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A POST-GRADUATE LECTURE ON MISTAKEN DIAGNOSIS.

Delivered in the National Hospital for the Paralysed and Epileptic.

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GENTLEMEN,—It is always a pleasant thing to be right, but it is generally a much more useful thing to be wrong. If you are right, all that you do, as a rule, is to confirm your previous opinion, your previous habits of reasoning, and your previous self-esteem. But if you are wrong you generally gain in knowledge and gain perception of the way in which your method of diagnosis needs improvement, and the influence on self-esteem is not likely to do you harm. At least that is my own experience, and I think I have observed it confirmed in others. But the result is dependent on deliberate effort. There is a strong temptation to smooth down error, and it is very easy not to gain from it its precious lesson. It is more easy to fancy that there is some accidental cause for the mistake than frankly to perceive that it is a fault. But if you make a deliberate effort to realise and to face in your own mind the mistake you have made, to discern its cause, and to employ this perception as far as you can to remove the cause and prevent a like mistake in the future—if you do this, almost every error becomes one of the precious experiences of your practical life.

Yet you will note that I have not said this quite absolutely. I said it is "generally" more useful to be wrong, that "almost" every error is useful. As a matter of fact, there are errors you cannot avoid. Beware, however, of thinking that any individual instance of error is of that character. The chances are great that it is not, that it might have been avoided, and they are considerable that it will be avoided in the future as a consequence of its occurrence. At least I hope so.

Still, there are cases in which error is inevitable. I should like to mention to you an instance which illustrates the conditions on which the relation depends. But this is not the chief subject I desire to bring before you. My chief object is to seize the opportunity afforded me by the courtesy of a private patient and his desire to be useful—the opportunity of illustrating avoidable mistakes by an example almost perfect in its character, almost unique in its features, and seldom equalled in the variety and importance of the instruction it affords. The case is indeed full of important lessons, and it is one the like of which, I venture to say, not one of you is likely to have seen before or is likely to see again.

But, first let me say a few words about inevitable errors. There is a patient in the hospital at this moment whom I cannot show you now, but whose case is an example of mistakes that must be. I saw him first about two months ago, at the commencement of his illness. I then made a diagnosis, of the correctness of which I felt assured, and which I am now certain was wrong. Yet if I saw a like case to-morrow with the same symptoms, with all the knowledge I have gained from this case, I should make the same diagnosis, that which proved to be wrong; and the chances are fifty to one, or more, that it would be right. Why, in this instance, was it wrong? Because all diagnosis that rests on

reasoning is a matter of probability; only that which is simple observation is certain. The probability may be great, or may be only that of a slight preponderance of the balance of evidence, but wherever inference comes in there is no certainty. Remember that inference plays a part which you can discern only by an effort, in a large part of diagnosis. You think you observe the presence of consolidation of the lung or of pleural effusion. You do nothing of the kind. You infer its existence from certain physical signs. I remember an incident which illustrates the risk of error thus involved. A skilled physician gave orders to his house-physician that a surgeon should be called in to tap a chest, one side of which was full of fluid. When the surgeon came he took notice of the chest before plunging in his trocar, and, being a man of a thoroughly scientific mind and used to observation, he was struck by the fact that there was no enlargement of the chest. Although he was a surgeon, he percussed carefully, and found that every other sign of pleural effusion was present except enlargement of the side. He declined to tap. A little later the patient died, and the lung was found to be a solid mass of cancer. That was a case of incomplete observation, but it illustrates the fact that even a condition like pleural effusion, which you seem to observe, is really recognised by complex inference, and if either the process of reasoning or the observation is deficient, conclusion may be wrong.

To return now to the case I mentioned. The patient is a man of 48 years. I saw him a few hours after he had been seized with hemiplegia, which had come on in a few minutes. Such a sudden onset means, a vascular lesion, the rupture or closure of an artery. The onset had occurred without any loss of consciousness, and without prodromata. There was no sign of degeneration or of kidney disease. The ophthalmoscopic appearances were normal. The hemiplegia was complete; but the entire absence of any loss of consciousness made it distinctly unlikely to be hæmorrhage; and the facts that there was no tension in the pulse, and that there was a perfectly normal heart free from hypertrophy, made rupture of a vessel still more improbable. The absence of kidney disease made atheroma, at that age, most improbable, common as it is at a later time in life. No source of embolism could be found. As an almost invariable rule the source of an embolus can be discovered soon after the onset; if no source can be found the process may safely be excluded. When no evidence of any other cause of arterial occlusion can be discovered, and there is no condition to cause the rare spontaneous thrombosis in a healthy vessel, syphilitic arterial disease is probable. It is the condition left by the exclusion of others, and it can very seldom be excluded. I came, therefore, to the conclusion that it was a case of syphilitic arterial disease leading to the sudden formation of clot in a branch coming off from the diseased part of the artery. But not only could syphilis not be excluded in this case; there was a history of it. The patient was perfectly conscious and able to talk, and gave me a history of syphilis more than twenty years ago; an intimate friend, moreover, told me of a further history of syphilis as recently as eight years ago. Under these circumstances the diagnosis of syphilitic arterial disease and thrombosis was the proper diagnosis, and treatment was arranged accordingly.

