On fatty degeneration of the small blood-vessels of the brain, and its relation to apoplexy : communicated to the Abernethian Society of St. Bartholomew's Hospital / by James Paget.

ON

FATTY DEGENERATION

OF THE

SMALL BLOOD-VESSELS OF THE BRAIN,

AND ITS

RELATION TO APOPLEXY;

Communicated to the Abernethian Society of St. Bartholomew's Hospital,

BY

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THE following pages include the substance of a communication lately made to the Abernethian Society of Saint Bartholomew's Hospital. It is not without hesitation that I publish observations so incomplete as these are; nor would I do so, if it were not that they seem to give sufficient promise of utility to merit at once the attention of other observers, and that the necessity of engaging in other investigations must, for some time, hinder my pursuing these.

In the least degrees of the disease which I propose to describe, the only apparent change of structure is, that minute, shining, black-edged particles, like molecules of oil, are thinly and irregularly scattered beneath the outer surface of the small bloodvessels of the brain. Such a change may be seen in the vessels of portions of the brain that appear quite healthy, as well in the capillaries as in branches of both arteries and veins of all sizes, from 1-150th of an inch in diameter, to those of smallest dimension.

As the disease makes progress, the oil-particles may increase in number till the whole extent of the affected vessels is thick-set with them, and the natural structures, even if not quite wasted, can hardly be discerned. While their number thus increases, there is, also, usually, a considerable increase of the size of many of the oil-particles, and they may be seen of every size, from an immeasurable minuteness to the diameter of 1-2000th of an inch. In other places, one sees, instead of this increase of scattered oil-particles, or together with it, groups or clusters of similar minute particles, which are conglomerated, sometimes in regular oval or round masses, like large granule-cells,* but more often in irregular masses or patches in the wall of a great part of the circumference of a bloodvessel.

In a single fortunately selected specimen, one may see, in different branches of a vessel, all these degrees or states of the disease—the less and the more thickly scattered minute oil-particles, the clusters of such particles in various sizes and shapes, and the larger particles like drops of oil.

When the fatty degeneration has made much progress, changes in the structure, and, not rarely, changes in the shape also, of the affected bloodvessels may be observed. The chief change of structure appears to consist in a gradual wasting of the more developed proper structures of the vessels: growing fainter in, apparently, the same proportion as the disease makes progress, the various nuclei or fibres are at length altogether lost, and bloodvessels of even 1-150th of an inch in diameter appear like tubes of homogeneous pellucid membrane, thick-set with the fatty particles. The structures of the vessels are not merely obscured by the abnormal deposits: they waste and totally disappear.

The changes of shape which the vessels may at the same time undergo are various. Very commonly, the outer layer of the wall is lifted up by one or more clusters of oil-particles, and the outline of the vessel appears uneven, as if it were tuberous or knotted.* Sometimes the outer or cellular coat of the vessels is for some distance raised far from the middle coat, as if it were inflated, and the space between them contains numerous particles of oil; (but, perhaps, this raising up of the outer coat is often produced by water being imbibed while preparing the specimen for examination.) Sometimes, but I think only

* I mean such bodies as Dr. Hughes Bennett calls "exudation-corpuscles" (Treatise on Inflammation, fig. 15); such as Reinhardt (Traube's Beiträge, H. II. and Virchow's Archiv, H. I.) has described, in relation to their multiform origins, as Körnchenzellen; and Virchow, under the same name, in his Archiv, H. I. 142. Similar corpuscles occurring among the products of inflammation were described by Gluge as "composite inflammation-globules;" but Vogel (Pathologische Anatomie, p. 126) gives good reasons for using the term "granule-cells" for these corpuscles also.

