

tetraspores in the *Florideæ*, by the *proliferations* and *propagative gemmules* which are found in the *Fucaceæ* and the other *Fucoidæ*, and by the zoospores which are widely distributed among the marine and fresh-water *Algæ*. The sexual function is probably fulfilled in the *Florideæ* by the cells of the *antheridia* and the *conceptacular spores*; in the *Fucaceæ* certainly by the spermatozoids and the contents of the so-termed "spores;" in the *Confervæ* by spermatozoids and the contents of the quiescent spores.

The spores of the *Fucoidæ* and the *quiescent spores of the fresh water Algæ*, however, are properly spore-fruits (*sporangia*), whose contents are fertilized sometimes *within*, sometimes *without the sporangium*.

The *Algæ*, moreover, are sometimes *diœcious*—and this is the case with the greater number—some *monœcious*. The individuals, lastly, which form the *asexual* organs of multiplication are usually *sexually sterile*; but at the same time in their vegetative parts *more strongly developed* than the fertile; this holds good both of the individuals with tetraspores among the *Florideæ*, as well as of the individuals of the fresh-water *Algæ*, which form zoospores. The latter condition, which has as yet not been noticed, promises to afford much aid in the classification of allied forms.

On the COURSE of the AMYLOID DEGENERATION. By RUDOLPH VIRCHOW. (Abstracted from the Archiv. f. Patholog. Anatomie und Physiologie. Bd. viii., p. 364.)

IN former communications on the subject of "amyloid degeneration" the Author was able to adduce, as instances of the affection, besides the *corpora amylacea* in the nervous system, only the waxy degeneration of the spleen, liver, and kidneys; but since then some more recent cases have afforded him the opportunity of extending his researches, and of making, as he thinks, a very important advance in the knowledge of the remarkable changes included under the term.

In all these cases there existed chronic, and very considerable disease in some part of the *osseous system*. Even in his former communication, respecting the "waxy spleen," he had noticed that it was especially in persons affected with chronic disease of the bones that this form of degeneration of the organ was presented, and he has since seen scarcely a single case in which the same complication did not exist. This frequent association cannot, he thinks, be explained except upon the supposition that the disease in the bone exerts a

determinate influence upon the production of the affection in the spleen, liver, and kidneys. It is usually the case that primary, long-continued disease of the bones, especially *caries* and *necrosis* of the larger bones or portions of the skeleton, in their subsequent course, induce cachexia and dropsy, and particularly *albuminuria* and degeneration of the kidneys, but how is the connexion between the primary and secondary affections to be explained? Two hypotheses, with respect to this, might be entertained, either the disease in the osseous system may so far interfere with the general nutrition that the constituent elements of the spleen, kidneys, and liver may be deprived of their normal supply of nutriment, and disposed to undergo the amyloid change, or the disease in the bones may actually produce the amyloid matter, which is deposited secondarily in the other organs. In the former case there would be a peculiar metamorphosis, an idiopathic, morbid change in the elements of the spleen, liver, and kidneys; and in the second an instance of metastasis, in which the glandular organs would be merely the seat of the deposition of the morbid material.

Hitherto Virchow has not found in the *bone* itself a substance corresponding to that which occurs in the abdominal glands, whilst he has always detected its presence in the *cartilages*. In an aged individual, who presented in many of the joints the changes peculiar to senile arthritis, the pubic symphysis in particular, towards the interior aspect, was much enlarged, and unusually moveable. When cut across, there was apparent in the middle of it an irregular, vertical fissure, with uneven, somewhat tuberos walls, and without any fluid contents. The layers of cartilage on each side were considerably thickened, of a dirty, yellowish colour, and very unequal density; the parts immediately contiguous to the fissure were more especially softened in places, greasy, and as it were, broken up, so that portions, of considerable size, were almost separated from the rest, or were held together only by slender connexions. Microscopic examination disclosed a great variety of constituents. The cartilage cells were generally enlarged, their capsules very thick and wide; in many places considerable-sized groups of them might be observed in a proliferous state, but in some might also be seen minute, roundish, or flattened corpuscles. Towards the surface of the fissure many cartilage cells were in a state of fatty degeneration, the matrix being, at the same time, transformed into a soft, clouded, streaked, and granular substance, in which the presence of cholesterin was here and there perceptible. In these situations the condition might be described as "*atheromatous dege-*

