REMARKS
ON
THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE BRAIN.

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(Concluded from p. 63.)

I NEXT speak in some detail of the methodical investigation of particular cases of brain disease, and shall deal with questions of treatment at several stages of the inquiry. The clinical problem of what we call *a* disease is threefold—anatomical, seat of lesion; physiological, functional nature of lesion; pathological, disorder of the nutritive process. The division into structure, function, and nutrition is, of course, arbitrary, but it is a convenient one. I may now say, once for all, that I use the term functional in its meaning as the adjective of the word function. I do not believe that there can be any kind of symptoms without abnormal changes, however slight they may be in some cases (see an able paper by Dr. Allchin, *Westminster Hospital Reports*, vol. ii). Hence, when speaking of cerebral and cerebellar tumours, and other masses, I used the expression *gross* organic disease, not doubting that there is some organic change, however minute it may be, and, as yet undiscoverable, even in epilepsy proper, in chorea, in neuralgia, etc. There are two diametrically opposite kinds of functional changes. 1. Degrees from slight defect to loss of function. 2. Degrees from slight to excessive exaltation of function. The former, negative state of function, exists in cases of paralysis, the latter, positive (super-positive) state of function in cases of epilepsy, chorea, tetanus, etc. I never use the expression "disorder of function," but speak of degrees of negative functional states, and of degrees of states of over-function. The two may co-exist. Some elements of the set of motor nervous arrangements representing a muscular region may have lost function, whilst other elements of the same set may be in over-function. For example, we find not rarely persisting hemiplegia and occasional convulsion of the muscular region paralysed.

One advantage of the scheme of investigation by the triple division is that we learn by it where our knowledge is deficient. Indeed, of some cases of nervous disease it would be commonly said that we know symptoms only. The scheme enables us to separate definitely what we know from what we only suppose. In chorea we know that there is the second kind of functional lesion; at any rate, it is an irresistible inference that the movements depend on unduly high instability of nerve cells.[8] But we do not know the seat of that lesion, nor the pathological processes leading to it. On the anatomy and pathology of chorea all of us have hypotheses only, My speculation is that, anatomically, the lesion is of some convolutions of the motor area, and that the pathology in most cases is plugging of arterioles.

In illustration of the triple method I shall take a case in which our knowledge is fairly complete, an ordinary case of hemiplegia. Before I do this I will once more speak of types. As to range, I make two types of hemiplegia. In most cases the arm suffers more than the leg, in some the leg more than the arm. The division arm-type and leg-type is of practical importance. Were I obliged to be paralysed of the left side I should prefer the ordinary variety of hemiplegia, in which the arm suffers more than the leg, as I could do indifferently well without the use of the *left* arm, and could get about if the leg were only slightly paralysed. If the paralysis were to be of the right side, I would far rather that the leg suffered more than the arm, particularly because I should, the cerebral lesion being farther back, have little or no defect of speech.

Taking for illustration the arm-type of hemiplegia, we may conveniently make three degrees of it. 1. Paralysis of the face, tongue, arm, and leg. 2. Greater paralysis of these parts, and also turning of the head and eyes from the side of the body paralysed. 3. Universal powerlessness (strictly not a degree of, but one beyond, hemiplegia). I pass over the third degree, as the situation is too complex for illustration. I remark of the second that the additional symptoms, so to call them, betoken a grave lesion. I speak of the first degree only when illustrating the triple method of investigation.

From the external region affected we infer, let us say, that there is a lesion of the motor, anterior, part of the internal capsule; that is the anatomical part of the clinical problem. Next, since the phenomena in the muscular region affected are negative, paralytic, we conclude that the function of fibres of the internal capsule is lost; most often they are destroyed. This is the physiological part of the clinical problem.

It may seem a pedantic refinement to distinguish between loss of function and pathological process in cases where, for example, a clot has destroyed fibres, where the function and the fibres are gone together by one blow. Not so, since the hemiplegia depends on loss of function, *however produced*—by softening, by clot, by tumour, or by mechanical injury; we may be sure of the abnormal *physiological* state, loss of function, and yet have to wait for the necropsy to tell us the nature of the *pathological* process which produced it. Again, although in most cases of hemiplegia there is destruction of fibres, there is in the epileptic hemiplegia of Dr. Todd—post-epileptiform hemiplegia, I call it—(temporary) loss of function of fibres and no destruction of them. As some would put it, hemiplegia is "only a symptom;" but it is a symptom always signifying the abnormal physiological state, loss of function, although the pathological processes effecting that loss are various. When we come to consider the other kind of functional change—exaltation of function, hyper-physiological states—the distinction between abnormal (crude) physiological states and the pathological processes producing them is of supreme importance; hence, one reason for insisting now on the distinction in simple cases between loss of function and the pathological processes producing it.

So far we have dealt expressly with but two elements, anatomical and physiological, of the threefold clinical problem; we have not yet, except incidentally, said anything on the most medically important element, the pathological. Whilst anatomically we say of a case of hemiplegia that the lesion is (1) of the internal capsule, that (2) physiologically it is a negative functional state, we may be able to complete the clinical problem by concluding that (3) the pathology is cerebral hæmorrhage. I speak first of what I may call the rough and immediate pathology of hemiplegia. I say rough and immediate because, for example, to speak of the pathology of a case of hemiplegia as being cerebral hæmorrhage is to speak very inadequately. Destruction of fibres by clot is a quasi-traumatic lesion; cerebral hæmorrhage is often but an incident—a very calamitous one—in an exceedingly wide, indeed universal, pathology. We have two kinds of evidence bearing on the "rough pathology" of hemiplegia: (A) mode of onset; (B) the patient's general pathology. I can only consider some modes of onset.

(1) If the paralysis begins very locally—say in the hand—increases in degree and in range very slowly, day by day and week by week, there is great likelihood of tumour of the opposite cerebral hemisphere. I confess that I have twice been wrong in the diagnosis of cerebral tumour from "slow hemiplegia." If with such hemiplegia there be also double optic neuritis, we may be confident of tumour or some other kind of adventitious product. Again, if there be no severe headache and no optic neuritis with this "slow hemiplegia," yet if there be with it gradual and "even" degradation of mind, there is most probably a large tumour (or other mass) deep in the white substance of the opposite cerebral hemisphere. (I should not in such a case advise operation.) In young children, when the adventitious product in one cerebral hemisphere is very large, the head gets bigger, the sutures widening, as happens also in some cases of tumour of the middle lobe of the cerebellum; in the former there is some hemiplegia, in the latter reeling gait. When the motor symptoms are little marked, and when the child is young and very ill or indocile, the differential diagnosis is far from easy.

