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CELLULAR PATHOLOGY.

CASE

OF

SYPHILITIC DEPOSIT

IN

THE SUBSTANCE OF THE HEART.

BY

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PHYSICIAN, LATE PATHOLOGIST TO THE ROYAL INFIRMARY.

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CELLULAR PATHOLOGY.

In a paper recently published, on the coexistence of tubercle and cancer, I alluded to the two opinions entertained by pathologists regarding the origin of new growths, and I expressed my belief in the essential truth of the doctrine which maintains that cells do not arise independently, but that all are produced from similar pre-existing structures. While numerous observations confirmatory of this view have been published in Germany, the subject has not in this country met with the attention it deserved, and as the question is one which can only be decided by observation, I propose at present to detail the particulars of a case in which, as it appears to me, the strongest testimony is borne to the correctness of the modern or cellular pathology. I must, however, premise a few observations on the general question.

The observations of Schleiden and Schwann were unquestionably among the most important of modern times. They established the truth of what is called the cell-theory, which maintains that the vegetable and animal tissues are formed from cells, originally simple, but which in process of development undergo various modifications. This doctrine was soon applied to pathology, and it was supposed that a new growth, such as pus, arose in the following way:—A fluid containing in solution animal and mineral matter is poured out from the blood-vessels; in this fluid, at first structureless, molecules and granules make their appearance, these become grouped together and surrounded by a membrane so as to form a nucleus, around which the cell itself is formed. This doctrine, though plausible, has been almost universally abandoned in Germany; the description of what is supposed to take place is essentially theoretical; positive facts cannot be advanced in its favour; and the appearances adduced in support of it admit of another interpretation.

Twenty years ago, Professor Goodsir described the development of new cells from what he denominated "centres of nutrition;" each centre of nutrition was described as a cell, from the nucleus of which successive broods of young cells proceeded and passed off in various directions, and under various forms, according to the texture

or organ of which their parent formed a part.[1] Virchow, however, first clearly announced the doctrine of continuous development in its full integrity as applied to new formations. The almost simultaneous discovery by himself and Donders of the existence of connective tissue corpuscles, was the first important step in this direction. The close analogy existing between these, and the corpuscles of bones and the cells of cartilage, was speedily discovered. These cells, and their anastomising branches, were soon recognised as the channels by which parts not in direct communication with capillaries are nourished. Their arrangement is perhaps most typical in the case of bone. The osseous structure, around each of the Haversian canals, is studded with bone-corpuscles or lacunæ, from which fine pores or canaliculi proceed, which freely anastomose, and by which adjoining lacunæ communicate with their neighbours. These canaliculi extend to the surface of the vascular canal, and there can be little doubt that they take up nutritive fluids from the blood, and distribute it by means of their mutual anastomoses throughout the whole of the bone-substance. The existence of similar channels in tendinous structures was demonstrated by Wittich,[2] and has been established in the case of almost all the tissues of the body.

Virchow had from the first recognised the importance of these anastomosing cells, or connective tissue corpuscles; he saw in them the starting point of various new formations; and he soon enunciated the doctrine that no development of any kind begins de novo, that where a cell arises, there a cell must have previously existed (omnis cellula e cellula), just as an animal can spring only from an animal, a plant only from a plant.[3] Of course this doctrine, which revolutionized the older pathological theories, did not meet with universal acceptance; by many of those who had identified themselves with the earlier views, it was regarded as no more than a baseless though brilliant theory. Later observations have, however, all tended to show that it is essentially correct, and the admirable observations of Weber, His, Rindfleisch, and others, have convinced many of its original opponents of its correctness.

The most important objection made to this theory is, that new cellular growths arise in situations where no cells previously existed. Thus Professor Bennett says, "the fallacy of this theory, though it has many facts which seem to give it support, is easily demonstrated. For instance, pus cells may occur in tissues where there are no epithelial cells, as among muscles; and cancer, pus, and tubercle are all found in the white substance of the brain, where no cells have been demonstrated to exist, capable of increasing on the one hand or degenerating on the other."[4]

[1] Goodsir's Anatomical and Pathological Observations, "Centres of Nutrition."