The patient was admitted here a short time afterwards, and, instead of improving as he should have done, he has got worse. By "improving" I mean in the general cerebral symptoms, not necessarily improvement in the hemiplegia. You cannot by treatment restore the lumen of the vessel or the tissue destroyed by necrotic softening. The treatment is capable only of influencing the morbid process in the wall, and

not its consequence. Not only has the hemiplegia continued unchanged, as would be compatible with the diagnosis, but the general cerebral symptoms have become gravely worse; his mental state has become increasingly dull, weakness of the sixth nerves has developed, and, although the optic discs were perfectly normal when I saw him, optic neuritis has developed with a rapidity and to a degree of intensity that I think I have never seen before. It is certain that he is suffering from a tumour of the brain which is not syphilitic, and in some way by pressing on an artery has led to the sudden formation of clot in the vessels or in a branch. This must have been the process by which the cause of the symptoms we now see caused the sudden attack.

Of course I need hardly add that he was treated by iodide of potassium in full doses, and soon afterwards mercury was added and pushed just to the degree of affecting the gums; yet not only without improvement, but with the contrary. I may incidentally add that the mercury was pushed to the degree of affecting the gums, because, unless you see indications by the gums that there is enough mercury in the blood to act upon the tissues, the presumption is that the mercury is eliminated so fast that there is not enough in the blood to act upon the syphilitic tissue.

Such a combination of symptoms is seldom met with; but we do occasionally meet with a combination of symptoms which illustrates the same rule—that the diagnosis which it is right to make is wrong in fact.

I remember another instance of inevitable error in diagnosis, which I will briefly mention. An old woman, aged 60, was admitted in profound stupor and with indications of bilateral hemiplegia and irregular damage to the cranial nerves. This state had come on so suddenly we had no doubt that there was occlusion of the basilar artery. She was 60, and presented signs of degeneration: therefore thrombosis in a branch of an atheromatous artery was probable. But she had also mitral constriction, the cardiac lesion which of all others is most prone to cause embolism. Embolism of the basilar artery, curiously enough, has been thought to be impossible, because the artery is larger than either of those by which the blood reaches it, but manifestly a plug may pass through one of the vertebrals which cannot pass through either of the posterior cerebral arteries, which are smaller than the vertebrals. As a matter of fact, I have seen a distinct embolus in the anterior extremity of the basilar. Therefore embolism was also probable, for no age excludes it. The patient died, and was found to have syphilitic disease of the basilar, perfectly characteristic. This we had no reason to suspect. It is another instance of a case in which a correct diagnosis was impossible, and error was inevitable. From such cases only the general lesson can be learnt, that accuracy is occasionally impossible; we can only be right in nineteen cases by being wrong in the twentieth. It is well to realise this. But remember that in practice we have to treat that which is only probable as if it were certain. We could not treat two-thirds of our cases properly without doing this. But always discern the degree of probability, and if the probability is low, reduce or modify your treatment so as to do as much good as you can, if your opinion is right, without certainly doing harm if your opinion is wrong. You will find that this principle is applicable to many and various contingencies.

And now we pass to the case which I want especially to make the subject of your attention to-day. The patient is a man who first consulted me on February 9th, complaining of numbness in his hands and feet, with pains and twitching of the muscles, which were increased when he walked. These symptoms were of three years' duration and had gradually become worse. They began after over-work. He had sharp momentary pains in both feet, sometimes in the toes, sometimes in the soles, and sometimes in the balls of the feet—not much in the legs, and none in the arms. There was no trace of knee-jerk; although there was a little complaint of unsteadiness, he could stand, with his eyes shut, fairly well. There was no inco-ordination in the hands, and no deficiency in their sensitiveness. The pupils acted to light. He had had slight brief double vision. There was diminution in sexual power but no difficulty in micturition. These symptoms, especially the loss of the knee-jerk and the sharp pains, afforded a strong presumption

of tabes. Inquiry after the common antecedent of tabes gave no evidence of it, but did not enable it to be absolutely excluded. He came late one morning, after I had finished my work, and I had no time to examine the state of sensibility upon the legs; I made a note that it was to be examined next time I saw him. I generally refuse to see a patient unless there is adequate time for investigation, but it is not easy to resist the urgent desire for an interview when a patient has come from a distance. I made the diagnosis of probable tabes, and ordered him a mixture containing belladonna, quinine, and arsenic. He came again, about five weeks afterwards, saying that he was about the same. The pains were a little less, but the other symptoms were still troublesome. I then proceeded to do what I had not been able to do on the first interview—to test his sensibility.

