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REPORT XCIX.

LESIONS OF SPINAL AND CRANIAL NERVES EXPERIMENTALLY PRODUCED BY TOXINS.*

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IN a previous paper[1] we described the lesions in the posterior columns of the spinal cord in cases of general paralysis, and pointed out their similarity with those in early tabes. We showed that the degeneration always commenced at or close to the point where the posterior roots enter the cord. It is here that the sensory fibres become part of the central nervous system and lose their neurilemma sheath; and in all cases we found that precisely at this point degeneration began.

While studying these lesions we had indications that it would be advisable to inquire into what was known of the lymphatic system of the posterior roots and columns, and we found evidence of a very convincing nature that there was a continuous flow of lymph upwards along the nerves to the cord; it is believed that the main lymph current lies at the periphery of the nerve bundles immediately under the fibrous sheath.

We have in three previous publications[1 2 3] referred to the data on which these assertions are based, and in this would put forward several additional arguments of importance.

It is well known that tetanus and rabies spread to the cord by the nerve paths, and in this connexion we might mention the experiments of Marie and Morax,[4] who, after cutting the nerve to the fore-limb of an animal, and later injecting a lethal dose of the toxin into its paw, found that no convulsions followed. Homén and Laitinen[2] after injection of streptococci into the sciatic nerve traced the organisms upwards into the meninges of the cord; while Pirrone,[4] experimenting with the pneumococcus, found changes in the cord, but limited to that side on which the nerve was injected. But in addition to organisms, chemical and inert substances have been used with like results, for example, Guillain[4] injected ferric chloride into the sciatic nerve, subsequently introducing potassium ferrocyanide into the general circulation, and then found prussian blue in the posterior roots. Then Sicard and Bauer,[4] using China ink, found after injection into the nerve that the granules ascended along the nerves towards the cord.

It was evident that if these views were correct we ought to find in the cord of cases in which some septic focus existed, lesions of the posterior columns occasioned by the presence of toxins ascending in the lymph stream. On examining cases of brachial neuritis (infective), bed-sores, suppurating knee-joint, and septic psoas abscess, we found in the cord of all the lesions expected.[3] We then submitted our theories to experimental test, and have been successful in inducing posterior column lesions in rabbits exactly similar to those already found in man.

The method which we adopted—at the suggestion of Professor Lorrain Smith, and in whose laboratory the experiments were carried out—consisted in filling a celloidin capsule with a broth culture of a certain organism. The sciatic nerve being exposed, the sealed capsule was placed in apposition with it, after which the gluteal muscles were stitched in their original position and the wound closed. As toxins are known to diffuse through the wall of these capsules, we assumed they would find their way into the ascending lymph stream of the nerve and so to the cord, where their presence would be demonstrated by the ensuing degeneration. The organisms we first employed were *Staphylococcus pyogenes aureus Bacillus pyocyaneus*, Gaertner's bacillus, and the *Bacillus coli*; later we used the organisms taken from cases of acute colitis.

We commenced our experiments at the beginning of 1905, and at first used organisms whose virulence had not been raised in any way. We found, however, that, in order to obtain definite lesions, it was necessary to do so; and, further, that it was advantageous to renew the capsule from time to time in order to maintain the supply of toxin. We purposely at this stage ignored the question as to the predilection of certain organisms for the nervous system, and kept strictly to our original purpose of testing our own views and those of others on the direction of the lymph stream in the spinal roots and the possibility of cord infection by this channel.

The lesions of the posterior columns in the rabbit's cord were very definite. The degeneration commenced at the point where the sensory fibres lost their neurilemma sheath, and spread inwards to the root-entry zone. The collaterals springing from this area and passing into the grey matter were also affected. The degeneration, studied by the osmic acid method, was, in its distribution, quite indistinguishable from the early system lesions already described by us—namely, the exogenous zones were much more affected than the endogenous ones. The appearance of the affected fibres in both transverse and longitudinal sections shows that the degeneration in its early phase is essentially a primary one of the myelin sheath alone. In a more advanced phase we have observed in longitudinal sections of the posterior columns long rows of black globules showing the typical arrangement met with in Wallerian degeneration. In no case did the posterior spinal roots outside the cord or the sciatic nerves show any change when treated with osmic acid.

