Neurological Section.

January 19, 1911.

Dr. J. A. ORMEROD, President of the Section, in the Chair.

Progressive Spinal Muscular Atrophy of Infants and Young Children.

By FREDERICK E. BATTEN, M.D.

INTRODUCTION.

THE occurrence of progressive paralysis and muscular atrophy due to a lesion of the lower motor neuron is a condition of some rarity both in infants and young children. During the past ten years I have seen some eight cases which may be placed under such a heading. Some of these have been under my own care, others under the care of my colleagues, but I have made the pathological examination in all cases in which an autopsy has been obtainable. Some of these cases have already been published. It is from a consideration of these cases that I propose to deal with the somewhat difficult problem of progressive spinal muscular atrophy of infants and young children. It will be well in the first place to mention certain classes of cases, which though they may show progressive muscular atrophy dependent or independent of spinal disease, it is not intended to deal with in this paper. Into this category are placed: (1) The primary muscular atrophies (myopathies), and with these I include the condition known as "myatonia congenita"; (2) the effects of acute poliomyelitis; (3) spinal or spinal root injury; (4) congenital defects of the cord; (5) the peroneal type of muscular atrophy (Charcot-Marie-Tooth); (6) von Recklinghausen's disease; (7) the effects of spinal caries and spinal growth.

The eight cases on which this paper is based may be arranged in three classes; each class will be dealt with in a separate chapter. A short statement of the clinical and pathological features of the cases belonging to each class will be found at the beginning of the chapter; but for a full clinical report and details of pathological examination reference should be made to the appendix for those cases not already published, and to the article referred to for those which have been published.

Of the eight cases *six* belong to the first class, *one* to the second class, and *one* to the third class. The characters of these three classes may be stated as follows:—

(1) A type of case in which progressive muscular weakness occurs during the first weeks or months of life, gradually progresses, and terminates in death after a variable period of weeks, months, or years. Sometimes more than one member of the family may be affected. Atrophy of the cells of the anterior horn is the constant pathological change found in such cases, but it may be associated with other changes in the central nervous system (Werdnig-Hoffmann type).

(2) A type of case in which progressive muscular weakness and atrophy begins somewhat later in life, after the child has already walked, and slowly progresses till death occurs from respiratory failure or pneumonia. The pathological changes found in such cases consist in a degeneration of the lower motor and sensory neurons resembling those occurring in a "toxic neuritis."

(3) A type of case in which progressive muscular weakness and atrophy begin in later life after the child has already walked, slowly progress, and are attended by very marked degeneration of the spinal cord, not limited to any one group of cells or tracts (a "myelitis").

Chapter I.—Werdnig-Hoffmann Type.

The cases which belong to this type are six in number, and the following is a short abstract of the clinical features and pathological changes in those cases in which a post-mortem was obtained:—

Case I.—C. H., aged 4 weeks. First child of healthy parents; no miscarriages. Said by the mother to be healthy at birth. Took breast well for fourteen days; then fed on goat's milk. Wasting and weakness of the limbs noted when 14 days old; got tired when sucking. The child never cried well. On admission to hospital, small child, 5⅛ lb., feeble cry. A complete flaccid paralysis of arms and legs, with slight movements of fingers and toes; neck

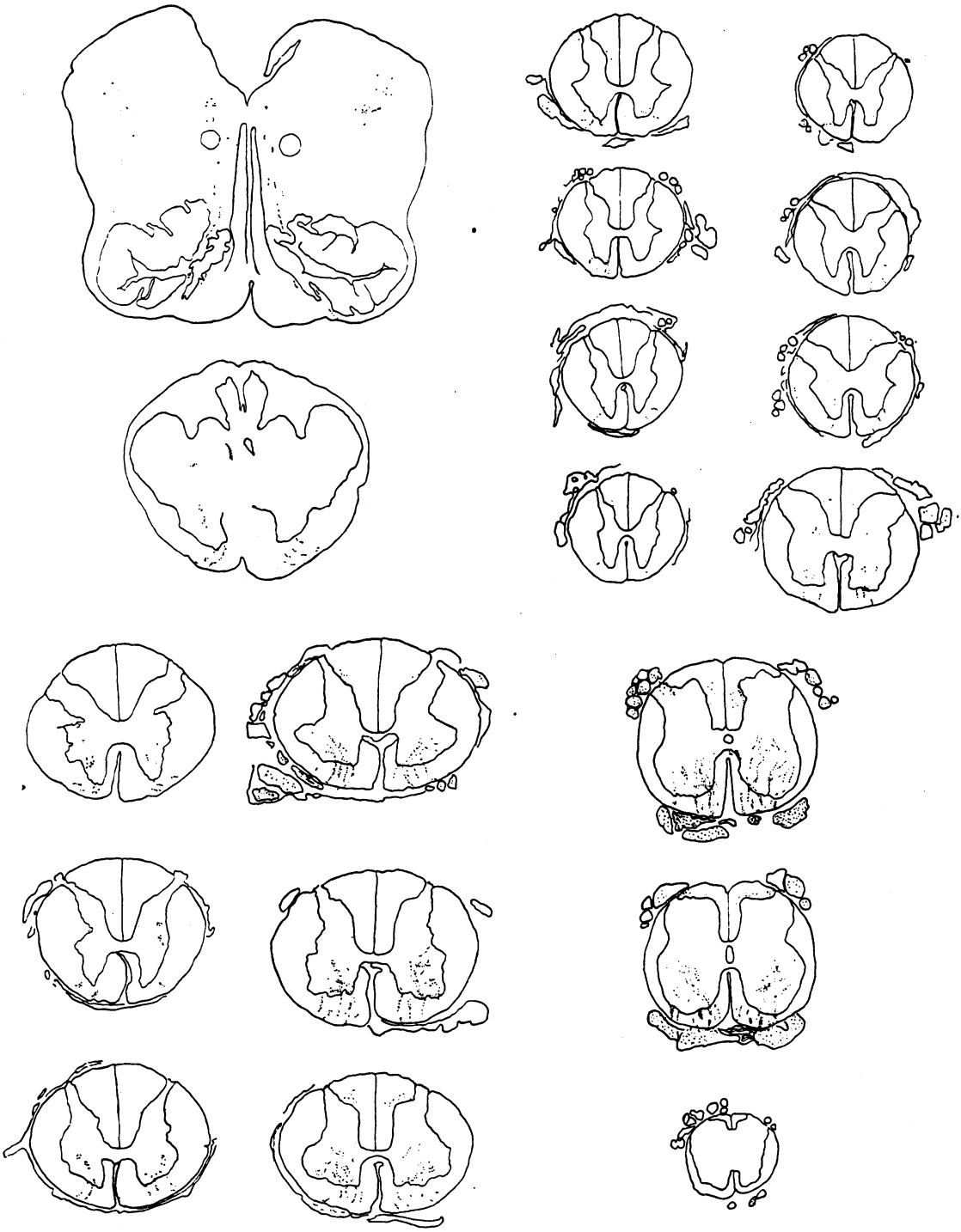

FIG. 1.—Series of section through the spinal cord, from Case I, C. H., stained by the Marchi method, showing the degeneration of the anterior root. The stress of the disease is seen to fall on the lumbar and the cervical region of the spinal cord, but some degeneration is present throughout the whole length of the cord and medulla.

muscles flaccid. Sucks well, no regurgitation; deep reflexes absent, sensation apparently normal, no reaction obtained in muscles by strong faradic current. Death after three days.

Post-mortem: Nothing abnormal to naked eye in visceral or nervous system. No evidence of birth injury. Microscopical examination: Marked degeneration of anterior nerve-roots throughout the cord; some chromatolysis of anterior horn cells; no evidence of muscular degeneration. (*See* figs. 1, 2, 3, 4, 5, 6.) (*See* Appendix.)

Case II.—W. G., aged 5 weeks. The eighth of eight children, three of whom have died of a similar complaint within the first few months of life.

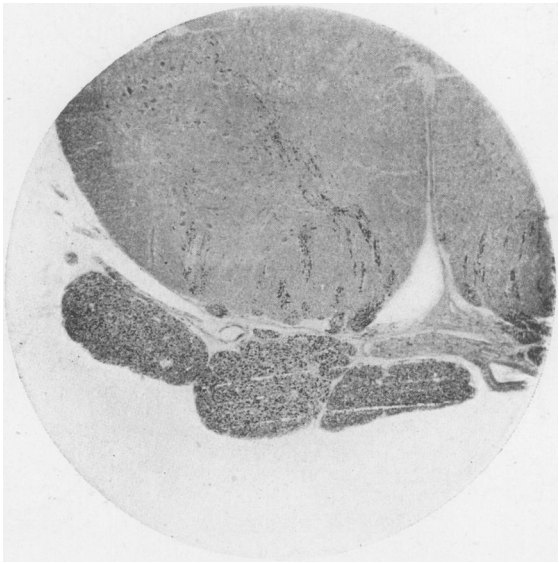

FIG. 2.

