

On the nature of the substance found in the amyloid degeneration of various organs of the human body / by Francis Harris.

Contributors

Harris, Francis.

Publication/Creation

Westminster (London)] : T. Brettell, 1860.

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With the Dedication complimentary

ON THE

NATURE OF THE SUBSTANCE

FOUND IN

THE AMYLOID DEGENERATION

OF VARIOUS ORGANS OF

THE HUMAN BODY.

(A THESIS FOR A MEDICAL ACT IN THE UNIVERSITY OF CAMBRIDGE.)

BY

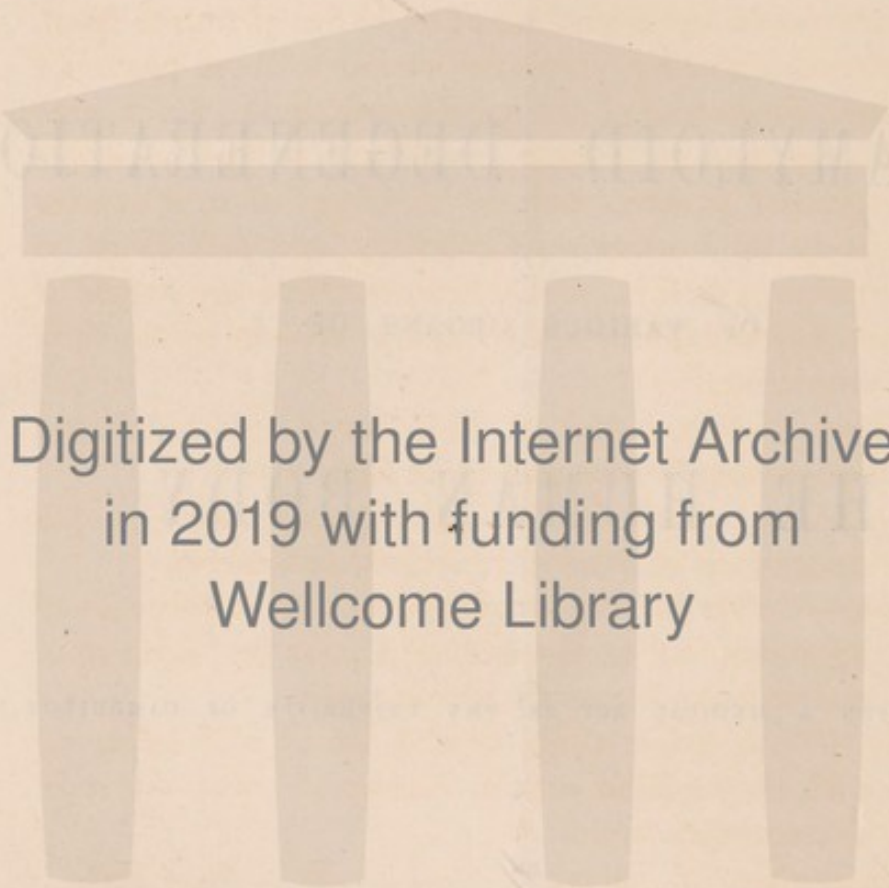
FRANCIS HARRIS, M.D. (CANTAB),

DEMONSTRATOR OF PATHOLOGICAL ANATOMY AT ST. BARTHOLOMEW'S HOSPITAL,
ASSISTANT PHYSICIAN TO THE HOSPITAL FOR SICK CHILDREN, ETC.

Westminster:

PRINTED BY THOMAS BRETTELL, RUPERT STREET, HAYMARKET.

1860.



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THE occurrence in the animal kingdom either of Starch itself, or of substances exhibiting properties similar to those possessed by the different substances of the amylaceous group (which were at one time supposed to belong exclusively to the vegetable kingdom), is at the present moment a subject of considerable interest, both in its bearing on Physiology, and still more on Pathology, inasmuch as it is calculated to elucidate the nature of some of those degenerations with which at present we are only imperfectly acquainted.

The general characteristics of the Starch group of the vegetable kingdom may be summed up as follows :—

First,—These substances are non-nitrogenous,—simple compounds of oxygen, hydrogen, and carbon.

Secondly,—Under certain circumstances they are capable of appropriating to themselves oxygen and hydrogen, and so become converted into sugar.

Thirdly,—With iodine alone, or with iodine and sulphuric acid, they exhibit certain changes of colour—certain characteristic reactions.

The composition of Starch is $C_{12} \cdot H_9 \cdot O_9 + HO$.

„ „ of Cellulose $C_{12} \cdot H_{10} \cdot O_{10}$.

„ „ of Grape Sugar $C_{12} \cdot H_{14} \cdot O_{14}$.

All these substances, therefore, possess this peculiarity, that they contain 12 eq. of carbon, and amounts of oxygen and hydrogen in the proportions to form water.

The conversion of these substances into glucose, or grape sugar, by prolonged boiling with dilute mineral acids, is a fact which requires only a passing mention.

The characteristic blue colour, which is formed when free iodine comes into contact with starch, is also so well known as to require no description.

With cellulose, however, iodine alone produces little change of colour, and it is only when sulphuric acid is added that a blue colour is perceptible. If, for instance, a solution of iodine be

applied to cotton wool, the individual fibres are seen under the microscope to assume a faint pinkish brown tinge, and this tinge is readily removed by washing them in a stream of water; if, however, sulphuric acid be also added, the fibres swell up, take a deep blue colour, and ultimately dissolve;—even this colour vanishes after a few hours' exposure.

To shew, then, that any substance which is found in the animal kingdom is strictly analogous to this amylaceous group, it would be necessary not only to shew that it formed with iodine colours more or less resembling those produced by starch, but that also it was a non-nitrogenous substance; nor would these two characters alone be sufficient, as another substance possesses both these peculiarities,—Cholesterine is a non-nitrogenous body,—a compound of carbon, oxygen, and hydrogen alone—its formula being $C_{87} H_{82} O$. and with iodine and sulphuric acid it exhibits a blue colour, much resembling that which cellulose shews under the same circumstances. So that it is also necessary, in order to prove the amylaceous nature of any animal substance, that it should, in addition to these two properties, be also convertible into sugar.