[2] Virchow's Archivs, 1855.

[3] Cellular Pathology, p. 27.

[4] Principles and Practice of Medicine, 3d edit., p. 153.

Such objections are founded on a misconception or imperfect acquaintance with Virchow's views. Virchow does not maintain that pus cells are always developed from *epithelial* cells, but that they always arise from *cells;* and that in the case of the non-epithelial structures, they take their origin from the connective tissue corpuscles of the part. No epithelial or glandular cells are found in muscles, or in the white substance of the brain; but in the former we find nuclei within the fibres, and corpuscles of interstitial connective tissue between the fasciculi; while in the latter, the existence of a form of connective tissue which binds together the nervous elements has been demonstrated.

It is not, however, to be supposed that the demonstration of these connective tissue corpuscles is at all times easy, or that the appearances met with never admit of misinterpretation. With certain precautions, however, we may generally satisfy ourselves of the presence of this cellular element even in the fibrous structures. The mode of demonstration which I have found most convenient, is the following: the tendo Achillis of a child, or one of the semilunar cartilages of the knee-joint, is to be cut in pieces and soaked in diluted acetic acid (one part of pyroligneous acid to seven of water), until it swells up and becomes translucent. The pieces are then to be dried in the air: in this process they shrink considerably, and assume a horny appearance. When it is desired to examine the structure, the surface is to be moistened with water, and slices are to be removed with a razor or a very sharp knife. In this way specimens of any degree of thinness may be obtained, and these are to be examined under the microscope (a drop of water, or still better of glycerine, having been previously added), when the anastomosing cells will in general be distinctly seen. The only source of fallacy with which I am acquainted is this, that it is sometimes exceedingly difficult to distinguish the branches of cells from fibres of elastic tissue. This source of fallacy is not surprising, and becomes of little consequence when it is borne in mind that Donders has proved that elastic tissue is formed by a conversion of the cells and tubules of connective tissue into compact and tough fibres, which retain the original plan of the tissue, and are arranged in the form of a net-work; it is indeed impossible to say whether the cavity of the original cell is completely obliterated, or whether a small canal is left in its interior.

It is, however, in pathological processes that we have the most convincing proofs of the truth of the doctrine of continuous development, and that we can actually trace the changes in process of taking place. The tissues may be divided into two groups; those which consist exclusively of cells, and those in which the individual cells are separated from one another by an intervening material.[1] The first group embraces the epithelial, the second the connective tissues. Now, pathological processes differ considerably, according

[1] Virchow's Cellular Pathology, p. 28.

as the former or the latter of these is affected. The phenomena of suppuration, for instance, are different according as it starts from epithelial cells or from connective tissue corpuscles; for in the first case there is not necessarily any great loss of substance, while in the second this invariably takes place. In either case, however, the process is essentially the same; the nuclei, originally single, divide and increase in number, new cells are formed, and so the process of multiplication goes on. We must not indeed expect to be able, in the case of every abscess or purulent discharge, to be able to trace thus distinctly the origin of the pus-cells; there is only a certain stage in pathological as in physiological growths, in which the actual mode of development can be followed; we might as well expect to be able to discover, by an examination of the mature fœtus, the different steps by which its organs had been formed, as to be able, in a ripe abscess or a well-organized cancerous mass, to determine in what way normal had been converted into abnormal tissues.

Two years ago, I had several admirable opportunities of witnessing the mode of formation of pus upon mucous surfaces. During the winter 1860–61, several fatal cases of small-pox occurred in the Royal Infirmary, and in almost all, the lining membrane of the larynx and trachea was found coated with a very soft, dirty-looking deposit. This, on microscopic examination, was found to consist essentially of pus corpuscles; but, on gently scraping the surface of the membrane, a remarkable change was found to have taken place in many of the cells of its epithelial lining. The cells in this situation are of the cylindrical variety, and in the normal condition each contains a single nucleus. But in the cases to which I am alluding many of the cells were enlarged, and, in place of a single nucleus, each contained several nuclei, three, four, or more. These it was evident had been derived from the division or proliferation of the original nucleus; while external to the cells were young ones in all stages of development, some of which corresponded perfectly to those still retained within the parent one.