Photograph of the anterior region of the sacral cord from Case I, C. H., showing the degeneration of the anterior nerve-roots in their intramedullary course. Stained by the Marchi method.

The labour was difficult. On admission to hospital the child was well nourished, looked healthy, and took food well. There was complete flaccid paralysis of all four limbs, except for slight movements of the fingers. There was complete paralysis of the trunk muscles and intercostals, but the diaphragm acted well. All the deep reflexes were absent; there was analgesia below the second rib. The child died when 8 weeks old of broncho-pneumonia.

Post-mortem: Nothing abnormal on macroscopical examination; but on microscopical examination widespread atrophy of the cells of the anterior horn, and degeneration of the fibres of the posterior column. (*See* figs. 7 and 8.) (See *Brain*, 1902, xxv, p. 85.)

Case III.—E. T., aged 4 months. Fourth of four children, one of whom was said to have died of a similar complaint. Easy labour. General helplessness noticed one week after birth ; gradually increased. On admission, flaccid paralysis of arms and legs, absence of deep reflexes, paralysis of intercostals. Death. No post-mortem. (*See* Appendix.)

Case IV.—P. B., aged 6 months. Fourth of four children. Full term ; normal labour. Healthy at birth. Gradual onset of weakness first noticed in the arms when 4 months old. Well nourished, intelligent child. Flaccid paralysis of arms, legs, trunk, neck. Paralysis of intercostals. Absent reflexes. Sensation apparently normal. Death. No post-mortem. (*See* Appendix.)

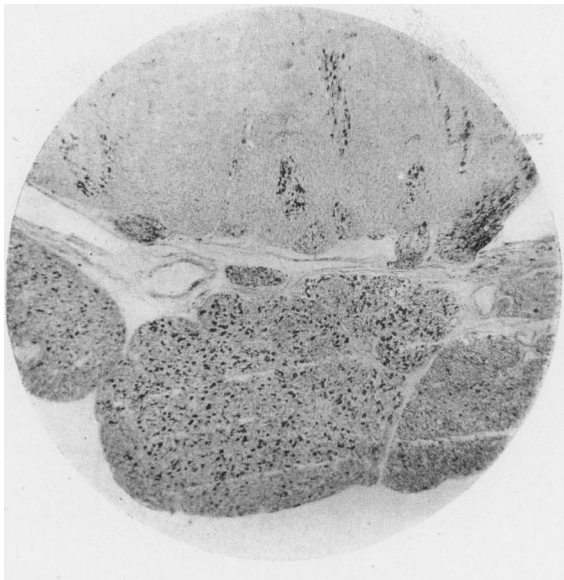

FIG. 3.

Photograph of anterior roots showing degeneration of the anterior roots in their extramedullary course. Stained by the Marchi method.

Case V.—H. C., aged 8 months. Third of three children, others healthy. Breast-fed. Normal labour. Always weak ; never able to sit up or hold its head up. Weakness has increased. There was flaccid paralysis of both arms and both legs. Weakness of back muscles with lateral curvature of the spine. Knee-jerks only obtainable with difficulty. Death after four days in hospital.

Post-mortem : Nothing abnormal on macroscopical examination. On microscopical examination some degeneration of the anterior roots and some chromatolysis and atrophy of the cells of the anterior horn. (*See* Appendix.)

Case VI.—R. A., aged 3½, one of twins. Never learnt to sit up. Learnt to talk early. When 15 months old could not move his legs, but could move

the arms. When first seen in June, 1910, he was quite intelligent, had flaccid paralysis of both legs, was quite unable to sit up or maintain a sitting position; he could, however, hold up his head. Sensation was perfect. The knee-jerks were absent. The intercostals paralysed. He died from broncho-pneumonia in September, 1910.

Post mortem: Broncho-pneumonia. Microscopical examination showed smallness of anterior nerve-roots of the spinal cord, and marked atrophy of the cells of the anterior horns. No Marchi degeneration. No vascular change. (*See* figs. 9 and 10.) (*See* Appendix.)

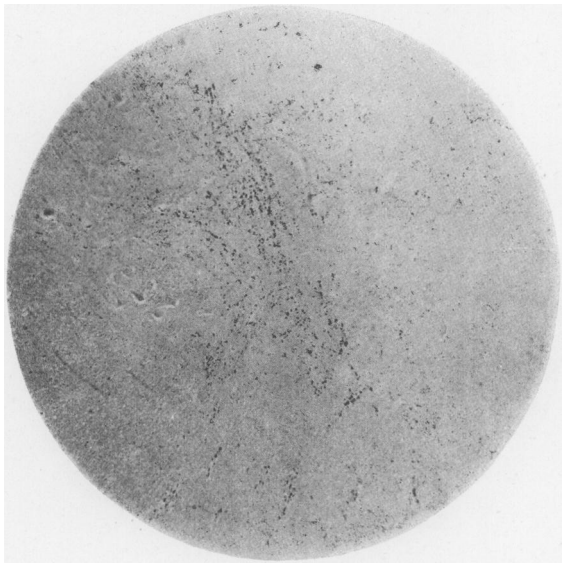

FIG. 4.

Photograph of grey matter, showing degeneration of fine fibres arising from cells of anterior horns. Stained by the Marchi method.

Clinical Features of Class I.

An infant born at full term and apparently normal at birth begins in the first few weeks of life to show weakness of the trunk and limbs. The infant appears of normal intelligence. The weakness steadily progresses, so that there is a complete flaccid paralysis of both arms and legs, and only a little movement is preserved in the fingers and toes. The intercostal muscles become paralysed and the child dies from some intercurrent disease, generally of broncho-pneumonia. Several members of a family may in succession be affected, as in the Case II, where four children out of a family of eight were thus affected. In Case III,

another member of the family is said to have died from the same disease.

The clinical picture which these infants present is very striking: The infant lies in bed, happy and contented, taking his food well, but completely unable to move either arms or legs, the limbs being perfectly flaccid. The disease tends to affect the proximal muscles before the distal, so that all movements of the fingers and toes are still possible after power has been lost in the shoulders and hips. If an attempt is made to lift up the child the extreme flaccidity of the trunk muscles is easily recognized. The actual wasting of muscles in some cases is not obvious, for it is covered up by the subcutaneous fat. The child will, as

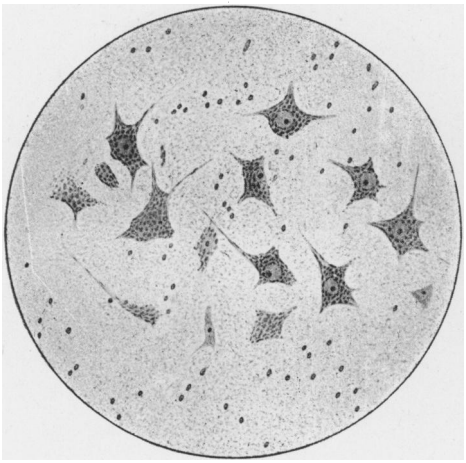

FIG. 5.

Cells of the anterior horns of cervical region, stained by the Nissl method, from Case I, C. H. Most of the cells appear normal; some, however, show slight chromatolysis.

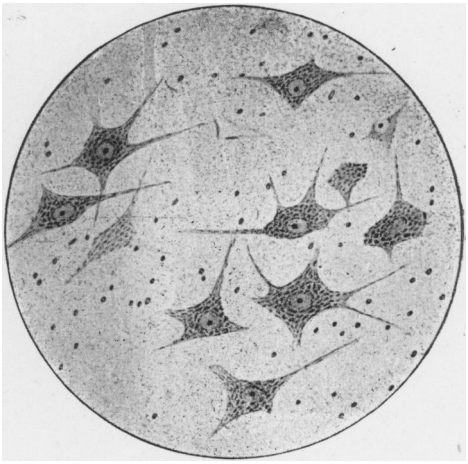

FIG. 6.

Cells of the anterior horns of the lumbar region, stained by the Nissl method, from Case I, C. H. The cells as a whole appear strikingly normal in appearance, considering the marked change seen by the Marchi method; some, however, show slight chromatolysis.

a rule, rapidly respond by crying when pricked by a pin, and as far as can be judged, sensation is perfect. All the tendon reflexes are either absent or greatly diminished. In those cases in which the electrical reactions have been examined the absence or great diminution of excitability to the faradic current is a most striking feature. The duration of life in most of these cases is limited by months, but in one case of the present series it was considerably longer—viz., three and a half years.

Pathological Features of Class I.