I should in early stages of "slow hemiplegia" treat for syphi-

NOTE.—On page 61 of last week's issue, second column, third and fourth line from bottom, omit "*an explanation of difficult problems.*"

[8] There is, however, with the over-development of some movements loss of other movements of the same muscles; the two opposite functional lesions, the inference is, co-exist in chorea. In some cases the paralysis (that is, loss of movements) preponderates (see Gowers's *Diseases of the Nervous System*, vol. ii, p. 554, on "Paralytic Chorea."

lis. But I wish to say very prominently that hemiplegia so coming on is, in my experience, exceedingly rarely owing to syphilis. In an article, "The Syphilitic Affections of the Nervous System," *Journal of Mental Science*, July, 1875 (also *Medical Times and Gazette*, May 23rd, 1868, p. 551, *et seq.*), I put down "slow hemiplegia" as one of three varieties of "syphilitic hemiplegia;" but since that time I have not seen a single case of such hemiplegia owing to a syphilitic tumour—of course I speak of cases completed by necropsy. Two other very common types or varieties of "syphilitic hemiplegia" will be spoken of further on.

(2) If the hemiplegia is found immediately after an epileptiform seizure which began very locally—say in one thumb—I should conclude that there was disease of some part of the cortex in the Rolandic region of the opposite side of the brain.[9] Of course the practical question in diagnosis here is the cause of the fit of which the hemiplegia is a consequence; it is a post-epileptiform hemiplegia. In such cases the disease is most often tumour; it certainly is not always so; there may be plugging of cortical arteries. I say nothing of guessing, but submit that we can only confidently *diagnose* tumour as the cause of epileptiform seizures if there be also double optic neuritis. I have not yet seen a case followed by necropsy, the two symptoms—the epileptiform seizure and double optic neuritis—co-existing, in which I did not find cerebral tumour.

To ascertain whether epileptiform seizures do or do not depend on cortical tumour is important with regard to surgical interference. Were I subject to frequent epileptiform seizures always beginning in the *left* thumb, I would have the "discharging lesion" cut out, even if I could know that there was no tumour as an inducing cause of it; if tumour were found, of course that should be cut out too. In the case mentioned (page 63, operation by Horsley) I advised operation, although I could not tell whether or not that patient's fits depended on tumour. Enough of the cortex should, for cure of the fits, be cut out to produce considerable paralysis of the part in which the convulsion begins. I spoke of fits beginning left-sidedly; on account of the "speech centre," operations on the left cerebral hemisphere are more serious than operations on the right.

To return to the hemiplegia. Although post-epileptiform hemiplegia so often depends on tumour, it is transitory; it depends very indirectly on the tumour. We now come to some further considerations also of practical value.

The tumour causing epileptiform fits is sometimes syphilitic; the sequent hemiplegia is one type or variety of "syphilitic hemiplegia." But to say that syphilis (a syphilitic tumour, gumma, of the cortex) "caused the hemiplegia," is to speak very vaguely. Here we have a most excellent example of the indirect way in which syphilis "causes" nervous symptoms. It is a long cry from syphilis to this variety of what we call "syphilitic hemiplegia;" let us look at the stages from syphilis to the paralysis. First there is slowly formed a syphilitic tumour; next this *causes the cause* (the direct cause) of the fits. By some process, there is produced high instability of cells near the growth (presumably in the order from smallest towards largest) a persisting local condition which, although produced by, is secondary to, the syphilitic tumour and is itself not syphilitic. This secondary and non-syphilitic change has become independent of the syphilitic tumour, being established it is automonous; it is then an energetic "hyper-physiological parasite;" there is what I call it a "discharging lesion" or "physiological fulminate," or, sometimes using Horsley's term, an "epileptogenous focus." In still other words there is produced a functional change, in the proper sense of the term functional, one of high instability of nerve cells. This change is not a pathological one, but is an hyper-physiological state, a crude physiological state; it is the *result* of a pathological process entailing, no doubt, destruction of some cells, but yet increased nutrition (presumably of an inferior kind), and consequently unduly high tension and instability of others. There is, I imagine, an encephalitis provoked by the syphilitic tumour, not in its individual character as a *syphilitic* product, nor even in its more general character as a tumour, but in its most general character, that of a "foreign body." So to speak between the "foreign body" and the high instability of cells making up the "discharging lesion," comes the active pathological process, a local encephalitis. Putting part of the foregoing otherwise: the secondary change induced is the same, whether the tumour be a glioma or a syphiloma.[10] So then the change on which the fits directly depend is *post*-syphilitic, or, if we take into account the disordered nutritive process, which I imagine to be a local and limited encephalitis, it is *post-post*-syphilitic. The hemiplegia, on any hypothesis as to the exact nature of the negative central change immediately answering to it, is a still more indirect result of syphilis; I imagine, essentially adopting Todd and Robertson's hypothesis, that it depends directly on loss of function of fibres of the pyramidal tract; they being, it is suggested, exhausted by the excessive discharge in the preceding fit. At any rate there is some negative central change.[11] Here we have in sequence the two opposite kinds of functional, abnormal physiological, change; there is high instability of cells, over-function, and following sudden, etc., discharge of those cells, there is temporary loss of function of nerve fibres. Neglecting the hypothetical encephalitis, this type of "syphilitic hemiplegia" is "caused by syphilis" in a triply indirect way.

We have two kinds of treatment for this variety of "syphilitic hemiplegia;" treatment for syphilis, and treatment, for the most part empirical (bromides), for the fits; the post-epileptiform hemiplegia (or, after partial fits, monoplegia) requires no treatment.

3. If the hemiplegia comes on deliberately, say in half-an-hour, or if the patient tells us that he was paralysed on getting up in the morning—hemiplegia without defect of consciousness—the presumption is for local softening from plugging of the middle cerebral artery, or more likely of some branch of that vessel.

4. If the hemiplegia comes on rapidly with loss of consciousness, or if coma soon follows a deliberate onset, the presumption is for cerebral hæmorrhage.

We have, however, to bear in mind that 3 and 4 are only empirical rules. Strictly, we should speak of degrees of "gravity" of lesions, using that term to include both quantity destroyed and rate of destruction. Comparatively slow blocking of the main trunk of the middle cerebral artery (as in a third type of "syphilitic hemiplegia" I have yet to remark on) may be unattended by what would be commonly called *loss* of consciousness, whereas sudden blocking of that main trunk by an embolon might entail temporary coma. There are other qualifications to the Rules 3 and 4. We have to rely upon the patient's general pathology. I give but one illustration. If the patient have atheromatous arteries, hypertrophy of the left ventricle, and chronic renal disease, we conclude for clot, in whatever way the hemiplegia came on, and whether it be slight and transient or perfect and permanent.

Omitting much, I make two further remarks on diagnosis between clot and softening. If a patient have double, or even unilocular, optic neuritis (the latter is very rare in physicians' practice), the hemiplegia coming on rapidly with, or even without, loss of consciousness, is probably owing to hæmorrhage from a vascular tumour of the opposite cerebral hemisphere.[12] Here we must, however, exclude Bright's disease, it being remembered that sometimes with Bright's disease, and without intra-cranial tumour, we have optic neuritis indistinguishable from that which tumour most often produces. Certain well-known abnormal changes in the fundi in Bright's disease are not always "characteristic," as we used very many years ago to say, of that disease. Again, suppose

[9] Beevor and Horsley find that, in the monkey, the particular part of the cerebral cortex where the thumb, which has a wide representation in the cortex, is *most especially* represented is about the junction of the lowest and middle thirds of the ascending parietal convolution.

