ON THE PATHOLOGY OF URÆMIA AND THE SO-CALLED URÆMIC CONVULSIONS.*

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THAT Bright's disease is the most frequent cause of cerebral hæmorrhage is, perhaps, one of the most universally admitted pathological facts; but the statement is usually made with regard to the grosser hæmorrhages, which cause death from apoplexy. It is also generally admitted that small capillary hæmorrhages frequently accompany and are seen on the outskirts of the grosser lesions; but that such minute hæmorrhages occur alone, and without association with the larger ones, though under the same conditions, does not appear very generally recognised, and certainly the symptoms to which they give rise are altogether overlooked. All pathologists mention such conditions as occurring, usually in connection with disease of the vessels and other conditions to be considered hereafter, but very few attempt to associate them with any symptoms.

Wilks and Moxon, speaking of them, say: "This condition of the brain denotes a diseased state of the blood or the vessels generally, and is found in purpura, in idiopathic anæmia, and sometimes in fever. We think it interesting in connection with paralysis which may come on in cases of fever shortly before death; we have then found this state of capillary apoplexy to exist. It is often present also after the convulsive attacks occasionally observed in typhus."

Dr. Hughlings Jackson, in his admirable article on Apoplexy, in Reynolds's *System of Medicine*, comes nearer the truth. While discussing the frequent association of Bright's disease with apoplexy, he mentions capillary hæmorrhages, which, he states, are sometimes found, and he thinks often occur in this disease; concerning them, he speaks thus: "We have, unfortunately, very little precise information about the symptoms they produce, as they do not cause death."

Rindfleisch describes these capillary hæmorrhages more accurately than any other pathologist, and altogether places them in a more important position, though chiefly using them as types of cerebral hæmorrhage, which are serviceable for microscopic demonstration of the minute changes produced by hæmorrhage into the brain-tissue. He mentions their association with grosser hæmorrhages in Bright's disease; and indicates that, in this condition, hæmorrhages various in extent may occur and clots of various sizes result. He, moreover, divides them into two classes: punctiform hæmorrhages, the results of "diapedesis" or simple exudation, as in purpura, etc.; and those the result of absolute rupture of walls of vessels, such as occur in Bright's disease, the result of degeneration of the walls of the vessel by endarteritis or periarteritis, and of the increased tension within them. He, moreover, points out that the extent of the hæmorrhage depends upon this amount of arterial tension.

Niemeyer suggests that these capillary hæmorrhages give rise to the so called "warnings" preceding an attack of apoplexy.

To form an opinion, first, as to the question what evidence there is that these punctiform hæmorrhages may give rise to convulsions such as we meet with in so-called uræmia, let us examine the pathological conditions under which it occurs and the symptoms associated with them. On examining that admirably arranged storehouse of facts the *post mortem* records at Guy's Hospital, limiting my inquiries to the last six years, the conditions in which punctiform hæmorrhages have been found in the brain may be tabulated with some from other sources as follows.

I. Hæmorrhages from simple exudation, due to altered blood: hæmorrhages by "diapedesis".

1. Purpura.
2. Leukæmia.
3. Malaria.

II. From bruising, due to laceration of vessels: hæmorrhages by "ecchymosis".

1. Injuries to skull and lacerations of brain, from blows, etc.

III. From inflammations or congestions.

1. Cerebritis, including also
 - a. Red softening;
 - b. Invasion of cortex by meningitis.
2. Embolism.
3. Fevers.
4. Sunstroke.

5. Occasionally the vicinity of tumours, aneurisms, hydatids, etc.

IV. From diseases of vessels, permitting rupture by blood-pressure.

1. The psychoses (Rindfleisch). General paralysis.

2. Bright's disease:

- a. In the neighbourhood of larger clots;
- b. Alone, in deaths from uræmia in which convulsions have been present during life.