The clinical features of the disease are fairly constant. The pathological features differ somewhat. These differences may depend upon the length of time the disease exists before a fatal issue ensues; for that issue, although dependent in part on the progress of the disease, and especially on the paralysis of the intercostal muscles, is often accelerated by the occurrence of broncho-pneumonia.

In four of the six cases belonging to this class a pathological examination was made—viz., Cases I, II, V, VI.

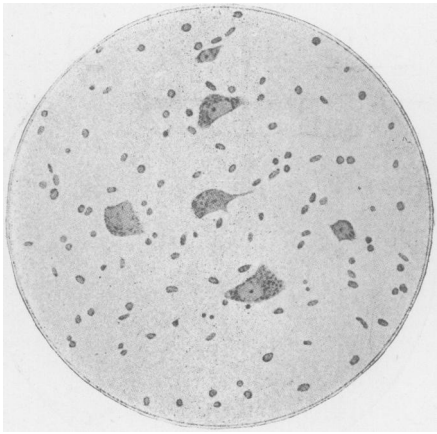

FIG. 7.

Cells from the anterior horns of the cervical region, stained by the Nissl method, from Case II, W. G., showing marked atrophy. Compare them with the normal-sized cells of fig. 5. (Drawn under same magnification, 170 diameters.)

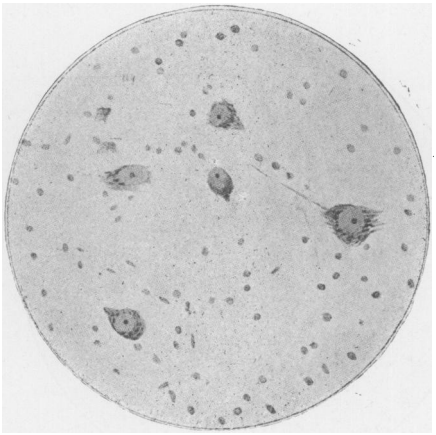

FIG. 8.

Cells from the anterior horns of lumbar region from Case II, showing same condition.

In Case I there is the most marked degeneration of the medullary sheath of the fibres of the anterior roots of the spinal cord from their origin in the cells of the anterior horns, in their intramedullary course through the cord, and in their extramedullary course (figs. 1, 2, 3, 4). This degeneration is most strikingly shown by the Marchi method. The peripheral nerves show but little change. The cells of the anterior horns show but little change, when considered in relation to the marked change in the fibres. Some few cells undoubtedly show chromatolysis (figs. 5 and 6), but only a few compared to the numbers of fibres which are affected. (Compare figs. 1, 2, 3, 4, 5, 6.)

The muscles in Case I do not show any marked change, the muscle-fibres being in the condition seen in a late fœtal or infantile life.

The changes met with in Case II are somewhat different. In this case there is a marked atrophy of the cells of the anterior horn throughout the cord (figs. 7 and 8), without the striking degeneration of the anterior roots as shown by the Marchi method. There is some degeneration of the posterior column of the spinal cord. The muscle shows a cruious mixture of atrophy and hypertrophy of muscle-fibre, but no fibrosis.

The changes met with in Case V are similar to those in the two former cases, but differ in the following respects, viz., that the Marchi

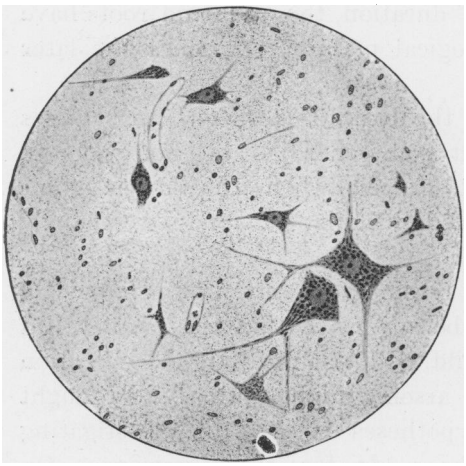

FIG. 9.

Cells from the anterior horns of the cervical region, stained by Nissl method, from Case VI, R. A., showing marked atrophy of cells, two normal cells alone remaining.

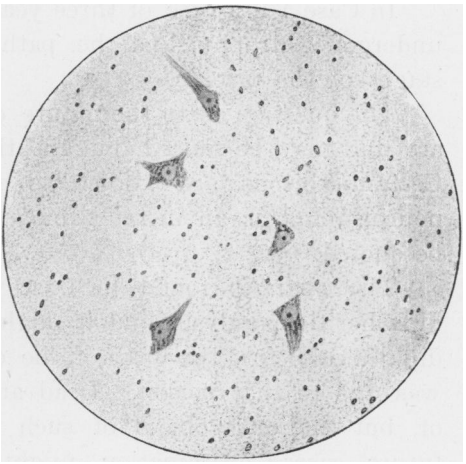

FIG. 10.

Cells from lumbar region of Case VI, showing similar changes. (Magnification 170 diameters.)

degeneration is less marked than in Case I, and more marked than in Case II, while the chromatolysis is more marked than in Case I and less marked than in Case II.

The changes met with in Case VI are similar to those seen in Cases II and V—viz., the marked atrophy of the cells of the anterior horns, and of the anterior roots, only a few normal cells persisting. (Figs. 9 and 10.)

If the pathological findings in these four cases are carefully considered together, may not the differences be explained partly by the

intensity of the poison, and partly by the duration of the disease? In Case I the appearance is very similar to that met with in diphtheritic paralysis, the most marked changes being visible in the medullated sheath of the nerve, whilst the cells exhibit but little chromatolysis. At a later stage the products of degeneration shown by the Marchi method become absorbed, whilst the chromatolysis and atrophy of the cells as shown by the Nissl method become more marked. Such a condition is well exemplified in Case V, where there is a condition both of chromatolysis and atrophy of the cells, with some degeneration of the myelin sheath of the fibres, an appearance compatible with a more chronic course, dependent on a lesser dose of the toxin. The longer clinical history of this case corresponds with such a result.

In Case VI, a case of three years' duration, the cells and roots have undergone atrophy, and the pathological picture represents the later stages of the disease.

The question as to the nature of the toxin to which these changes are due may be raised, but on that point there is yet no evidence. Certain poisons are known to act especially on the lower motor neurons, and as an instance of such, diphtheria, lead and arsenic may be quoted.

The changes found in Case I resemble closely those found in diphtheritic paralysis, and it might be suggested that the mother had diphtheria before the birth of the child, and the resulting degeneration was due to that poison. Lead and arsenic might similarly be thought of, but the only object of such hypotheses is that in investigating future cases, examination might be made for these poisons. On the other hand, the occurrence of the disease in families, although not absolutely excluding the toxin theory, yet renders such a view improbable, and would seem to point to the condition being due to what Sir William Gowers has termed an "abiotrophy," that is, a "degeneration dependent on a defective vital endurance."

Recently Catola has examined the nervous system of infants born of parents suffering from various diseases. The changes which he figures and describes in the cells of the anterior horns and in the anterior roots in the child of an eclamptic mother and in that of a syphilitic mother are strikingly similar to those described in Case I of my series.

Chapter II.—Toxic Neuritis.

Abstract of Case.

Case VII.—H. M., aged 3. Weakness of limbs first noticed when 3 years old; the weakness gradually progressed, but there were considerable remissions, during which the child improved. Deep reflexes became abolished. Muscles of trunk, intercostals and diaphragm became involved. Death from broncho-pneumonia fourteen months after onset.

Post-mortem: No macroscopic change in nervous system. On microscopical examination chromatolysis of the cells of the anterior horns and degeneration of the peripheral nerves. Fatty degeneration of muscles. (Figs. 10 and 11.)

Clinical Features of Class II.

The case which is placed in this class is one which was under the care of my colleague Dr. Voelcker, and was shown by him at the Medical Society, November, 1908, and February, 1909. I saw the child on various occasions. One of the most striking features of the case was, that although the disease was slowly progressive, yet there were periods during which improvement took place. The disease ran its course in a period of fourteen months.

The clinical features of this class as based on this case are as follows:—

An apparently healthy and intelligent child, who had made normal progress, without any obvious cause was noticed one morning to be unable to walk properly and to fall after taking a few steps. This weakness gradually progressed, so that the child became unable to walk and unable to feed herself. There was incontinence of urine and fæces for a time. There was a transient weakness of the muscles of the face. All the deep reflexes became abolished. The muscles showed the reaction of degeneration. The respiratory muscles became affected. Sensation was unaffected, and there was no pain.

Some improvement took place for a few months, then the disease steadily advanced and the child died some fourteen months after the first symptom.

Pathological Features of Class II.

The brain and spinal cord to the naked eye appears quite normal, and on microscopical examination no change could be shown by the Weigert-Pal method. Some slight degeneration is seen by the Marchi

method, both in the white matter of the cord and in the anterior and posterior roots. Some of the cells of the anterior horn, both in the cervical, dorsal and lumbar region show chromatolysis, others have already undergone atrophy. (Figs. 11 and 12.)