Within the last few months I have had two opportunities of tracing the origin of other morbid growths in the case of non-epithelial tissues. To the first of these I shall allude in a very cursory manner. On the 19th of May, I examined the body of a man who had died of cancer. The disease had had its starting points from the dorsal vertebræ, the scapula, and the sternum; it had spread very rapidly, and had formed large tumours anteriorly and posteriorly. The growth had increased by a gradual involvment of surrounding parts: the appearance of the muscles was remarkable; near the bones from which the disease had had its origin, and in the centre of the tumours, none of the normal tissues could be distinguished; but in the outskirts of the growths the gradual involvment of the normal structures could be traced; one portion of a muscle, for instance, was lost in the mass; in the adjoining portion the fibres

could be recognised, but pale and of altered appearance; while external to this the muscular structure retained its healthy appearance.

On microscopic examination, the mass of the tumour was found to consist of an immense number of small cells, apparently naked nuclei; while within the muscular fibres adjoining the diseased growth, similar cells could be seen, evidently formed by a division or proliferation of the original nuclei. The growth then evidently extended by means of an abundant production of cells from the nuclei of the muscular fibres, and from the connective tissue corpuscles interposed between them, the muscular fibre itself gradually wasting and disappearing. In this case it would have been impossible to tell, from a mere examination of the muscular fibre, what the cells contained within it were ultimately to become; for in the early stage of such formations we cannot say whether we have merely to do with a multiplication of natural textures as the result of irritation, or with the development of a heteroplastic or so-called malignant growth. The concomitant circumstances in this case, however, left no doubt that the latter condition was in progress.

The following case of a somewhat different character is of great interest for its own sake, and also as an illustration of some of the preceding statements.

On the 13th of last June, in conjunction with Dr Littlejohn, I examined, by direction of the authorities of police, the body of a woman who had died under somewhat suspicious circumstances. We were informed that between ten and eleven o'clock on the night of the 11th of June, a woman had rushed out of a brothel in the High Street, exclaiming that her sister had been murdered. The police immediately entered the house, and found a woman lying in the passage apparently lifeless; the body was at once conveyed to the Royal Infirmary, where it was found by Dr Simpson, resident clinical assistant, that life was extinct. Subsequently to the examination of the body, I obtained a few additional particulars, which, with a view to perspicuity, I may introduce here.

M. H., about twenty-five years of age, the daughter of respectable working people, began to lead a dissipated life about eight years before her death, and had for the last three years been an inmate of a brothel in the High Street. She habitually drank freely, and was frequently intoxicated. Her health had for a long time been good, in fact robust, but latterly she had become very fat, and had for some time back occasionally complained of difficulty of breathing. I made special inquiries as to whether she had been known to have had any syphilitic affection, but could obtain no satisfactory information. The woman, in whose house she had been residing, stated positively that she had had no such complaint for the last three years, but I could trace the history no farther back.

About nine o'clock in the evening of the 11th of June, her "fancy man" came to see M. H. She told him she was hungry, and went with her companion to a public-house, where she ate sandwiches, and drank some ginger-beer, with about a wine-glassful of whisky. They returned to the house, and were together in a bed-room for about an hour. She then left the room in

order to empty the chamber utensil; this she appears to have done, and was next seen by one of the inmates of the house sitting in the passage in a crouching attitude. The latter addressed M. H., but received no answer; supposing she was asleep or intoxicated, she gave her a slight push, whereupon the body fell down and remained motionless. The sister of the subject of this observation, herself an inmate of the establishment, was immediately summoned, and finding her sister apparently dead, she rushed into the street shrieking out that her sister had been murdered.