neration," similar to that which takes place in the arteries. Crystalline cholesterin existed only on the surface, beneath which, however, the matrix presented numerous alterations; isolated portions were composed, in great part, of the unchanged, hyaline, dense substance, close to which might be noticed considerable tracts and masses in which the matrix was streaky and fibrous. The fibres in some parts resembled the rigid filaments in the well-known asbestos-like portions of the costal cartilages, and in others assumed more the aspect of hard, wavy, and strongly refractive *strivæ*. On the addition of solutions of iodine, either the simply aqueous, or made with iodide of potassium, some portions of the microscopic section at once assumed an intense reddish-yellow (iodine-red) colour, whilst others remained perfectly clear and colourless; the greater part presented a yellowish, and, on more prolonged action of the reagent, a yellowish-brown hue. If sulphuric acid or chloride of zinc be now added, the reddish-yellow spots are immediately rendered of a violet, or occasionally, bright blue colour, although a strong reddish tinge is always retained. Under the action of a very concentrated solution of iodine, also, the colour becomes at once dark red, or nearly violet-red, especially when the section so treated is dried and again moistened with water. The places in the section where the iodine reaction took place might be very distinctly recognized, even by the naked eye, as dark, reddish, or blackish-red points, particularly when thin sections were viewed over a clean, white surface. When examined with the microscope it was readily seen that it was not cholesterin in any form which afforded the simple reaction with iodine; as is usual, this substance, even after the addition of iodine, remained colourless, and did not exhibit any of the often-noticed changes of colour, except under the energetic action of sulphuric acid or of chloride of zinc.

It was now a point of much interest to determine in which of the structural elements the reaction took place; with respect to which it was at once evident that both the matrix-substance and the corpuscles participated in it, either each singly, or both, though less extensively, conjointly. Of the corpuscles, again, it was quite evident that it was the thick capsules which afforded the deepest colouring, which was intense in proportion as the corpuscles were of larger size, and more free in the surrounding matrix; but in some places the true cell (contents of the capsules) also appeared to be similarly affected; and, especially in the smaller ones, Virchow often noticed the entire corpuscles coloured red or violet throughout.

It was remarkable that no microscopic characters could be

discerned, from which it might be concluded *a priori* whether the parts would be acted upon by the iodine or not; neither in the matrix, nor in corpuscles, did the spots, which were afterwards coloured, exhibit before the addition of the iodine, any difference from those which remained uncoloured; nor, excepting the rather remarkable *microscopical* condition of the whole cartilage, could it be said that these cartilages presented any appearance by which they could be distinguished from many other senile cartilages in which the reaction did not occur. This circumstance, with regard to the cartilages, is perhaps of the more importance to be noted, as a strong contrast in this respect was presented in other parts, and especially in the glandular organs, in all of which, especially in more advanced stages of the affection, in the portions where the amyloid change had taken place, a degree of softening independent of any reagent might be recognised, and particularly the presence of a brilliant, pale, thickening substance.

A farther step in advance was made on the inspection of the body of a boy aged 13 years, who had died of albuminuria and dropsy, following *spondylarthrocasis*. In this case there existed almost complete destruction of the intervertebral substance between the last lumbar *vertebra* and *sacrum*, together with caries of the contiguous bodies of the *vertebrae*, and extensive sinuses passing through the sciatic notch and over the *crista ili*, running far between the muscles of the buttock and thigh which were in a state of fatty degeneration, and opening externally by large fistulous orifices. No tubercles existed in any part, not even in the lungs; a single gland in the mediastinum only was enlarged, and filled with a cheesy, necrotic matter. On the other hand, there was very far advanced parenchymatous nephritis, with amyloid degeneration of the *glomeruli*, sago-spleen, and slight enlargement of the liver, whose cells, close to the portal vessels, were filled with fat, whilst the interior of the *acini* was occupied with amyloid substance. All the waxy parts of the spleen, liver, and kidneys afforded, with iodine alone, a distinct reaction, obvious even to the naked eye, and on the addition of sulphuric acid, a beautiful violet and blue colour.