In considering this table especially in relation to the question of convulsions accompanying the diseases mentioned, the results are, I think, most striking and important. In the first class, in which blood exudes passively and without any increase of pressure upon or laceration of the cerebral substance, convulsions are not present, or, if ever, very rarely. In the second class, due to injuries, all symptoms are masked by those of concussion and paralysis. Moreover, in them the pressure on the cerebral tissue is not increased. In the last two classes, which are characterised by hæmorrhages with increased blood-pressure, convulsions are most common, in many of them almost invariable; and, inasmuch as hæmorrhages do not occur in *all* these cases, it would not be too much to say, I think, as there is some evidence to support it, that those cases in which convulsions occur are those in which these capillary hæmorrhages are present, though not to such a degree as to cause absolute paralysis, which it appears equally certain that they may do if very numerous.

But it may be said, Why, if these hæmorrhages be the cause of uræmic convulsions, are they not more frequently found in the deadhouse associated with Bright's disease? I think there are sufficient reasons to answer this question satisfactorily. First, such small hæmorrhages as these would be rapidly absorbed; and, if the convulsions had not occurred within a few days of death, they would not be found. Secondly, cases dying in this manner, though not unusual, are not so very common. Thirdly, the head is sometimes not examined at all; and, if examined, it may be done without very great care. Fourthly, it is impossible to examine the grey matter of each convolution minutely, so that such small hæmorrhages might easily be overlooked even by a most careful pathologist. Now, however, thanks to our ability to localise the disease more accurately, we may hope to discover them with greater ease.

It is of interest also to note, as bearing upon the question of these hæmorrhages, that uræmic convulsions are more common in acute Bright's disease; while larger hæmorrhages, causing death from apoplexy, occur more frequently in the chronic form and in more advanced life. The reason for this is very evident. It is not difficult to rupture the capillaries by increased blood-tension, owing to the thinness of their walls, as seen in the kidney when bloody urine is produced, this being undoubtedly due to rupture of capillaries; while in the chronic disease the larger vessels have had time to undergo degeneration, so that they become equally, if not more, liable to rupture.

Another question may be put, and one which bears strongly upon this subject, and indeed forms part of it. Supposing these hæmorrhages are the cause of uræmic convulsions, how do you account for the other symptoms of uræmia? To this I would answer: By oedema of the brain-tissue. I know that the occurrence of such a thing as oedema of the brain has been denied by many eminent pathologists; but, on the other hand, it has been supported by others. Of late years, I think, many new facts have been obtained in relation to this question and very strongly supporting such a view. The most important of these is the hyaline exudation found by Sir William Gull and Dr. Sutton around capillaries in nervous tissues: this they have found, if I remember rightly, in acute Bright's disease associated with dropsy elsewhere. I know that it was under conditions of increased vascular tension. This hyaline exudation is, moreover, also described by Rindfleisch, and by Cornil and Ranvier. It is of the same nature as oedema of the brain, only the exudation has been highly fibrinous and has coagulated, thus forming the only condition under which it could be examined microscopically. Another fact of a somewhat similar nature is the extreme hyperæmia, accompanied by transudation of leucocytes through the walls of the vessels, found in hydrophobia by Dr. Coats, Dr. Gowers, and others. Moreover, accepting the mechanical theory of the production of dropsy, which now-a-days must surely be almost universally admitted, I can see no reason why the greatly increased blood-pressure in Bright's disease should not cause transudation of serum through the walls of the cerebral capillaries, which are among the most delicate in the body, as through those of other parts. Of course, owing to the density of the structure surrounding them, and the intracranial pressure, we should expect it to be the last place in which it occurred; but so indeed it usually is, as evidenced by the symptoms produced. But we also know that there are times at which the pressure in the blood-vessels in the brain exceeds the pressure outside them, as must necessarily be the case in all hæmorrhages; when this occurs in the capillaries, what more probable than

* Concluded from page 12 of last number.

exudation of serum or rupture and punctiform hæmorrhages, according to the degree of intensity of blood-pressure? If, then, œdema be admitted as possible, the other symptoms of uræmia—the coma, drowsiness, and typhoid state—are completely accounted for by compression of the brain-tissue.

