a mild enteritis, however produced, is sufficient to produce an attack. It would appear that in such cases the absorption of poisonous cleavage-products of proteins may be the exciting cause, and even histamine has been held by some writers to be responsible. If you have in mind what I stated, in dealing with experimental anaphylaxis, concerning the generally enhanced sensitiveness of the anaphylactic animal to poisons of this type, you will find no difficulty in reconciling the occurrence of such attacks with a specific, anaphylactic origin of the asthmatic condition, in the patient in whom they occur. Nor should the evidence brought forward by Auld and others, as to the improvement of such patients under treatment with small injections of poisonous protein derivatives, such as Witte's peptone, present much difficulty of interpretation, if you remember my statement that the anaphylactic guinea-pig can be partially desensitized by a similar non-specific intoxication.

I am by no means suggesting that every case of so called asthma is of the anaphylactic type. Even if the so-called cardiac asthma and renal dyspnoea are excluded, I imagine that there are many cases in which the symptoms are asthmatic, but which have a different origin altogether. When the question is raised of sensitization to the proteins of infecting organisms, the distinction between a primary toxic action of their products and an anaphylactic reaction to their proteins becomes difficult to draw. Especially is this the case with an infection of the respiratory passages themselves. There seem to be some clear cases; however, of infection at a distant site, causing, not a local trouble, but a genuine general anaphylactic reaction. But the discussion of the relation of anaphylaxis to bacterial proteins, full of suggestion though it is for a rational conception of the genesis of certain chronic morbid conditions, would lead us into such inadequately charted waters that I shall not attempt the rôle of pilot. My object has been to provide, from the experimental side, a more definite conception of the nature of those conditions in which sensitization to foreign proteins is clearly established; such a conception as may help to focus ideas, to stimulate observation, and even to rationalize treatment.

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A British Medical Association Lecture

ON THE

DIAGNOSIS AND TREATMENT OF INTRATHECAL TUMOURS OF THE SPINAL CORD.*

BY

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In this lecture I shall not endeavour to advance any original ideas, but will present certain aspects of an important topic which, although they are familiar to the neurologist, are, I fear, not so well known as they ought to be to the general body of the profession. The subject is important because we have in the treatment of intrathecal tumours of the spinal cord one of the most, if not the most, reliable developments of the surgery of the nervous system, and yet I am convinced that in this country many cases which could be readily and almost dramatically cured are allowed to pass without recognition or radical treatment and to run unaided their inevitable course to death.

I propose to illustrate my remarks by showing two patients, both operated upon sufficiently long ago to demonstrate what may reasonably be called "end results." The first will serve to illustrate all the salient points of an intrathecal tumour; the second is one of a more obscure condition liable to be confused therewith.

H. H., a motor driver, aged 43, came under my observation in the Manchester Royal Infirmary in March, 1920, when I was asked to see him by my colleague, Dr. Ramsbottom, and the first point which I must note is that, as these cases rarely come directly before the surgeon, it will quite properly lie with the general

practitioner and the physician to make the preliminary diagnosis, without which nothing further can be done.

The patient, whose complaint may be briefly described as "paraplegia," gave a clinical history of the utmost importance. About the end of 1918, while in an army hospital with an attack alleged to be one of influenza, he noticed what is described as an indefinite pain about and just below the left costal margin. At first this pain was felt only in the morning, and it passed away throughout the day, but it tended gradually to become more constant. In March of 1919, when demobilized, he had no great amount of pain, but suffered a little from what he and his advisers called lumbago. He was, however, able to return to civil work and to continue thereat until October. During this period he noticed a gradually increasing weakness of the left lower limb, which at first used occasionally to "give" a little, and which later began to "drag." In the autumn of 1919 the right leg also began to show similar symptoms, and he then had to give up his work, although still able to walk about with the aid of a stick. In the month of January, 1920, he became rapidly weaker, and in the first days of February he was entirely confined to bed. From that time until I saw him in March he was in hospital and only growing feebler.

I have dwelt in detail upon this clinical history for reasons to which I shall return directly, but we may now turn to his condition as first seen.