* In such cases, the masses of oil-particles often appear to lie outside the vessels, but examination with well-adjusted light will always find the outer layer of the wall, as a distinct dark line, raised up and continued over the surface of the cluster of oil-particles, or lost on its most prominent part. Dr. Hughes Bennett, in his Researches on Inflammation of the Nervous Centres, must, I think, have overlooked this fact. His attention being directed primarily to the changes of the structure of the brain itself, and to the products of inflammation in it, he appears to have less minutely examined the state of the bloodvessels in the diseased parts. Some of the appearances produced by fatty degeneration are represented by him (in the Edinburgh Medical and Surgical Journal, vol. lviii., pl. v. fig. 56, and very accurately in vol. lix., pl. i., fig. 5); but he refers them to the vessels becoming coated externally with exudation-granules, the products of inflammation.

in vessels of less than 1-500th of an inch in diameter, partial enlargements, like aneurismal dilatations or pouches of their walls, are found.

The vessels most liable to this disease are, I think, the arteries of about 1-300th of an inch in diameter; but it exists, generally, at the same time, in the veins of the same or of less size. As a general rule (judging from the specimens hitherto examined), the disease decreases in nearly the same proportion as the size of the vessels, and the smallest capillaries are least, if at all, affected. But there are many exceptions to this rule; and it is not rare to find vessels of from 1-2000th to 1-3000th of an inch in diameter, having parts of their walls nearly covered with the abnormal deposits.

The principal and first seat of the deposits is, in arteries, in the more or less developed muscular or transversely fibrous coat:—in veins, it is in the corresponding layer, immediately within their external fibro-cellular nucleated coat:—in vessels, whether arteries or veins, whose walls consist of only a simple pellucid membrane bearing nuclei, the substance of this membrane is the first seat of the deposits. In some cases the outer fibro-cellular coat of both arteries and veins appears to contain abundant fatty matter. But it is seldom that, in an advanced stage of the affection, any of the several coats of a bloodvessel can be assigned as its chief seat; for even in large four-coated arteries they wholly waste, and their remains appear united in a single pellucid layer, of which the whole thickness may be occupied by the deposit.

The figures represent some of the most usual appearances of the degeneration.

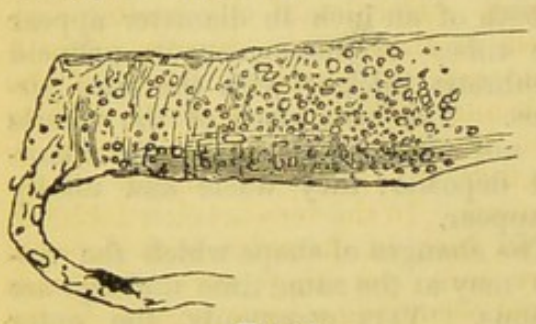

FIG. 1.

FIG. 3.

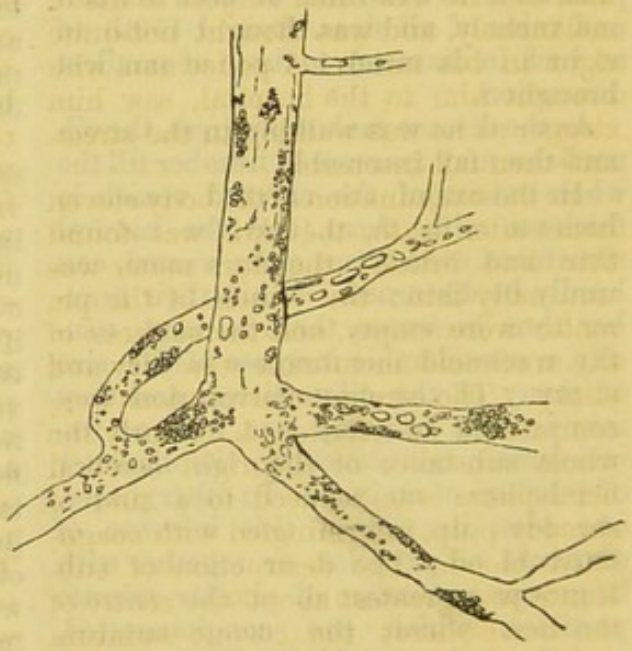

FIG. 2.

FIG. 1. An artery, of 1-300th of an inch in diameter, and a branch given from it, from the softened corpus striatum in the third of the related cases. Numerous oil-particles of various sizes are scattered in the muscular coat, traces of the tissue of which appear in obscure transverse marks.

