A CONTRIBUTION
TO THE
PATHOLOGY OF DIPHTHERITIC
PARALYSIS.

BY
PERCY KIDD, M.A., M.D. OXON.,
ASSISTANT PHYSICIAN TO THE HOSPITAL FOR CONSUMPTION, BROMPTON.

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THE clinical features of diphtheritic paralysis are now well known. Some difference of opinion, it is true, still prevails concerning the frequency of its occurrence and the danger which it entails. But there is a more or less general agreement as to the clinical aspects of the disease.

Much uncertainty, however, has from the first attached to its pathology. It is only in more or less recent times that there has been any record of definite facts bearing on the question. Consequently the literature relating to the pathological anatomy of diphtheritic paralysis is somewhat limited.

Charcot and Vulpian,¹ as far back as 1862, described fatty and granular degeneration of the palatine nerves and their corresponding muscles. In this case the paralysis of

¹ 'Compte rendu de la Soc. de Biol.,' 1862.

the palate developed eight or nine days after the angina appeared.

There was no paralysis of other parts, and no mention is made of any microscopic examination of the spinal cord.

A few years later Lorain and Lépine¹ stated that they had observed changes similar to those described by the last authors but gave no further details.

Liouville² found similar degeneration of the phrenic nerves in one case.

Buhl,³ in an article entitled "Einiges über Diphtherie," related the results of an autopsy of a case of diphtheria in which he found marked lesions of the nervous system. The examination revealed extravasations of blood in almost every organ, and also in the cerebral pia mater and cortex. Infarcts were found in the white matter of the brain, in the central ganglia, crura cerebri, pons, cerebellum, medulla, and spinal cord. The spinal ganglia, and the anterior and posterior roots at their points of junction, were swollen. The nerve sheath and ganglia being infiltrated with nuclear bodies, which Buhl considered to be characteristic of the false membranes of diphtheria. These appearances were most evident in the lumbar region. No mention is made of any affection of the spinal cord itself. The absence of any clinical history of paralysis forbids any stress being laid on this interesting case.

Hermann Weber, "Ueber Lähmungen nach Diphtherie,"⁴ gives an account of paralysis in an adult. Four weeks after the sorethroat began this patient had recovered completely. But two weeks later he was seized with paralysis of sensation and movement, first in the legs, then in the arms, and lastly, he had symptoms of paralysis of the sphincter vesicæ. The paralysis came on after the patient had walked a great distance and had got wet through.

¹ Art. "Diphthérie," 'Nouv. Dict. de Med. et Chir. pratique,' 1869.

² Quoted by Bailly, 'Thèse de Paris,' 1872.

³ 'Zeitschrift f. Biol.,' 1867.

⁴ 'Virch. Arch.,' xxv, p. 130.

Death occurred twelve days after the paralysis began and was preceded by great dyspnœa. The autopsy revealed fatty degeneration of the heart, œdema of the lungs, congestion of the kidneys; no naked-eye or microscopic change in the nervous system.

Leyden¹ found in one case the appearances of a "neuritis migrans" ascending towards the nerve centres.

Oertel² in one case met with multiplication of nuclei in the spinal cord, especially in the anterior cornua, and hæmorrhagic patches in the cord and pia mater.

Vulpian³ in 1870 published the results of an examination of three fatal cases but without any clinical details. In two of these he found what he calls "rarefaction" of the connective tissue in the outer and posterior parts of the anterior horns, and alterations in the motor nerve-cells. The affected cells were globular in shape, their contents had become homogeneous, and the nucleus was obscured. There was also a slight increase in the number of nuclei in the spinal cord. Vulpian did not, however, attach any precise importance to these changes.

Pierret⁴ a few years later described a case of paralysis in an adult, in which he found disseminated patches of meningitis with perineuritis of the adjacent spinal roots.

It was reserved for Dejerine⁵ to bring forward the first definite facts in favour of diphtheritic paralysis being due to a degeneration of the motor nerve-cells of the spinal cord.

In three cases of his own and in two others to which he had access, he found constant lesions of an inflammatory nature in the anterior cornua, with consecutive neuritis of the corresponding anterior spinal roots. The posterior roots in each case were unaffected. The lesions of the anterior horns were both parenchymatous and inter-

¹ "Ueber Reflex Lähmungen," 'Sammlung Klin. Vorträge v. Volkmann.'

² 'Deutsches Arch. f. Klin. Med.' viii, 1871.

³ 'Malad. d. Syst. Nerv.,' 1870.