Quite recently the investigations of M. Berthelot* have shewn that there exist in the animal kingdom two substances capable of fulfilling all these conditions. The one of these, Chitine, has been long known; for the other M. Berthelot proposes the name of Tunicine. It had, however, already been described as animal cellulose, by Schmidt in 1845, by Löwig and Kölliker in 1846, and by Professor Huxley in 1853.

The organic matter of the envelopes and external skeletons of certain invertebrate animals differs from the organic matter of the bone of vertebrate animals, by its insolubility in solutions of caustic potash; in this respect it presents a remarkable analogy to certain vegetable tissues.

From the envelopes of certain of the Tunicata (the Ascidians were used in the experiments) M. Berthelot obtained the organic principle, for which he proposes the name of Tunicine, in the following manner:—

The envelopes were first boiled in concentrated hydrochloric acid for some hours, in order to free them from any earthy substance; they were then washed frequently with water, till all trace of the acid had disappeared. Afterwards they were boiled

* Brown-Séguard's *Journal de la Physiologie*, No. VII. p. 577. Oct. 1859.

with a solution of caustic potash, and again washed, till they became perfectly neutral.

There was then left a white opaque substance, of almost horny consistence, and non-crystalline in structure. When moist it was soft, supple, and tenacious. Under the microscope it presented a fibrous structure, like animal tissues, and quite different in this respect from vegetable cellulose.

By the ultimate organic analysis of this substance, he found that 100 parts yielded 44.6 of carbon, and 6.1 of hydrogen.

The formula $C_{12}H_{10}O_{10}$, the formula of cellulose, requires 44.4 of carbon, and 6.2 of hydrogen, so that tunicine may be considered isomeric with cellulose.

This analysis coincides very closely with two analyses, given by Schlossberger* ; one by Schmidt, which gives

Carbon	45.38
Hydrogen	6.47
Oxygen	48.15

The other, by Löwig, gives

Carbon	43.40
Hydrogen	5.68
Oxygen	51.32

A mere identity in the ultimate chemical composition would, however, prove but little, unless some of the properties of this substance resembled those of the vegetable tissue.

M. Berthelot found that, with iodine and concentrated sulphuric acid, this substance assumed a very pale blue colour. The colour, he states, resembled rather that which cholesterine produced, than that of cellulose.

Schlossberger†, however, and Professor Huxley‡, both found that it coloured in a manner precisely similar to that of vegetable cellulose. This substance, however, differs from cellulose by its far greater resistance to acids. M. Berthelot found that it could be boiled with dilute acids for several weeks, without any change into sugar taking place in it.

Its resistance was so great, that it was necessary to employ re-agents of so strong a nature, that they were calculated not to produce sugar, but to destroy it, if it had already been formed.

Yet, after many failures, he was completely successful, in the following manner :—

* *Thier-Chemie*, Vol. I. p. 255. 1856.

† *Op. cit.*

‡ *Microscopical Journal*, Vol. I. p. 22. 1853.

Dried tunicine was mixed with cold concentrated sulphuric acid. By degrees it dissolved without becoming coloured. The fluid was then poured, drop by drop, into a hundred times its weight of boiling water. The mixture was then kept boiling for an hour. It was then saturated with chalk, and, after having been filtered, was evaporated to a syrupy consistence.

This syrupy fluid was a mixture of sugar with some substance of an indeterminate nature. It reduced energetically the potassio-tartrate of copper, and assumed a dark brown colour when boiled with caustic potash.

To a mixture of this syrup with water, yeast was added, and fermentation was readily set up, with the production of carbonic acid and alcohol.

The conversion of this substance into sugar was therefore fully proved.

The other substance, chitine, is the organic basis of the external skeleton of crustacea arachnida, insecta, &c. It may be obtained by a method similar to that employed for the preparation of tunicine. As early as 1823, M. Odier* considered it to be a substance approaching in its nature to cellulose. It differs from tunicine in one very important particular—it has not yet been obtained free from nitrogen.

M. Berthelot states that he boiled the chitine, which he obtained from the shells of lobsters, for several weeks with dilute sulphuric acid; and that the mixture was then left for a period of fourteen months at the ordinary temperature of the air, but that after this time the chitine was found almost intact, and still contained 5 to 7 per cent. of nitrogen.

Various other analyses of it have been made at different times. In one by Messrs. Children and Daniell† its composition is stated to be

Carbon	46.08
Hydrogen	5.96
Nitrogen	10.29
Oxygen	37.41

Schmidt found it to contain‡

Carbon	46.69
Hydrogen	6.69
Nitrogen	6.33

but found in it no trace of phosphorus or sulphur.

* *Mémoires de la Société d'Histoire Nat. de Paris*, Tome I. p. 29. 1823.

† *Todd's Cyclop. of Anat.* Vol. II. p. 882.

‡ *Zur vergleich. Physiologie der Wirbellosen*, p. 39. 1845.

Frémy* however considered it a non-nitrogenous substance isomeric with cellulose.

But on the other hand Lehmann and Schlossberger† both found in it 6.5 of nitrogen.

Frémy was unable to obtain sugar from it, nor could he form a detonating mixture with it and the elements of nitric acid, and stated therefore that it had the composition, but not the properties, of cellulose.

Schmidt formulated‡ it $C_{17} H_{14} N O_{11}$, and considered it a union of two substances; the one a proteine compound $C_8 H_6 N O_8$; the other a hydro-carbon $C_9 H_8 O_3$.

He obtained this latter formula by subtracting the formula for the muscular tissue of the crab, $C_8 H_6 N O_8$ from the formula for chitine above stated.

M. Berthelot inclines to this latter hypothesis in so far that he considers it a union of two substances, the one non-nitrogenous and the other analogous to horny matter. By means of a process exactly similar to that employed with the tunicine he was enabled to obtain a syrup which reduced the potassio-tartrate of copper, and with yeast fermented with the production of carbonic acid and alcohol.