Among the many aphorisms I heard from the lips of the greatest bedside teacher whom any living person remembers, was one that flashed across my mind when, to test sensation, the patient's skin was bared. I remember hearing Sir William Jenner once say: "Gentlemen, more mistakes are made, many more, by not looking than by not knowing." To my astonishment, almost to my consternation, I saw that the skin presented everywhere the characteristic pigmentation produced by arsenic. It was a case of arsenical poisoning simulating tabes. And I had prescribed arsenic for him! Before his illness, and during its first year, he was by occupation an oil and colour merchant, handling papers of various tints, and all sorts of pigments, many no doubt containing arsenic. He had also during the first year he began to suffer taken a tonic mixture containing arsenic; but he did not take this long enough for it to do more than intensify the poisoning, which had no doubt been the result of his occupation. He had been exposed for many years; and it is probable that during the two years which elapsed between the development of his symptoms and the time I saw him, that which I did others had done. Arsenic had been given him to cure his symptoms.

I need hardly say that I changed the prescription. He has not, however, improved. I gave him iodide of potassium, which seems to have a definite action in eliminating arsenic from the system; but the course of his symptoms during the last three months is curious; they have rather increased than lessened, and especially the condition of the skin that I will show you in a moment, has become more intense. Unless there is some continued cause of arsenical poisoning, and we cannot discover it in any way, I think the iodide of potassium must have been eliminating the arsenic from the tissues to such an extent as to increase the amount in the blood to a degree that has further irritated the damaged structures.

Before, however, we examine the skin, let me remind you that the nerve symptoms in arsenical poisoning are most important. In acute poisoning they are met with after the acute symptoms have subsided; they come on gradually, and for a time increase. The arsenic taken in during the acute poisoning seems to enter into the nutrition of the nerve elements and gradually to derange their function and their structure. In chronic poisoning there is a gradual interference with function.

This fact, that arsenic passing into the nerve structures, perhaps partly in place of phosphorus, should first gradually modify their function, is not surprising. Function depends upon the release of force—nerve force—by chemical combinations; and the amount of nerve energy latent in complex compounds, released when simpler compounds are formed, depends upon the constituents; so also does the readiness with which it is evolved and the kind of stimulus that excites the release. But the change in nutrition which at first disturbs function, in greater degree, changes the structure, and leads even to disintegration of the substance of the nerve elements. As a fact, this is what arsenic and other metallic poisons do. Their action presents certain features which you should always bear in mind. They reach the structures by the blood. The structures on the two sides have bilateral symmetry in intimate constitution as in outward form, and that involves a similar susceptibility on the two sides. Hence it is that these poisons produce symptoms that are bilaterally symmetrical.

Moreover, they produce symptoms which are limited

according to function. There we have a mystery, and yet it is a mystery we must recognise as an indication of fact. Function must be related to the chemical and molecular constitution of the nerve elements. The difference in susceptibility to different forms of force must depend on atomic constitution and molecular arrangement. We cannot conceive that the nerve endings in the skin which produce a nerve impulse on the slightest touch are quite the same in constitution as those which produce a nerve impulse when warmth is applied. We cannot believe that the same kind of structure can subserve the susceptibility to the massive motion of a touch or to the wave motion, only a little less frequent than the waves of light, which constitutes heat. And that difference, we can understand, is equal or greater in the motor and sensory terminal structures on which toxic influences for the most part primarily act. This enables us to understand why it is that poisons act specially upon structures with certain functions, and should even act first on one set of sensory nerves and not on another set. So we have, from different poisons, different effects upon the nerves, and we have also different effects from the same poison, probably dependent on the fact that it enters the blood in a somewhat different form, or with greater or less rapidity, and thus is assimilated by and deranges certain structures rather than others. Thus we have, from arsenic, palsy of the extensors of the arms and feet, as we have from alcohol. We have sometimes a perfect simulation of tabes, ataxy, muscular anæsthesia, and loss of knee-jerk, in consequence of the preponderant affection of the afferent muscle nerves, and sometimes we have chiefly sensory cutaneous symptoms, although scarcely ever without loss of the knee-jerk. Remember, that loss of the knee-jerk only indicates affection of the afferent muscle nerves, and that we know that the impairment of these nerves has many causes. To all toxic influences they seem specially susceptible.

Hence, I beg you to remember, above all things, as a practical rule, that whenever you have bilateral disturbance of the peripheral nerves, symmetrical, with a distinct limitation to function, sensory or motor, it is almost certainly due to a blood state. There is reason to believe that the degenerations which may appear to constitute an exception are really due to a blood poison. Many are the cases in which the recognition of that fact will save from grave error.