The peripheral nerves show a considerable amount of degeneration by the Marchi method. The changes appear to be more marked in the peripheral nerves than in the central nervous system.

The muscles and fibres of the diaphragm show a marked fatty degeneration by the Marchi method.

The changes found are probably the result of some toxin affecting the lower neurons ("toxic neuritis").

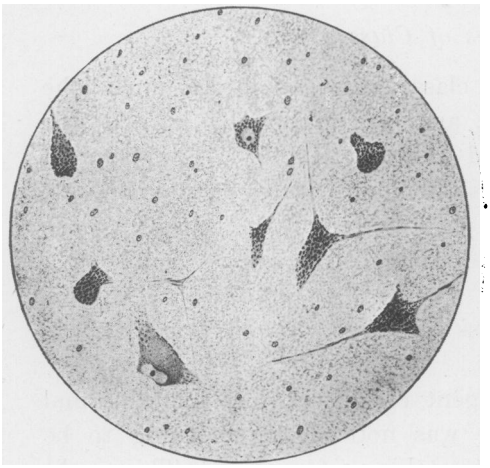

FIG. 11.

Cell from anterior horn of the cervical region from Case VII, H. M., showing marked chromatolytic changes. Stained by Nissl method. (Magnified 170 diameters.)

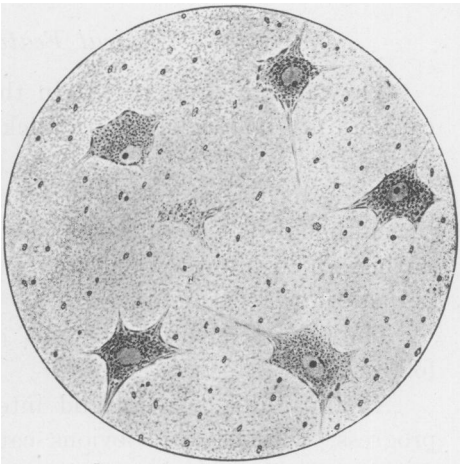

FIG. 12.

Cells from anterior horn of lumbar region, from Case VII, H. M., showing marked chromatolytic changes similar to those in the cervical region. Stained by Nissl method. (Magnified 170 diameters).

This case has been classed as a "toxic neuritis," partly on clinical grounds, partly on pathological grounds. The clinical history of the case is distinct from that of the cases which form Class I. The onset of the disease, the irregular course, the reaction of degeneration, the affections of the diaphragm, are all symptoms to which, if taken singly, no special value in the differential diagnosis could be attached, but if taken together suggest a poison acting diffusely in the lower neurons, rather than a poison which is acting primarily on the cells of the anterior horn.

On pathological grounds the extensive degeneration of the peripheral

nerves as compared to the slighter changes in the cells of the anterior horns, together with the character of those changes, seem to me to be points in favour of regarding this case as one belonging to the class of "toxic neuritis."

It is admittedly one of the most difficult problems in neurology to differentiate between cases of "toxic neuritis" and those due to degeneration of the cells of the anterior horn.

On clinical grounds there is no doubt that the distinction is useful; on pathological grounds it seems to me doubtful if the distinction can be drawn between affections of various portions of the lower motor neuron, but for the present I would classify those cases which show rather diffuse changes in the peripheral nerves, and but little change in the anterior horn cells or anterior roots, as "toxic neuritis," and those cases which show marked changes in the anterior horn cells and anterior roots, and but little or scattered degeneration in the peripheral neurons, as "spinal atrophies."

The question as to the advisability of including such a case in a series of cases described as progressive spinal muscular atrophy might be raised. Few, I think, will be disposed to press this objection against the obvious advantages of considering together cases which have a marked clinical similarity.

Chapter III.—Chronic Myelitis.

Abstract of Case.

Case VIII.—M. L., aged 11. Twelve months' weakness of hands, four months' weakness of legs. Gradual increase of weakness and muscular atrophy. Reaction of degeneration in some muscles. Sudden death from respiratory failure eighteen months after onset of illness.

Post-mortem: Extensive myelitis of both grey and white matter of the spinal cord, giving rise to atrophy of the cells of the anterior horns. (*Brain*, 1903, xxvi, p. 473.)

Clinical Features of Class III.

The case on which the third class is described is one which was published in *Brain*, 1903, by Dr. Morley Fletcher and myself. It is in its clinical and pathological manifestation entirely distinct from the other two groups, and yet it possesses the characteristic feature—viz., progressive muscular atrophy of spinal origin.

The clinical features are given in the following short abstract :—

A girl, aged 11. Twelve months' weakness of hands; seven months

unable to button clothes; four months' weakness of legs. Two months ago adenoids removed and much worse since that operation. Fourteen days' pain in back and increased difficulty in swallowing. Intelligent, deaf, some atrophy of tongue, palate moves well on phonation, weakness of neck, respiration thoracic, upper intercostals only in use. Claw-hand, wrist-drop, weakness of upper arm and shoulder muscles. Can walk but feebly; knee-jerks brisk, plantars flexor. Sensation natural to all forms. Electrical reaction shows R.D. in some muscles, in others only diminution of excitability.

Sudden death from respiratory failure six months later.

Pathological Features of Class III.

There is extensive destruction and atrophy of the cells of the anterior horn from the upper cervical to the lower thoracic segments, these changes being most marked at the level of the sixth thoracic segment; the cells of Clarke's column being also affected. There is extensive degeneration of the whole of the ventral region of the cord in the thoracic segments, the lesion being most marked at the level of the sixth thoracic segment, and diminishing in extent both towards the medulla and caudally. There is extensive degeneration of the direct cerebellar tracts, both dorsal and ventral, beginning in the lower thoracic segments and extending up to their respective termination in the cerebellum. The degeneration affects both grey and white matters alike.

There is a marked increase of the connective tissue in the ventral portion of the cord. The walls of the vessels show no change. The cords show both recent and old degeneration. (*Brain*, 1903, xxvi, p. 473.)

This case must be regarded as a chronic form of diffuse myelitis, secondary to some vascular changes and toxic blood state. The origin and cause of the myelitis and of the peculiar distribution is unexplained.

Chapter IV.—Diagnosis.

The differential diagnosis in the first class of cases above described is one of the greatest difficulties. A child who at the *time of birth* has a complete flaccid paralysis of all four extremities is probably the subject of a spinal hæmorrhage, due to traumatism at birth. The child who

during the first few weeks or months of life *develops* a flaccid paralysis of all four extremities is probably the subject of a spinal atrophy; but the difficulty of differentiating these two conditions is well shown in the two cases recorded by Dr. Beevor. Two children, when a few weeks old, exhibited the same clinical picture, viz., that of a complete flaccid paralysis, and yet on pathological examination it was found that in the one case the condition was due to spinal hæmorrhage, in the other to an atrophy of the anterior horn cells. In children rather more advanced in age other questions come up for consideration, and one of the most difficult is the distinction of a primary spinal condition from a primary muscular condition or myopathy.

The forms of myopathy which occur in young children become year by year more generally recognized. The "simple atrophic" type of Erb and the condition known under the name "myatonia congenita" may easily be mistaken for the Werdnig-Hoffmann paralysis. Myatonia congenita is a disease of early childhood, characterized by an extreme degree of loss of tone and feebleness in all the muscles of the body. The condition is stated to improve as the child advances in age.

A child with this disease can, as a rule, perform all movements in a feeble manner, and there is not the marked degree of flaccid *paralysis* seen in the case of spinal atrophy. Although hypotonia is present in cases of spinal atrophy, yet it is not so marked as in cases of myatonia congenita. Again, the intercostal muscles are commonly paralysed in the spinal atrophy of infants, whereas in myatonia they are less affected.

Shortly, it may be said that in spinal atrophy the paralysis is more marked and the hypotonia less marked than in cases of myatonia congenita.

The difficulty of diagnosis is well exemplified by the three cases in one family described by Finkelnburg. These would, on clinical grounds alone, be assigned to the Werdnig-Hoffmann group, and yet on pathological examination he has shown that they belong to the myopathic group—there being no change in the spinal cord, and changes in the muscles typical of myopathy.

Spinal caries may, under certain circumstances, rather closely simulate this disease, especially when the tuberculous process has spread in through the membranes and invaded the spinal cord. Cases of widespread poliomyelitis occurring during infant life may clinically resemble Werdnig-Hoffmann paralysis, but the paralysis and atrophy of muscles is rarely symmetrical, and groups of muscles tend to be picked out, others being left unaffected.

In the second and third class the diagnosis is no more easy than in the first group, and even with the pathological knowledge obtained from the examination of these cases, it would be most difficult to assert in cases presenting similar symptoms what was the cause of the widespread progressive muscular atrophy.