He could not stand or walk unless supported. The right leg was very weak; the left could not be moved in the bed. When assisted he attempted to walk, but did so with an extremely spastic gait, more marked on the left side. There was no marked atrophy of the limbs, but the left was thinner than the right. As regards anaesthesia, he presented fairly good appreciation and localization of contact throughout, although there was a little delay in response. The appreciation of heat and cold and the sense of pain were lost in both lower limbs, and thence upwards to a level of about 2 in. above the umbilicus. Knee-jerks were exaggerated on both sides, and he had marked ankle clonus, especially on the left; the plantar reaction was extensor; the lower abdominal skin reflexes and the cremasteric reflexes were very sluggish. Bladder and rectum showed no abnormality. Pain was of the girdle type, running round immediately above the umbilicus, although in the early stages it had been assigned to a higher level; it was sufficiently severe to require a nightly dose of opium.

So far, then, we have a sufficiently typical case of a transverse lesion of the spinal cord more advanced on the left side, but on a very slight consideration of the symptoms and onset, we can go much further and recognize with almost absolute certainty an intrathecal tumour which may readily and most hopefully be removed—a diagnosis founded on both negative and positive indications.

About traumatic lesions we need not trouble. I have seen several cases of haemorrhage into the lower dorsal region of the cord, generally occurring in boys or young men and often after bathing in cold water, but in such, as in trauma, the onset is acute. Tuberculous disease of the spine is excluded by the absence of any evidence of bone disease either clinical or radiographic, and by the very slow onset; in this connexion I may say that local tenderness on tapping the spinous processes, and even local kyphosis may be present in the case of intradural growths, and that such symptoms must not be taken as excluding the presence of such growths, but here this possible source of error had not arisen. For similar reasons it is not at all probable that we have a growth—generally malignant—of the vertebrae themselves; the pain is not the intense pain of "paraplegia dolorosa" met with in such cases, and, while vertebral growths are generally secondary, there is here no indication of any primary growth elsewhere. Syphilis is excluded; so far as exclusion is possible, by the total absence of any indication of that disease, and by the fact that the cerebro-spinal fluid gave a negative Wassermann reaction. Growths, tuberculous masses, and cysts within the cord itself are all comparatively rare, especially in the lower dorsal region, and are not as a rule accompanied by pain. Cysts, such as hydatid cysts, in the meninges would, of course, produce the same symptoms as true tumours, but their treatment is identical. Of a remaining possible source of error I shall speak in connexion with our second case.

So much may be said for the negative side of our diagnosis. On the positive side we have a very strong argument. The essential feature of the clinical history was, as we have seen, pain long precedent to the paraplegia, of varying intensity and associated with remissions, while it was not localized in the back, but extended vaguely along one or more spinal segments. Such pains are almost invariably present as an early symptom of intrathecal tumours; I have traced back their history to as long as two years before any paraplegic phenomena were noted, and I have known them to be in abeyance for many months. They may or may not be associated with paraesthesiae or with a certain amount of anaesthesia. They may be bilateral or, as in the early stages of

* Delivered to the Birmingham Branch, November 17th, 1921.

this case, unilateral. Of somewhat vague nature, they are not often in themselves diagnostic until other symptoms supervene. They are generally described and treated as "rheumatic," or they may be regarded as due to visceral disease, as in one case in which a most eminent surgeon had advised operation upon the gall bladder in a man from whom I removed an intraspinal growth. Themselves, therefore, almost useless as a guide, they are of the utmost value when other medullary symptoms have developed, and it follows as a matter of course that every case of such radiating pain demands a most careful and, if necessary, a repeated search for indications of a transverse lesion of the cord, which may, as in our patient, approach most insidiously, and which show a strong tendency to be at first unilateral only.

Our diagnosis in the present case being, in my opinion, a matter of almost absolute certainty, it remained only to localize the level of and to remove the growth. The localization of the level demands, first, an accurate examination to ascertain the highest level of sensory or motor phenomena; secondly, a knowledge of the distribution of the spinal segments; thirdly, a recognition of the relation of these segments to the spinous processes; and fourthly, a correct enumeration of the processes themselves. It is doubtless due to a want of appreciation of these anatomical difficulties that many errors have occurred, and that the tumour has been missed through its having been sought too low down.

With regard to the appreciation of the highest level of symptoms it is not sufficient to accept the upper limit of what I may call "gross anaesthesia." The line of limitation is often very ill defined and only careful and repeated examination will enable us to determine it. In the present case a casual examination might readily have limited the level to a point below the umbilicus, whereas greater care showed some sensory loss as high as two inches above that landmark; pain had, indeed, been felt at a still higher level, but the overlap of segments causes pain to radiate far beyond the obvious anatomical distribution of the affected nerve and hence the ninth dorsal segment was regarded as the true level of the lesion. The peripheral distribution of the various spinal segments is now well recognized, and its consideration at this date would be merely a historical discussion into which I do not propose to enter, more especially as, with my old teacher James Ross, I may perhaps claim to have laid the basis upon which it rests. Moreover, in the case of the trunk, it is a peculiarly simple problem and the great majority of intrathecal tumours lie below the brachial and above the lumbar enlargement.