It may be objected to this, that uræmia occurs in chronic Bright's disease in which there is no dropsy. I have before pointed out a probable reason for the absence of dropsy in this condition; namely, the insidious nature of the disease, the gradual increase of the blood-tension, and the accompanying gradual thickening of the capillaries, which are thus enabled to withstand the increased blood-pressure. But, when this is still further suddenly increased, as by the supervention of an acute attack on the chronic disease, dropsy does occur, and so does uræmia; but, apart from this, the occurrence of a great increase of tension, causing distension of capillaries without exudation, would, by increased pressure on the nervous structures, produce some of the slighter symptoms of uræmia, such as the characteristic headache of Bright's disease.

To return, however, to the convulsions, other grave objections may be raised to my theory of their production.

1. Experimental evidence may be adduced to show that the grey matter of the cortex may be cut, bruised, burnt by caustics, and irritated by various methods, without the production of convulsions. But, on the other hand, besides its irritation by electricity, Nothnagel produced convulsions by the injection of a solution of chromic acid into the grey matter of the cortex. But, more than that—for experimental evidence, unless supported by pathological facts, is worth but little—I think I have already adduced sufficiently strong evidence of the association between punctiform hæmorrhages and convulsions to be found in the deadhouse.

2. It may be said that the convulsions produced the hæmorrhage, and not the hæmorrhage the convulsions; but the entire weight of pathological evidence is the other way. People dying of epilepsy do not usually present these hæmorrhages; in fact, all authorities on this disease emphasise greatly the fact of their great rarity. While in the deadhouse it is common to see ecchymoses below the skin, serous and mucous membranes, the result of impeded venous circulation, as in death by asphyxia from any cause, it is extremely rare to see these hæmorrhages in the brain-tissue under these conditions: though they will occur beneath the arachnoid, I have never seen them, nor can I find any record of their occurrence, in the substance of the brain, from this cause.

3. Epilepsy may be quoted as a fact against my theory, for not only are these hæmorrhages not found in epileptics, but epilepsy is believed by many eminent authorities to be associated with anæmia of the brain rather than hyperæmia; but this view is at least open to question. It would be impossible to discuss this subject here; but however strong the evidence of anæmia of the brain in epilepsy may be, the side of hyperæmia is almost equally strong. If Kussmaul and Tenner think they have proved *experimentally* that anæmia of the brain produces convulsions, so also Schroeder van der Kolk has beyond doubt, I think, proved that dilatation of the capillaries occurs as the result of hyperæmia in epileptics; and this, be it remembered, not generally throughout the brain, which might be the result of general turgescence owing to impeded venous return, but in that centre in the medulla to which he refers the irritation producing the convulsions. He is even able to divide his cases into two classes: tongue-biters, in which the capillaries of the hypoglossal nucleus are especially affected; and those who do not bite the tongue, in which those of the pneumogastric nucleus are alone dilated.

While suggesting capillary hæmorrhage as a cause for convulsions, let it be clearly understood that my remarks are confined to those occurring in conditions of high arterial tension, as in Bright's disease, pregnancy, and other conditions in which so-called uræmia occurs. The convulsions of epilepsy are probably due to some hyperæsthetic or irritable condition of nerve-cells, which may be due to a local hyperæmia, or to some other cause, but certainly not to capillary hæmorrhage.

4. Dr. Hughlings Jackson's theory of spasm of cerebral arteries as a cause for uræmic convulsions remains to be contested: it must stand or fall in great measure with the anæmic theory of epilepsy; but, even admitting that to be true, it appears to me difficult to conceive such severe spasm of cerebral arteries as to so completely cut off all blood-supply to the brain, as Kussmaul and Tenner's experiments seem to indicate as necessary for the production of epilepsy; for, according to them, if but one vessel out of the four large arteries supplying the brain be left uncompressed, the convulsions did not ensue.