FIG. 2. From the same part, a vein 1-600th of an inch in diameter, with branches from 1-1200th to 1-1800th, and portions of capillaries. Scattered oil-particles, and groups, like broken irregular granule-cells, are seen in the homogeneous pellucid walls of all the vessels.

FIG. 3. A vessel of 1-600th of an inch in diameter, and another of 1-1800th, with a branch of 1-3000th of an inch. Groups and scattered oil-particles are thick-set in the simple, pellucid, membranous walls. From the second of the related cases.

The changes of structure just described indicate an affection of the small blood-vessels similar in its nature to those which form the large class of "fatty degenerations." Viewed in its relations to them it presents many points of interest; but, reserving these, I prefer now to illustrate the fatty degeneration of the bloodvessels of the brain in its connection with cerebral apoplexy, of which it may be suspected to be the ordinary precursor, or even the immediately predisposing cause. In the following cases the connection was well-marked.

Case I.—Joseph Collett, a tall thin labourer, 64 years old, was admitted into Mark's Ward, under Dr. Hue, on the 15th of January. He was completely comatose, and soon after admission was found to have hemiplegia on the left side. Scarce any change occurred in his state: he remained quite unconscious, and died in two days. The only history that could be obtained of him was, that he was often subject to fits of melancholy, and was thought not quite right in his mind. A policeman, who brought him to the hospital, saw him stagger as he was walking in the street, and then fall insensible.

In the examination of the body eleven hours after death, the skull was found thin and brittle; the dura mater was unusually thin; the vessels of the pia mater were empty, and the surfaces of the arachnoid membrane were dry and sticky. The cerebral convolutions were compressed and flattened. Nearly the whole substance of the right cerebral hemisphere was reduced to a kind of shreddy pulp, intermingled with coagulated blood. The destruction of substance was greatest about the centre of the hemisphere; the corpus striatum and optic thalamus were completely broken down, scarcely a trace of either remaining. The peripheral parts of the hemisphere were moderately firm, and looked healthy. No yellow softening existed. The blood extravasated might have filled a wine-glass. The septum lucidum was entire The left lateral ventricle contained about three drachms of a light brownish fluid. The whole of the left cerebral hemisphere and its ganglia appeared healthy

The anterior border of the right hemisphere of the cerebellum was broken down, and contained recent blood, which was probably derived from the extravasation in the cerebrum. The pons Varolii also contained several little masses of recent clotted blood, separately effused.

The longitudinal sinus contained only a small black clot at its lower part; the lateral sinuses contained thick dark blood. Small deposits of yellow matter existed about the junction of the anterior and middle cerebral arteries, and a streak or two of similar deposit along each of their trunks, but there was no disease sufficient to impede the passage of blood through them.

The brain alone was allowed to be examined.*

In examinations of numerous minute arteries and veins taken from the ruptured parts of the cerebral hemisphere, I found that nearly all, but especially the arteries from 1-200th to 1-1200th of an inch in diameter, had abundant minute molecules of oily matter scattered in their coats, directly beneath their external surface. Some of the molecules appeared to lie in the cellular coat, but more in the coat beneath it, whether muscular or simply mem branous. In the vessels below 1-1200th of an inch in diameter such deposits were rare, yet they were sometimes found occupying a large portion of the wall. In a cluster of vessels drawn from the wall of the cavity in which a small clot of blood was effused in the pons, I found the degeneration in its most advanced form. Thick-set oil-particles, and larger drops of oil, large clusters of molecules, like granule-cells, and patches of granules, and some almost like pigment-cells, abounded on nearly every part of these blood-vessels. The proper structure of the vessels had so disappeared that I could not tell whether they were arteries or veins.

No inflammatory or other morbid deposit existed in the many portions of the substance of the brain that were examined together with the blood-vessels.