Chapter V.—Literature.

Since the year 1898 there are only some five cases of the disease recorded in which there has been a pathological examination. These are the cases recorded, one by Hoffmann, one by Beevor, two by von Ritter, and one by Armand-Delille and Boudet. Previous to that date there are the well-known cases of Werdnig and Hoffmann on which the clinical features and pathology of the disease are founded, to which may be added the case recorded by Thomson and Bruce—i.e., ten cases; to these may be added the three cases in this paper, making thirteen cases in all.

Of cases without autopsy there are those recorded by Senator, Sevestre, Bruns, Wimmer, Haushalter, Lange. Some of these, and notably those of Bruns, Senator, Haushalter, and Lange, and the second case of Wimmers, should almost certainly be classified as myopathies and not with the Werdnig-Hoffmann group. The earlier cases of Werdnig and Hoffmann have already been reviewed in *Brain*, 1897. The later case of Hoffmann and those of Beevor, von Ritter, Armand-Delille and Boudet will be considered.

Hoffmann in 1900 recorded the result of the autopsy on the child M. G., the details of whose case had already been published in 1897. The paralysis slowly progressed, only feeble movements of the hands and feet remaining till the end. The face, tongue, muscles of deglutition, remained unaffected. The higher senses were normal, and there was no affection of the bladder or rectum. Sensation remained intact. The child died when 5 years old of pneumonia. On examination of the spinal cord there was found to be atrophy of the intra- and extra-medullary portions of the anterior roots, degeneration and wasting of the multipolar ganglion cells, and degeneration of the peripheral nerves. The pyramidal tracts showed no change. There was wasting of the muscle-fibres with fatty degeneration and interstitial fat.

Beevor's case, published in 1902, is recorded in the Appendix, and is one of those included in the substance of the paper. Shortly, the leading

features are as follows: An infant, the eighth of a family of eight, four of whom had been similarly affected, had flaccid paralysis of all four limbs. The child died at 2 months old, and extensive atrophy of the cells of the anterior horns was found.

Von Ritter, in 1904, described two cases. The first, a female child, 15 months old at the time of death, the only child of healthy parents, born in normal labour, and suckled till 10 months old. When 5 months old it was noticed that the child moved its legs but little, and she seemed to get weaker in the upper extremities. The child was fat, not rickety, and had a flaccid paralysis of all its limbs. The face, mental condition, sight, and hearing were quite normal. On examination, the spinal cord showed marked atrophy of the cells of the anterior horns and atrophy of the muscle-fibres, with fatty degeneration. The second case, a female child, the second of two children, the first being quite healthy. The birth was normal. During the first year of life the parents noticed nothing amiss. In the second year of life the child gradually began to develop weakness in the lower extremities, and she had, by the end of the second year, complete loss of power in the legs, and had paresis of the arms. There was marked wasting of the buttocks, standing was impossible, sitting was possible, all the visceral functions were normal, the deep reflexes were abolished. The child died when 2 years old. On pathological examination, the anterior roots of the spinal cord were found to be very wasted, and very few normal ganglion cells remained. The muscles showed atrophy of the muscle-fibres and a marked lipomatosis. The cord does not seem to have been examined by the Marchi method.

Armand-Delille and Boudet, in 1908, described the case of a child, 5 months old, the first of two healthy parents. The infant had made normal movements of the new-born during the first weeks of life, but when 2 months old weakness of the limbs was noticed. The muscles of the neck were also weak, and the head flopped to the side.

On examination there was almost complete paralysis of the four limbs and muscles of the neck. There was paralysis of the intercostal muscles. The diaphragm alone carried on respiration. The thorax was deformed. Cutaneous sensation was preserved. All the deep reflexes were abolished. There was absence of response in the muscles, both to faradic and galvanic currents. The sphincters were intact. On account of the subcutaneous fat it was impossible to feel the muscles, which were paralysed and in the course of atrophy. The child died when

5 months old. On examination of the muscle, the nuclei appeared very abundant, and the muscle-fibres markedly degenerate. Some bundles were completely replaced by connective tissue, some of the muscle-fibres preserved their striation, but most were already in a stage of advanced atrophy. A perivascular and interstitial sclerosis was present. The muscle-fibres of the diaphragm were normal. In the peripheral nerves a number of the fibres had disappeared. The anterior roots were atrophied, the posterior roots were intact. The posterior root ganglia showed no change. The white matter of the cord was normal. There was very marked atrophy of the cells of the anterior horns and of the anterior roots. The cells which were less affected showed chromatolysis. The atrophy of the cells of the anterior horn contrasts with the normal appearance of those of Clarke's column. The meninges were intact. All these cases may be accepted as examples of the disease.

The cases, without autopsy, arrange themselves in two groups—those which from their clinical symptoms may be considered as examples of the disease, and those which from their clinical symptoms it would not seem justifiable in the absence of any pathological evidence to the contrary, to include under the Werdnig-Hoffmann group.

Group I.—Cases which, from their Clinical Symptoms, and without an Autopsy, may be considered as Examples of the Werdnig-Hoffmann Type.

In the first group may be placed the cases of Sevestre and Wimmer's first case, while in the latter group I should place those of Haushalter, Bruns, Senator, and Lange.

Sevestre showed the case of an infant $2\frac{1}{2}$ months old, with complete flaccid paralysis of the body, only the muscles of the head, neck, and diaphragm remaining normal. The muscles of the extremities were atrophic, and they had lost their faradic irritability and gave an anodal contraction on galvanic stimulation. The thorax was deformed. Two other members of the family of six had had the same affection and had died when a few months old. In the discussion Hutinel said he had seen a similar condition in two children born in a breech presentation, and he attributed the condition to spinal hæmorrhage. In one case, however, in which an autopsy was obtained, no such hæmorrhage was present.

Wimmer's case is that of a boy, aged 16 months. The labour was normal, and no other members of the family were affected. A few

months after birth difficulty in sucking was noticed. The infant was always very weak, could not raise the arms, but could move the fingers and hands. The child could move the toes, but not the legs or thighs. The neck muscles were weak. The child was not imbecile, had no enlargement of the head, and the movements of the face, eyes, and tongue were normal. The child was a cryptorchid. The deep reflexes were absent. The muscles showed altered electrical reactions. He compares it to Beevor's case and says that it most resembles that.

GROUP II.—CASES WHICH, FROM THEIR CLINICAL SYMPTOMS, AND WITHOUT AN AUTOPSY, SHOULD NOT, IN THE OPINION OF THE WRITER, BE REGARDED AS BELONGING TO THE WERDNIG-HOFFMANN TYPE.

With regard to the second group of cases without autopsy, recorded by Haushalter, Bruns, Senator, and Lange, I am unwilling to accept any of these as cases of muscular atrophy due primarily to atrophy of the cells of the anterior horn. Haushalter, indeed, regards his cases as primarily myopathic, though described under the title "Amyotrophie primitive progressive dans l'enfance," the first being a fairly typical case of facio-scapulo-humeral type, the second belonging to the simple atrophic type, and the third probably to the myatonia congenita type, though in many features this case most closely resembles the Werdnig-Hoffmann type.

Bruns records three cases from different families. In the first family two sisters had died of the same complaint. In the second family there was no other case. In the third family the two elder and one of the younger members were healthy. Bruns counts these as five cases, and added to the nineteen cases already published by Hoffmann, and the two cases by Werdnig, and one by Bruce, says that there are now twenty-eight recorded cases of the disease.

The first case is that of a girl, I. R., aged 10, the fourth of four children. The family history was as follows: The first child, a boy, stood and walked at 9 months. Paralysis then occurred and he died when 4 years old. The second, a girl, died from inflammation of the lungs when 3 years old. The third, a boy, normal at birth, developed well till 9 months old, began to sit up, but could not stand, the hands were unsteady. When 2½ years old he was examined. The child could just sit up, but easily fell backward. The legs could not be bent at the hips, the weakness of the quadriceps extensor was

very marked. There was loss of faradic irritability in the muscles, and a very weak reaction to galvanism. The weakness gradually extended and the child died when 3 years old. There was no post-mortem.

The girl, I. R., developed fairly well in the first two years of life. She nearly walked at $1\frac{3}{4}$ years, after which no progress was made. She frequently fell, and her gait became progressively worse. Weakness of the arms came on at a later date. When seen in 1894 there was very marked curving of the spine, wasting and feebleness of the arms, a weakness of the legs. The paralysis was of a flaccid character. The deep reflexes were absent. The lower arm and hands were less affected than the shoulder muscles, and the toes less affected than the upper portion of the leg. Fibrillary tremors were present. There was loss of electrical excitability, but no distinct reaction of degeneration. Intelligence, sensation and sphincters were normal. In 1896 the weakness had increased and she had difficulty in holding up the head. In 1898 there was still more weakness, atrophy of the shoulder girdle and the thighs, and more wasting of the calf muscles. In 1900 she died, when 16 years old. There was no autopsy.

