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PROGRESSIVE SPINAL MUSCULAR ATROPHY OF INFANTS.
(WERDNIG-HOFFMANN PARALYSIS).

The object of this communication is to record six cases of Werdnig-Hoffmann paralysis which were investigated in life and post-mortem by the author. These six cases were under the care of his colleagues at The Hospital for Sick Children, Great Ormond Street, London, W.C.1., while the author was acting as Medical Registrar and Pathologist there. It is due to their kind permission that he is able to use these cases.
History of the Disease.

This form of muscular atrophy was first described by Werdnig of Gratz in 1891 (1). His description is as follows:

"In a family without neuropathic taint, two or more children, who had been well up to that time, become sick about the tenth month of life without fever, convulsions or other signs of infection. The disease begins very gradually, in that they cannot use their legs as well as formerly; the children never learn to walk and cannot stand without
help. There is atrophy and paralysis of the muscles of the back and pelvic girdle (marked in the gluteal muscles), but especially in the quadriceps. The disease, in a chronic, progressive, centrifugal and symmetrical course, involves the shoulder-girdle, neck and throat muscles, later the muscles of the thigh and arm, then the leg and forearm and last the muscles of the hands and feet. There is atrophy of the muscles en masse; there is no hypertrophy or pseudohypertrophy. Bulbar symptoms, fibrillary twitchings and secondary
contractures may be present. There is marked flaccid paralysis with complete loss of the tendon reflexes and a partial loss of the skin reflexes; sitting up is very difficult or impossible. There is lordosis of the lumbar spine. There is no pain or tenderness anywhere, nor objective disturbance of sensation. The sphincters are normal. Mental development is good. There is extreme atrophy of the muscles, but not of the subcutaneous fat. There is involvement of the muscles of respiration and the
disease runs a quick, fatal course; in the mildest cases within several years. The pathologic findings are primary symmetrical disease of the spinal cord, consisting of atrophy of the anterior horn cells, without evidence of any inflammatory process; a marked degeneration of anterior nerve-roots; secondary simple atrophy of the muscles with more or less marked increase of nuclei; in places, degenerative atrophy and lipomatoses of the muscles."

Hoffmann of Heidelberg confirmed
Werdnig's description in 1893 (2). Since this date a number of similar cases have been described.

In 1900 Oppenheim (3) described a syndrome which was "congenital, but not hereditary nor familial; present in full bloom at birth, consisting of a hypotonia of most of the muscles of the body, with absence of tendon reflexes and no reaction of degeneration, and a tendency to progressive improvement." This clinical picture has often been confused with that of Werdnig-
Icy Hoffmann paralysis and vice versa. Latterly neurologists of repute (4) have contended that Werdnig-Hoffmann paralysis and Oppenheim's disease were one and the same thing, and that their pathology was identical.

**Aetiology.**

Nothing is definitely known as to the aetiology, and certainly the analysis of these cases has thrown no light on the cause of the disease. Batten (5) suggests that it may be due to a toxin acting during intra- or extra-uterine life, or may be due to what
Gowers called "abiotrophy, a degeneration depending on a defective vital endurance."

Greenfield and Stern (4) state that "the pathological evidence is altogether in favour of the disease being due to a degeneration of the neurons of the ventral horns, a process which may begin either before birth or within the first year of life, and which may be either rapid or slow in its progress or may even cease to advance." Huenekens and Bell (6) quoted Marburg of Vienna (7) as having given the differential diagnosis between Amyotonia Congenita
(Oppenheim's disease) and Werdnig-Hoffmann paralysis as follows:

Amyotonia Congenita.  

Werdnig-Hoffmann.


   Acquired in early life.

   In this series of cases four were definitely present from birth. Of the others, one was probably present from birth and one was certainly acquired very early in life.

2. Usually single, rarely familial.

   Usually familial.

   In two cases of this series the disease was clearly familial.


   Localised atrophies, beginning in the pelvic region and spreading.
Amyotonia Congenita.  Werdnig-Hoffmann.