The relation of the affected segment to the spinous processes which are our guide to the site of operation is variable within somewhat wide limits, so that the operation must be sufficiently extensive to allow for individual differences. In the region with which we are now dealing the segment is generally about two vertebrae higher than the spinous process which bears the same number, so that for our ninth dorsal segment the centre of the incision will be at or even a little above the seventh dorsal spine, which again corresponds to the body of the eighth dorsal vertebra. Again, the determination on the operating table of the spine desired as a landmark is often far more difficult than might be supposed, especially in a stout or deformed person, and it may be necessary to find it beforehand by means of a radiogram with an indicator fixed to the skin, or even, as in one of my cases, by previously imbedding a piece of wire at the region required and then checking it by a radiogram.

In the case which we are now considering the operation, with the details of which I do not propose to trouble you, was performed on March 23rd, 1920, or, say, twenty months ago. The laminae of the seventh, eighth, and ninth dorsal vertebrae were cut across with the saw, the ligaments between the sixth and seventh divided with scissors, and the flap thus made turned downwards. There was at once observed an obvious fullness of the dura mater, which was laid open. The spinal cord was found to be pushed backwards and to the right, and a tumour was exposed to the left of and in front of it. One of the spinal roots, presumed to be the ninth dorsal, lay across its lower pole, and was divided to allow of the cord being gently drawn still further to the right, when there was fully exposed a firm, deeply red, encapsuled mass, which proved to be 3 cm. long, 1.5 cm. wide at its lower end, and very much of the size and shape of the terminal phalanx of the index finger. This was most readily shelled out, its attachments being, as is usual, quite loose. The actual seat of origin of the growth could not be determined owing to the very lightness of these attachments,

which almost give the impression that the tumour is lying free in the meningeal space; moreover, very little bleeding follows the blunt separation of the connecting bands. In structure the tumour was described by the pathological department as a "fibroma of rather cellular and vascular type."

Such an operation may be regarded as typical, except that it is more difficult in stout patients to turn down spines, laminae, and their connexions as a continuous osteoplastic flap. On the other hand, in this case the anterior position of the growth and its rather unusually large size rendered necessary a good deal of traction on the already markedly displaced cord. I must, however, again insist on the readiness with which these growths can be enucleated, those which are situated a little further back upon the cord almost giving the impression that, if the patient were rolled over, they would fall out as—to use a war-time illustration—a shrapnel bullet might fall out of a mass of granulation tissue.

The rather unusual difficulty in shelling out the tumour in the present case explains the fact that for a short period the patient had aggravated symptoms. For the first four days anaesthesia was a little deeper than before operation, but sensation to heat and cold then began to return and was rapidly followed by return of sensation to pain. Urine was retained and the catheter was required for the first eight days after operation, while he had a mild attack of cystitis, which quickly passed away. Return of motor power was more gradual but perfectly steady. On the twenty-eighth day both legs were quite movable in bed, the right being more so, but both still felt stiff; the right knee-jerk presented no exaggeration, the left slight only; the plantar response on both sides was an extension followed by flexion. At the end of six weeks he could walk about the ward with a stick and was able to go home. A month later the aid of the stick was dispensed with. Examination of his condition to-day will show that from a subjective point of view he is perfectly healthy and that the only peculiarities which can be detected are a faint linear scar upon the back and a slight irritability of the knee-jerks.