The second case, E. F., aged 11. Nothing is known of the family history. She had general weakness of the shoulders and hips, standing was impossible, there was a marked kyphosis, fibrillary tremor in the shoulder muscles, diminished electrical reaction, absence of the deep reflexes. She remained in this condition.

The third case, A. N., boy, aged 3; two older brothers, aged respectively 7 and 5, are healthy, as is also the sister, aged 8 months. This child walked and talked at 1 year and 3 months. When 2 years old the mother noticed gradually increasing weakness. The child lost the power of walking, developed a tremor of the hands and weakness of the back. The legs showed the greatest amount of weakness. The face, eye, muscles of the tongue were unaffected. There was fibrillary tremor of the muscles of both hands. Kyphosis was present in the lumbar region and the deep reflexes were absent.

Bruns, in considering these cases, says they are undoubted cases of Werdnig-Hoffmann's disease. He notes the difference in age between his cases and those of Werdnig and Hoffmann, but he says that they cannot be mistaken for any progessive form of muscular dystrophy. He suggests that the Charcot-Marie-Tooth, or peroneal, is the type which most resembles these cases, but the atrophy in these begins in the peripheral portion of the limbs and extends upwards.

I should not be prepared to agree with this statement, for the cases rather closely resemble some of the forms of dystrophy, which begin in the proximal muscle, and a very similar case with curvature of the spine has been figured by Jendrassik.[1] Without a pathological

[1] *See* Case 10, *Deutsch. Zeitschr. f. Nervenheilk.*, 1902, xxii, p. 444.

examination Bruns is hardly justified in placing in the Werdnig-Hoffmann group a type of case which differs so markedly in course and clinical features from that group.

Senator describes two cases, a brother and sister, under the title "Zur Kenntniss der familiaren progressiven Muskelatrophie im Kindesalter."

The first case is that of a boy, aged 8, healthy at birth. He walked at 11 months. When 2 years old he often fell. Walking and standing became more difficult, so that when 3 years he had nearly always to be carried. He learnt to write, but when between 6 and 7 he lost this power, owing to the shaking of his hands. His memory also began to fail. There was atrophy of the shoulder and upper arm muscles, atrophy of the back muscles, moderate lordosis and the muscles showed fibrillary tremors. The knee-jerks were absent, sensation was natural. There was altered electrical excitability. Six months later the atrophy of the buttocks and shoulders had made further progress. The gait was unaltered. He was neither better nor worse.

The second case, G. S., a girl, aged 5½, walked at 10 months. When 18 months old she had a fit. When 2 years old she became unsteady on her legs, like her brother, and at the same time there was tremor of the hands. She walked with a wide base, was shaky, had marked lordosis and a lateral curvature with the convexity to the right. There was wasting of the back muscles and to a lesser degree of the upper arm and pectoral muscles. The buttock muscles were flabby, but the lower legs appeared well developed. Fibrillary tremor was present in some muscles. There was diminished excitability in the muscles.

Senator, in considering the differential diagnosis of these cases, questions whether they belong to the neuropathic form of Werdnig and Hoffmann, or to Erb's myopathic form of simple atrophy. He says that Heubner, Schulz and Preisz have shown changes in the nervous system in some cases of myopathy. He thinks these two cases are probably spinal in origin.

Lange describes two cases, a brother and sister, aged 11 and 6 respectively, the first and fourth children of a family of six. The second child was said to have died of a similar complaint when 3 years old.

The first case, a boy, did well for the first nine months of life, then he began to lose power in the limbs, lost the power of sitting up, and also the power in the neck muscles. When 3 he developed double cataract.

When 11 years old he was unable to stand, there was marked wasting of the proximal muscles of the limbs. The shoulders were loose. The knee-jerks were absent.

The second child, sister of the above, aged 6, was quite well till 9 months. Then the legs began to waste. She never learnt to walk. When 3 years old she, like her brother, developed cataract. She could only sit when propped up.

Lange is inclined to attribute these cases to the Werdnig-Hoffmann group, but he says it is impossible to separate such cases from the myopathies without a pathological examination.

In conclusion, as belonging to the Werdnig-Hoffmann group one would accept in addition to the case of Hoffmann, published in 1900, Beevor's case, von Ritter's two cases, Armand-Delille and Boudet's case, all with the pathological examination, and also Sevestre's and Wimmer's first case without a pathological examination. I should not, however, be prepared to accept as belonging to this group the cases of Bruns, Senator and Lange without a pathological examination.

The following list of thirteen cases comprises all those in which the diagnosis has been confirmed by autopsy, and may be accepted as belonging to the Werdnig-Hoffmann type. They have been arranged according to the age at which death occurred. The list shows the marked variation in the duration of symptoms.

Recorder	Age of onset	Sex	Age of child	Family history	Year of publication
1. Batten ...	14 days ...	M.	5 weeks ...	0	1911
2. Beevor ...	Birth	M.	2 months ...	Yes	1900
3. Armand-Delille and Boudet	2 months ...	M.	6 months ...	0	1908
4. Batten ...	Always weak ...	M.	8 months ...	0	1911
5. v. Ritter ...	5 months ...	F.	15 months ...	0	1904
6. v. Ritter ...	12 months ...	F.	2 years	0	1904
7. Hoffmann ...	7 months ...	F.	2½ years ...	Yes	1897
8. Werdnig ...	10 months ...	M.	3 years	Yes	1891
9. Batten ...	Always weak ...	M.	3½ years ...	0	1911
10. Hoffmann ...	9 months ...	F.	5 years	Yes	1893
11. Hoffmann ...	4 months ...	F.	5 years	Yes	1900
12. Werdnig ...	10 months ...	M.	6 years	Yes	1894
13. Bruce and Thomson	12 months ...	F.	6 years	0	1893

SUMMARY.

The paper deals with the widespread progressive muscular atrophy of infants and young children due to a spinal lesion. The paper is based on the clinical and pathological examination of eight cases. These, on pathological grounds, are divided into three classes:—

(1) A type of case in which progressive muscular weakness occurs

during the first week or month of life, gradually progresses, and terminates in death after a variable period of weeks, months, or years. Sometimes more than one member of the family may be affected. The pathological change found in these cases is a degeneration of the lower motor neurons, the character of the change depending on the time after the onset of the disease at which death takes place. The type corresponds to the cases described by Werdnig and Hoffmann.

(2) A type of case in which progressive muscular weakness and atrophy begins somewhat later in life, after the child has already walked, and slowly progresses till death occurs from respiratory failure or pneumonia. The pathological changes found in such a case resemble those found in a toxic neuritis.

(3) A type of case in which progressive muscular weakness and atrophy begin in later life, after the child has already walked, slowly progresses, and is attended by a widespread myelitis of the spinal cord.

Six of the recorded cases are assigned to the first group, one to the second, and one to the third.

The literature is then considered. Ten cases belonging to the first group are at present on record with a pathological examination; two recorded by Werdnig, three by Hoffmann, two by von Ritter, one by Bruce and Thomson, one by Beevor, and one by Armand-Delille and Boudet.

Of recorded cases assigned to the Werdnig-Hoffmann group without an autopsy, the writer is unwilling to accept those of Senator, Bruns, Lange, and the second case of Wimmer's, but would accept Wimmer's first case, and that recorded by Sevestre.

The great difficulty in the diagnosis of these cases from cases of primary myopathy is recognized, and reference is made to cases recorded by Finkelnburg, which on clinical grounds might well be assigned to primary spinal atrophy, but on pathological grounds were shown to belong to the myopathic group.

Appendix.

Case I.—C. H., aged 4 weeks, was seen at the Children's Hospital, Great Ormond Street, in May, 1903. The child was the first. The parents were healthy. There had been no miscarriages, the labour had been prolonged, but no instruments had been used. At birth the cord was round the child's neck, and the child was cyanosed. The child was breast-fed for the first fourteen days and seemed to thrive. It was then fed on goats' milk. Wasting and loss of power in the limbs was first noticed when the child was 14 days old, and the child gradually became feebler. The child sucked well, but seemed to get easily tired. There was no vomiting. The child had been rather constipated. On examination the child was small, wasted, weighing 5½ lb. It lay with the arms at its side and did not attempt any movement. Respiration was feeble, the pulse from 84 to 96 per minute. The child seemed to see and to take notice. The eye movements were good, it sucked well, and there was no paralysis of the tongue or palate. There was no regurgitation; it cried fairly well; there was complete flaccid paralysis of the muscles of the neck.

