile might yield any of the fatty acids, and sugar the glycerol. But the proof of any of these processes actually occurring has not yet been furnished, and the transformation of cholic acid would not be easy to explain in view of the probability of its containing an aromatic radicle.

CHEMICAL CONSTITUTION OF CARTILAGE AND SIMILAR TISSUES.

CARTILAGE contains peculiar *cells*, or nucleated centres of bioplasm capable of multiplication by division. These cells are chemically distinguished by great resistance to solvent agents. They are imbedded in an apparently homogeneous material produced by themselves, the *intercellular substance*, termed *chondrinogen*, because by boiling with water it is transformed into *chondrin*. According to some, this matter gelatinizes like glue, according to others, it is not gelatinizing, and when it becomes a jelly this is due to the admixture of gelatin. Again, it is alleged that chondrinogen is collogen simply, but in a denser form, and requires a more prolonged influence of hot water ; now, as such an influence transforms gelatin into a non-gelatinizing modification, chondrin might be such a product. Anyhow, chondrin and gelatin have very different chemical constitutions ; chemolysis leading to the following proportion as the simplest expression of the elements contained in them :

$$\text{Gelatin, } C_{3\cdot 66}H_{7\cdot 20}NO_{2\cdot 08}$$
$$\text{Chondrin, } C_{4\cdot 676}H_{8\cdot 49}NO_{2\cdot 57}$$
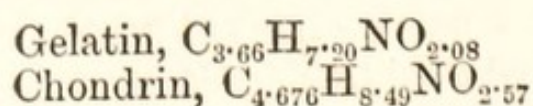
The cartilages are subject to degeneration which ends in ossification, or infiltration with calcium phosphate. The

cartilaginous surfaces of joints are lubricated by a fluid which is termed *synovia*. It contains about 94 per cent. of water, 3·5 of albumen, 0·5 of mucin, and more than 1 per cent. of ash. Its origin is not yet satisfactorily explained, but is probably connected with bioplastic activity of the cartilage cells. During diseased or irritated condition of joints much synovia is formed : the collection of an excess of synovia in a joint constitutes *hydrarthron*. A matter similar to chondrinogen is *hyalin*, of which the cysts of old echinococci are composed. Boiled with dilute sulphuric acid it yields a substance which reduces alkaline copper solution, and is supposed to be a sugar (*hyalose*).

The chemical composition of the *cornea* is similar to that of cartilage, particularly the hyaline variety.

CHEMICAL CONSTITUTION OF BONES AND TEETH.

THE *Bones* consist of a peculiar combination of organic matter with mineral earthy phosphates, and contain as accessory matters marrow, blood-vessels, and cellular nuclei in the cavities called bone-corpuscles. The organic substratum is called *ossein*, the mineral matter is termed bone-earth. The ossein is obtained by extracting the bone-earth by dilute hydrochloric acid. It retains the structure of the bone substance, which is disposed in concentric layers round a tubular centre. Ossein when boiled in water dissolves like collogen, but differs from the latter in several particulars, although the product of the solution in hot water is true gelatine. Of ossein purified bone contains from 29·5 to 30·9 per cent., with which 68·1 to 69·4 per cent. of earthy salts are in combination. The regularity of these proportions has led to the assumption that bone is a chemical compound in definite atomic proportions of ossein and earthy salts, and not merely a tissue in which earthy salts are deposited. Experiment shows that an attraction