The body was examined in the Pathological Theatre of the Royal Infirmary, on the 13th of June, in the presence of Professor Laycock and the members of the clinical class. The following were the appearances found :—

There was great lividity of the face and neck; no mark of injury on the surface. The mammæ were much developed; there was a large deposit of adipose matter in the cellular tissue of the thoracic and abdominal parietes; in the latter situation there was a layer of fat more than two inches in thickness. There was not a corresponding deposit of fat upon the limbs.

On examining the head, the dura mater was found firmly united to the skull; in the occipital region these adhesions were so firm that the membrane gave way in the attempt to separate them. There was no appearance of any abnormal deposit in this situation, or at any other part of the membranes of the brain. There was a moderate degree of congestion of the pia mater and of the cerebral substance, but nothing abnormal was discovered.

The mucous membrane of the larynx and trachea was congested, and lined with frothy mucus.

The right lung was non-adherent; the left pleura was universally and firmly adherent. Both lungs were much congested, in some places to such a degree as to have led to a very slight degree of hæmorrhagic extravasation.

The heart was moderately distended with fluid and loosely coagulated blood, divided pretty equally between the two sides; there was rather more fat around it than is generally found at the age of five-and-twenty; it weighed 11¾ ounces. The valves were tested and found competent. On the anterior surface of the left ventricle, near the septum, a flattened mass was noticed, about a quarter of an inch long and half that breadth, projecting slightly above the general level; it was cut into and found to be of a moderately firm consistence, and a pinkish grey colour, and to extend one-eighth of an inch into the muscular substance. On laying open the left ventricle, the greater part of the septum presented, instead of the ordinary smooth fleshy appearance, a greyish or yellowish pink colour, as if portions of the muscular substance had been converted into fat, which shone through the endocardium. The surface of the septum had not a quite uniform tint, but had a somewhat mottled appearance, as if the new matter had been deposited in separate masses, with slight intervals between them. The surface of the septum looking to the right ventricle had a similar appearance, except that the deposit was in the form of distinct lobules, generally about the size of peas. When the septum was cut through, the deposit was found to extend through its entire thickness; it had a considerable resemblance to fat, but was of a pinker colour, and tougher consistence; a small quantity of a watery juice exuded from it on pressure; intermixed with it, chiefly near the endocardium, was a material which, to the naked eye, resembled fibrous tissue, being tough and of a bluish or greyish colour. The wall of a portion of the left ventricle, extending from the base half way to

the apex, and situated near the septum, was in a precisely similar condition; some of the pectinate muscles appeared to be completely converted into this material. On the right side the deposit was confined to the septum, with the exception of a single nodule, which was continuous with the material in that situation. The substance of the auricles was natural. There were very minute traces of atheroma in the ascending aorta, and on the anterior flap of the mitral valve.

The stomach was distended with flatus; it contained a few ounces of pultaceous matter of a pinkish colour, in which could be distinguished morsels of meat, apparently of salt beef, and little bits of bread. The contents of the stomach had a sour smell, but no distinctly alcoholic odour. There was no abnormal condition of the gastric mucous membrane. The whole of the intestinal canal was examined and found healthy. The liver weighed four pounds; it was moderately congested, and the hepatic cells contained a little more fat than natural. The kidneys and spleen were healthy. There was matting together of the parts in and around the broad ligaments. The uterus was a little enlarged. The os uteri was small and regular; a little muco-purulent discharge issued from it. There were no indications of syphilitic disease about either the external or the internal genital organs.