The arms lay quite flaccid by the side or across the abdomen, or wherever placed. The child was just able to move the fingers, the arms were thin and wasted. There was no power in the muscles of the back, and very little in the intercostal or abdominal muscles. There was almost complete flaccid palsy of all the muscles of the leg, but some slight movement remained in the toes. The knee-jerks were absent. The child certainly felt a pinprick all over the body.

On electrical examination of the muscles no contraction could be obtained to strong faradic current in any of the muscles of the arm, trunk, or leg. The child died three days after admission to the hospital. On post-mortem examination nothing abnormal could be found on naked-eye examination in the visceral or nervous system. The brain and spinal cord, the right median, the right phrenic, left sciatic nerves, and biceps muscle were preserved for examination.

The examination of the tissues was carried out by the Marchi, Nissl, Weigert-Pal, and Van Gieson methods.

Microscopical examination: The spinal cord by the Marchi method showed at the level of a third sacral segment marked degeneration in the finer fibres of the grey matter of the anterior horns (fig. 4). These degenerate fibres arising from the cells of the anterior horn form bundles which can be seen passing through the white matter of the cord towards the peripheral, where they form, after their exit from the cord, the anterior roots. Numerous degenerate fibres can be seen in these anterior roots (figs. 2 and 3). The fibres of both anterior horns are about equally affected. The cells of the anterior horn appear for the most part normal and show no evidence of pigmentation or degeneration. It is not possible to assert that one group of cells have more

degenerate fibres arising from them than another group. No degenerate fibres could be seen in the antero-lateral tracts other than those above mentioned, which were passing outwards to the anterior roots. In the posterior columns, however, a few degenerate fibres could be seen in the posterior root zone, and also in the posterior roots both within the cord and outside.

At the level of the third lumbar a similar condition was present—viz., degeneration of the fine fibres passing from the anterior horns to the anterior roots. A few degenerate fibres were also present in the posterior columns and roots.

At the level of the first lumbar the degeneration becomes less marked, but a few degenerate fibres can now be seen in the region of Clarke's column, and although they cannot be traced to the direct cerebellar tract, yet they tend in that direction, and scattered degenerate fibres can be seen in this tract. A few degenerate fibres are present also in the posterior columns and roots.

Throughout the dorsal region but little degeneration can be seen (fig. 1). There are a few degenerate fibres in the anterior horns and also in the posterior columns, but the cells of Clarke's column appear normal, and there are no degenerate fibres in that region. (Figs. 1, 2, 3, 4.)

At the level of the first and second dorsal segments degenerate fibres again become more numerous, and at the level of the sixth cervical segment marked degeneration is again present in the grey matter of the anterior horns (fig. 1). The degeneration is more marked about the median group of cells, and least about the lateral group. In the posterior columns there are a few degenerate fibres, whilst there are practically no degenerate fibres in the antero-lateral tract. All through the cervical region there is considerable degeneration which, however, becomes less marked again in the upper cervical segments. There is a small bundle of fibres situated at the root of the posterior horn, which contains degenerate fibres; this can be traced from the seventh cervical segment upwards to the lower portion of the medulla, where it apparently leaves the cord by a lateral nerve-root (spinal accessory fibres).

By the Nissl method the cells of the anterior horn appear numerous, and for the most part well stained. Here and there individual cells may show some chromatolysis, but the greater part of the cells are normal, both as to number and character (figs. 5 and 6).

By the Weigert-Pal method the cord appears normal for a child of this age, although the pyramidal tracts are not fully medullated.

By the Van Gieson method there is no evidence of vascular or interstitial change.

Brain: No change could be found in the cortex of the cerebral hemispheres, in the cerebellum, or in the pons. In the medulla a few degenerate fibres can be seen in the intramedullary course of the twelfth nerve.

The peripheral nerves, the right phrenic, the left sciatic, the right median, examined by the Marchi method, do not show any degeneration, and also appear normal by other methods of examination.

The biceps muscle does not show any marked change. The muscle-fibres

are in the infantile condition, uniform in size, there is no fibrosis, and the intramuscular nerves are relatively well stained.

The result of the examination of this case is to show that degeneration has taken place in the lower motor neurons. The changes present are similar to those seen in diphtheritic paralysis—viz., a marked degeneration of the myelin sheath, as shown by the Marchi method, and comparatively little change in the cells of the anterior horn.

Case II.—W. G., aged 5 weeks, was admitted to the National Hospital under the care of Dr. Beevor. The child was the eighth of eight children, four of whom had been similarly affected—viz., the first died at $4\frac{1}{2}$ months, the second died at 8 months, the fourth died at 7 months, and the eighth (the patient) died at 2 months.

The child was full term, there was difficulty with the labour, and he was noticed to be paralysed at birth.

On examination there was complete flaccid paralysis of all four limbs, with the exception of very slight involuntary movements of the fingers of the left hand. Sensation was said to be lost on the limbs and on the trunk to the second rib. All the deep reflexes were absent.

The pathological examination showed no macroscopic change, but on microscopical examination atrophy of the cells of the anterior horns (figs. 7 and 8) and degeneration of the posterior columns were found.

For a full clinical and pathological report of this case see *Brain*, 1902, xxv, p. 85.

Case III.—E. T., aged 4 months, was admitted to the Children's Hospital, Great Ormond Street, under the care of Dr. Penrose, in October, 1901.

History: General helplessness was first noticed one week after birth, and had steadily increased since. The limbs wasted and the breathing became difficult. There was some difficulty in swallowing at times. The child is the fourth of four children. The first is alive, aged 4, and is well. The third child died at 5 months and is said to have had a similar condition to the present patient.

Present condition: The child lies on its back, crying feebly, but employing all its facial muscles. There is no facial asymmetry. The thorax is quite motionless in breathing; while the abdomen moves freely. There is marked wasting of the shoulder muscles and those of the limbs. The child can apparently do nothing except make a slight movement of the toes. The forearm can be feebly flexed and extended and all movements of the upper arm are capable of being feebly performed, though the child does not raise the arms above the shoulders. The wrists are dropped. The child is absolutely unable to sit up, and when raised the head falls about helplessly. Fibrillary tremor is noticed in the muscles of the arm. The movements of the tongue and eyes appear normal. The deep reflexes are absent and the plantar response, when it can be elicited, is in the direction of the extension of the small toes. The child died. No post-mortem was obtainable.

Case IV.—P. B., aged 6 months, fourth of four children. One died of fits at 4 months, due to injury at birth. One died of tuberculosis. The boy was born at full term, and the labour was natural. He was said by the mother to be healthy at birth. When 4 months old it was noticed that the child could not move the arms. The onset seems to have been quite gradual.

On admission to hospital the child was well nourished, lay on its back taking notice of all around it, smiling, and seemed quite intelligent.

Both arms lay by the side absolutely flaccid, except for some movements of the fingers. Both legs were quite flaccid and powerless. Respiration was almost entirely abdominal, and there seemed to be paralysis of the intercostals. The neck muscles were quite powerless. All the deep reflexes were absent; superficial reflexes indefinite. Sensation apparently perfect. On electrical examination practically no contraction could be obtained to faradic stimulation, except in the flexors of the fingers, and then only with a current which will produce a tetanus in the muscles of a normal individual. To galvanism no definite contraction obtained.

The fundus of the eyes was examined and appeared normal. The child developed broncho-pneumonia and died. No autopsy was obtainable.

The clinical features which this child presented seem to be almost typical of the progressive muscular atrophy of infants, but without the verification of a post-mortem the case loses much of its importance.

Case V.—H. C., aged 8 months, was the third of three children, the other two being healthy. The child had been breast-fed; he had had no difficulty in swallowing and had had no illness. The birth of the child was natural. The history was that the child had always been weak and had never been able to sit up, nor could he hold up the head. The weakness seems to have increased, and when first seen, besides the weakness of the neck muscles above described, the arms were perfectly flaccid, the deltoids being especially weak. The legs were flaccid, only the slightest movement being possible. The knee-jerks were present, but only obtained with difficulty, and the plantar usually gave a flexor response.

There was marked weakness of the back, with a lateral curvature, the concavity being to the left. The pupils were equal.

The child developed broncho-pneumonia and died in a few days.

At the autopsy there was extensive broncho-pneumonia. There was a marked lateral curvature of the spine to the left. The spinal cord and membranes appeared normal. There was no wasting of the cord. Brain appeared normal. All the muscles very pale, but not atrophied. Diaphragm looked a good colour.

Pathological examination: The cord was examined by the Marchi, Nissl, and Van Gieson methods. The cells of the spinal cord appear to be fairly numerous, and show only slight chromatolysis. In most of the cells the nucleus is centrally placed. The anterior nerve-roots do not appear unduly small.

Examination by Marchi method shows a certain amount of degeneration in the anterior roots very similar to that found in the Case I, but to a far less degree.

There was in this case no microscopical examination of the peripheral nerves or muscles.