Turning our attention next to the pons and medulla, we found that lesions of the cranial nerves in general paralysis commenced exactly at a corresponding point to those of the spinal nerves; the degeneration affected not only sensory but also motor nerves, and by the experimental method described we have been able to induce similar cranial nerve lesions in rabbits by implanting a bacteria-laden capsule under the skin of the cheek. This, the latter portion of our research, from our recognition of the importance of using organisms of adequate virulence and of maintaining the supply of toxins, has yielded more constant results and thrown more light on the initial changes affecting nerves in their intramedullary course where they are devoid of neurilemma. Up to the present we have only completed the serial examination of the pons and medulla taken from two experiments.

In the first experiment the fifth and sixth nerves alone showed definite degeneration; in the other nerves the degree of affection was very slight. In the second experiment the degeneration was much more marked and more widely spread, affecting the third, fourth, fifth, sixth, seventh and eighth, and the twelfth to a very slight extent. No appreciable change could be observed in the other—ninth, tenth, eleventh—nerves. The degeneration affected only the intramedullary part of the nerve, and in the case of the motor nerves could be traced as far inwards as the nuclei of origin, especially in the third and sixth, which readily lent themselves to examination. The changes in these two, as revealed by the osmic-acid method, consisted in an acute necrosis of the myelin sheath, which assumed various morbid forms—for example, long and short oval masses, elongated threads of varying thickness, mostly slender, on which were moniliform swellings. The degenerative products stained intensely black, and in the motor nerves the myelin affection was a little less marked towards the nucleus of origin. In one of the degenerated fifth nerves there was Wallerian degeneration in the descending root as far as the lower end of the medulla. All the degenerations were sharply defined from the surrounding tissues, into which obviously no appreciable diffusion of toxins had taken place from the nerve paths. In both cases the extramedullary portion of the nerves showed no reaction to osmic acid.

Conclusions.

1. Toxins readily travel up spinal and cranial nerves to the central nervous system.

2. While these nerves in their extramedullary portion possess a neurilemma sheath and are protected by its

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vital action, in their intramedullary part, having lost their neurilemma, they immediately undergo degeneration.

3. The first change is a primary degeneration of the myelin; axis cylinders and nerve cells are evidently affected later.

It seems to us that the results of our investigations suggest the possible lymphogenous origin of some nervous affections. We know that tabetiform and cranial nerve lesions in general paralysis, and even those in tabes, are not the result of nerve-cell degeneration, but are a primary affection of the myelin sheath, commencing where the neurilemma is lost. In our clinical cases, and also experimentally, we have found similar lesions starting at the same point, the result of absorption from a definite toxic focus situated outside the central nervous system, the toxins gaining access by the lymph stream. May it not be possible that the former lesions are also the result of toxins passing to the cord, medulla, and pons by the lymph stream from some external but as yet unknown focus? In support of the lymphogenous theory of infection, we have lately added two additional clinical cases, namely, one of chronic middle ear and mastoid disease in which the eighth nerve was markedly degenerated in its intramedullary portion; and another of multiple abscesses in the right trapezius in which the right eleventh nerve was attacked within the medulla.

References.
[1] *Brain*, Winter, 1904. [2] *Rev. Neurol. and Psych.*, October, 1903. [3] Ibid., January, 1906. [4] *Manuel d'Histologie Pathologique*, Cornil and Ranvier, T. 3, 1907, pp. 718 to 725.

REPORT C.

AN INVESTIGATION ON THE REGENERATION OF NERVES, WITH REGARD TO SURGICAL TREATMENT OF CERTAIN PARALYSES.

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In this article some experiments will be detailed on nerve crossing in the spinal canal, and their surgical bearing discussed.

It is generally admitted that regeneration is impossible in the nerve tracts and fibres in the cord. This faculty of repair ceases at the point of entrance and exit of the nerve bundles from the cord itself, and corresponds to the place where the primitive sheath ends. The latter seems in some way to be essential for regeneration. In the case of the posterior roots useful regeneration can only take place when the lesion is distal to the posterior root ganglion. Section and suture central to this are doubtless followed by regeneration as far as the cord, but it ceases there, and the result is of no value.

In the case of the anterior root, the recovery can follow a lesion anywhere in the neural canal if the ends be brought into satisfactory apposition. There is anatomically a considerable scope for the nerve surgery within the spinal canal. It has long been recognized that injury to the cauda equina can sometimes be successfully treated by laminectomy and suture of the individual trunks, exactly as lesions of peripheral nerves can. Up to the present, I believe, nerve crossing has never been suggested within the spinal canal, and I wish to show that it is possible and has practical importance. The experiments were performed on dogs, and consisted in suturing the central ends of one of the limb nerves to the peripheral ends of the nerve supplying the rectum and bladder, with the object of innervating these structures by the higher nerve. The results were very encouraging. Before giving details of the experiments the bladder supply of the dog may be briefly given.