It remains to consider, as in all cases of tumour removal, what are the prospects as regards recurrence. Into the difficult question of the pathological nature of these intrathecal growths I do not propose to enter. Probably all arise from dura, arachnoid, or pia mater. Among my own cases I have had various descriptions from pathologists, such as haemangioma, lymphangioma, endothelioma, and fibroma, occasionally also sarcoma; far more extensive investigations have been made from *post-mortem* examinations, and many operators have recorded psammomata, which, curiously enough, I have not met with, or at least not recognized; hydatid cysts are not by any means unknown, but again I have not seen such. The important practical point is that I know of no case of recurrence even in patients operated upon many years ago. I have met with one case only of infiltrating sarcoma, which invaded the *conus medullaris* and the *cauda equina* for many inches, and in which excision was out of the question; I have met with one case of long standing in which functional recovery after excision was very imperfect; I have had one case in which, on clinical grounds, I advised operation, but the misreading of a radiogram (now many years ago) was taken to show a large ossifying sarcoma—nothing was done, and the patient died, when the autopsy revealed a condition quite similar to that of H. H. On the other hand, I have had at least a score of cases in which the operation was as simple and the results as satisfactory as in the one before you. The operation mortality is *nil*, as I have found it to be in all cases of laminectomy for exploration, rhizotomy, spinal drainage, and the like. But I regret to say that I know of a good many cases in which operation has been refused and death ensued. It is my earnest hope, gentlemen, that such cases will become more rare than they now are, and that in all which are doubtful the safe and simple expedient of exploration will be adopted.

And now I will ask you to turn to my second patient, whose case illustrates some difficulties of diagnosis and some of the advantages of exploring when in doubt.

R. C., aged 22, consulted me on December 6th, 1920. From boyhood he appears to have suffered from vesical catarrh for which I have found no cause or explanation and from which he had no practical inconvenience. In the year 1917 he had an attack of fever of unknown nature while on naval service in Cuba; other-

wise he has been perfectly healthy. Nine weeks before I saw him he had a disagreeable sensation which he describes "as if his toes were tied together." His legs then became weak and stiff and he was unable properly to control their movements. He had a little pain on bending strongly to the left and appeared to have some tenderness of the left kidney, but these symptoms were so slight as to be quite doubtful. Incompletely paraplegic, he had great and increasing difficulty in moving about the room with the aid of a stick. Anaesthesia, which was nowhere complete, extended to a fading margin a short distance above Poupart's ligament. Knee-jerks and ankle clonus were markedly exaggerated. There was some difficulty in commencing to micturate but no retention of urine.

A week later when he came into hospital paraplegia was almost complete; he could neither stand nor walk. Anaesthesia was more marked and extended nearly to the waist line. The knee-jerks and the ankle clonus were more marked on the left side; the plantar reactions were flexor. Three weeks in hospital were devoted to the attempt to define symptoms a little more closely, to look for any sign of improvement from complete rest, and to search for any of the more common causes of transverse lesion of the cord. We found no evidence of tubercle or other bone disease. There was no indication of syphilis, and the Wassermann reaction of the cerebro-spinal fluid was negative. There was equally no evidence of past or present gonorrhoea; the urine contained small quantities of pus, but no organisms were discovered. Anaesthesia varied a good deal in its intensity and slightly in its upper limit, but sensation was normal above the line of the umbilicus. Paraplegia increased, so that he could not move his lower limbs in the bed.

Here, then, we have a clinical picture which I may describe as the blurred image of an intrathecal tumour. Anaesthesia could not be recorded in diagrams as it was vague and changeable but with a tendency to extend upwards. Paraplegia was steadily increasing in intensity. The reflexes were those of a transverse lesion except for the plantar reaction. There was no longer any pain, and pain had always been of the slightest. Such a condition reminds us at once of the cases described by Horsley as "chronic spinal meningitis" and by Spiller as "circumscribed serous spinal meningitis." The general outline as given by Horsley resembles that of a tumour of the cord, but pain is less definitely localized and there are often widely spread hyperaesthetic areas; anaesthesia is incomplete and without dissociation; paralysis comes on as a widely spread weakness, often unilateral; there are no vasomotor symptoms; the patients are almost always adults, and the upper level of anaesthesia is usually mid-dorsal. Some of Horsley's cases were regarded as syphilitic, several as due to recent gonorrhoea, and others were assigned to influenza.

Operating on 21 cases of this type which had been originally regarded as tumours Horsley found excess of cerebro-spinal fluid, thickening of the arachnoid, "matting of nerve roots," and compression of the cord. He opened the dura mater, irrigated with strong solutions of mercuric chloride, and left the theca open for drainage. The good results which he obtained he compares to those which follow laparotomy in tuberculous peritonitis.¹

When this description appeared I had already met with a few similar cases—notably one in which I thought that the symptoms of a tumour of the cauda equina were unequivocal, but in which I found only thickening of the dura mater with very large quantities of cerebro-spinal fluid; after this had been opened up and drained recovery was to my surprise complete, but I fear that I then dismissed the matter from my mind as an unexplained error in diagnosis.