⁴ 'Comptes rendus de la Soc. de Biol.,' 1876.

⁵ 'Arch. de Phys. Norm. et Path.,' tome v, p. 107, 1878.

stitial. These nerve-cells were swollen in some instances, shrunken in others. The affected cells were indistinct, had lost their processes, and were globular in shape.

The number of nerve-cells in the anterior cornua was diminished. These changes were most marked in certain parts of the spinal cord.

The neuroglia showed multiplication of its nuclei and took up carmine very readily, an evidence of irritation as Dejerine thinks.

The small vessels were distended with blood and dilated. Hæmorrhages due to rupture of vessels were found in the anterior cornua, together with perivascular collections of small cells.

Around the central canal he found cell infiltration of an inflammatory nature. This affection of the spinal cord is regarded by Dejerine as a "subacute tephromyelitis," the neuritis of the anterior spinal roots being secondary to the spinal lesion.

Dr. Abercrombie at the last International Medical Congress in London gave the results of a microscopical examination of the spinal cord in seven cases of diphtheritic paralysis. In all of these cases he found evidences of a more or less advanced degeneration affecting the motor cells of the anterior horns in different parts of the cord.

These changes resembled closely those described by Dejerine, but though the small vessels were filled with blood no hæmorrhage was seen. There was a doubtful increase in the nuclei of the neuroglia, but no stress is laid by Dr. Abercrombie on this point. This author also considers the spinal lesion to be due to a "subacute myelitis."

It will be seen from this short historical sketch that although Vulpian was the first to recognise changes in the motor cells of the spinal cord, he did not attach the importance to this degeneration for which Dejerine and Dr. Abercrombie have since contended.

I shall now proceed to give a short description of a fatal case of diphtheritic paralysis that came under my

own observation and in which I had the opportunity of examining the nerve centres.

In the present state of the pathology of this affection every fatal case is of the greatest importance.

This must be my excuse for bringing forward an account of a single case.

Ernest H—, æt. 7, was brought to me by his father at the out-patient department of the Brompton Hospital with the following history :

Two months ago the boy had diphtheria, ever since he had the sorethroat his voice has been nasal, and food has sometimes come through his nose. He has been very weak all along, and never regained his strength properly. Two weeks ago he began to cough and since that time he has had some shortness of breath.

Present condition.—The patient is a pale, thin boy. Voice distinctly nasal. Seems very weak and walks in a tottering way. Muscular power of arms small, grasp of hands very feeble. Legs weak but less so than arms. Knee-jerk feeble on both sides. No distinct loss of cutaneous sensation. Micturition and defæcation unaffected. Tongue protruded straight, movements rather tremulous. Pupils contract with accommodation and react to light. Soft palate hangs motionless. No distinct action of the intercostal muscles. Breathing diaphragmatic, rapid. Chest: physical signs of general bronchitis.

As the intercostal paralysis was evidently a source of danger, I advised the father to try to procure admission for him at once into a general hospital, and ordered him an expectorant for his bronchitis. Three days later the father came and told me that the child was dead. He had been unable to get him admitted at the hospital where he applied, and had therefore kept him at home.

His breathing became gradually shorter and he died rather suddenly, before a doctor could be summoned. Death occurred two days after I saw the patient.

I regret that the clinical account of the case is not more complete, but on the only occasion in which I saw

the patient his general condition necessitated a somewhat hurried examination.

I proceeded to make the autopsy twenty hours after death. But when I had removed the brain and spinal cord the father interfered and refused to allow me to complete the examination.

The brain, spinal cord, and the membranes presented no alteration to the naked eye. The spinal cord, medulla, and pons were placed in weak alcohol for twelve hours, and were then transferred to a 2-per cent. solution of bichromate of potassium for three weeks. Hardening was subsequently completed with alcohol.

The pons, medulla, and spinal cord throughout were examined systematically. Sections were cut with the freezing microtome, and after staining with hæmatoxylin or picro-carmin were mounted in Canada balsam.

Results of microscopical examination.—Certain slight changes of a similar character were observed throughout the parts examined. These consisted in an accumulation of leucocytes in the smallest veins and in the capillaries. In a few instances the small veins were seen to be crammed with red corpuscles, especially in the pons and medulla. There was also distension of the capillaries and smallest veins in places. Collections of small cells, for the most part contained in capillaries, were observed around the cerebral canal throughout the cord.