Microscopical Examination.—The deposit in the septum of the ventricles was first examined by scraping off a little of it, and mixing it with water, when it was found to consist of an immense number of small cells mixed up with granular matter, and a finely fibrous or fibrillated material. The cells were a little larger than blood globules, being from $\frac{1}{3000}$ to $\frac{1}{2400}$ of an inch ($\frac{1}{120}$ to $\frac{1}{100}$ millimètre) in diameter, and contained minute granules in their interior. On the addition of diluted acetic acid they became more distinct and sharply defined, and presented a strong resemblance to the spores of some fungus, or other vegetable growth. They were, however, at once dissolved by a solution of caustic potash. Mixed up with them were fragments of muscular fibres, smaller than natural, in some of which striæ were still visible, in others these were almost entirely gone, and were replaced by fine dots. There were no free fat cells. When a section was made with the double-bladed knife the central portion of the deposit presented the appearances above described, except that the portions of muscular fibre were somewhat better seen than before. The transition from this to the healthy-looking tissue could be distinctly traced. On the margin of the deposit the muscular fibres were clearly seen, although the striæ were less distinct than natural. Lying on, between, and within the muscular fibres were bodies similar to those above described. In the tissue in the immediate neighbourhood of the deposit, which to the eye seemed natural, well-formed muscular fibres were seen, but they were at once distinguished by the large number of nuclei in their interior; instead of a single nucleus occurring at comparatively rare intervals, there could be seen groups of five or six in close contact; in other situations they were of larger size than natural, and evidently in process of splitting up. This splitting up took place sometimes transversely, at others and more seldom longitudinally; in one case four could be seen arranged linearly, apparently within one cell. These cells, though varying somewhat, possessed the same general characters; they were larger than those seen in the centre of the deposit, varying from the $\frac{1}{2500}$ to the $\frac{1}{1800}$ of an inch (from $\frac{1}{100}$ to $\frac{1}{75}$ of a millimètre) in diameter, were of a rounded or oval form, and generally contained one or two granules in their interior.

The annexed engravings give representations of the changes which had taken place in the muscular fibres adjoining and involved in the new material.[1]

Fig. 1.

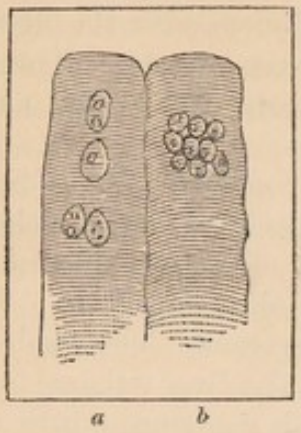


Fig. 2.

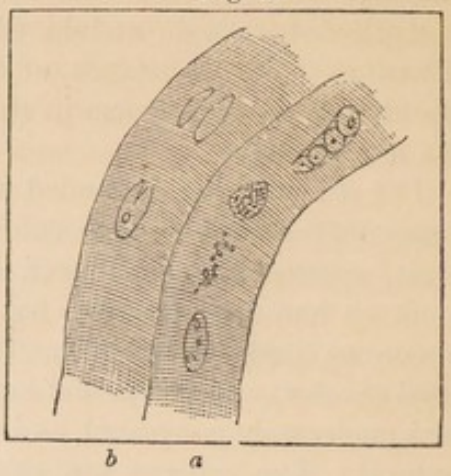


Fig. 3.

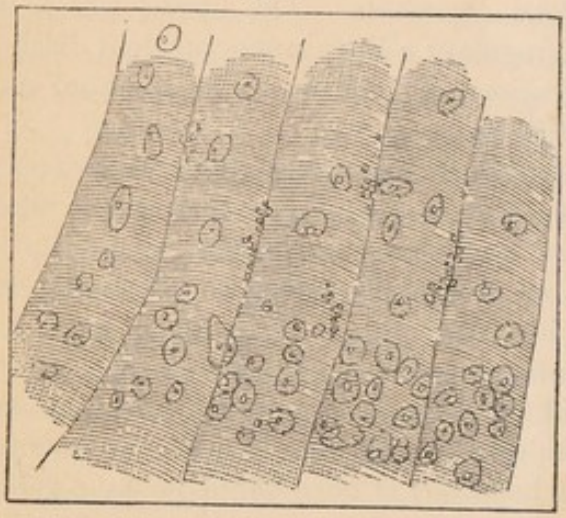
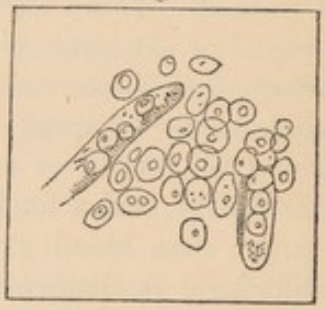


Fig. 4.