The existence in the animal kingdom of these two substances which seem capable of fulfilling in every respect the conditions necessary to establish their perfect analogy with the group of amylaceous substances is a most interesting fact, and a very important link in the chain of evidence which tends to point out the starchy nature of the substances found in certain degenerations of the human tissues, of which I will presently speak.

To Virchow§ we are indebted for a knowledge of the fact, that certain structures in the human body when brought into contact either with iodine alone, or with iodine and sulphuric acid, exhibit changes of colour similar to those produced under the same circumstances with starch and cellulose.

* *Annales de Chimie*, Tome XLIII. p. 95. 1855.

† *Thier-Chemie*, Vol. I. p. 228.

‡ *Op. cit.* p. 50.

§ *Arch. für Patholog. Anatom.* Vol. VI. p. 135.

In 1854 he first shewed that certain of the round concentric bodies found in the so-called lining membrane of the ventricles of the brain (ependyma ventriculorum) exhibit a pale blue colour on the addition of iodine, and on the further addition of sulphuric acid, a beautiful violet. This reaction separated these from certain other forms of concentric granules (Brain-sand), and to the class thus distinguished he restricted the name "Corpora Amylacea." He considered that this reaction alone was sufficient to indicate their cellulose nature; for though he was unable to isolate them in sufficient quantity to subject them to chemical analysis, he considered their cellulose nature beyond doubt, as there was no other known substance in the whole range of animal tissues which produced similar reactions.

These observations of Virchow's were repeated by Mr. Busk*, who, however, arrived at the conclusion that these bodies were not cellulose but genuine starch, since they "possessed all the structural, chemical, and optical properties of starch as it occurs in plants." They exhibited concentric markings,—they coloured blue with iodine,—they acted upon polarized light in the same manner as starch does. Other observers, however, have not been able to convince themselves of the actual starch-nature of these bodies†. Schmidt while distinctly expressing his opinion that the covering of the tunicata is actual cellulose, still thought that the cellulose nature of the corpora amylacea had not at that time been determined.

Until, then, these bodies have been shewn to be convertible into sugar, some doubt must exist as to their nature.

The occurrence of starch itself, as starch in the human body, has been maintained by Mr. Carter‡. In endeavouring to make out the structure of a tumor of the optic nerve, he found a large number of bodies (corresponding to the corpora amylacea of Virchow), which, when brought into contact with iodine, passed through various shades of purple to the densest black. He afterwards examined a long series of tissues, some healthy, others variously diseased, both in the human subject, and in the

* *Quarterly Journal of Microscopical Science*, Vol. II. p. 105. 1853.

† *Thier-Chemie*, p. 255.

‡ *Edinburgh Medical Journal*, Vol. I. p. 133. 1855. And *Ibid*, March 1858.

sheep and ox ; and he found in the cerebrum, cerebellum, liver, lungs, spleen, kidneys, striped muscular, and connective tissues, bodies which in every way corresponded with starch—in their size and shape and concentric marking,—in their colouring with iodine, and in the phenomena they exhibited when viewed by polarized light. Indeed, no doubt can exist that these bodies were actually starch ; the only doubt that remains is, as to how their presence is to be accounted for.

Were they really formed in the tissue ? or, were they only accidentally present in the microscopical preparation ?

Mr. Carter has no doubt that they were really formed in the tissue. He states that two varieties of them existed ; the one resembling wheat starch, the other, the rarer kind, “corresponding in every particular with the starch derived from “potatoes.” He most frequently found them diffused through the tissues, either isolated, or aggregated and united by interposed homogeneous matter, but in some exceptional cases occupying the cavity of flaccid cells. This last is certainly a strong point in favour of their actual formation in the tissue.

On the other hand, M. Rouget has recently investigated the subject, and, from the number and extent of his experiments, many curious facts have been brought to light.

In examining the epithelial glycogenic papillæ of the Amnion of Ruminants, he found, when he had crushed the pulpy substance between his fingers, a considerable number of grains of starch ; but he found that these grains were always on the surface, never in the substance of the epithelial layers. He suspected, from this circumstance, their origin ; and he found that, even after repeated washings, the fingers deposited grains of starch on all surfaces, especially when they were moistened. M. Balbiani found, too, that the most frequent washings could not remove the starch grains from the hands. He therefore washed one of his hands in a solution of potash, and then covered this hand with a glove : at the end of eight hours he could not discover a single grain on the hand which had been thus protected, whilst on his other hand he found the starch grains as numerous as before. M. Rouget found starch grains also in the dust on the outside of windows, on roofs, on stones, in the layer of dust deposited daily in his laboratory, on glass slides exposed to the air ; in

short, on almost everything to which the ordinary air had access.

My own more limited experience tends to confirm that of M. Rouget: for I have certainly found starch granules in the dust on books, on glass slides, and in the scrapings of my hands, but in far less numbers than I was led to suppose from M. Rouget's description. Perhaps the rarity of corn mills in London may account for the difference. In microscopical preparations, too, I have occasionally found a few starch grains, but I never could persuade myself that their presence was other than accidental.

On the whole, I think it must be concluded that the presence of starch, as starch, in the human tissues, is a matter at present "not proven."

The formation in the healthy liver of a substance which is converted during life into sugar, even in animals fed exclusively on meat, is a fact which renders it probable that in certain states of disordered nutrition a substance analagous to starch may be accumulated in the liver and other organs. This substance, which has been named by M. Bernard*, Glycogène, exists in the hepatic cells, and may be obtained from them by pounding in a mortar the liver-substance of recently killed animals, and then treating it with boiling water, and adding to the expressed fluid four or five times its volume of alcohol; a precipitate instantly falls, and when this is boiled with a solution of caustic potash to free it from any nitrogenous matter and again purified by alcohol, there is at last obtained a white amorphous powder, of neutral reaction, without colour or taste, which becomes blue when brought into contact with iodine, but does not reduce the potassio-tartrate of copper nor ferment on the addition of yeast. This powder is soluble in warm water but not in alcohol, and is readily converted into sugar by all the agents which produce this transformation in starch and cellulose.