According to Langley and Anderson and Sherrington,[1] the nerve supply of the bladder in the dog is variable. The second and third sacral nerves always give bladder contraction sufficient to expel the contents.

The first sacral in a few cases gives bladder contraction, but not enough to cause micturition. It is very rare for the last lumbar (the seventh) to innervate the bladder, and even when it does the amount is insignificant.

The experiments were performed on three large dogs; in one the first sacral was sutured to the second and third, and in the other two the last lumbar was joined to the second and third sacral, leaving the first untouched. Preparatory to the operation a large area of the skin of the back was shaved, and cleaned with turpentine, ether, and warm perchloride solution. The single median incision was made over the vertebral spines. On each side the spinal muscles were rapidly cleared from the laminae till several of the bones were bared. The very free oozing was then arrested by firm pressure with a sponge wrung out of hot antiseptic solution. Then the laminae were chipped away with bone forceps and the nerve roots exposed in the spinal canal. The ones to be used were hooked up in their sheath with an aneurysm needle, and the dura mater was not opened. It was found that the seventh lumbar was the highest that could be sutured to the second and third sacral without any tension, and only a single thin chromic catgut suture was used. The muscles were sutured over the exposed dura to form a protection, and finally the skin. Several animals were operated on, but only three which healed by first intention were kept. The after-results produced were some awkwardness in the hind leg on the side operated upon, which partly disappeared in time. Nothing peculiar about the bladder function was noticed.

In order to identify the nerves, the following points were observed. A line joining the two posterior superior iliac spines crosses the point where the second sacral pierces the dura. The first sacral was very much larger than the second and third, and the last lumbar is nearly as big as the first sacral. The key to the position lies in identifying the second sacral, and counting the roots upwards and downwards.

The following are the details of the experiments:

Dog 1.—Operated on June 29th, 1906. The central end of both roots of the first sacral nerve were fixed to the distal end of both roots of the second and third sacral on the left side. The first sacral was cut out of the intervetebral foramen, and the second and third where they come out of the cord. There was no chance of the two ends of the same nerve joining in any way.

October 15th, 1906. The spinal canal was again opened up, and the nerves isolated. There is always considerable difficulty in this, as the outer surface of the dura is roughened and adherent to the surrounding structures at the time of the second operation. Faradic stimulation of the first sacral nerve caused no sensory reflexes as the posterior root had been divided central to the ganglion. Stimulation of the first sacral produced strong movement of the tail and contraction of the pelvic diaphragm, and usually started bladder contraction with expulsion of contents. A cannula tied in the bladder and connected with a manometer showed a rise in the intravesical pressure. It seemed as if the contraction of the pelvic floor started the bladder reflex rather than caused the bladder contraction directly. This was not quite certain, however, but the practical results were the same in either case. Stimulation of the first sacral on the right side produced none of these effects.

Dog 2.—Operated on August 20th, 1906. The anterior root of the seventh lumbar was joined to both roots of the second and third sacral nerves on the left side; in the latter case both roots were used, because they were so small that it was impossible to separate anterior from posterior without causing much damage. An endeavour to do this in one animal spoiled the operation.

February 12th, 1907 (176 days after). Stimulation was performed, after cutting the spinal cord across at the level of the sixth lumbar nerve. The faradic current on the seventh nerve produced: (*a*) A vigorous contraction of the muscles of the pelvic floor; (*b*) vigorous contraction of the sphincter ani, and after ceasing the stimulation, extrusion of faeces; (*c*) expulsion of some of the bladder contents through the urethra in a jet (the organ having been previously filled with fluid), though no definite and visible contraction of the bladder or rectal wall was noticed. These organs were exposed by making a large incision in the abdominal wall. As a control, the seventh lumbar of the opposite side was stimulated and produced no contraction of the pelvic floor, sphincter ani, or expulsion of bladder contents. On the sound side stimulation of the second and third sacral produced exactly the effects of the seventh lumbar on the opposite side, but here, too, there was no contraction of the bladder or rectal walls detectable by the eye alone.

Dog 3.—Operated on October 18th, 1906. Both roots of the last lumbar nerve on the left side were fixed to the two roots of the second and third sacral nerves. The posterior root of the lumbar was cut distal to the ganglion, and the second and third sacral central to this. There were thus two ganglia in connexion with the posterior roots connected with the regenerating second and third sacrals. The first sacral was left untouched.

February 28th, 1907 (123 days after). Stimulation was performed. On the left side the faradic current, when applied to