Case VI.—R. A., a boy, aged 3½, was admitted into the Hospital for Sick Children, Great Ormond Street, under the care of Dr. Garrod, June, 1910. He was one of twins; the other (a male) is healthy. This child cut his first tooth at 8 months, and learnt to talk early. The boy never learnt to sit up, and when 15 months old it was noticed that he could not move his legs. He, however, moved his arms quite well. When 2½ years old he was seen by a surgeon, who ordered him a Phelps's box in which he was kept lying down.

The boy is the result of the fifth pregnancy. The eldest child, aged 15, is alive. There has been one miscarriage and two children stillborn.

The boy lies on his back and he can be freely moved about without pain. He is intelligent and can talk well. There is no affection of the ocular nerves. He is quite unable to sit up, nor can he maintain the sitting posture when sat up. He can, however, hold up his head. He can move the arms about fairly well, but there is some contraction of the outer phalangeal joints which limits his movements. There is a peculiar "athetoid" movement of both hands, and when he grasps an object he overdoes the action. The legs lie flaccid in bed, but the right knee-joint cannot be extended more than 35°. The legs are generally wasted and flabby and there is wasting of both lower limbs, especially above the knee, and this is rather more marked on the right side than the left. The right thigh is adducted and the adductor muscle is contracted. There is genu valgum and talipes valgus on the right side. There is no power of movement in the lower limbs, but they can be freely moved passively, and there is marked flaccidity, except for the contraction above mentioned.

There was well-marked lateral curvature in the lower dorsal region, with convexity to the right. The muscles of the back were wasted. There was no tenderness.

The left knee-jerk was present, the right was absent. No plantar response was obtained. The abdominal reflex was present on the left, absent on the right side. Sensation was perfect. Electrical examination showed greatly diminished excitability to both faradic and galvanic current.

I saw the boy in June, 1910, and from the clinical features came to the conclusion that the case was probably one of old and extensive poliomyelitis. I failed to recognize the progressive nature of the case and attributed his continued weakness to the fact that he had been kept for a year in a Phelps's box. On July 8 he had some retention of urine, which was relieved by the catheter. This retention passed off on the 12th. X-rays showed no disease of spine.

On August 24 intercostals became very weak. Broncho-pneumonia developed, and the child died on September 3.

The post-mortem showed some patchy broncho-pneumonia. The brain and

spinal cord appeared normal to the naked eye, except that the anterior roots appeared smaller than normal. The posterior roots were well developed. The spinal cord was examined by the Marchi, Weigert-Pal, Nissl, and Van Gieson methods.

By the Marchi method practically no recent degeneration could be found. There were in the grey matter of the anterior horns in the cervical region a few fibres which showed degeneration, but they were very few in number.

By the Weigert-Pal method the whole of the white matter of the antero-lateral tracts was paler than the posterior columns, but no tract could be said to be definitely affected. There was no diminution in the size of the grey matter, and the medullated fibres in the grey matter appeared fairly normal. The most striking feature was the smallness of the anterior roots as compared with the posterior, and the great diminution of fibres. The most marked change was to be seen in sections stained by the Nissl and Van Gieson methods. The absence of cells in the anterior horns, both in the lumbar, thoracic and cervical region, is most striking. In any given section one or two normal cells can generally be seen, but the other cells are small, apparently well formed, but only about half the size of the normal cell. Many cells must have entirely disappeared. If the number of cells of moderate size are counted in a series of sections in the lumbar region, they average out about ten to a section, whereas the normal average out to about forty, and these figures do not truly represent the state of affairs, for the size of the cells in this cord is somewhat smaller than in the normal cord (figs. 9 and 10.)

Case VII.—H. M., aged 3, the youngest of four healthy children, was admitted to the Children's Hospital, Great Ormond Street, under the care of Dr. Voelcker, in October, 1908. She was healthy at birth, and well up till ten weeks ago, when it was noticed one morning that she was unable to walk properly and fell backwards into a sitting position after taking a few steps. On stooping she was unable to regain the upright position. She had incontinence of urine and fæces. The arms were said to be unaffected and the child was able to feed herself. There had been no constitutional symptoms.

Seven weeks later the arms became weak, causing her difficulty in feeding herself. There was irritability, but no evidence of pain.

She is a bright, intelligent, and well-nourished child. She can move her legs, but cannot stand. There is weakness of both deltoids, but the forearm muscles are good. The cranial nerves, optic disks, and trunk muscles are normal. Sensation is unimpaired. All the deep reflexes are absent, but the abdominals are present and the plantars give an indefinite response.

When at first in the hospital there was a definite increase of muscular weakness. The arms became powerless, only movements of the fingers and slight movements of the wrists remained. The back muscles were weak, and there was a curvature, with the convexity to the right. The legs became weaker and more wasted. A definite weakness of the right side of the face developed. This passed off in a few days. There was the reaction of degeneration in the muscles of the lower limbs.

In December, some two months after admission to the hospital, there was a gradual improvement, so that the child could now get the hand up to the mouth and move its legs. The knee-jerks were still absent. This improvement was maintained till February, 1909. The weakness then again began to increase, the intercostal muscles and diaphragm became affected, and in October, 1909, the child died, twelve months after admission to the hospital, and fourteen months after the onset of the disease.

On post-mortem examination nothing abnormal to the naked eye could be found in the brain or spinal cord.

The cord and medulla were examined by the Weigert-Pal, Nissl, Marchi, and Van Gieson methods.

The cord, examined by Weigert-Pal method, appeared perfectly normal.

By the Marchi method: There was scattered degeneration throughout the length of the spinal cord. The amount of the degeneration was slight, and could not be said to affect any particular tract of the cord. If anything, the anterior and posterior roots in their passage through the white matter of the cord were rather more affected than other parts. There was a little fine degeneration in the grey matter in the region of the anterior horns. The intramedullary portions of the twelfth nerve also show some fine degeneration. The extramedullary portion of the anterior and posterior roots practically show no change.

By the Nissl method: The cells of the grey matter are well stained. Many of the cells of the anterior horns in the lumbar, thoracic, and cervical regions of the cord appear perfectly normal. Some cells, however, in each region of the cord show chromatolytic changes. These changes are not confined to any one group of cells, but affect individual cells in any group, a cell in close proximity being perfectly normal (figs. 11 and 12).

The changes which these cells exhibit are a somewhat swollen appearance, the nucleus being eccentric, but the nucleolus well stained.

The chromophylic substance of the cells stains diffusely, and it is only at the margin of the cell that the normal chromophylic granules can be seen.

There are very few cells that can be said to be in a state of profound degeneration, and in most of those affected the change is comparatively slight.

The cells of Clarke's column also show some changes.

By the Van Gieson method: The interstitial tissue and the vessels of the cord appear perfectly normal, and there is no evidence of either past or present inflammation.

The peripheral nerves examined were those of the sciatic and brachial plexus.

By the Marchi method: A very considerable amount of degeneration of the myelin sheath could be seen. This was more marked in the nerves of the brachial plexus than in the sciatic.

By the Van Gieson method: The same nerves appear perfectly normal, and there is no evidence of interstitial inflammation.

The muscle-fibres of the diaphragm show most marked fatty degeneration when stained by the Marchi method.

The changes found in this case point to a toxic degeneration of the lower motor and sensory neurons. Since the changes are more marked in the peripheral nerves than in the cell body, the case would fall into the group known as toxic neuritis. The clinical course and symptoms do not, however, correspond with those commonly associated with that disease.

Case VIII.—M. L., aged 11. Twelve months, weakness of hands. Seven months, unable to button clothes. Four months, weakness of legs. Two months, adenoids removed, and much worse since that operation. Fourteen days, pain in back, and increasing difficulty in swallowing.

Intelligent, deaf, some atrophy of tongue, palate moves well on phonation, weakness of neck, respiration thoracic, upper intercostals only in use. Claw hand, wrist-drop. Weakness of upper arm and shoulder muscles. Can walk, but only feebly. Knee-jerks brisk, plantar flexor, sensation natural to all forms.

Electrical reaction R.D. in some muscles, in others only diminution of irritability. Sudden death from respiratory failure six months later, eighteen months after onset of disease.

Pathological examination showed an extensive destruction and atrophy of the cells of the anterior horn, from the upper cervical to the lower thoracic segment, extensive degeneration of the whole of the ventral region of the cord in the thoracic segments. Degeneration of the direct cerebellar tracts both dorsal and ventral.

There was a marked increase of the connective tissue in the ventral portion of the cord in the thoracic region.

The walls of the vessels showed no change. The cord showed both recent and old degeneration.

The change in the cord is attributed to a chronic myelitis secondary to some vascular change and toxic blood state. For full clinical and pathological report of the case, see *Brain*, 1903, xxvi, p. 473.

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