M. Rouget† has shewn that this substance is produced by other tissues as well as by the liver; that it is not produced by special glycogenic cells but by epithelial cells in general; he found it in epithelial cells of the skin, of the palate, of the tongue,

* *Nysten, Dictionnaire de Médecine, Article Glycogène.*

† *Gazette Hebdomadaire, 1859, p. 266, and Journal de la Physiologie, No. VI. p. 312.*

stomach, and intestines. From these and other facts he concluded that the presence of this matter must not be attributed to a special function of the elements of any tissue in particular, but that it must be regarded as a peculiarity in the constitution of the elements themselves, thus establishing one analogy more between the animal and the vegetable tissues.

Dr. Pavey* has recently endeavoured to shew that the conversion of this glycogenic matter into sugar does not actually occur during life, but that the sugar which is found in the blood of the right side of the heart is really due to a post-mortem change, for in the blood that he obtained from the right ventricle of living animals, by passing a catheter down the jugular vein into the right side of the heart, he found only a trace of sugar. His conclusions have however been disputed by later observers.

These facts shew that the formation of an amyloid substance in the human body is not only extremely probable, but that such a substance is really physiologically produced.

The proof of the actual existence however of an amyloid matter as a pathological phenomenon must rest upon other evidence.

Certain pathological conditions of the liver, spleen and kidneys, in which these organs became infiltrated with a peculiar wax-like substance, had been long known, and had been described under the name of Waxy, Lardaceous, or Albuminous Infiltrations; but neither the nature of the substance to which this change was due nor the exact anatomical seat of this deposit had been clearly defined until Virchow pushed his investigations in pursuit of animal cellulose into the regions of pathology.

In 1854† he shewed that this waxy degeneration of the spleen commenced in its malpighian bodies, that while the whole spleen became enlarged, indurated, and anæmic, it was at the same time studded through with dull, gelatinous-looking bodies, varying in size from a pin's head to a hempseed, more or less resembling in general appearance little granules of boiled sago; and that these bodies were due to a deposit within the malpighian follicles of roundish or somewhat angular granules, rather larger

* *Guy's Hospital Reports*, Vol. IV. p. 291. 1858.

† *Arch. für patholog. Anatom.*, Vol. VI. p. 268.

than a lymph cell; and that moreover when a solution of iodine was applied to them their colour changed to a dark yellowish red, which on the addition of sulphuric acid passed into a deep violet. From these changes in colour he was led to infer that the substance was of a similar nature to that which he had described as cellulose in the corpora amylacea of the brain. Shortly* after this time he pointed out that changes of a similar nature occurred in many other organs and tissues, namely, in the kidney, liver, cartilages, intestinal canal, &c.

In his lectures on "Cellular Pathology†," he has given his last opinion as to the nature of the substance, its anatomical seat, and the character of the constitutional symptoms which accompany it.

His views are as follows :—

Almost all parts of the body are capable of undergoing this process of degeneration. The affected parts become enlarged, somewhat indurated and anæmic; the cut surface is semi-transparent, but dull; the natural colour of the parts is lost, but the colour of the neighbouring parts and vessels being seen through, gives them a yellowish or brownish tinge. The coats of the small arteries are the most frequent primary seat of this infiltration, and from them it spreads to the parenchyma of the organs; the walls of the arteries become thickened, and their calibre reduced, and hence the anæmic condition of the organs. The muscular fibres of the middle coat are the parts first affected. In the place of each muscular cell a compact homogeneous body is seen, in which, in the earlier stages, the centre of the nucleus appears as a hole; this afterwards disappears, so that a kind of spindle-shaped body remains, from which all trace of cell structure has vanished, no distinction being left between cell-wall, contents and nucleus. When the infiltration has reached this point, it commences to invade the parenchyma of the organs. In the liver, the cells in the immediate neighbourhood of the hepatic arteries are first affected; the liver-cells gradually become homogeneous; nucleus and cell-wall gradually disappear; and at last nothing is left but an absolutely homogeneous shining body; the cells are thus converted into a kind of corpora amylacea. In the kidney, the vessels of the malpighian bodies and the afferent

* *Arch. für patholog. Anatomie*, Vol. VI. p. 410; and Vol. VIII. pp. 140 and 364.

† *Die Cellularpathologie*. Berlin, 1858, p. 331.

arteries first undergo this change. In the earlier stages, but little alteration is perceptible to the naked eye; the kidney appears merely indurated and anæmic, and only when a solution of iodine has been applied to it, does the change it has undergone become apparent; then, throughout the cortex, numerous fine red dots appear, corresponding in their size and position to the glomeruli, and fine red streaks, running from them, indicate the afferent arteries.

The disease is constitutional; one organ alone is rarely affected; the only spot, where as yet an independent development of this change had been remarked, was in the permanent cartilages. The organs thus affected cease to discharge their functions. The patients assume a cachectic appearance, and gradually waste away. Dropsy frequently supervenes. Sometimes, too, the whole digestive tract is affected by this degeneration. During life this is rendered manifest by continual diarrhœa, and by diminished powers of absorption.

During the last four months I have in all met with four cases of this degeneration, two of them were affected by chronic albuminuria, and in these the kidney was the seat of the change; in the other two the liver was the organ chiefly affected.

I will now relate them,—

Sarah Ann P., æt. 24, was admitted into Hope Ward of St. Bartholomew's Hospital on November 14th. She was a servant, and had been in good health till about two years before her admission, at which time she had met with a fall and struck her back severely; this was followed by a severe illness attended with great pain in the abdomen; an abscess had formed internally, had burst, and had continued to discharge till about June last. About the beginning of last year she noticed that her feet began to swell towards evening; the swelling gradually increased and gained her legs and thighs. She had, it seems, never suffered from any acute renal attack, though she stated that some time ago the urine had become scanty, but she was certain that it had never looked bloody. She stated also that she had been more swollen a few days previously.