[10] Illustrating by another secondary change; optic neuritis from syphilis is not syphilitic optic neuritis; any sort of tumour or mass in the brain produces just the same kind of change in the optic discs as any other does.

[11] I suppose that the negative post-epileptiform change answering to the paralysis is above the anterior horns (except perhaps for exhaustion of inhibitory centres, Gowers's), where there are exaggerated knee-jerk and foot clonus. I published a case of this kind (*Medical Times and Gazette*, February 12th, 1881, On a Case of Temporary Left Hemiplegia, with Foot Clonus and Exaggerated Knee Phenomenon, after an Epileptiform Seizure beginning in the Left Foot). The estimation of the different conditions of the "deep reflexes" after epileptiform and epileptic fits is very important. (See a very important paper by Beevor, *Brain*, 1882, On Knee-jerk, and Foot Clonus, Plantar Reflex and Conjugate Deviation of the Eye, after Epileptic Fits.) When there is exaggeration of the "deep reflexes," there is a degree of functional change not spoken of in the text; certain anterior horns are in over-function from, I think, loss of control. This degree of functional change is not the result, not the direct result, of any pathological process; it ought to be most carefully distinguished from the degree constituting a "discharging lesion," or we shall misinterpret some symptomatic conditions, post-epileptic states (mania, etc.), for example.

[12] I have spoken, it will be seen, of three very different ways in which hemiplegia may be associated with tumour of the cerebral hemisphere (1) slow hemiplegia from gradual destruction, (2) post-epileptiform hemiplegia, and (3) hemiplegia by hæmorrhage from a tumour.

a patient, say a young patient, has cardiac valvular disease, then, if hemiplegia comes on suddenly with deep loss of consciousness, we must not be sure that there is embolism; there may be cerebral hæmorrhage from rupture of a large aneurysm of some branch of the middle cerebral artery. I do not know how to distinguish be the two possibilities.

To shorten my subject, I shall now arbitrarily suppose that the lesion causing the hemiplegia is local cerebral softening from plugging of an artery. Some general remarks are needed before going further. Cerebral softening is always local; and (excluding softening about tumours and other obviously exceptional cases), it is localised by vessels, mostly arteries, and, as a matter of fact, the middle cerebral artery, or some branch of it, is nearly always the vessel plugged; thus, the two great symptoms of softening of the brain are hemiplegia and aphasia, sometimes both together. There is no such disease as "general softening" of the brain. Some cases so-called are cases of cerebral atrophy, of general paresis, or are cases of cerebral tumour. Reasserting that softening of the brain is local, and that it is practically an affair of plugging of cerebral arteries, the next remark is that there are two processes of plugging—thrombotic and embolic. In the former, the vessel is "crusted up," because the artery, mostly atheromatous, but sometimes the subject of a syphilitic change, is roughened in its interior, or narrowed, or both; here the artery is in *fault*. In embolism the artery may be, and often is, quite healthy, *innocent*, and is corked up by something coming from a distance, in most cases, from the valves of the heart. No doubt there is sometimes partial occlusion by an embolon, complete closure of the artery being effected by superinduced thrombosis. We sometimes hear of "extension of softening." I know of none, except possibly by plugging of other arterial branches, supplying parts near the already softened part; this is not, however, properly speaking, *extension* of, but additional softening. It is common enough to find general mental deterioration slowly following a local cerebral lesion, clot, or softening, which has produced hemiplegia. The patient suffers from defect of memory, and is incapable of sustained intellectual exertion. He is "more emotional" (really there is here loss or defect of the highest ["finest"] with increased manifestation of the lower ["coarser"] emotions). But I presume that the intellectual and emotional deterioration are owing, not to softening nor to extension of softening, but to widespread partial atrophy of convolutions.

It is needless, for my present narrow purpose, to speak of the differential diagnosis between thrombosis and embolism as a cause of the local softening which produces hemiplegia. The commonest condition for the thrombotic process is arterial atheroma. I wish to speak of a rarer cause of thrombosis of the middle cerebral artery—of a third Type or variety of "syphilitic hemiplegia." We shall see another way in which syphilis produces nervous symptoms indirectly.

I do not deny that syphilis may "attack" proper nervous elements, nerve cells, and fibres of nervous organs directly, or be an important factor towards their degeneration. I say nothing here on that question. In cases of "syphilitic nervous affections" of which we *know* the morbid anatomy, the direct "attack" is upon non-nervous ingredients of nervous organs. When there is a syphilitic neuroma, as it is often called, say the trunk of the third nerve is affected, the action of syphilis on nervous elements is indirect, but yet most nearly direct; an overgrowth of connective tissue there and then squeezes nerve fibres. The process by which syphilis produces the type or variety of "syphilitic hemiplegia" I am about to remark on is far more indirect, although not so indirect as is the one whereby the type recently considered (post-epileptiform hemiplegia) is produced. There is first slowly established syphilitic disease of the middle cerebral artery or of some branch of it: so far all may go indifferently well. But the diseased artery becoming narrowed, something happens which is not syphilitic. Thrombosis occurs, and thereupon ensues local softening of the brain, causing hemiplegia of deliberate onset, without loss of consciousness, but, perhaps, if the main trunk be plugged, with considerable stupor. I fear that it is not always realised that in this type of "syphilitic hemiplegia" there is softening of the brain; that there is essentially the same change (I have not yet seen red softening in such cases) as that which occurs when an atheromatous artery is thrombosed, or when a healthy one is corked up by an embolon. The real nervous change, the one on which the paralysis in this type of "syphilitic hemiplegia" *directly* depends is not a syphilitic change at all; it is post-syphilitic. I have assumed that the arterial disease is syphilitic, have spoken as if we had had the necropsy first. I must next speak generally of the diagnosis of "syphilitic affections of the nervous system," in order methodically to answer the question, "Is this patient's hemiplegia syphilitic?"

It would be wasting time to speak of such evidence as clear signs of syphilis in visible parts of the patient's body; this is, of course, the best kind of evidence, and no one is likely to ignore it. There is another kind of evidence which is of great value in diagnosis when that just spoken of is not to be had. I must premise that the hemiplegia itself, its kind, degree, and mode of onset do not help us. I submit three dicta on syphilitic nervous affections: (1) *No single nervous symptom is characteristic of syphilis:* (2) *It is the disorderly grouping (random association) of certain nervous symptoms, or the disorderly or random succession of certain nervous symptoms which is most characteristic of syphilis.* The third dictum, *that syphilis produces nervous symptoms indirectly*, has been insisted on when dealing with the two types of "syphilitic hemiplegia." I will give but one illustration of a medley of symptoms often pointing to syphilis. If a man have paralysis of parts supplied by one third nerve and hemiplegia of the *same* side, there are certainly two lesions, and there is in that "random association" very strong empirical evidence of syphilis. I now speak of treatment of "syphilitic hemiplegia." We must take a realistic view of the situation. Although it is, for many clinical purposes, convenient to use the term "syphilitic hemiplegia," it would be monstrous to think of a case of hemiplegia as "caused by a syphilis," without tacit analysis of the real state of things in each case.