4. Atrophy masked, not grossly apparent.  Atrophy easily recognized and apparent.

Atrophy was not apparent in any of these cases, but it was very clearly seen in all at post-mortem examination, when the thick subcutaneous fat was cut through.

5. Tendon reflexes absent.  Proportional to the atrophies.

The tendon reflexes were absent in all these cases.

6. Stimulated by electricity or the hypotonic reaction given. (Farad. 0., Galv. plus.)  Reaction of degeneration.
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<td>7. Progressive improvement.</td>
<td>Progressively worse, a mere skeleton at 4 to 5 years.</td>
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All the cases in this series were rapidly fatal.

**Similarities between Werdnig-Hoffmann Paralysis and Oppenheim's disease.**

Greenfield and Stern (4) refer to three points where these two diseases merge clinically. They note that the course of the disease is not always progressively downward in Werdnig-Hoffmann paralysis, there being periods when the disease seems to come to a standstill or even to improve.
This tendency to improve was definitely noted in one of the cases investigated (Case III).

Again, there is a constant sparing of the diaphragm in both diseases. Over-action of the diaphragm, with protruding abdomen, is very typical of the clinical picture in both cases.

Finally, they note that cranial nerve paralyses occur very rarely, the majority of cases showing none. None occurred in this series of cases.

A little weakness of the tongue and facial muscles has been suggested in both conditions, but in none of this series were they present.
Examining such a classification with this series of cases in mind it would be quite impossible to say into which class they should be put, and since the pathology of all was identical this adds very strong proof to the contention of Greenfield and Stern (4) that the two conditions are one and the same disease with a wide variety of clinical manifestations.

Pathology.

In the cases being described, on cutting down on the muscles of the extremities at post-mortal examination, there was an unusually thick
layer of subcutaneous fat, and when the muscle was reached, it appeared extremely thin and pale, in fact, a mere sheet only. Beyond the changes in the cord, all other organs appeared normal, with the exception of the lungs, which showed a pneumonia secondary to the condition.

Microscopically, in all cases the cord showed an atrophy of the anterior horn cells. Some of the cells were merely smaller in size, but in all there was a great decrease in their number, compared with the cells in a normal infant of the same age. The muscle
fibres were atrophied and of small size, and were interspaced with globules of fat.

Occasionally a muscle fibre or two appeared normal and was therefore noticeably large.

Batten (5), Greenfield and Stern (4), and others state that, seen with the naked eye, there is atrophy of the anterior roots of the cord, and the muscles of the trunk and limbs are thin, flabby and pale. Microscopically, there is much atrophy and degeneration of the anterior horn cells, and also atrophy of the lower motor-neuron, passing away from the
anterior horns. Some of the muscle-fibres are left unaffected, while other bundles of fibres show marked atrophy, with much fat replacing them. The appearance is similar to that of muscle which has atrophied secondary to a spinal change. Greenfield and Stern (4) state that:

1. In the medulla there is a diminution in the number of cells in the hypoglossal nucleus.

2. In the spinal cord there is diminution in the number and size of the anterior horn.
cells, with definite chromatolytic changes in some of those remaining.

3. The anterior nerve roots are small compared with the posterior roots and show a loss of myeline.

4. In the peripheral nerves there is an unduly high proportion of minute, finely myelinated fibres.

5. The muscles all showed the features of a simple atrophy.

Huenekens and Bell (6) point out the fact that the pathology of Oppenheim's
disease and Werdnig-Hoffmann paralysis are similar, although the clinical picture is not quite identical, and they suggest that possibly these two conditions are extreme types of the same disease. A case described by Holmes (8) in the "American Journal of Diseases of Children" as Amyotonia Congenita or Oppenheim's disease seems in every respect like the cases in this series, showing that, whatever name be given to it, both clinically and pathologically we are describing the same disease.
Familial Nature of the Disease.

Both Werdnig and Hoffmann insisted that this was a feature, whereas Oppenheim did not. Batten (5) stresses the familial character of the complaint. In this series it was shown very clearly in Cases IV and VI. In Cases I and III the patient was the first and only child. In Cases II and V the condition was clearly not familial.