When admitted she had a fatigued expression, her face was pale and sallow, somewhat puffed under the eyes, pupils dilated, skin cool and dry, pulse 120, very weak, tongue red, raw-looking with aphthous ulceration on the sides; no appetite. Bowels open many times a day with watery motions; this diarrhœa had continued for a long time. She had no pain in the loins. She complained of no particular pain anywhere, but only of excessive weakness.

On the following day I examined the urine and found it copious, of a light amber colour, clear, depositing scarcely any sediment, of specific gravity 1008. On boiling and adding nitric acid a well marked cloud of albumen formed, but the quantity of albumen was small. On examining the sediment under the microscope, only a few kidney-epithelium cells, containing minute oil globules, were found, but no casts or blood-cells. The epithelium-cells presented no unusual appearances on the addition of iodine.

The diarrhœa persisted in spite of treatment. On the 22nd a considerable amount of blood passed with each motion. She gradually sank, and on November 29th she died.

I made the post-mortem examination on the following day.

There was still a moderate amount of fat in the subcutaneous tissue.

The brain and its membranes were anæmic, but otherwise healthy.

Heart was small ($5\frac{1}{2}$ oz. avoird.); its substance pale, its valves quite healthy; in all its cavities very firm pale clots were found.

In the right pleura there were some old and very firm adhesions about the apex of lung, and in this part the lung tissue was found condensed around a smooth-walled cavity of about the size of a walnut. This cavity opened at its inferior and inner angle into the superior branch of the right bronchus. No recent tubercular deposit was found anywhere.

The liver was larger than usual (wt. 3 lb 8 oz.), pale mottled, greasy, of diminished consistence, under the microscope found to be generally fattily degenerated. No reactions were obtained with iodine and sulphuric acid.

Spleen, 6 oz., apparently quite normal; no appearance of sago-like bodies.

The intestines were all matted together by old and firm adhesions, in the form of thin layers of connective tissue.

The walls of the intestines were thin and very pale; with the

exception of this exceeding paleness no change was remarkable in them by the naked eye until the lower part of the colon was reached ; here there were a few small circular superficial ulcers : these increased in number as the rectum was approached. All the pelvic organs were matted together into a firm mass, and at the same time were united firmly to the walls of the pelvis—no doubt this was caused by an attack of pelvic cellulitis at the time of the formation of the abscess mentioned in the patient's history.

On brushing a solution of iodine over the mucous membrane of the intestines, innumerable little dark red dots, corresponding with the villi, appeared, and on placing on the part thus changed a drop of dilute sulphuric acid, the whole surface previously coloured by the iodine changed to bluish-steel colour.

The right kidney weighed $7\frac{3}{4}$ oz., the left $6\frac{1}{4}$ oz. The right measured 5 inches in length, $2\frac{1}{2}$ in breadth, $1\frac{1}{2}$ in thickness.

The capsules stripped off readily, leaving the surface smooth, and not torn. The surface was of a pale yellowish white colour, here and there irregularly depressed, the depressions giving the surface an uneven lobular appearance. Little, very opaque, white specks and streaks indicated fatty degeneration of the contents of the tubuli. The depressed portions appeared somewhat darker ; in colour of a pale pink, and semi-translucent. A few stellate veins stood out on the surface of the kidney. On the cut surface—the pyramids and cortex were very pale. From the apex of a central pyramid to the circumference of the kidney measured $1\frac{9}{12}$ inch along a line drawn perpendicular to the base of the pyramid. Of this the pyramid measured $\frac{7}{12}$; the cortex $\frac{3}{12}$. The cortical substance was of a pale yellowish white colour—the portions occupied by the straight tubes of the cortex being semi-translucent : the intermediate portions occupied by the convolutions of these tubes were opaque white, with little dots and streaks similar to those seen on the surface of the organ. The malpighian bodies were scarcely apparent, but on brushing the cut surface over with a solution of iodine, numerous dark red dots instantly appeared, which by their size and position were recognizable as malpighian bodies.

On a microscopical examination of a thin section, those parts which to the naked eye had appeared most opaque (namely, the convolutions of the cortical tubes), appeared black. This black deposit was contained within the tubules, many of them being considerably swollen out by it. With a higher power this deposit was seen to consist of granular matter, set through with innu-

merable minute oil globules. Between the convolutions of the tubules the malpighian bodies were seen pale and semi-translucent, about $\frac{1}{10}$ of an inch in diameter, their capsules not thickened, but in parts dotted with oil globules. On examining with a higher power isolated malpighian bodies, which had become shelled out of their capsules, they appeared confused, translucent, colourless, and refracted the light very strongly, in this respect presenting an appearance very similar to minute calcified arteries of the brain; no nuclei were visible in them. (See fig. 2.)

On applying a solution* of iodine, the malpighian bodies changed to a bright transparent carmine (see fig. 3) colour, that is when seen by transmitted light (by daylight there was a tinge of orange in the red). The colour in some instances was seen to extend for a short distance into the afferent arteries of the bodies; and a few streaks, of a similar colour, were visible among the straight tubes of the pyramids. The other parts of the kidney were stained only of a pale brownish colour.

On the addition of a drop of dilute sulphuric acid, the colour of the malpighian bodies instantly began to change, becoming more of a port-wine colour, which gradually deepened till they assumed an indigo black. Those bodies on which the acid had acted less, still, however, retained a shade of violet. (See fig. 4.)

These colours were evanescent, and after a few days disappeared, leaving the kidney structure just as at first; but a fresh application of iodine reproduced the colours, but not so vivid as before. The same thing occurs with vegetable cellulose; if the preparation is left uncovered, the colours quickly fade away, and may be reproduced in a similar manner.

The second case that I met with was in the beginning of this year†. The patient, a gentleman twenty-seven years of age, had been known to be passing albumen in his urine for five years. Three years previously to this he had suffered from a slight attack of syphilis. Two years before his death his sight became troubled, and almost complete blindness followed. After a time, however, the sight of one eye was regained. Some months before his death he had a series of severe epileptiform convulsions, followed by coma. These convulsions recurred a fortnight before

* The strength of the solutions and method employed were fully described by me in *The Lancet*, December 24, 1859.