The case of R. C. appeared to me to be most probably of similar nature, and the source of infection as vesical or renal, and I decided upon an exploratory operation, which was performed on December 28th, 1920. The sixth, seventh, eighth, and ninth dorsal laminae were totally removed, it being difficult to do an osteoplastic operation on account of the rather free haemorrhage and depth of the wound rendering unsafe the use of the saw. In the centre of the exposed area of the theca it was at once obvious that there was some change; above this point pulsation was very marked; below it ceased entirely and abruptly; there was also an appearance of a slight constriction. An incision four inches long was then made into the dura from below upwards, and cerebro-spinal fluid only began to flow when the incision was carried above the point noted; above this point the flow was very free, from which I concluded that there was here some slight adhesion of the meninges, although there was no visible cicatrix. As the patient's condition was giving a good deal of anxiety to the anaesthetist, while free bleeding and escape of cerebro-spinal fluid obscured the view, I decided to complete the exploration a few days later. Four days afterwards, when the wound was reopened, there gushed out from its deeper part at least two or three ounces of cerebro-

spinal fluid, but nothing further was discovered after a most careful search, including the anterior aspect of the cord, and the wound was again closed, the dura mater being left freely open.

For four or five days after this second operation there was a good deal of pain; at the end of a week the lower limbs could be moved, and at the end of a fortnight were freely movable, while sensation was distinct everywhere, although still somewhat wanting in acuteness. On account of the amount of injury inflicted upon the bones of the spine I kept the patient in bed longer than usual, but after two months he could walk, although with difficulty. He can, as you will see, now go about quite easily, and he says that the only thing that he cannot do is to run; he is, as he will tell you, not conscious of any physical defect, although his knee-jerks are still exaggerated, and probably always will be so. His old vesical condition is naturally not affected by the operation, and I am hoping that it may now be found possible to do something to correct it.

I have brought this case before you more particularly to illustrate three points—namely, first, the great importance of exploring doubtful cases of transverse lesion of the cord—that is to say, *all* cases which are not obviously hopeless; secondly, that you are more likely to do good than harm should a diagnosis of a thecal tumour prove incorrect; and thirdly, because I hold that there is a strong probability that many early cases of transverse myelitis may be arrested and cured by incision and drainage of the dura mater—a possibility fully in accord with the view that such myelitis is often due to infection spreading along the spinal nerves and then necessarily crossing the meninges and the intradural space before the cord itself is attacked. If this view of the causation of transverse myelitis be correct—and there is strong evidence in its favour—we may then hope to arrest the infection in its course and to save the cord before it is irretrievably damaged. When once a portion of the cord has been converted into a cicatrix there is nothing to be done, but if we can arrest infection at its onset it is reasonable to hope that the patient may be saved. In all other regions of the body we aim at the drainage of infections at the earliest possible moment; in this, the most vulnerable of all regions, we can only hope to save by exceptionally early drainage of even the mildest of infections. And, before leaving this side-issue of the present address, I may add that I think the infections usually derive from the urinary organs—a view in accord with the cases which I have myself seen, with the tendency of transverse myelitis to attack the levels connected with the kidney, and with the fully recognized tendency of the kidney itself to collect and harbour organisms of all types.

Gentlemen, I have, with the exception of a single reference to the great pioneer of the surgery of the nervous system, given you only the results of personal experience, and I am only too well aware that as surgeon to a general hospital I have not the advantage of those practising in hospitals specially devoted to the diseases of the nervous system. For this reason I cannot bring before you extensive statistics, nor can I hope to do more than help to throw a very little light upon neurological questions. But the more obscure and limited field of to-day becomes the commonplace of tomorrow, and I am convinced that the search for and the recognition of cases such as I have described to you will result in the discovery and the salvation of many which are now lost. The neurologist and the surgeon are fully prepared to deal with them, although the neurological physician perhaps hardly realizes the safety of laminectomy. It is therefore now necessary only to make such cases more widely known to the great body of the profession in order that we may realize an advance in treatment similar to that which has occurred in other branches of practice.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, February 27th, 1909.

THE International Grenfell Association now has five hospitals established on the shores of Newfoundland and Western Labrador; an orphanage was built at St. Anthony, on the north coast of Newfoundland, last summer.

THE Federation of the American Society of Experimental Biology, composed of five societies, held its annual meeting at New Haven, U.S.A., from December 28th to 30th, under the auspices of Yale University. Dr. J. J. R. McLeod, of the University of Toronto, president of the American Physiological Society, was president. The annual meeting of the American Association of Anatomists was held at the same time.