The third type of syphilitic hemiplegia is for direct treatment of the paralysis itself, a case of local cerebral softening, a non-syphilitic change, although produced by thrombosis of a *syphilitically* diseased artery. What will drugs do towards ridding the patient of his paralysis? Nothing. No drugs can do anything whatever, good or bad, for cerebral softening; softened brain is not brain at all, it is dirt in the brain. More generally, he who is treating by drugs hemiplegia owing to softening, however produced, or to clot, is treating a hole in the brain. Even supposing that vigorous anti-syphilitic treatment had swept away all syphilitic changes from every part of the patient's body, it would have done nothing for the *post-syphilitic change*, the softening. And if we had drugs which could dissipate the plug in the vessel (I know of none), they would have to do it with marvellous quickness, or the nerve tissue would be dead by starvation before circulation was re-established. And yet, without any inconsistency, I treat actively by mercurials and iodides in early stages of the variety of "syphilitic hemiplegia" under remark; for there is a reasonable probability that other cerebral arteries may be syphilitically diseased, and, by acting on them in early stages of syphilitic growth, we may obviate plugging of them, and thus prevent other local cerebral softenings. We must bear in mind that many syphilitic diseases of the nervous system are post-syphilitic *in time*. It is only in recent syphilitic changes most nearly directly affecting nervous elements, as when nerve trunks are diseased, that we can hope for very happy results. I imagine that most cortical gummata are well established ("firmly rooted") before they produce serious symptoms in their character of "foreign bodies;" hence the importance of active treatment of headaches in the syphilitic, especially if the pain be of one side of the head. There is a fallacy as to the effects of treatment of the third type of "syphilitic hemiplegia" to be now pointed out.

It may be said that, as a matter of fact, some of the patients who present this type of "syphilitic hemiplegia" get rid of their paralysis on treatment by mercury and iodides. To that I can testify, but I submit that our drugs do not cure them. Why, then, does the patient get well? Not from roundabout supply of blood, by anastomosing vessels, to the part of which the proper artery is blocked, for the central branches of the middle cerebral artery have no, or next to no, anastomosis; the boycotting is effectual. Nor will it do to invoke shrinking or abrogation of the plug; that would occur too late. The *fact* is that patients recover from hemiplegia when the destruction which caused that paralysis remains, provided the lesion be limited in extent. For after such recoveries we may find when, later on, the patient dies from some non-cerebral disease, that a small part of the brain has been annihilated: there is a hole where nervous elements once were.[13] Degree of re-

[13] I here quote from the abstract of the report of a case of a patient of mine published in the JOURNAL, August 30th, 1873, p. 254. A gentleman, aged 38, in apparently good general health, was first seen in July, 1867, for recent (July 14th) paralysis of the parts supplied by the left portio dura nerve, and for recent

covery depends to some extent on the exact position of the lesion; I am speaking of cases of patients who do recover; and I mean what we call recovery, not contending that there is absolute restoration of power in any case. Deficient dexterity may show loss of some "fine" (most special) movements; and too early fatigue of the "recovered" limbs means some paralysis, as does, also, undue slowness of motion of them. Speaking generally of all kinds of destructive lesions, I would suggest (I cannot speak definitely) that if a small quantity of a nervous organ be destroyed, there is recovery; if a large quantity, there is some recovery; if of a very large quantity, scarcely any. Some cases of hemiplegia, where the paralysis is very slight and also transitory, may be explained by the hypotheses that they are "functional," or that they are "owing to gout," or to liver and stomach derangement, or to constipation, and so on. The simplest hypothesis for these cases is, I submit, that there is a local destructive lesion, but a very small one.

The process of recovery is obviously of vast importance for our consideration in regard to rational treatment of some cases of very serious brain disease; for if recovery be spontaneous, we may err in attributing it to the effects of our remedies, and thus our opinions on therapeutics become untrustworthy. Why do patients recover from hemiplegia when the loss of nerve tissue is permanent? The reply is hypothetical. There are, according to degrees of gravity of the destructive lesion, degrees of recovery. I should put down paralysis at the onset to the destruction effected, and attribute degrees of recovery to degrees of compensation; nervous arrangements near to those destroyed, having closely similar duties, come to serve, not as well, but, according to the degree of gravity of the lesion, next and next as well as those destroyed. Let us take for illlustration the second degree of hemiplegia, supposing it to be owing to hæmorrhage. I should attribute the paralysis which the lateral deviation of the eyes (neglecting that of the head) signifies to the same cause as I should the rest of the paralysis, should say that nervous arrangements[14] for some ocular movements had been annihilated, should do so if I could at that time know that the deviation would pass away. I should not explain the recovery from this very definite and most particular symptom by the hypothesis of subsidence of initial shock, or by that of diminished congestion or œdema round about the lesion; these may be slight factors. When the patient recovers from the second to the first degree of hemiplegia, that is, when the lateral deviation of the eyes has gone, the recovery on my hypothesis could not be owing to restoration of lost nervous arrangements for ocular movements. But there are, I contend, innumerable other nervous arrangements for ocular movements remaining, and by them there is compensation for those annihilated, so that the patient seemingly moves the eyes as well as ever. I insist strongly that there may be loss of some *movements* of a parts when there is no discoverable *inability in the muscles* of that part for all other movements. We must most carefully distinguish between loss of movements and inabilities in muscular regions. As perhaps the two expressions are not clear I give an illustration. Loss of speech, say an ordinary case of perfect aphasia, is a psychical loss, and we have nothing to do with it except as evidence of a correlative physical negative condition. This is destruction of nervous arrangements for certain very complex, etc., *movements* of the muscles of the tongue, lips, palate, etc. (surely there is loss of those movements the patient can no longer make); but the muscles of those parts are not unable for all other *movements;* indeed, they may even serve elaborately in articulation when the speechless patient swears. There is here, to my thinking, as certainly paralysis, *in the sense of loss of movements*, as there is in the same sense in the hemiplegia along with the aphasia, there being greatly more compensation in the former.

Let me give what I think is a crucial demonstration of the general truth of the dictum that there may be paralysis in the sense of loss of movements without discoverable muscular inability. Horsley and Semon find that faradaic excitation of a certain part of the cortex of a monkey on either side of its brain puts both vocal cords in activity; this shows that movements of *both* cords are represented in *each* of the bilateral centres. Next, ablation of either of the twin centres produces no obvious inability in either of the two cords, although of necessity "half" the *movements* of them are permanently lost, so to say, have been cut at. There is here immediate and, apparently, absolutely complete compensation. The facts of these experiments are in accord with Broadbent's well-known hypothesis, now just twenty-two years old. I consider that in cases of aphasia there is loss of many movements of the vocal cords, although the patient's voice is not morbidly affected; he may be able to sing. Before leaving this part of my subject I would say that the foregoing remarks on Compensation imply that I do not accept the current hypothesis as to the nature of Localisation ("abrupt localisation") any more than I do the one sometimes called Universalisation. I have restated the hypothesis I hold in the third Croonian lecture, 1884 (BRITISH MEDICAL JOURNAL, April 12th, 1884). Questions as to the correct principle of localisation are not of mere theoretical interest; their discussion is not out of place in this address if they bear on the process of recovery. I would refer those interested in localisation to a paper, very important in many other ways, by Beevor and Horsley (*Phil. Trans.*, vol. 178 (1887), B. pp. 153—167). Without, of course, committing these able observers to any hypothesis of mine, I may say that the facts of certain experiments they made on part of the cerebral cortex of monkeys seem to me to be in great disaccord with the current doctrine of localisation.