Case II.—Hannah Bailey, a large and fat washerwoman, 47 years old, was admitted into Faith Ward, under Dr. Burrows, on the 4th of January. She had always enjoyed good health, and was troubled with only a winter cough, till the 27th of December,

* I am indebted for the particulars of both this and the next case to Dr. Kirkes.

when at breakfast, after complaining of headache, she suddenly became unconscious. She recovered her consciousness in about half an hour, and went about her work; but about four hours afterwards she felt faint, sat down, and then fell to the right side. She was insensible for a few minutes; and on recovering had lost the use of both right limbs, but could speak distinctly. In about three hours afterwards she had another attack, and remained unconscious till midnight, when she partially recovered.

Till the last day of her life she remained almost always in a half-conscious state; hemiplegic on the right side, and generally unable to speak. In the last day she became more and more comatose, and so died.

In the examination after death, diseased mitral valve, enlarged heart, and signs of bronchitis, were found. In the aortic valves and the arch of the aorta, and about the orifices of its great branches, were numerous scattered deposits of fatty matter; and similar deposits were abundant in the coronary arteries.

The skull and dura mater were thick. On the upper surface of the left cerebral hemisphere, the substance of the brain, for about two inches in length, and one in breadth, near the longitudinal fissure, was flattened, soft, and spotted with deep red. The parts immediately around this portion were of a light yellow tint, and much softer than the rest of the cerebral substance. Beneath the red-spotted part, and to within a line of the roof of the lateral ventricle, was a brownish-red mass, consisting of clotted and partially decolorized blood, intimately mixed with cerebral sub stance. The portion of brain around this was softened and yellowish, but the portion between the clots and the lateral ventricle appeared healthy. So, also, did all the other parts of the brain.

Several portions of yellow fatty deposit existed in the walls of the branches of the arterial circle of Willis, and in the walls of the anterior and middle cere bral arteries; but the deposit did not anywhere appear sufficient to impede the stream of blood.

In microscopic examinations of portions of this brain, I found fatty degeneration, in the forms described above, affecting alike the vessels of the healthy, the broken, and the softened portions of the brain; but the vessels of the healthy parts were affected in a less degree than those of the others. Some vessels, not less than 1-200th of an inch in diameter, appeared to have almost totally lost their natural structures, though presenting but little fatty degeneration. A similar loss of natural structure was observable wherever the degeneration existed. The disease affected principally the bloodvessels of about 1-400th of an inch in diameter, but in some parts it existed also in even the smallest capillaries; such as, when collapsed, measured not more than 1-3000th of an inch. In many specimens it was easy to trace both an inner and an outer line at the sides of the deposits,—proving that they lay in the very substance of the coats of the vessels.

In and about some of the affected bloodvessels were numerous lozenge-shaped, dark, blood-red crystals, some of which lay among the clusters of fatty particles in the walls, while others appeared to be within the cavities of the bloodvessels.*

Some, also, of the small bloodvessels presented well-marked partial dilatations, like aneurismal pouches, or like more extended varicose enlargements of their walls. In these, as in others, but in no greater degree, the fatty degeneration existed.

The cerebral substance appeared generally healthy, but in the softest parts granule-cells existed,—not, however, in great abundance.

Case III.—E. Rose, a sempstress, 21 years old, was admitted on the 8th of October into Harley's ward, under Mr. Stanley, with an outward dislocation of the patella that had existed two months. The dislocation was with much difficulty reduced on the 16th of October, and, with equal difficulty, was prevented from recurring. The pressure of apparatus on the reduced patella caused slight sloughing of the integuments over it, and she was under treatment for this, when, on the 29th of November, symptoms of affection of the

* Respecting these singular crystals, the reader may consult Virchow, who believes them to be formed of modified hæmatin (Ueber pathol. Pigmente; in his Archiv, B. i. p. 390, Tab. iii.) or Zwicky (De corporum luteorum origine). Köliker also has some remarks on them in his Zeitschrift für wissensch. Zoologie, B. i. p. 266.