exists yet even between gelatin and earthy phosphates. Thus a mixture of gelatin and bone-earth dissolved in hydrochloric acid, when neutralized by ammonia, deposits bone-earth with 20 per cent. of gelatin ; when tannic acid is added to such a solution, tannate of gelatin with much bone-earth is precipitated. Bone-earth contains 9·1 per cent. of calcium carbonate, 87·7 per cent. of calcium phosphate, $Ca_3P_2O_8$, 1·7 per cent. of magnesium phosphate, $Mg_3P_2O_8$, and 3 per cent. of calcium fluoride, $CaFl_2$. The nutrition of the bones proceeds from their surface towards their cavities ; their renovation after injuries proceeds in the same order ; both nutrition and renovation are the function of the bioplasm of the *periosteum*. Certain dyes, such as a pigment contained in madder, when given with food, penetrate into the bones and stain them. The conclusion formerly drawn from this experiment, namely, that the bone was rapidly renewed from without and absorbed in the marrow cavity, is probably quite untenable. In several important diseases the bones are greatly affected, and become either brittle, so as to break easily, or soft and slowly bending. Such diseases are rhachitis, or rickets, common in children, the osteomalacia of pregnant women, and that particular form which attacks aged persons. In these diseases the amount of bone-earth present in the bone falls from the normal 68 per cent. to about 30 per cent. of the dry bones, while the ossein rises to 60 and 80 per cent. The ossein at the same time changes its chemical character, and simultaneously undergoes a curious tissue transformation, starting from the marrow cavities, and now no longer yields gelatin. It seems that one of the agents by means of which in this no doubt complicated process the earths are removed is lactic acid, which under these circumstances, and not in health, is found in and about the bone. These diseases urgently call for chemical investigation.

The teeth are peculiar bone-like structures, of which a

part, the root, is covered by a material like ordinary bone, termed *cement*, while the top or crown is formed upon a particular plan, round many minute tubes ; this latter tissue is termed *dentin* or *ivory*. The outer hard covering, the *enamel*, is a third specific formation of dental bioplasm, and contains only 4 per cent of organic matter, 92 per cent. of earthy phosphates, and 4 per cent. of calcium fluoride. Dentin has very nearly the composition of bone, but in some mammals contains more magnesium phosphate than bone, namely, up to 2·5 per cent.

CHEMICAL CONSTITUTION OF THE SPLEEN, SUPRARENAL CAPSULES, THYMUS, AND THYROID GLANDS.

The function of *the spleen* is not well known, but seems connected with the elaboration of certain constituents of the blood, and certain processes of digestion. The organ contains much blood, and a separation of its tissue and juice from its blood has not yet been effected. The fresh spleen is alkaline, but soon becomes acid. The watery extract contains hemochrom and the other ingredients of the blood, besides a peculiar albuminous matter which on combustion leaves phosphoric acid and ferric oxide. It encloses some cholesterin. After removal of all albuminous matters there are in the extract, of fixed acids, the lactic and succinic ; of volatile fatty acids, formic, acetic, and butyric ; of amidoacids, leucin ; of ureides, hypoxanthin, xanthin, and uric acid ; there is also inosite in considerable quantity. The pulp contains a phosphatide, besides the cytophosphatide and plastin of white lymph-corpuscles. The spleen of old horses when dried and burnt yields up to 5 per cent. of ferric oxide. These ingredients show that chemical processes of various kinds must be carried on actively in the spleen. They are, however, not indispensable to life, as animals from which the spleen has been removed by operation, continue to live without any perceptible disturbance. In leukocythæmia the spleen

is frequently very large, and weighs up to nine or ten pounds. If it be found small in that disease, the lymphatic glands are certainly enlarged instead. The spleen is sometimes subject to an albuminous infiltration; the material passes into a colloid state, becomes hardened, and is indigestible in artificial gastric juice. It gives no sugar by treatment with sulphuric acid, and is little prone to change by artificial or natural influences.

The thymus gland is a mysterious organ situated in the chest in front of the lungs. It becomes of less importance to the adult than it probably is to the fœtus in the womb. It contains albumen, collogen, elastic tissue, a little fat, leucin, xanthin, hypoxanthin, succinic and lactic acid, and perhaps also volatile fatty acids and sugar. In the progress of the involution of the thymus the amount of sodium contained in it is nearly doubled, while the fat is increased to more than ten times the amount which it contains shortly after birth. Denis considers the bioplasm of the thymus to contain globulin with little fibrin, besides albumen and serin. The washed pulp yields to salt water this globulin (or plastin) with the usual properties.