I go on to speak further of the treatment of cases of hemiplegia, or rather, I should say, of the patients who present this symptom, now supposing syphilis to be excluded. In many of them there is an imperious necessity for treatment. This time the illustration shall be hemiplegia owing to cerebral hæmorrhage, the clot being the rough and immediate pathology of the case. Since we can do nothing for the clot (which although *in the brain* is really *out of the body*, being to all intents and purposes a "foreign body"), and since the nerve fibres broke up are non-existent, we widen our investigation to find out what we can do for our patient. We examine him all over, our aim being to discover why a diseased cerebral artery burst, in order that, by properly directed treatment, we may prevent bursting of other arteries. Let us take *part of* a hemiplegia, slight facial monoplegia, sufficiently described for our present purpose by saying that it is of the cerebral type. This paralysis is sometimes very transitory, but when it has disappeared we have often enough serious conditions to treat. If the patient's arteries be unsound (atheromatous and probably then miliary aneurysms of the cerebral vessels), and if he have hypertrophy of the left ventricle and renal disease, the probability is that the facial paralysis is owing to a cerebral hæmorrhage; because of the slightness and transitoriness of it, we conclude that the clot is a very small one. In all cases of cerebral hæmorrhage the condition of the arteries (statical as atheroma, dynamical as degrees of tension) is a thing of first importance; by instinct, so to speak, I feel the pulse first of all in the examination of a case of brain disease; we never fail to examine the urine. If we could imagine a doctor neglecting one part of his patient's case, he had better neglect the paralysis than the evil triad I have mentioned, important parts of the wide universal pathology which is the basis of the incidental pathology, clot, which I call the rough and immediate pathology of some cases of hemiplegia. The wide pathology is the proper field of our treatment. To give "nervous remedies," hypophosphites, strychnine, and so forth, for the cure of paralysis from cerebral hæmorrhage, is really to do nothing of value in a formal way; we have to neglect the paralysis so far as drug-treatment of it goes. Massage and gentle faradisation of the paralysed limbs will be of some service whilst we are waiting for Compensation; they will be useful as an artificial exercise. To diminish the quantity of highly nitrogenised food, to look after the digestion, to keep the patient's bowels free, is the best style of treatment. If arterial tension be high we may give small doses of mercury and saline aperients. I forbid cold bathing. I never prescribe strychnine, having no faith in it as a "nervous remedy" for lesions answering to cerebral paralysis; it, among other doings, stimulates the vasomotor centre, and thus will help to increase arterial tension. Our general treatment would be the same if the "rough pathology" of a case was epistaxis or retinal hæmorrhage,

partial deafness of the left ear. There were also remains of paralysis of the right leg, which had begun in April. He rapidly got rid of all his nervous symptoms after taking iodide of potassium; but he did not continue the drug, because he believed all his ailments to be owing to ague poison. He had been in the West Indies, and still remained subject to slight shivering attacks; he had had primary syphilis fifteen years before. He remained well until March 2nd, 1868, when he became hemiplegic of the left side. *He would not take any drugs except aperients.* Nevertheless, in about a week he was apparently well again; but on March 21st he was found apoplectic and again hemiplegic—this time of the right side. He died next day. At the necropsy there were found diffluent softening of part of the right corpus striatum, and also softening of the left corpus striatum. There was syphilitic disease of each middle cerebral artery. Thrombosis of each at the part diseased accounted for the two local softenings, and for the two attacks of hemiplegia related to them.

[14] Strictly, annihilation of fibres passing between nervous arrangements of the middle and lowest motor centres.

events of very evil significance in cases of chronic Bright's disease.

The results of the measures one adopts for diminishing arterial tension are not always pleasing to the patient; perhaps sometimes we have too much zeal. A certain degree of arterial tonus is necessary for everybody's well-being; the more blood is in the arteries, the less is in the capillaries, that is, the less is close to the tissues. To an increased degree of arterial tonus the cheering effects of a cold bath are due, a luxury few people after fifty ought to indulge in. I submit that a healthy degree of arterial tonus is kept up by a normal degree of waste nitrogenised products in the blood, the "natural stimulant," I imagine, of the vasomotor centre, as venous blood is the natural stimulant of the respiratory centres.[15] In Bright's disease and in gouty states there is an excess of these "natural" stimulants and very likely presence of some unnatural ones, whereby I suppose the vasomotor centre is over-stimulated; hence excess of arterial tonus, or, as we call it when morbid, high tension. I have heard an eminent medical man say that he felt best when a little gouty; I suppose he had then a slight extra degree of tonus, so that his brain had a better supply of blood; the cerebral arteries, having less muscular tissue than most other arteries, would be less constricted. But in a high degree of tonus, high tension, such a feeling of well-being is more pleasant than safe. I think there is something in the statements we hear about patients who die of apoplexy, that they had felt unusually well just before the onset of their illness, that is, before a fatal cerebral hæmorrhage, that is, before the bursting of a cerebral artery. If we reduce our patient's arterial tension, perhaps sometimes too much, by low diet and purgatives, he "feels weak" and is very naturally dissatisfied until it is explained to him that he had better be safe than have a feeling of well-being from undue arterial tension. Many a man with chronic Bright's disease lives on the brink of cerebral hæmorrhage; the less he lives the longer will he live; but if he tries to get the most out of himself and is careless of his diet and of the state of his bowels he may be high up in a certain kind of health, so to call it, only for a sudden fall to a low level of disability or to death.

I will now speak more generally on the essentially non-nervous nature of many diseases called nervous. For a realistic consideration of the pathology of any case of disease of the brain we have to consider whether or not the morbid change *begins in* nervous or in non-nervous *elements* of nervous *organs*. Hemiplegia is not a nervous disease at all in the strict sense; it is in most cases an arterial affair. For my part I do not believe in the existence of "emotional hemiplegia" (or of emotional aphasia either); at any rate, I shall ignore it here, and also cases of so-called hysterical hemiplegia. I go on to say of nearly all diseases of the brain of which there is a known morbid anatomy, that they are not nervous diseases in the strict sense; they are damages of nervous organs, but their pathology is not primarily nervous, that is, the morbid change does not *begin in nervous elements* of the nervous organ damaged. Here is a very important question regarding fundamental pathological diagnosis and also treatment. A nervous organ, besides what we may call its proper ingredients, nerve cells and fibres, contains connective tissue and blood vessels; the latter for some purposes we may call compound tissues. It may be that in some diseases the nervous elements are the first to go wrong, as in what is called parenchymatous atrophy of the optic nerves, and in the "degenerative diseases" of the nervous system. Saying nothing whatever for or against this hypothesis, I urge again that most nervous diseases of which we *know* the morbid anatomy are not nervous in the sense that the pathological changes begin in the proper, nervous, *elements* of nervous *organs*. This dogma I have already repeatedly illustrated in this address, especially when analysing the state of things in "syphilitic hemiplegia."