Great pains were taken to determine whether the cells arose within or between the muscular fibres. At first the greater part seemed to be within them; but careful observation determined that this was not invariably or even generally the case,—many which at first sight appeared to be so, turning out to be in reality between adjoining primitive muscular fasciculi. In some situations, however, it was established with certainty that the cells were actually within the muscular fibres. I may add that I submitted the demonstrations from which the annexed drawings were taken to Dr W. T. Gairdner, Dr Sanders, and Mr Turner, who satisfied themselves of the correctness of the observation.

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[1] Figs. 1–4.—Sections of the left ventricle in the neighbourhood of the new material, magnified 400 diameters.

Fig. 1.—Muscular fibres from an apparently healthy part at the margin of the deposit, showing increased growth of nuclei.
a. Nuclei enlarged, division about to take place.
b. Proliferation of nuclei.

Fig. 2.—Muscular fibres from the same situation as the last.
At the upper part of *a* four cells are seen arranged linearly, apparently within the same cell-wall.
b. A nucleus in process of dividing longitudinally.

Fig. 3.—Muscular fibres from a part involved in the deposit.
Numerous cells upon, within, and between the muscular fibres.

Fig. 4.—From near the centre of the mass.
Fragments of muscular fibres seen.

The preceding case bears strong testimony in favour of the view of the German pathologists. There was no possible source of fallacy: cells could be seen to arise either from a division or a multiplication of pre-existing cells. As stated above, it was by no means easy to determine whether they arose in general from the nuclei of the muscular fibres, or from the intermediate connective tissue corpuscles. In reference to this point, it may be remarked that two opinions are entertained regarding the nuclei of muscular fibre. The generally received opinion is, that they are the actual nuclei of the sarcolemma; the other, that they are the nuclei of anastomosing connective tissue corpuscles with extremely fine walls, which penetrate and surround the primitive muscular bundles.[1] Whether we adopt one or other view is of no great consequence; for on either hypothesis the further process of development must be the same.

The only point which remains to be considered is the nature of the new material found in the muscular substance of the heart. My first impression was, that it was of a syphilitic character. The absence of a similar deposit from any of the other situations where it is more commonly met with, and the comparatively high degree of its organization in the heart, subsequently raised doubts in my mind as to the justice of this impression; after mature consideration, however, I came to the conclusion that the original opinion was the correct one. To this conclusion I was led by a consideration of the characters of the growth, and by a reference to a few somewhat similar cases. Only three explanations of the character of the deposit appear to me possible: the first, that it was due to a simple inflammatory process; the second, that it was the result of a cancerous degeneration; the third, that it was the manifestation of a constitutional syphilitic affection.

The first of these hypotheses may be disposed of in a very few words. Myocarditis, more common than has often been supposed, leads either to abscess, or more frequently to fibroid degeneration of the muscular substance. In the case under consideration, a certain amount of fibroid degeneration had taken place, indicative, no doubt, of a certain degree of simple inflammation; the deposit, however, was of a different character. No one could have taken it for an abscess in course of formation; and it had none of the characters of purulent matter altered by age. Microscopic examination, too, showed cells in process of growth, not of decay. For these reasons the idea of simple inflammation must be rejected. Neither can I believe the deposit to have been cancerous. It had, indeed, some of the physical characters of cancer, although there was an almost entire absence of the juice which can generally be expressed from growths of that kind. But, putting this aside, and even keeping out of view the extreme rarity of primary cancerous degeneration of muscular fibre, the other facts do not tally with

[1] See Weber, in Virchow's Archivs, vol. xv. p. 480.