The condition of the lumbar glands was especially worthy of attention. They were much enlarged, and presented externally a peculiar bluish-green, transparent aspect. On section, the medullary substance (*hilus*) appeared unchanged, whilst the cortical portion was more or less completely transformed into a clear, anæmic, transparent, nearly colourless gelatiniform substance. This condition was most apparent in the glands situated nearest to the diseased portion of the spine, and in

these it extended almost through the entire thickness of the cortical substance. Higher up the alteration was more confined to the peripheral portions of the glands in which the afferent lymphatics open, the substance surrounding the *hilus* and the inner portion of the cortical substance retaining their normal aspect. It could be readily perceived even with the naked eye, but still better with a lens, that the substance was not uniformly affected, but that the change had taken place in the points, which in a normal lymphatic gland, are visible as white, round, vesicular spots—the follicles or *alveoli*.

Microscopic examination entirely confirmed this supposition, and the chemical reaction fully established the identity of this morbid condition of the lymphatic glands with that formerly described by the Author under the term *sago-spleen*. In the lymphatic glands, as in the spleen, the follicles appear to constitute the proper seat of the affection, and in the one case, as in the other, the proper gland-cells (lymph-corpuscles) are destroyed in proportion to the amount in which the new substance is deposited. The follicles or *alveoli* enlarge at the same time, so as to attain to the size of a small pin's head, although the enlargement is never so considerable as in the splenic follicles. The deposited substance consists of comparatively large (0·04—0·05^{mm}), rounded, or subangular corpuscles, of a pale, colourless, homogeneous aspect, and breaking up under pressure in such a way that their solid structure is plainly discernible. In many cases might be perceived minute, superficial depressions, rounded or stelliform, and usually one or two in number, in which a minute, nucleiform body was often seen lying. Amongst them was spread a fine network, composed of stellate elements, in the nodular points of which 1—2 manifest nuclei were usually contained. Even on the simple addition of iodine the pale corpuscles assumed a beautiful yellowish-red colour, and on the application of a solution of iodine in hydriodate of potass, they were rendered distinctly bluish-red, which, on the subsequent addition of sulphuric acid, or of ioduretted chloride of zinc, became the most beautiful violet, gradually passing into a deep blue.

This degeneration, however, was not confined solely to the follicular elements, it being evident that the fine arterial vessels of the interstitial tissue had undergone a similar change in their tunics. They were thickened, and the lumen was contracted; whilst the walls, which appeared shining and almost homogeneous, afforded the most marked reaction. This change in the vessels, however, was also confined to the proper cortical substance of the gland; neither in the medullary substance, nor externally to the gland, was anything of

the kind observable in the blood- or lymphatic vessels. Nor in the interior of the gland did the vascular plexus there situated present any colouring.

This discovery is of considerable importance as regards the development of the *corpora amyloacea*. On comparison with the figures given by Kölliker ('Mik. Anat.' ii. 2, figs. 365-367) of the normal lymphatic glands, it will be satisfactorily seen that each individual amyloid granule corresponds, not with a single cell, but with an entire group. For since the fine net-work remains in the interior of the *alveoli*, and, speaking generally, only one *corpus amyloaceum* lies in each areola, it is obvious that it must represent an entire mass of the pre-existing cells. In this case, also, the amyloid degeneration cannot be regarded as a simple transformation of individual cells; as in the arterial vessels all parts of the wall—connective tissue, and muscular fibres—are ultimately fused into a homogeneous substance, so is it with the cells in the lymphatic follicles.

The morbid condition in the case last cited extended very widely upwards. The epigastric lymphatic glands were also extensively implicated, and on close examination some of the bronchial glands also exhibited scattered waxy spots, though it must be confessed to a very limited extent. At first it appeared as if the process in the blood-vascular system was limited to the minute arterioles of the lymphatic glands, spleen, and kidneys; but it was afterwards found that the arterial vessels of the digestive tract were also largely implicated.