The thyroid gland contains nearly the same chemical constituents as the thymus. It would, however, be erroneous to assume that *all* the constituents of glands of the most varied connection and situation are identical, for the defined ingredients are perhaps only one-fourth or one-sixth of the whole of the ingredients, and specific differences may therefore be discovered upon the ingredients which are at present undefined. The thyroid contains the constituents of bioplasm, plastin, and cytophosphatide; mucin, particularly in the state termed colloid degeneration; it then also contains cholesterin. When containing brown fluids in the disease termed struma, a sediment of blood-corpuscles is mostly present, which, however, contains only decomposed hemochrom in the form of *hematin.*

The suprarenal glands have a dark colour of their own, and yield many curious coloured reactions. Their watery extracts are coloured red by iodine, and blackish blue by ferric chloride ; they contain leucin. Alcohol extracts from these glands a peculiar substance, *renculin*, which is deposited on cooling, and requires further examination. The alcoholic, or ethereal, extracts become yellow and red when exposed to the air, and show a green fluorescence due to the specific ingredient just alluded to. In certain chronic diseases (Addison's, or bronzed skin disease) in which the skin is more or less copper or brown coloured, the suprarenal glands are specifically diseased.

CHEMICAL CONSTITUTION OF THE PROCREATIVE GLANDS, OVARIES, AND TESTICLES.

THE *Ovaries* are composed of the anatomical stroma, the Graafian follicles, and the corpora lutea. The latter contain *fluid and coagulable serum*, particularly while they possess an internal cavity ; this lymph is gradually absorbed by the cellular bioplasm, which grows from the walls of the cavity, gradually fills it entirely, and constitutes the solid corpus luteum. This bioplasm contains the usual constituents, but is distinguished by the deposition in its cells, as granules (microsomata), of *ovariolutein*, a yellow matter soluble in alcohol, ether, and chloroform, and distinguished spectroscopically by three absorption bands, which its solutions show in the blue and violet part of the spectrum. A similar yellow matter is contained in the yelk of eggs. The yellow colour is not due to hematin or hematoidin, as was formerly generally supposed.

In some forms of *ovarian cyst* a yellow albuminous fluid is contained, which shows the spectrum of lutein without any preparation ; in this morbid fluid the lutein, which must be distinguished as *cystolutein*, is therefore contained in solution, while in the normal corpora lutea it is con-

tained in granules, and this should be distinguished as *ovariolutein.*

The *ovum*, or primary female germ, before impregnation is the true protoplasm ; of this we can guess the composition only by analogy. Eggs, so-called, of bird and reptiles, etc., are *impregnated* ova, to which an independent existence has been secured by the accumulation around them of reserve matter from which the germs can draw materials for their growth. These reserve matters are *yelk* and *albumen.* The yelk contains an albuminous matter, *vitellin ; phosphatides ;* of these lecithin is, perhaps, present in hen's yelk; but there are also other *phosphatides,* not being lecithin ; then *cholesterin,* and *fats.* It is on account of these fats that the yelk is difficult to analyze as regards the phosphatides contained in it. The opinion that the *vitellin* and *phosphatides* of the yelk are in a kind of chemical combination is not improbable; the yelk contains *yelk plates,* supposed to be nucleolar elements, cytophosphatides. But the yelk is not a bioplasm ; like the albumen, it is only a material produced by a specific bioplasm (ovarioplasm), from which true protoplasm may take its material for further development.