There is a class of nervous diseases (often called the "neuroses") in which there is no morbid change. I mean, of course, that there is not one yet for us. There is a morbid change, no doubt a minute one, but we have not discovered it. The term "functional" is sometimes applied to some cases of this class in the sense that there is no morbid change answering to the symptoms. I never use the term functional in that way in scientific exposition (*vide supra*). In cases of the two neuroses, epilepsy and chorea, there is evidently abnormal function in the true sense of the word (an exaltation of function issuing in strong discharges), implying abnormally increased nutrition (pathological process) from some cause. What we do not know is the pathological process productive of this functional abnormality. Strange to say, confident opinions are expressed that the neuroses are of purely nervous origin and that they occur, in "neurotic" families, interchangeably by inheritance. Is this because they have as yet for us *no* "morbid anatomy?" Of course, it is quite a legitimate hypothesis that the neuroses are nervous diseases in the sense that nervous elements are primarily in fault. But, as we *know* nothing of their pathology, it is an hypothesis only. It is equally legitimate for me to put forward another hypothesis as to one of them—epilepsy proper. That hypothesis is that, in most cases of this disease, the pathology is primarily arterial (sometimes, I think, venous) and only secondarily nervous, in the same way that most cases of hemiplegia are primarily arterial and only secondarily nervous. The facts that an epileptic patient's blood relatives had apoplexy, hemiplegia, meningitis, tumour of the brain, etc., supply no evidence whatever towards proving that he inherits a tendency to disease *beginning in* nervous elements; do not warrant the inference that his epilepsy is strictly a nervous affection—one primarily nervous. On the contrary, such evidence tells quite the other way. If it have any bearing it points to a primarily non-nervous and to only a secondarily-nervous pathology of the epilepsy, because the "nervous diseases" in the patient's family are not nervous diseases at all in the strict sense, although they are damages of nervous organs. The occurrence of chorea and migraine in the patient's blood relatives does not decide the question either way, because we have no certain knowledge of the pathology of these two morbid affections. The hypothesis I put forward as to the pathology of most cases of epilepsy (and for most cases of migraine and chorea too[16]) is that it is plugging of small cerebral arteries and its consequences.

It is quite reasonable to consider first simpler cases of "fits," epileptiform seizures, to see if their pathology countenances the hypothetical pathology I have submitted of epilepsy proper. I am not aware that anybody believes that the pathology in any case of epileptiform seizures is primarily nervous; that there is a nervous change (one of exaltation of function) is obvious enough, the occasional nervous discharges (liberations of energy) declare that there is. The nervous change is secondary, and is often determined by tumours and other masses; on this matter I have, in an earlier part of this address, said enough. But in some cases the (secondary) nervous state is a result of plugging of arteries;[17] in these cases the hyper-physiological or functional change, that of the nerve cells ("discharging lesion") is in an arterio-cortical region, and is a very local one. The group of highly over-unstable cells making up the "discharging lesion" is certainly in but one side of the cerebrum, although sudden, etc., discharge of that lesion will, if

[15] The hypothesis more generally is that there is in health Chemical Regulation, so to call it, by natural stimulants in addition to, or rather as an aid to, physiological regulation by nerve centres and nerves, and that some particular morbid effects are the results of excess of those stimulants. I have (*Brain*, April, 1886) suggested that the convulsion in laryngismus stridulus is owing to supervenosity, to an excess of a "natural stimulant" of the respiratory centres. In the same way I think it likely that rigor is owing to an excess of the natural stimulant of the vasomotor centre, and very likely that some convulsions in kidney disease (not those which are unilateral) are owing to excessive stimulation, primarily of various "regulating centres" in the medulla oblongata, by waste products which the kidneys ought to, but cannot efficiently, eliminate. [Consider in this connection convulsions in animals after injection of the poison absinthe, and especially Dr. George Johnson's researches on convulsions in man consequent on poisoning by camphor. (*Medical Lectures and Essays*, p. 311.)] Dr. Maclagan, in his work on Fever, makes the very interesting and, as I think, most important remark, that heat is the natural stimulus of the heat-inhibiting function and that accumulation of heat in the system naturally excites that function to increased activity and may at length exhaust it. In some cases of jaundice the pulse is less frequent than normal, possibly by action of bile acids. The mode of action of bile acids on the circulation is not known, and it would be premature, for several reasons, to conclude that there is in such cases an excess of a natural stimulant to the ends of the vagi.

[16] Dr. George Johnson, *op. cit.*, p. 510, writes: "Chorea is sometimes associated with, and apparently caused by, capillary embolism in some portions of the brain near the corpus striatum."

[17] I have never believed that the local high instability of cells *directly* causative of epileptiform seizures is produced by tumour only. I put forward the speculation that seizures of this kind (I then called them unilateral convulsions) sometimes depend on embolism (*London Hospital Reports*, 1864, vol. i, pp. 465-6), making the crude and, at that time, the following much too-confident statement: "They are, I am convinced, not infrequently the result of plugging of branches of the middle cerebral, partial occlusion of its main trunk or some of its branches." To the same effect: *Med. Times and Gazette*, August 13th, 1864, p. 167. I have re-stated the hypothesis I hope more clearly and correctly (*St. Andrews Med. Grad. Trans.*, vol. iii, 1870; *Reynold's System of Medicine*, vol. ii, second edition, pp. 284-5). I have stated it with regard to both epileptiform seizures and epilepsy proper (*West Riding Asylum Reports*, 1873, vol. iii, pp. 328 and 329; *Med. Press and Circular*, January 26th, 1876; *Med. Times and Gazette*, January, 1879.) Frank and Pitres (*Archives de Physiologie*, August 15th, 1883, No. 6) found that out of seventy-one cases of what I call epileptiform seizures, there were tumours in thirty-two cases. "ramollisements inflammatoires ou emboliques" in sixteen; in the rest various other lesions.

the discharge be strong enough, produce *universal* convulsion. The conclusion is that in some cases of epileptiform seizures a local "discharging lesion" is a secondary result of abnormal nutrition consequent on plugging of arterioles; in other words, that the pathology is exactly the same as that of most cases of hemiplegia. The abnormal *physiological* state of nervous elements (the secondary nervous state) in the two is diametrically opposite; in the former case the change we are concerned with is a *plus*, in the latter a *minus* functional change, and is often actual destruction; in both cases the secondary—the nervous—state is persistent; in the former there are occasional excessive developments of movements (convulsions); in the latter there is permanent loss of movements. Why in the former case there is produced high instability of cells (and no doubt destruction of many others) and in the latter destruction only, may possibly depend on differences in the degree of anastomosis of central and cortical branches of the middle cerebral artery; the former having none or next to none, the latter varying in that respect in different persons and in the same brain in different branches. Complete arrest of circulation in an arterio-cortical area would produce destruction of nervous elements; but some anastomosis might lead to a comparative restoration of circulation, otherwise to *comparative stagnation*—to a semi-stagnant patch. Such a condition is likely to cause destruction of cells in the central part of the arterial area, and is one favourable for over-nutrition of an inferior kind of those at its periphery. I have suggested that there is substitution nutrition, a replacement of phosphorus by nitrogen; the nervous matter resulting, although of a different composition and more "explosive," being of the same constitution as in health. I have since my earliest scientific studies of epilepsy (1864) been interested in its arterial pathology, having been so long ago much impressed by the occurrence of convulsions beginning in parts presumably paralysed from the effects of embolism.