In the nerve symptoms of this patient there is little more for you to observe than I have told you, but if you ascertain for yourselves the absence of the knee-jerk, the fact may be more securely fixed in your mind, and it cannot be too surely held. But, as regards the cutaneous symptoms, there is a picture for you to study such as you will not see again. This arsenical pigmentation is so characteristic that the moment I saw it I was sure of its nature, but I never like my own certainty to be without corroboration if it is outside my own special region. So I sent the case to Dr. Radcliffe Crocker, and he is also absolutely certain. He has seen, he said, one more intense case, and he has kindly allowed me to show you a plate from his *Atlas*, which illustrates it.

I have myself become familiar with the pigmentation that is caused by arsenic because I have often seen it in the cases of epilepsy. I have also seen it in well-marked form, in a lady whose love for working on muslins led her to their continuous handling, and she preferred æsthetic tints. The result was that she began to suffer from pains that were ascribed to gout, until there came progressive palsy of the extensor muscles of arms and feet. This showed a toxic influence, by the symmetry and limitation I have mentioned. Then the pigmentation was discerned, although, I believe, chemical analysis had already made certain the cause. But the troublesome pustular eruption which bromide causes in most persons can only be prevented, or kept down to insignificant degree, by arsenic. No other drug, no modification of the way or form in which bromide is given, has any influence. Some patients are peculiarly prone to the rash, and have to take the drug for a long time; they have to take arsenic also. A slight degree of pigmentation is often produced in such cases. It has, therefore, several times happened to me that I have had to put to the patient the two evils, and say, "Which will you have, the spots or the pigmentation?" There is no other help for it; they must have one or the other. They always choose the pigmentation. It does not, however, increase to

a really serious degree in such cases, and I have not met with any other symptoms of chronic arsenical poisoning in consequence of the use of arsenic to prevent the bromide rash.

If you observe carefully the skin of this patient, you will see that the pigmentation begins as small round spots which seem to increase in size and coalesce, but leave small rounded areas of unpigmented skin. These appear whiter than normal, perhaps only by contrast. The pigmentation is abundant everywhere, but extreme on the neck, front and back of the trunk, arms, and thighs. For the most part it appears a simple deposit of pigment, dark brown in tint. But in many places you will observe small round spots of congestion, of the same size, which suggest that, at least when the process is going on actively, congestion may be the first part of the process. Moreover, in the neck, where the skin has been subjected to habitual friction, the pigmentation is so intense as to be practically continuous, and with it so much congestion is combined as to give the pigmented area a reddish or purplish-brown aspect. The congestion is also conspicuous on the hands, and there, on the palms especially, the spots are attended with distinct elevation. Indeed, where the epidermis is thick, there are minute raised elevations, at which no indication of congestion or pigmentation can be discerned.

The great fact is the pigmentation, at first essentially punctate or in small spots. It is that that is so characteristic. You will at once understand how important it is to be able at once to recognise a sign so distinctive and so significant. You cannot note the state too carefully. Once firmly fixed in the visual memory, it will not be lost. It is seldom easy to retain an image securely from a single opportunity of inspection, but this condition is one, I think, which you are not likely to mistake when you see it again. You may have some other opportunity of observing a similar condition. You probably will have such if you carefully examine the skin of patients who have been, for long, taking arsenic with bromide. But the story of the origin of this patient's illness suggests that a careful inspection of the skin of a number of men employed in shops where paints and papers are sold might afford an inquiring student opportunities of observing the pigmentation, which would be beneficial not to himself alone. It is certain that the change in the skin may long precede any other symptom.

Having helped you so far, gentlemen, I must now ask you to help yourselves. Observe, also, what I have not mentioned, the bilateral symmetry of the rash, a feature that you will recognise, from what I have said, to be inevitable. Connect it with the bilateral pains and loss of knee-jerk, and fix these features of limitation and symmetry in your minds in association with the toxic cause. For a moment, indeed, forget what the cause here is; forget the precise character of the symptoms, in order that the general facts of combined functional limitation and bilateral symmetry may stand out more clearly in your view, as landmarks which, whenever and wherever they are seen, will always guide you surely.

THE CROONIAN LECTURES

ON

A NEW DEPARTURE IN DIABETES.

Delivered before the Royal College of Physicians of London.

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[*Special Abstract Report.*]

LECTURE III.

AMOUNT OF SUGAR IN THE BLOOD.

AFTER recapitulating briefly the arguments of the two opening lectures, Dr. Pavy proceeded to state the result of his investigations as to the amount of sugar in the blood under normal conditions. This he said was in the general circulation very small. The results from upwards of 100 determinations of the amount of sugar present under natural conditions in various animals showed a range of from about 0.6 to 1.0, or a little over 1.0, per 1,000. The cupric-oxide reducing power