this hypothesis. The great majority of the cells were not such as are seen in cancer; for, as previously stated, they were generally of small size, little larger than blood-globules, and presented a remarkable resemblance to the spores of some vegetable growth. It is very true that animal cells cannot in general be distinguished in an absolute manner from one another, for, with altered nutrition and altered activity, cells may adopt a new form, analogous to that of some other kind of cell. Still, the general characters of cells in the same tissue are the same; it may be impossible to recognise and differentiate a special cancer-cell, but there is no doubt but that cancer as a whole presents certain special histological characters. Consequently, although in the above case some cells were met with which presented a striking resemblance to cancer-cells, or the nuclei of cancer-cells, the general microscopical characters of the deposit were different, and suggested the idea of a growth less highly organized than cancer, and not proceeding so far in its development. It is also worthy of remark, that it is not usual to find in the centre of cancerous masses such distinct remains of the original textures as were met with here, where, in the very centre of the deposit, fragments of muscular fibre were still recognisable—a circumstance not to have been anticipated in the case of a neoplasm, which, like cancer, tends to absorb and assimilate to itself all the previously-existing structures.

By way of exclusion, therefore, I was led to believe that the deposit was of a syphilitic character; and arguments in favour of this view are not wanting. The later stages of syphilis are characterized by lesions, which are distinguished from the earlier venereal affections by their situation as well as by their anatomical peculiarities. Ricord and his school base the differences between the different stages of the disease almost exclusively upon the organs affected. The primary affection is purely local, and affects the part through which the contagion is contracted; in the secondary stage, the skin, the mucous membranes, the iris, and the other superficial tissues suffer; while, in the tertiary, the cellular tissue, the bones, the muscles, the liver, the brain, and other deep organs are affected. A division founded upon the anatomical characters of the lesions is, however, more satisfactory. Thus, in the primary and secondary affections, we have to do only with congestions, inflammations, and simple exudations (modified, no doubt, by the specific virus), while in the tertiary there is a deposit of a peculiar material which takes the place of the atrophied natural textures. This deposit occurs in the form of gummy tumours or tubercles, and is met with frequently in the cellular tissue, in the testicles, in the bones, in the liver, and in the brain, occasionally, though unfrequently, in the muscles, and very rarely in the substance of the heart.

Virchow, in an admirable article "On the Nature of Constitutional Syphilitic Affections,"[1] describes a case of syphilitic deposit in

[1] Archivs, vol. xv. p. 217.

the heart, and refers to two similar cases recorded respectively by Ricord and Lebert. These cases, though in some respects similar to that which I have described, present certain differences. In Ricord's case,[1] the subject of observation, a man, died suddenly, and, on examination, firm, yellow, cheesy masses were found in the substance of the ventricles of the heart. There was no doubt as to the fact of the individual having suffered from constitutional syphilis: there was a history of old chancres, and of ulcerated tubercles of the skin. In the case of a woman, recorded by Lebert,[2] three tumours at a comparatively early stage of development were found in the wall of the right ventricle; here also there were syphilitic tubercles of the skin, of the subcutaneous cellular tissue, of the genital organs, and of the bones of the skull. In Virchow's own case, the patient, a man forty-seven years of age, had a history of a syphilitic affection dating back fourteen years. He died somewhat suddenly, and masses of deposit were found in the substance of his heart, chiefly in the septum; there was also syphilitic disease of the testicles.

The case which I have recorded is not so complete as these; it does not so distinctly carry along with it testimony as to the nature of the lesion. In the first place, there is no history of syphilis; but this, considering the circumstances under which the examination took place, is not surprising, and I attach no importance to it. A much more serious deficiency is the absence of any other evidence of a syphilitic affection: peculiar as this is, it does not lead me to modify the conclusion already expressed. The adhesions of the dura mater may indeed have been the result of a specific disease, but as this is not certain, little importance can be attached to their existence. The structure of the deposit in the heart was, however, so like what I have met with in undoubted syphilitic lesions in other organs, especially the brain, and it agrees so closely with that of the tumours described by Lebert and Virchow, that I have no doubt that the disease was due to a venereal affection, the history of which could not be recovered, and the other traces of which had been obliterated from the economy.

[1] Clinique Icongraphique, pl. xxix.
[2] Anatomie Pathologique, pl. lxviii. fig. 5.

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