brain ensued. Her general health had not been materially affected, but for three or four days she had complained of want of sleep, and headache. On the 29th she became, almost suddenly, hemiplegic, losing all sensation and power of voluntary motion on her right side. She appeared, too, very drowsy, and half comatose. From this time she seemed occasionally to improve, but, on the whole, became gradually worse: she passed restless nights, often shrieking and delirious, and was once or twice severely convulsed; her tongue was usually dry, and nearly black, and she had intense headache. A week after the attack of hemiplegia, sloughs formed in the skin of the right leg where the bed-clothes pressed on it: a few days later the skin and other tissues began to slough on the nates on both sides, on the sacrum, the right arm, the back of the head, and the right ear. She died in extreme emaciation on the 31st of December.*

In the examination after death, the tissue of the pia mater was found containing a large quantity of pellucid fluid. All the brain appeared quite healthy, except the left corpus striatum, of which nearly the whole was reduced to a soft pulpy substance, with mingled shades of pink, greyish, and pale yellow, and with small spots of blood here and there scattered through it.

On the mitral valve there was a thick patch of recently deposited lymph, and in the upper part of the left kidney was a large collection of pus in a cavity with sloughing walls.

Tufts of small blood-vessels drawn from the diseased part of the brain showed the most striking degeneration. It was best marked in vessels from 1-150th to 1-400th of an inch in diameter. These presented no change of shape, no dilatations: their outlines were distinct and uniform, but of the several tissues of their coats scarcely a trace remained: they appeared as if formed of pellucid simple membrane, varied only by the fatty deposits, which existed in all the varieties of form already described. In blood-vessels less than 1-400th of an inch in diameter, both the loss of proper structures and the fatty degeneration were less, and both seemed to diminish with the size of the vessels: many of the capillaries appeared nearly healthy; others, however, were thickly sprinkled with oil-particles.

The softened cerebral substance contained abundant granule-cells, with cell-shaped clusters of granules, and diffused granular matter. Some corpuscles, also, were seen like those of lymph formed in inflammation; but these might be colourless blood-corpuscles, such as existed abundantly in the blood. Groups of dark blood-red crystals, of apparently prismatic form, were numerous in the softened substance of the brain.

In the blood-vessels of other and healthy-looking parts of the brain, scarcely any appearance of fatty degeneration was observed. The great arteries of the brain appeared quite healthy, and there were only very trivial deposits of fatty matter in the aorta.

In the foregoing cases, the fatty degeneration of the small blood-vessels of the brain existed in an extreme degree. In a less degree I have observed it in the brain of a man, 51 years old, who died with suppression of urine; in that of an epileptic woman, 45 years old; and in such other cases that I think it will be found a frequent condition in the apparently healthy brains of persons past the middle period of adult life. In all such cases, when the disease is far advanced in any of the blood-vessels, the loss of their proper structures, and the weakening of the remains of their walls by the copious deposits of fatty matter in them, must make them peculiarly liable to rupture. It cannot but be that this affection should constitute a predisposition to apoplexy, whether occurring in its simplest form or in connection with cerebral softening; indeed, how readily vessels thus affected may be torn, we may see in the frequency with which, in the microscopic examinations of them, specimens of considerable blood-vessels are found torn across at or near the anormal deposits.

If what I have written should induce others to investigate this subject, I venture to suggest that they should especially examine the connection of this form of degeneration with the common fatty or atheromatous degeneration of the larger arteries, and with the morbid softenings and other errors of

* For many of the particulars of this case I have to thank Mr. H. O. Thorold, who was the patient's dresser.

nutrition in the brain. The foregoing cases make it probable that the degeneration may advance far in the vessels of the brain, while affecting the larger arteries in only a trivial degree. In two of these cases partial softening of the brain existed; but in one, at least, of them this change was most probably subsequent to the rupture of the blood-vessels. Dr. Hughes Bennett's cases* show that the degeneration is frequently connected with cerebral softening, but not whether it is usually the precursor or the consequence of that change.

It may assist future researches if I add a short notice of the principal observations that have been lately made on the diseases of the small bloodvessels.