The testicles are rich in bioplastic substances belonging to the material which lines their tubes and produces the procreative elements. In the analysis of testicles it is even more difficult to distinguish between bioplasm and secretion, because the latter is organized, and because there is mostly a certain quantity of the secretion contained in the ducts of the gland. All testicles yield *plastin* (globulin) to salt water ; those of man least, those of fishes most, out of equal weight of dry material. The sperma of lower animals, *e.g.,* fishes, can be obtained in quantity of examination. It contains *albuminous matter ; spermatic filaments,* or *spermatozoa,* and peculiar *sulphurized* ingredients. The spermatic filaments contain a *cytophosphatide* (which on the assumption that the so-

called head of the spermatozoon corresponds to the nucleus of a cell may be termed a nuclein), which in the sperma of salmon is combined with a base, *protamin* (nearest formula, $C_8H_{16}N_{4\cdot5}O_2$). The sperma contains besides a *phosphatide*, which is supposed to be lecithin, and cholesterin. Human sperma yields a base, *spermatin*, C_2H_5N, which is also obtained from other bioplastic substances.[*]

CHEMICAL CONSTITUTION OF MILK-PRODUCING GLANDS, OR LACTOPLASM, AND THEIR SECRETION, MILK.

THE milk glands have never been adequately analyzed ; but their product, milk, has served as the material for many chemical and pseudo-chemical operations. Lactoplasm is endowed with a great amount of vital energy, if the latter can be measured by quantity of product. This energy is a function of the organic centre, termed cell ; it therefore resides mainly in the colloid albuminous and cytophosphatide matters, as is the case in all bioplasm. This is here repeated only in order to point out that future researches must be directed mainly towards the elucidation of the chemical nature of these albuminous bodies, and less than hitherto to the extraction of low crystalloids which may be results of retrogression, or materials for progressive metabole, but in any case are qualitatively and quantitatively subordinate factors of the vital process.

Milk contains *water, casein, albumen, lactoprotein, fats, sugar of milk* or *lactin, lactolutein, alkaloids* or so-called extractives, and *salts*. In the milk which is secreted by the females of mammals soon after they have given birth to their young, there are also shaped bioplastic elements,

[*] *Cf.* 'Spermatin, a new Organic Base in Animal Organisms.' 'Ann. Chem. Med.,' i., 301.

so-called *corpuscles of colostrum*, which disappear in the course of lactation.

Milk has a specific gravity from 1·018 to 1·045, and usually an alkaline, but sometimes an amphoteric, and in carnivora an acid reaction. It consists of a colourless serum in which *globules* float : these consist of *fat*, of which each particle is surrounded by an albuminous envelope. Milk contains about 10 per cent. of solid matter, of which from 0·1 to 0·5 per cent. are mineral and remain on combustion as ash. Of the 10 per cent. solids, from 2 to 4 per cent. are casein, from 1·5 to 4 per cent. fat, and from 4 to 5 per cent. milk-sugar (lactin).

The fats of milk when isolated are termed *butter*. They are mostly triglycerides ; some, however, are diglycerides. The acids which can be separated from the glycerol are almost all the members of the fatty acid series, with from C_4 to C_{20} : butyric, $C_4H_8O_2$; caproic, $C_6H_{12}O_2$; caprylic, $C_8H_{16}O_2$; caprinic, $C_{10}H_{20}O_2$; myristic, $C_{14}H_{28}O_2$; palmitic, $C_{16}H_{32}O_2$ (margaric, $C_{17}H_{34}O_2$, or isomeric with palmitic, an open question) ; stearic, $C_{18}H_{36}O_2$; arachinic, $C_{20}H_{40}O_2$; then there is oleic acid, $C_{18}H_{34}O_2$, which, though belonging to another series, by chemolysis yields fatty acids of the $C_nH_{2n}O_2$ series only.

Casein is an albuminous substance which contains not only carbon, hydrogen, nitrogen, oxygen, and sulphur in proportion, by which it is shown to be closely related to albumen, but also phosphorus, by which it is shown to be related to the phosphatides. On chemolysis it yields double the quantity of tyrosin which is obtained from albumen, and at least 34 crystalloid products which are the penultimate nuclei or radicles of its constitution, as well as of that of all albuminous substances. By its composition, therefore, casein is qualified to become the material from which the assimilating powers of the young organism may form all the different kinds of bioplasm which have been described in the foregoing.