Besides this vascular affection, definite changes were found in the grey matter. These changes concerned exclusively the anterior cornua, and were most marked in the dorsal region, less so in the cervical, and least of all in the lumbar division of the cord. The medulla and pons showed no alteration beyond the capillary and venous distension already alluded to.

The changes presented by the anterior cornua consisted in atrophy and alterations in the shape and appearance of their nerve-cells. As these changes attained their greatest development in the dorsal region a description of sections taken from this part will suffice for the cervical and

lumbar regions also. The changes in the latter parts differ from those in the dorsal cord only in degree.

Changes in the nerve-cells.—In many sections of the dorsal region examination with a low power shows numerical atrophy of the anterior nerve-cells, which in some cases is more marked on one side, in others is equally well marked on both sides. In such cases the sharp outline of the cells of Clarke's posterior vesicular column and of the tractus intermedio-lateralis contrasts strongly with the ill-defined appearance of the anterior nerve-cells.

However, on examining the anterior horns with a power of $\times 300$ in such cases I have invariably found evidence of the presence of more nerve-cells than one would expect from the previous examination.

These cells have undergone changes that readily explain the difficulty found in recognising their presence with a low power.

In the same anterior cornua, side by side with large, sharply-outlined, multipolar nerve-cells with branching processes, are seen small indistinct cells which have lost their processes. These cells have also a tendency to assume a more or less globular form in some instances, in other cases they are irregularly shaped.

As a rule, the cell protoplasm has become very pale and indistinct, and it is often somewhat difficult to distinguish such cells from the surrounding neuroglia. Vacuoles are found in some of these pale indistinct cells, and the nucleus is generally indistinct or invisible. The globular cells, on the contrary, are often more granular than natural, and stand out sharply.

These granular cells often show a well-marked nucleus. In nearly all these degenerate cells of both types careful focussing shows traces of the original cell processes. In no case did I see any swelling of the nerve-cells. The changes that I observed all tended towards atrophy.

In a few places the neuroglia is coarsely granular. In the neighbourhood of these granular patches are seen degenerate nerve-cells, which are partially encircled by a

somewhat crescentic, coarsely granular mass, resembling the surrounding neuroglia from which it is probably derived. These changes, however, have only a very limited distribution.

With this slight exception the neuroglia shows no change either in its intimate structure or in the number of its nuclei in any part of the spinal cord.

The affection of the motor cells, on the contrary, was found in almost every section from the dorsal region, and was not confined to any particular cell group of the anterior horns. The nerve-cells of the tractus intermediolateralis are unaffected in the dorsal region, though in the cervical segment similar but less marked alterations than those above described are seen in the cells of this group also.

The anterior nerve-cells of the cervical cord show exactly similar changes, but a relatively smaller number of cells is seen to be affected. A fairly large proportion of healthy cells is present in this region. Some sections show only very slight affection of the motor cells.

In the cervical as in the dorsal segment no particular group of nerve-cells is specially attacked.

In the lumbar region almost all the motor cells are quite healthy in appearance, here and there one or two small rather indistinct cells can be seen.

The nerve-cells of the pons and medulla are also quite healthy. No change is visible in the nerve nuclei on the floor of the fourth ventricle.

Drawings are given illustrating the appearances of the affected nerve-cells.

It now remains to estimate the importance of the foregoing changes in the spinal cord. There can be little doubt, I think, that evidence has been given in the present case of a distinct degenerative affection of the motor nerve-cells in special regions. In other words, we have to do with a "polio myelitis anterior."

This polio myelitis is characterised by a somewhat irregular distribution. Healthy and degenerate cells are

seen in one and the same cornu, although in those parts where this affection is most marked the latter decidedly outnumber the former.

This fact to my mind would be enough to negative the hypothesis of a more putrefactive change, if the general appearance of the tissues did not itself sufficiently discredit such an idea. The question as to whether a numerical atrophy of the motor cells is present or not in the affected parts is harder to answer.

This certainly seems to be the case in some sections from the dorsal segments. It will perhaps be objected that in this region the motor cells are least abundant in the normal spinal cord.

This is true as far as it goes, but I think the objection is hardly a sufficient one, as will appear on comparing these sections with those of a normal dorsal region. It may be that owing to their shrunken state the degenerate cells become loosened and so get detached in the various stages of cutting, staining, and mounting the sections. On the other hand, it is not improbable that total disappearance of the motor cells is the last link in the chain of pathological processes of which the degenerative change in the cell protoplasm is the starting point.