With the exception of the notices of the general dilatation of the small vessels of inflamed parts, scarcely any facts had been recorded in relation to this subject, till Kölliker and Hasse published their observations on the occurrence of "aneurismal capillaries," in a case of acute inflammatory softening of the brain, with capillary apoplexy. This affection, consisting, as the name implies, in partial pouch-like dilatations of the walls of small bloodvessels in inflamed parts, was subsequently observed by them in inflammations produced by severe injuries of the brains of rabbits.† Bruch‡ detected a similar condition of the small arteries in a case of traumatic inflammation of the peritoneum of a bitch; and Harting,§ in a case of diseased ovary. More lately, two cases have been described by Kölliker, and one by Rinecker, in which such aneurismal dilatations existed in the vessels of softened portions of brain;* but in all these cases the dilatations affected, not the smallest capillaries, but those of largest size and the small veins In all these cases, also, small blood-red points, characteristic of the so-called capillary apoplexy, and usually ascribed to effusions of blood, were found to be the aneurismally dilated vessels full of blood.

I lately observed this kind of dilatation in a case of acute softening of the brain, and could confirm all that Kölliker has described of it; but it existed in comparatively few of the blood-vessels of the diseased part. I have mentioned it, also, as occurring among the vessels of the brain in the second of the cases recorded above; and Dr. Ormerod tells me that he observed "fatty degeneration, with irregularly formed vessels and lateral expansions," in the neighbourhood of a large collection of pus in the brain. Doubtless, such partial dilatations are very frequent, if not constant, in cases of cerebral softening; but it has yet to be determined whether they are characteristic of inflammation, or whether, as I suspect, they may occur as well in the vessels weakened by fatty degeneration.

Kölliker† has recently described a disease, which he names "spurious aneurisms of the smallest arteries of the brain." It consists in effusions of blood between the middle and internal coats of arteries, from one-third of a line in diameter to those of smallest size: effusions resembling those of "dissecting aneurisms." He says this is, "according to my observations hitherto, the regular forerunner and accompaniment of common and capillary apoplexies." I have too much confidence in the accuracy of Professor Kölliker to doubt his observations; and though I have seldom, and only obscurely, seen what he describes and figures in his Tab. xix. fig. 1, yet I believe that these effusions of blood in the coats of the smallest arteries may be usual in cases of apoplexy. But I believe, also, that such effusions will be found to be only one of the consequences of previous degeneration of the arterial walls. Without such degeneration, neither the partial rupture of the vessels producing spurious aneurisms, nor the complete rupture permitting the effusion of an apoplexy, is likely to happen.

Respecting fatty degeneration in the small blood-vessels, the only notice I can find is by Virchow,‡ who says he has seen glistening red or yellowish little fat-drops in the epithelial cells of the capillary vessels of the kidney. This, however, must be quite a different

* In Edinburgh Med. and Surg. Journal, Vols. 58, 59, 60.

† Their observations are recorded in Henle and Pfeufer's Zeitschrift, B. iv. p. 1.

‡ In the same Journal, B. v. p. 69.

§ Nederlandsch Lancet, Jaarg. iv. No. 2. Dr. v. Leeuwen kindly gave me a specimen displaying the bloodvessels here described.

* The three cases, and a reference to one by Hasse, are in Kölliker's Zeitschrift für wissenschaftliche Zoologie, B. i. p. 262.

† In his Zeitschrift für wissensch. Zoologie, Bd. I. p. 264.

‡ In his Archiv, Bd. i. p. 145.

affection from that which I have described, and in which the fatty degeneration is seated in the muscular or other corresponding coat of bloodvessels, that, so far as I have observed, have no epithelium. So, too, it is a different, though it may be a related, affection which Rokitansky* describes as consisting in the excessive deposit of internal coat in very fine arteries, making their walls thicker, turbid, less transparent and brittle. This affection is well known in the bloodvessels of the brain just visible to the naked eye: it occurs, too, in those of the uterus, mammary gland, and perhaps many other organs in process of senile atrophy. Rokitansky "believes also that he has convinced himself of a similar state in the proper capillary vessels."

It will be observed, that nearly all the observations hitherto made relate to the bloodvessels of the brain. The facility with which these can be separated and cleaned for microscopic examination may explain this: but it is not likely that the brain should be the only organ whose small vessels are liable to these affections.

* Pathologische Anatomie, B. ii. p. 683.


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