† For the particulars of the case during life I am indebted to Dr. Baly, whom I assisted in making the *post-mortem* examination.

his death. During his whole illness he had never had any dropsy, nor had he had any pain in the loins. The urine was abundant, contained a large quantity of albumen ($\frac{1}{4}$ to $\frac{1}{3}$ the test tube); and an examination of the sediment showed numerous pale, transparent, smooth casts.

On examination after death, the skull was found much increased in thickness, the frontal bone, measuring $\frac{1}{2}$ inch in thickness, very hard and heavy. The optic nerves were thin, and apparently atrophied. Some adhesions were found on the under surface of the anterior lobes of the cerebrum, uniting them to the opposite layer of the arachnoid. The brain was otherwise normal.

The right pleural cavity contained some bloody serum, and there were some recent adhesions at the base of the right lung.

The pericardium, too, contained about 3 oz. of bloody serum.

The coils of the intestines were slightly matted together by layers of soft, yellowish, somewhat puriform lymph.

The liver was considerably increased in size and weight; its surface was everywhere drawn into large globular nodules, varying in size from a nutmeg to a hen's egg. On cutting into the fissure between these, a dense cicatrix tissue was found. The interior of the nodules themselves was composed of ordinary liver tissue, somewhat softened, and here and there fattily degenerated. Scattered indifferently through the substance of the liver were numerous small abscesses (the smallest of them apparently limited to a single lobule), filled with dirty sanious puriform matter. No reactions were obtained with iodine.

Spleen was large, its capsule thickened, at its upper edge were two wedge-shaped purulent deposits.

Kidneys were very large and soft. On stripping off the capsule the surface was left extremely uneven, a thin layer of kidney tissue being torn off with the capsule. The surface was of a yellowish colour, mottled with dark red. The numerous little prominences on its surface were white and opaque. On section the cortex was found much thickened of an opaque yellowish white colour, here and there mottled with red; this opaque deposit appeared to extend some little distance between the tubuli of the pyramids. The kidney tissue was very soft and pliable, and when cut into a considerable quantity of bloody serum drained away.

On microscopical examination the intertubular structure of the cortex was everywhere greatly thickened, by a transparent homogeneous substance in which nuclei were present in great

numbers, and here and there minute oil globules. The convoluted tubuli appeared compressed, much reduced in diameter, and in parts so constricted, that some of them presented little varicose bulgings; their epithelium was changed into a mass of oil globules, in which no trace of cell structure was any longer visible. In parts the intertubular substance appeared distinctly organised into connective tissue.

The malpighian bodies appeared solid, compact, and homogeneous, and refracted the light strongly, and on the addition of iodine, first alone, and afterwards with dilute sulphuric acid, they exhibited changes of colour exactly similar to those described in the last case, with this difference, however, that the change extended for a much greater distance into the arteries. Arteries even of considerable size had very thick homogeneous walls, quite equal in thickness to the calibre of the artery; the whole thickness of the walls became coloured by the iodine, so that under the microscope they appeared as if injected with some red preparation.

The third case was a young man, *æt.* 21, who about eleven months before his death was admitted into John Ward of St. Bartholomew's Hospital, under the care of Dr. Jeaffreson.

At the time of his admission his right pleural cavity was full of fluid. After some time a large quantity of pus was let out by paracentesis, and from time to time a discharge of pus issued from the opening thus made.

He slowly sank, and on December 21st he died.

I made the post-mortem examination on the following day.

The right pleural cavity was distended by about two pints of pus.

No trace of tubercle was found in either lung.

The liver was large, weighed 4lb. 10 oz. was considerably displaced to the left by the accumulation of fluid in the right pleural cavity, and was firmly adherent to the diaphragm on the right side, to the abdominal parietes anteriorly, and to the right kidney inferiorly, its peritoneal covering in these situations being much thickened.

Its edges were rounded. On section it was found very firm, cutting crisp and brawny. The colour of the cut surface was pale, pinkish, and semi-transparent, the lobules were distinctly marked out by white lines. The very centre of the lobules too,

immediately around the hepatic veins, exhibited little white opaque dots and streaks, the intermediate zone being semi-transparent. On the convex surface of the liver, the liver substance was opaque, white, soft, and greasy; this condition extended for about an inch into the substance of the liver, and terminated by a very irregular line.

A solution of iodine brushed over the cut surface instantly stained the transparent portions a deep reddish brown, leaving the opaque white parts unaltered. Some of the lymphatic glands in the gastro-hepatic omentum gave similar colours with iodine, but the intestinal mucous membrane and the kidneys remained unaltered.

The spleen too appeared perfectly normal.

A microscopical examination shewed that the opaque white lines surrounding the lobules and the specks in the centre were caused by a great accumulation of oil globules in the hepatic cells. The transparent portions yielded white translucent cells, strongly refracting the light, many appeared quite homogeneous and solid, other faintly granular, while some contained a few oil globules, and a nucleus. These changed to a carmine red with iodine, but the violet blue, with sulphuric acid, was not well marked, as the dilute acid produced but little change, and the strong acid acted too energetically.

The fourth case was a little boy *æt.* 10, one of my out-patients at the Children's Hospital. When brought, he looked very ill and pale. His mother told me that his illness began about ten months previously with an attack of rheumatic fever, and that since that time he had never regained his health. I admitted him into the hospital.

He complained of vague pains in his limbs, his pulse was quick and feeble, his tongue furred.

He gradually became feebler; symptoms of peritonitis manifested themselves; his breathing became hurried and oppressed. The left arm became suddenly *œdematous*; he began to vomit dark fluid, like coffee grounds, and ultimately blood,—and so died.

I made the post-mortem examination fourteen hours after death. There was no post-mortem rigidity. The left brachial vein was distended by a firm dark clot, to which it was firmly adherent for a distance of about two inches.