CHEMICAL CONSTITUTION OF PUS AND SEROUS EFFUSIONS.

PUS may be considered as *lymph* or *serum* which has been secreted into cavities or interstices of tissues under the influence of disease or injury. By disease we now mostly mean the condition produced in living bioplasms or liquids by the entrance into and action upon them of minute organisms, which have the power of multiplying and acting destructively, mechanically in **one** sense, chemically as instigators or instruments of decomposition, termed fermentations or zymoses. Hence these organisms are also termed microzymes, and as many are rod-shaped, bacteria. While, therefore, the material of pus, as furnished by the injured organism, is probably always the same—namely, serum, or lymph and lymph-corpuscles; the microzymes contained in pus will differ according to the accidents which introduce them into living beings. Pus may contain several kinds of microzymes at the same time; some of these are believed to be specific to pus, and to be found in that kind of pus which the ancients termed 'pus bonum et laudabile.' Other microzymes found in pus are either actually the bacteria of putrefaction, or are able to produce decomposition akin to putrefaction. When subjected to analysis, pus will therefore yield a great variety of ingredients; firstly, there are the corpuscles, with all their bioplastic constituents. These corpuscles accumulate in pus sometimes to the extent of making it a pasty mass, by the absorption of the serous liquid in which they were originally suspended. Then there are all the ingredients of serum, *serin* or *serum-albumen*, the *fibrin generators*, including fibrin ferment, and alkali-albumen. Mucin has never been found in pus. Chondrin and gelatin have been found in the filtrate of pus coagulated by boiling. Phosphatides found in pus probably

existed in the corpuscles ; *cholesterin*, however, is certainly in the serum. Good or healthy pus from wounds contains no volatile or fixed fatty acids, but decomposed pus yields formic, butyric, valerianic, palmitic, and stearic acid, besides other products of decomposition or putrefaction. Pus from abscesses, from phosphorus disease, and ulcerating cancers, contains an acid which, as it gives a rose-pink reaction with chlorine water, has been termed *chlorrhodinic acid*. A similar substance can be obtained from decomposing extracts of pancreas and lymphatic glands. Of low crystalloids, pus may contain *leucin*, *tyrosin*, xanthin, uric acid ; in the pus from jaundiced persons, biliary acids and pigments are found ; in that from diabetic persons, sugar. The so-called *blue pus* derives that colour from a kind of microzyme, which yields its pigment to chloroform, from which it is obtained in crystals and termed *pyocyanin*. The solid matters contained in pus amount to from 10 to 15 per cent. ; its ash is similar to that of blood, contains 72 per cent. of sodium chloride, and somewhat more potassium salt than blood-serum. A knowledge of the composition and products of decomposition of various kinds of pus from abscesses, ulcers, wounds, etc., is of the utmost importance for the study and treatment of reactive fever after wounds and operations, of various forms of blood-disease termed septohæmia and pyæmia. In all these affections, pus, or its microzymes, or its products of decomposition, are absorbed, or enter in a more crudely mechanical manner into the lymph and blood, and set up an acute patholytical process, which leads to violent attacks of shivering, fevers, sweating, diarrhœa ; then, in the case of septohæmia and pyæmia, to secondary deposits of pus or other fluids in various organs or cavities, caused mainly by multiplication of microzymes, and ultimately, and in nearly all cases, to death. For the prevention of this fatal disease the so-called *antiseptic treatment* has been devised. This consists in the measures which are calculated to keep

microzymes out of wounds, or to destroy any which may have obtained access to them, or to make albuminous substances in which they live incapable of supporting their life. For this purpose, *carbolic acid*, *salicylic acid*, *zinc chloride*, and *boracic acid* are used in the manner given in technical prescriptions.*

* The student will find a concise and practical account of these in an article, 'Chemical Surgery, with Special Reference to the Antiseptic Pharmacopœia.' 'Annals of Chemical Medicine, etc.,' vol. i., p. 309.

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THE END.