Dr. Jochmann was the first to notice that a strong iodine reaction was manifested in the gastric mucous membrane, and further investigation proved that this commenced in the vessels, and was always most strongly marked in them. Further research showed the same alteration in the vessels of the mucous membrane of the œsophagus, and of the whole intestinal canal, but particularly in the small intestine. It was limited in all parts to the fine arterial vessels of the mucous membrane, or at most involved only those of the uppermost layer of the submucous tissue, and it might be traced to some distance into the arterial side of the capillaries. Without re-agents, little appearance of change was discernible, the only indication of it consisting in the circumstance that the walls were slightly thickened and homogeneous; on the application of iodine and sulphuric acid, however, a very deep, dark-violet colour was manifested, which never passed into such a beautiful blue as that presented in the lymphatic glands, but was nevertheless very characteristic. Simple

iodine even, also produced a very strong colouring. The change to the naked eye was not very striking. The mucous membrane in all these parts had a very pale aspect; and in the stomach and œsophagus it was somewhat thickened, unusually transparent, and in parts of almost gelatinous consistence.

The above case indicated a much wider range of the amyloid degeneration than was previously known, and another observation showed the reliance which might be placed upon the truth of the discovery. A man, thirty years of age, who had long suffered from necrosis of the *femur*, with sinuous abscesses and fistulous openings, died, also, with albuminuria and ascites, but not until a subcutaneous abscess of the scrotum, suppurative inflammation of the parotid, and hemorrhagic pleurisy had taken place. There was found an enlarged waxy spleen, and parenchymatous nephritis, with very considerable amyloid degeneration of the *glomeruli*, as well as of the vessels and *tubuli uriniferi* in the *papillæ*, together with simple fatty liver and atrophic induration of the pancreas. The right femur was the seat of extensive hyperostosis, combined in the inferior third with a great loss of substance, whence proceeded fistulous passages; the surrounding parts had undergone a thickening and condensation, such as is seen in "white swelling." The lymphatic glands in the thigh and groin were enlarged, of a clear grey colour, in parts more transparent. Microscopic examination distinctly showed the commencement of amyloid degeneration in the follicles, some of which were wholly reduced to that condition, whilst others still retained lymph-corpuscles in some of the *areolæ*; and others, lastly, presented nothing but minute *corpora amylacea* amongst normal corpuscles.

Virchow was unable in this case to detect any indication of amyloid degeneration in the heart or any part of the muscular system, even in close contiguity with the diseased bone; nor in the mucous membrane of the respiratory organs and kidneys. The blood, also, contained no morphological particles which could be pronounced to be *corpora amylacea*.

Nevertheless, with respect to the course followed by the morbid change, it appears indubitable that the incitement to it proceeds from the diseased bones, whence it extends progressively to the lymphatic glands, then to the spleen, and ultimately to several of the secretory organs. Among these the first to suffer are invariably the kidneys, then the liver, probably lastly the mucous membrane of the digestive organs; and it is a circumstance of the greatest interest, that both in the kidneys and in the digestive mucous membrane

the morbid change always commences in the secretory vessels, in the same way as in the lymphatic glands, the spleen, and renal *papillæ*, the vessels, and especially the arterial, are very early affected. In all cases the normal tissue is removed in proportion to the amount of the new deposit, and it is not the individual elements which degenerate each separately, but the change involves all equally, so that the ultimate products present a very uniform, homogeneous constitution. From all that appears therefore, it is highly probable that the affection consists rather in a metastasis of a material formed in the site of the original diseased action, that is to say, in the bones, and which is transported to the different parts in a state of solution.

The constitution of the deposit is not everywhere alike, as has been before remarked by Virchow ('Archiv. Bd.' iii. p. 144) and Meckel. In particular, it would seem, that the substance in cases of less complete deposition, though assuming a beautiful red colour even under iodine alone, receives only an indistinct violet tint on the addition of sulphuric acid, and is never rendered blue. This was the case very remarkably in a boy, fourteen years of age, affected with disease of the lumbar vertebræ, whose liver weighed 5 lbs. 13 oz., the spleen about 7½ oz., one kidney nearly 4 and the other 3½ oz.; in whom the entire parenchyma of the liver, the spleen in its pulp, the kidneys in the *glomeruli*, the afferent arteries, and in the *papillæ*, exhibited the most complete waxy degeneration. With sulphuric acid the iodine-red colour was deepened, but rapidly became of a dirty violet, or rather of a dark bluish-red hue, and in parts greenish. In this case, therefore, the substance existed either in a less perfect form, or was more mixed with other matters.