There was a considerable quantity of turbid serous fluid in the left pleural cavity.

The apices of both lungs were solid and dark-coloured. The pericardium presented no sign of inflammation. The heart was large; its valves, with the exception of the mitral, on which there were some small firm granulations, quite healthy.

Some recent, yellowish, puriform lymph was smeared over the serous surfaces of the intestines. Spleen was firm and dark, but not enlarged; its malpighian bodies were very perceptible, but unaltered by iodine. The liver was large, weighed 2lb. 9 oz. (avoird.); the substance firmer than natural; on section there was seen throughout it little white semi-transparent streaks, not bounding, or limited to, the circumference of the lobules; these transparent parts changed to a deep red brown colour on the application of iodine; the other parts remained unaltered.

The kidneys were pale and firm; with iodine they gave no change of colour.

The stomach and intestines were full of dark discoloured blood; no lesion of their mucous surface was perceptible.

These cases are very far too few in number to admit of any general deductions being drawn from them. But it is remarkable that in all of them there had been a long debilitating illness, in three of them attended with a constant draining discharge. This coincides with the experience of Professor Virchow*, who pointed out the frequent coincidences of this degeneration with diseases of the bones; and with that of Dr. Bennett†, who has shewn its frequent connection with phthisis.

Another remarkable circumstance is that in both the cases of the kidney affection, although the malpighian bodies and the arteries leading to them were the seat of this degeneration, there was an almost constant excretion of a large amount of watery urine. If in a more extended experience this should be found to be invariably the case, might it not lead to some modification in our views of the functions of these organs?

In both the kidney cases, too, this degeneration was accompanied by extensive alterations in the tissue of the other parts of the kidney.

Another circumstance, which, however, may be only an acci-

* *Arch. für patholog. Anat.* Vol. VIII. p. 364.

† *Principles and Practice of Medicine.* Edinburgh, 1858. 2nd edit. p. 760.

dental coincidence, is, that in two of these four cases there was found after death those general inflammations of the serous membranes, in one accompanied by secondary purulent deposits, in the other with obstructions of the veins, which indicate the existence of blood poisoning,—the so-called pyæmia.

In considering, then, the nature of the substance to which these appearances are due, it is evident that we have to deal either with two substances or with two modifications of the same substance. The one, the material which forms the corpora amylacea of the brain, and the very similar prostatic concretions—for in the prostate gland there are very frequently found little oval or round concentric bodies, which assume a blue colour on the addition of iodine alone, just as the corpora amylacea do; and the other, the substance which is met with in the so-called waxy degeneration of the different organs.

If we inquire, then, how far these substances are capable of fulfilling the three conditions necessary to establish their perfect analogy with the substances of the amylaceous group, we are at once met by the difficulty that, owing to mechanical obstacles, we are not yet in possession of any exact analysis of their ultimate chemical composition.

Schmidt* has indeed attempted their analysis, and the results he has obtained are not favourable to the view that they are of an amylaceous nature. He made two analyses: the one of a choroid plexus rich in corpora amylacea, and the other of a waxy degenerated spleen. In the first he admits that, owing to the small size of these morphological elements, their mechanical separation from the surrounding tissues was impossible, and their chemical separation could be only very imperfectly attained, so that an elementary analysis could only give a partial explanation.

The argument which he follows may be thus briefly stated:—

Albuminous matters, such as albumen, fibrine, caseine, epithelial, and muscular tissue, &c. contain

Of Carbon,	from 50.	to 54.	per cent.
„ Hydrogen,	„ 5.7	„ 7.3	„
„ Nitrogen,	„ 15.	„ 18.	„

* Ueber das sogenannte thierische Amyloid.—*Annalen der Chemie, Sogenannte* Vol. CX. p. 250, 1859.

Gum, starch, and cellulose, the formula for which is $C_{12} H_{10} O_{10}$, contain

Of Carbon,	. . .	44.4 per cent.
„ Hydrogen,	. . .	6.1 „

If, then, in any mixture of these amyloid substances with albuminoid matter, the proportion of carbon sinks below 50 per cent., of hydrogen below 6.7, and of nitrogen below 15 per cent., and at the same time glucose is formed by treatment with sulphuric acid, these amyloid substances would belong to the second or starch group. If, however, the proportion of these elements rises above this per centage, and especially if the nitrogen rises above 15 per cent. these substances will belong to the albuminous class.

In the choroid plexus, after boiling it for half an hour with dilute sulphuric acid, he obtained no trace of sugar, either by the copper test or by yeast. He subsequently treated the plexus with concentrated sulphuric acid, in a manner similar to that described in the conversion of chitine, but without obtaining any traces of sugar.

From the spleen, too, he was unable to obtain any evidence of the presence of sugar. In an analysis of this spleen substance he found that the per centage of nitrogen = 15.56.

He concluded, therefore, that these substances were nitrogenous substances, to be classed with albuminous matters, and not with the non-nitrogenous hydrocarbons.

Virchow, too, admits that he has been unable to form sugar from either class of these amyloid matters.

The analysis above detailed is far from being completely satisfactory, and until a more extended series of experiments has been made, it will not be possible to arrive at any definite conclusion as to the ultimate composition of these substances.

In the absence of a complete analysis, are there any other relations of these bodies which may help us to form an opinion as to their nature?

In the *First* place, they possess a great resistance to putrid decomposition. Virchow found that after subjecting a spleen thus degenerated to a stream of water for three weeks, the amyloid granules were apparently unchanged.

Secondly,—In warm water the corpora amylacea of the brain swell up, and ultimately dissolve.

Thirdly,—They are insoluble in æther and alcohol.

Fourthly,—They offer to the actions of the alkalies and

acids a far greater resistance than albuminous matters do ; though, indeed, a less than is exhibited by vegetable cellulose.

And, *Lastly*,—They exhibit certain colours, when brought into contact with iodine and sulphuric acid.