In some cases of epileptiform seizures we may carry out the threefold investigation of the clinical problem they present to definite conclusions. *Anatomical*, the lesion is of this or that part of the cerebral cortex; *physiological*, it is local high instability of cells of that part; *pathological*, the disordered nutritive process is a result of occlusion of an artery supplying that part. Here the distinction between functional state and pathological process leading to it is not a pedantic refinement as it may have seemed to be in the case of hemiplegia.

I think the hypothesis that the primary change in most cases of epilepsy proper is arterial is countenanced by analogy—that there is in some cases of it as well as in some cases of epileptiform seizures a change of high instability of cells consequent on plugging of a small arterial branch—that there is thus produced what I call a "discharging lesion," a change of a few nerve cells of some limited part of the cortex, other than that of the so-called motor region, of one side of the brain; a persisting but yet varying, very local, hyper-physiological state.

It follows from what I have said that I no more believe that fright, overwork, indigestion, masturbation, etc., "cause epilepsy" than I believe that they cause hemiplegia; all that anybody can know is that such "causes" sometimes precede the first epileptic fit. Taking but one of these so-called causes, fright: if a patient has his first epileptic fit directly after a fright, I should conclude that there had been produced by some pathological process a "discharging lesion," one nearly ready to discharge, and that the physical disturbance during the emotion, fright, was only the determining cause of the first "explosion." Similarly for chorea. It is notorious that chorea frequently follows fright, and the current hypothesis is that fright is one of the causes of this disease; the hypothesis I hold as to the relation is that fright (its physical condition) is but a determining cause of discharge of nerve cells already highly over-unstable. To return to epilepsy. If arterial plugging (cortical) leads to the destruction of some cells and also to over-nutrition and consequent high instability of others, we have to account for loss of movements as well as for convulsion. For the highest centres ("organ of mind") are, I submit, sensori-motor, and the lesion in epilepsy proper is, one must suppose, of these centres. I think we may say that the higher the nervous centres the less serious (as to movements) is a "destructive lesion," and the more serious is a "discharging lesion;" for the higher the centre the more complex, etc., it is, and thus the greater is the compensation for negative functional lesions and also the greater the co-operation in excess for super-positive functional lesions. Compensation and Co-operation in excess will be greatest in the highest centres. The epileptic, so to say, carries about with him a hyper-physiological parasite, a part of his highest centres of no use for normal function (but for which, as a loss, there is nearly absolute compensation), and which is worse than useless (a "mad part"), for when it discharges it produces widespread or universal convulsion by compelling healthy nervous arrangements to co-operate in its excess. I suppose, however, there is loss of some movements from negative lesions of the highest centres, in spite of there being no discoverable inability in any muscular region (*vide supra*).

It follows from the hypothesis I hold as to the physiology and pathology of epilepsy that I do not entertain the hypothesis held by many medical men that there is *any relation of community of character* between epilepsy proper and insanity. There is, I think, no such relation between the pathological and physiological state of the brain in epilepsy and the pathological and physiological state of it in insanity. There is *a relation of sequence* often enough; not rarely there is temporary mania after a fit, and sometimes chronic mental failure occurs in epileptics; that relation of sequence is quite a different thing from a relation by community of character.

I will make a few remarks on the treatment of epilepsy proper. For the negative functional state in hemiplegia we can do nothing; nervous elements are in most cases gone, and in post-epileptiform hemiplegia the paralysis needs no treatment. In epilepsy the other, the diametrically opposite, kind of functional state is a very different thing in its therapeutical bearings. It is notorious that our treatment of epilepsy is deplorably unsatisfactory, and if my hypothesis be correct—that there is a persisting local lesion in the highest centres of one side of the brain—there are good reasons for it. The radical cure of epilepsy, as of epileptiform seizures, is for the surgeon to cut out the "discharging lesion;" but in no case of epilepsy proper do we as yet know its exact position; it will differ in different epilepsies. Still we may interfere for good in the local over-active process of nutrition, always going on, which keeps up the high instability of cells of the "discharging lesion."

Apart from any particular hypothesis as to its pathology, the excessive liberation of energy by the "discharging lesion" of necessity implies the taking in of a large amount of materials having potential energy—that is, increased nutrition. Some of the measures found beneficial in cases of epilepsy are presumably owing to reduction of the local nutritive process in the arterio-cortical area, so that there is less active nutrition and more stable tissue. It is a very old recommendation that epileptics should eat but little flesh-meat—highly nitrogenised food. On this I insist, excluding obvious exceptions. It is a good plan to name the number of ounces of meat, a guide being that the middle diet at hospitals is four ounces. Epileptics should eat less, regard being had to their work, etc. They must be content "to live on a lower level." They should have much exercise. The presumption is that the empirical remedy bromide, possibly by substitution nutrition, leads to formation of more stable nervous matter. Belladonna has had great repute, and no doubt does some good (I advise it especially in nocturnal epilepsy, a big dose at bedtime). I never give it alone, so can say nothing certain as to its individual value. Speaking very generally, we may say that, experimentally, belladonna induces a negative state of inhibitory and secretory nerves, leucenteric fibres; it stimulates centres which govern those parts of the body by intermediation of motor, polio-enteric nerves.[18] Its action is, however, very complex. Thus atropine injected into the carotid stimulates the vagus origins and renders the heart's beats less frequent; the latter action is on the vagus ends. In epilepsy we dare not give such large doses of belladonna as the experimentalists can to animals, but we should give the drug until some physiological effect is produced—drying of the mouth, for example. In the doses we can give it will not, I should imagine, influence the "discharging lesion;" but it may act beneficially in that the effects of the epileptic discharge will be less upon important parts of the body as they are supplied by inhibitory nerves, and more on them as they are supplied by motor nerves. I suppose it is better for the currents consequent on excessive cerebral discharge to pass by the accelerator fibres to the heart than by the inhibitory vagus fibres. I submit that the leucenteric fibres are those most affected by the epileptic discharge, and that they are those first exhausted (so during fear). They are pre-

[18] Here, once more using Gaskell's terms, I would urge that by aid of his thoroughly practical work and brilliant generalisations our scientific studies of many nervous diseases will be very much facilitated.

sumably later developed (hence great tolerance of belladonna by young children), and thus fail first in dissolution.