A "poliomyelitis" anterior of irregular distribution would sufficiently explain the paralysis that follows diphtheria. Lesions affecting units of a group of motor cells could hardly fail to result in imperfect function of the whole group. And it must be remembered that diphtheritic paralysis is usually rather a weakness or paresis than a complete paralysis.

The varying degree and extent of the poliomyelitis in the different segments of the spinal cord seem to have been accurately represented by the different degree of paralysis in the corresponding muscles. The capillary and venous distension and the accumulation of blood corpuscles in these vessels seems explicable from the fact, that the patient died of slow asphyxia. The collections of

cells around the central canal are probably to be explained in the same way.

In any case this last appearance has only a very doubtful significance in the present state of our knowledge.

No change in the motor nuclei of the medulla was found corresponding to the immobility of the palate. This is not to be wondered at when we remember that the patient's voice was said to have been nasal ever since the angina appeared.

Local causes seem accountable for this condition, whether the diphtheritic lesion affected primarily the muscle-fibres or their terminal nerve endings, though the latter supposition seems more likely.

True paralysis is a sequela of diphtheria, and rarely comes on before the second or third week, while it often develops much later. It is difficult to say when the general muscular weakness set in. But the palsy of the intercostal muscles probably commenced six weeks or so after the onset of the disease, about the time that cough and shortness of breath were noticed.

On this hypothesis death occurred about seventeen or eighteen days after the intercostal paralysis began.

From what has been said it will be seen that the changes in the spinal cord in my case agree very closely with those described by Dejerine and Dr. Abercrombie. The hæmorrhages, cell infiltration, and affection of the neuroglia which Dejerine observed were not present in my case. Dr. Abercrombie's description tallies with mine in this respect. The only changes I found in the grey matter were purely parenchymatous, no interstitial affection could be seen. Dr. Abercrombie's experience coincides with mine in this point too, and as his experience is based on an examination of seven cases I need hardly say that it carries much more weight than mine.

Through the kindness of Dr. Abercrombie I have had the opportunity of comparing his specimens with my own, I am consequently enabled to state that they agree very closely in almost every particular, though the cell degeneration in my case seems rather more advanced ; this may

be due to the fact that Dr. Abercrombie's cases proved more rapidly fatal than mine.

Now, if we enumerate the cases of diphtheritic paralysis which have been published in which changes in the motor cells of the spinal cord are described, we find that there are fifteen in all.¹ This includes five cases published by Dejerine, two by Vulpian, seven by Dr. Abercrombie, and lastly my own case.

Against these we have to put the negative results obtained by Hermann Weber, Oertel, Pierret, and Vulpian, making four in all.

We must omit from our calculation cases in which no mention is made of a microscopic examination of the spinal cord. Moreover, those cases where the palate was the only part paralysed, are open to the objection that the paralysis may have been due to local causes only. At any rate this possibility cannot be excluded.

These objections apply to the cases of Charcot and Vulpian, Lorain and Lépine, Liouville and Leyden. How, then, are we to account for the negative results obtained by Hermann Weber, Oertel, Pierret and Vulpian? I confess that this is very difficult in the case of such excellent observers. But I would suggest that in proportion to the length of time the paralysis has existed before death we may expect to find greater or less changes in the motor cells.

In rapidly fatal cases of paralysis the cell changes may be possibly so slight as to escape detection even by competent investigators. It was long before the spinal lesion of progressive muscular atrophy and infantile paralysis obtained full credence, but I believe that, like these diseases, diphtheritic muscular paralysis will be shown to depend upon a "poliomyelitis anterior."

¹ Since this paper was written similar changes have been found in a case of diphtheritic paralysis by Dr. Mott, of Liverpool.

DESCRIPTION OF PLATE IV.

(Pathology of Diphtheritic Paralysis. PERCY KIDD, M.D.)

FIG. 1.—Part of anterior horn, mid-dorsal region, showing contrast between indistinct shrunken nerve-cells (*a a*) and healthy ones (*b b*). $\times 300$.

FIG. 2.—Individual nerve-cells from anterior cornua, mid-dorsal region, in different conditions of degeneration; some granular, globular, and nucleated; others pale, indistinct, and showing no nucleus. (*x*) One large healthy cell from same cornu. $\times 300$.

FIG. 3.—Degenerate nerve-cells of different kinds, all of small size. One large healthy cell. Dorsal region. $\times 300$.

FIG. 4.—Degenerate nerve-cells from lower dorsal and cervical region. One pale irregular nerve-cell shows vacuoles in its protoplasm (*v*). $\times 300$.