The colour produced by iodine alone on organs which are the seat of this pathological process is perfectly distinctive. When, for example, a solution of iodine is brushed over a liver which has undergone this change, the affected parts in a few minutes assume a deep red brown colour, very different from the colour produced by iodine on organs in any other condition,—once seen it cannot be mistaken. In the last five months I have made or superintended more than sixty post-mortem examinations. In by far the greater majority of these I have applied iodine to the different organs ; indeed, it has been my rule to do so, whether this degeneration has been suspected or not—(only by inadvertence have I omitted it)—and only in the four cases related have I seen this peculiar colour. In these cases too the colour was precisely similar to the colour which Professor Virchow showed me at Berlin in the summer of 1858.

One cause of confusion however exists. Two, if not more very different pathological states have been confounded together under the name of waxy degeneration.

Not infrequently the malpighian bodies of the spleen are seen enlarged, forming small round white bodies, varying in size from a pin's head to a hemp seed, these are not so semi-transparent—not so sago-like—as the amyloid-degenerated corpuscles. Occasionally too the spleen is found occupied by numerous largish opaque white, or whitish yellow, irregularly-shaped, hardish masses. In two cases which have recently come under my observation this condition of the spleen was associated with great general enlargement of the lymphatic glands ; both of these cases were boys of the ages of eight and twelve respectively ; in one there was a considerable increase of the white corpuscles of the blood, in the other the blood, owing to an accident, was not examined. In neither case was any change of colour in the affected organs perceptible on the addition of iodine.

When to parts which have become thus reddened by iodine sulphuric acid is added, a change to a bluish red, or violet red, or deep blue purple, or even to an indigo black, speedily commences ; in some cases this colour quickly passes into a deep reddish brown. In the malpighian bodies and arteries of the kidney the bluish coloration is most marked, and in these the

dilute acid is sufficient to produce it, in the liver stronger acid is necessary and the colour is obtained with greater difficulty.

This blue coloration is so distinctive of amylaceous matter that up to the present time only one other substance has been found to exhibit it. Cholesterine when treated with strong sulphuric acid and iodine shows a very similar blue colour.

From this Meckel* was led to conclude that the substances in question were cholesterine or modifications of it.

From cholesterine they differ however, as Virchow has shewn, in many important particulars.

First,—Cholesterine is unchanged in colour by iodine alone.

Secondly,—The corpora amylacea dissolve in warm or boiling water. Cholestine is insoluble in water.

Thirdly,—Cholesterine melts on the application of heat; the amyloid bodies do not melt but only dry, and still give the same reactions with iodine.

Fourthly,—Cholesterine dissolves into a brown fluid on the addition of concentrated sulphuric acid. These other bodies swell but do not dissolve with a change of colour.

Fifthly,—Cholesterine is soluble in ether, amyloid not.

That, therefore, these substances are not cholesterine is abundantly manifest. One striking peculiarity in this reaction of cholesterine is, that the blue colour is not produced until the cholesterine has begun to oxidize under the influence of the acid. The formula for cholesteric acid is $C_8 H_4 O_4 + HO$, a formula much resembling the formula of the starch group. Is it not possible that this exceptional instance may indeed become an additional proof?

Are, then, those bodies found in the brain starch?

The pale blue colour with iodine alone differs considerably from the colour which starch assumes. And though sometimes the phenomena they exhibit with polarized light much resembles those exhibited by starch, yet until these bodies have been shewn to be convertible into sugar, I think we must answer this question in the negative.

Is the substance found in these amyloid degenerations of the different organs cellulose?

It differs from cellulose in the red brown colour produced by iodine alone, and by its less resistance to the action of alkalies.

* *Annalen der Berliner Charité-Krankenhäuser*, reference from Virchow's *Arch.*

All attempts, too, to convert it into sugar have, up to the present time, been unsuccessful.

So that, I think, all that we are justified in concluding is,—

That the reactions of these substances with iodine and sulphuric acid indicate their analogy, not their perfect identity, with the substances of the amylaceous group.

DESCRIPTION OF THE PLATE.

Fig. 1.

Epithelial cells, from the cortex of the kidney of Case 1.

Fig. 2.

A malpighian body, from the same kidney, in a state of amyloid degeneration. (250 diameters.)

Fig. 3.

A thin section of the same kidney, treated with a solution of iodine. The malpighian bodies are seen of a bright red colour.

Fig. 4.

Another section, treated with iodine and sulphuric acid. (inch power.)

The drawings were made by Mr. GODART, from microscopical preparations.

Fig. 1.



Fig. 2.



Fig. 3.

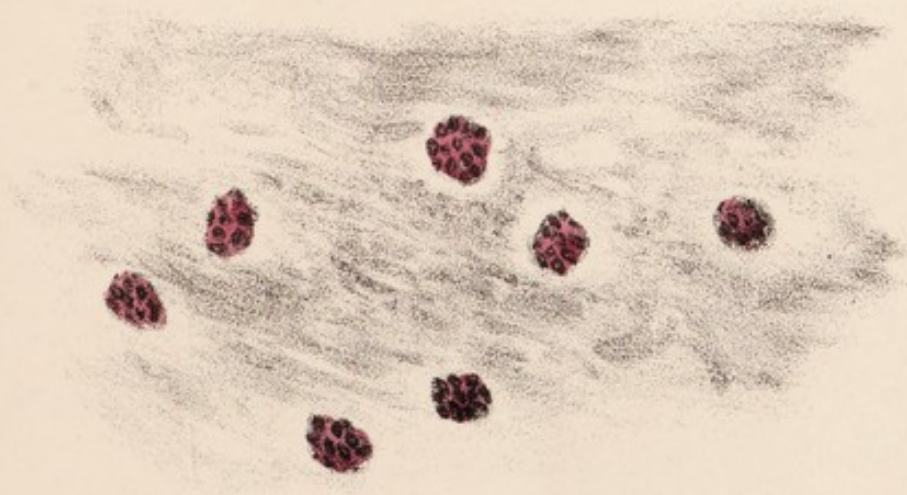


Fig. 4.