5. Dr. George Johnson's theory of "stopcock action" of arterioles, and Dr. Gowers' recent ophthalmoscopic observations in support of this, may also perhaps be adduced as reasons against the hæmorrhagic

theory of convulsions. To take the latter observations first, I think they are open to error. Any one who has used the sphygmograph extensively, will recognise the fact that arterial tension may be high—that is, the tidal wave sustained—even with a relaxed condition of at least the larger vessels, while in other cases the arterial system throughout is contracted; every degree, from great relaxation to tight cord-like contraction of the vessels, may accompany increased arterial tension. In all alike, cerebral hæmorrhages are liable to occur. I think Dr. Gowers' observations can only show this contracted state of the vessels generally or their relaxation, but I do not think that they are any test of arterial tension.

If Dr. Johnson's view of the stopcock action of the arterioles be true, then the tension in the capillaries must surely be low, or not increased, owing to the defending contraction of the arterioles; and it is this fact chiefly that makes me unable to accept his otherwise ingenious theory, for, without admitting that the high tension extends to the capillaries, I cannot see how to explain bloody urine and dropsy in acute Bright's disease, and the hyaline thickening around capillaries and absence of dropsy in chronic Bright's disease.

These, then, are the reasons for and against this theory of the *vascular* cause of what are known as uræmic symptoms, as far as they occur to me. I think they would be better described as the symptoms of high tension in the cerebral capillaries, or, more shortly, as those of *cerebral œdema* or hæmorrhage. They must always be regarded as a precursor of apoplexy, if they occur in a person advanced in life or with degenerate vessels. Should my view prove to be the correct one, the indications it affords for treatment by rapidly diminishing the blood-pressure are of the utmost importance for the safety of the patient.

REPLIES TO DR. C. J. B. WILLIAMS AND TO DR. BROADBENT ON THE MECHANISM OF THE HEART-SOUNDS.

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It is a matter of regret to me that the omission of a word in quoting from Dr. Williams' paper afforded him the occasion of making some sweeping and hardly justifiable assertions.* He says that my "misunderstandings and misquotations are something unusual; for example, he (Dr. Leared) quotes me as saying: 'The case is one of striking through a space at a tight barrier,' etc.; whereas my expression was: 'The case is *not* one of striking through a space at a tight barrier,' etc. This reversal of the sense makes nonsense, which he proceeds to deal with accordingly." In another part of the paper, the matter is again taken up. Dr. Williams says: "His omission of the word 'not' in the passage before quoted naturally throws Dr. Leared into a state of confusion, and it may be well to restate the argument in other terms." It is difficult to conceive why Dr. Williams could have allowed himself to make such a statement. But I am at the same time glad that he has put forward certain points of my theory with his own comments. To these I shall have occasion to return. First, let me dispose of the omission of a word and of its alleged effect upon my whole train of reasoning.

It is a remarkable circumstance that the insertion of the missing "not" in its place, instead of throwing me into "a state of confusion," strengthens my argument. I was combating Dr. Williams' assertion "that the whole movement is one of quiet displacement"; and I ask, has he "forgotten the force with which blood issued from the punctured aorta in his vivisection experiments? The force of the adult left ventricle was estimated by Valentin as sufficient to overcome a pressure of four pounds." Now, it is plain that, when I quoted Dr. Williams as saying the case was one of striking, instead of *not* striking, as it should have been, against a tight barrier, the force of my subsequent statement about the power of the ventricle was weakened by the omission of the word. Nevertheless, the mistake was unfortunate, and a cause of unnecessary trouble in this discussion.

Again, Dr. Williams says, in reference to the opinion of Dr. Stone, that "any person, whatever his scientific position, who declares the impossibility of sounds being produced in fluid alone, states a fallacy." "Either Dr. Leared misquoted, or his oracle misunderstood, my words, which were: 'I conclude, then, that the sounds of the heart are not produced by any motions or collisions of the blood, because I find that no such sounds can be produced in fluids alone.'" But, in the paragraph

* Dr. Williams' paper appeared in the BRITISH MEDICAL JOURNAL, February 3rd, 1877.—In Dr. Leared's absence from town, and from pressure on space, the insertion of this paper has been unavoidably delayed.