It is well known that in pernicious diabetes sugar disappears from the urine during febrile ailments, the explanation being, I suppose, that the dilated hepatic arterioles do not then get so much blood as when general arterial tension is normal. (If the splanchnic nerves are divided before experimental injury to an animal's "diabetic centre," there is no glycosuria.) It is known, too, that in febrile diseases epileptic attacks usually cease. I suppose that in this condition, arterial tension being relaxed, or during the stage of febrile disease when it is relaxed, the semi-stagnant patch—"discharging lesion"—in the cortex gets less blood. Is it possible that the good effects of a seton in some cases of epilepsy are owing to the induction of a slight, miniature febrile condition? I suppose that nitroglycerine is given in epilepsy to produce general arterial relaxation. I have as yet but little experience of this remedy. Increase of arterial tension would be another reason for diminishing in an epileptic's diet the quantity of highly-nitrogenised food; for during high arterial tension, which much food of that kind may induce, the "semi-stagnant patch" may get more blood than if the patient has a simpler diet. On the great importance of degrees of arterial tension in epileptics Dr. Broadbent insisted strongly in his Croonian Lectures (1886), and since hearing them I have paid very particular attention to states of the pulse in epileptics. Besides ordinary care of the bowels and dietetics, we may give occasional small doses of blue pill when there is undue arterial tension. We should in such cases not give strychnine.

In cases of epilepsy the patient should "avoid excitement." But in young people we may err in being too strict; we may narrow a young epileptic girl's life too much by forbidding the amusements proper to her age. If she have a fit soon after a hearty game or a dance, it is, I think, only the premature development of a fit nearly due.

ON THE EXCRETION OF REDUCTION PRODUCTS OF HÆMATIN IN DISEASE.[1]

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I MUST apologise for having brought a subject under your notice which may appear to be more of interest to pathological chemists than to medical men. I should not have presumed to do so were it not that some of the facts to which I wish to call attention have such an obvious bearing on pathogenesis, that they may be considered really more of medical than of chemical interest.

The subject is a difficult one, and to many may appear very dry, but that is not the fault of the subject, but is due to the fact that very few care to make themselves acquainted with the methods of spectrum analysis, and are not, therefore, in a position to understand the results.

For twelve years I have devoted much of my leisure time to the application of the spectroscope to biology in general, and, when I have had material to work upon, to that special branch of biology with which we are all concerned. During that time many new and interesting facts have presented themselves which, when their full significance is understood, must help to throw light on many now difficult problems.

In the present paper I wish to direct attention to the occasional presence of reduction products of hæmatin in pathological urine. In order to make this subject clearly understood it will be necessary to go somewhat into detail, and to refer incidentally to other kindred subjects.

Every medical man is more or less interested in the chemistry of urine, and most of us would like to know the cause of the increase of colour which that fluid undergoes in disease, or the actual change of colour from pale yellow to brown and black, which it often shows under certain conditions. It is easy enough to detect bile-colouring matter or blood-colouring matter by our rougher chemical tests; but there are other colouring matters present which cannot be detected by any other method but the spectroscopic one.

It may be asked, "And if you find out that a certain colouring matter is present, of what use is that knowledge?" So far, indeed, as the mere presence of a colouring matter is concerned, if we had to do only with that colouring matter, its detection could not add much to our knowledge, because we know that pigments in themselves are not poisonous substances. But if we can tell how these things are produced in the organism, we have a clue to the processes by means of which other things with which the pigments are associated are produced; and, considering how little we do really know of these processes, in other words, of the metabolic changes which characterise disease, anything must be considered of importance which will help us to understand these changes. If we know that a certain colouring matter can only be produced out of the body by a very energetic reduction or oxidation process, we know that in the body it must be produced in the same way. These pigments are, in fact, finger-posts, indicating accurately the metabolism that is taking place in the organism under normal and diseased conditions.

A definite and accurate knowledge of the colouring matters of urine will help the diagnosis of disease also, but we have a great deal to learn yet. We must not be content with a superficial examination of urine by means of the spectroscope. The colouring matters must be isolated, and the changes which their solutions undergo on the addition of different reagents must be studied patiently and carefully. The most apparently trifling differences have to be noted, for it is these things which teach us so much. The accusation of being careless in things chemical is frequently brought against the medical profession, and often with good reason; and yet if a man tries to bring in more refined methods of analysis, and devotes his time to their study, he is, on the other hand, liable to be called theoretical and a scientific enthusiast.

Most of the pigments in man's body are derived from the red colouring matter of the blood, hæmoglobin, either immediately or remotely, by destructive metabolism—catabolism; while others are built up from simpler radicals by a constructive metabolism—anabolism. Among the former are the colouring matters of bile, and some of those of urine, with others such as melanin (but it would appear that melanin may sometimes owe its source to other things). Among the latter, or those not derived from hæmoglobin, are the lipochromes or colouring matters of fat, formerly known as luteins, apparently the yellowish-red pigment of muscle, which I discovered and named "myohæmatin,"[2] and a class of pigments found in various tissues and organs, also discovered by me and named "histohæmatins." The products of decomposition of indoxyl-sulphate of potassium—indigo-blue and indigo-red, the derivatives of skatol and other pigments—also owe their origin to another source than hæmoglobin.

That bilirubin, the red colouring matter of bile, is derived from blood is proved by the fact that an identical substance occurs in old blood extravasations which is known as hæmatoidin, and that biliverdin, or the green colouring matter of bile, is also often directly derived from blood is proved by the fact that it occurs in the placenta of the bitch, also in the egg-shells of some birds, where it is often accompanied by hæmatoporphyrin (Sorby). Dr. Carter, of Birmingham, once sent me a bright green specimen of hydrocele fluid, the colour of which I found was due to biliverdin, and in that case its origin was definitely traced to an old hæmorrhage into the tunica vaginalis.[3] A curious proof was afforded of the truth of this assertion by an examination of the common red sea anemone, *Actinia mesembryanthemum*.[4] In this lowly organised animal I found that a substance occurred in ectoderm and endoderm which could be made to show the bands of reduced hæmatin by appropriate treatment, and between these layers is a bright green deposit, which I found to consist of a pigment which was quite indistinguishable from biliverdin. Hence, although the examination of the lowest animals may seem at first sight superfluous, yet we often come upon facts, during such examination, which throw a vivid light upon questions of physiology and pathology.

Colouring Matters of Urine.—If you will take up almost any book on the chemistry of urine, you will find a very confused account of the colouring matter of that fluid. Some of the German textbooks are not included under this statement, as doubtful matters are as a rule left out of them. In some of these manuals you will find Heller's test for "urophain" and tests for "urohæmatin," although these substances are only of historical value.

[1] Read before the Staffordshire Branch.

[2] MacMunn: Researches on Myohæmatin and the Histohæmatins, *Philos. Trans. Roy. Soc.*, Part I, 1886.

[3] MacMunn: Observations on the Colouring Matters of the so-called Bile of Invertebrates, etc., *Proc. Roy. Soc.*, No. 226, 1883.

[4] MacMunn: Observations on the Chromatology of Actiniæ, *Philos. Trans. Roy. Soc.*, Part II, 1885.