Sex and Age.

Four of the six cases were girls and two were boys. In a large series,
however, it is seen to affect males and females equally (Batten) (5). The youngest was five weeks and the oldest eight months of age when they first came under observation. Most cases reported have been much older than these, especially those reported by Batten (5). Out of 42 cases analysed by Huenekens and Bell (6), only 17 were eight months of age or less. Of 28 cases of Amyotonia Congenita analysed by Greenfield and Stern (4), death took place at eight months or less in 18 cases.
Duration of the Illness.

The shortest duration from the onset of the illness until death was five weeks and the longest 22 weeks, with an average of 13 weeks for all six cases. In four of the six cases the symptoms were definitely present at birth, and in the other two they were probably present at that time, although to a minor degree.

Symptoms.

The infant is born full-term of healthy parents, and appears perfectly normal,
well-formed, and healthy, but at birth or at varying periods up to a few months after birth, it is noted to be less active than a normal infant. On close examination the arms and legs are seen to move badly at the shoulders and hips, but movement from the elbows and knees and at the wrists and ankles remains normal. The head movements are also poor and the neck muscles are weak. There is a tendency for the head to fall backward or forward when the child is raised up. The abdomen is noted to be unduly prominent and
it will be seen that this is caused by over-
action of the diaphragm, as the breathing is
almost entirely diaphragmatic, the intercostal
muscles being paralysed. The voice becomes
progressively weaker, in fact it is because of
the weakness or absence of the cry that these
children are sometimes brought for attention.
Sucking is difficult because of dyspnoea, and
coughing becomes a most laboured process.
There is no apparent wasting, the limbs and
trunk appearing round and well-formed; but if
the child is lifted across the hand the lack of
muscular tone is at once evident, as the body curves over the hand, as shown in the illustrations of Cases II and IV. The cranial nerves are unaffected, the child smiling and looking about, taking a normal interest and showing the normal intelligence of a healthy child. The progress of the disease varies enormously. In some cases it is rapidly terminated by a massive collapse of the lung or with pneumonia. In others the child gains a little weight and actually seems to move the limbs a little better. There is a strong tendency for contractures, especially
of the hands, to take place, the forearms being pronated and the wrists flexed. The feeding becomes more and more difficult, and the usual termination is that of pneumonia.

Comparing this picture with that quoted by Batten (5), it will be seen that Batten states that an apparently healthy and intelligent child, making normal progress during the first few weeks or months of life, begins without any sudden onset manifestations of acute disease, or, without any known cause, to lose power. Four of the six cases in the present series were
definitely noticed from birth, and the other two were probably present from birth, certainly from five weeks old. This does not in the least correspond therefore to Batten's description. That the paralysis starts proximally and spreads distally, so that the fingers and hands can be moved while the upper arm is immobile, was true in this series. The intercostal and abdominal muscles are frequently affected, whereas the diaphragm remains unaffected. This also was found in all cases. The thick subcutaneous fat obscured the muscles, so that
fibrillary twitchings could not have been noticed. The neck muscles were weak in all the cases, and no bulbar symptoms were noted. Contractures tended to commence in one of the infants (Case IV). Sensation was not impaired. The mentality of the child was normal throughout and it took a normal interest in its surroundings. The cranial nerves were unaffected.

**Differential Diagnosis.**

Weakness in a new-born infant suggests various possibilities. A haemorrhage into
the brain produces a spastic condition with very often bulbar symptoms. Such a case should be easily differentiated. Haemorrhage into the cord, which is relatively uncommon, would produce a picture very similar to Werdnig-Hoffmann paralysis, but the paralysis of the intercostals without affection of the diaphragm, the paralysis of the neck-muscles without cranial nerve involvement, and the paralysis of the proximal rather than the distal muscles, is too definite to be simulated by spinal haemorrhage. Peripheral neuritis and toxic polyneuritis are
practically unknown at this age. Infantile poliomyelitis would be difficult or impossible to differentiate, but it would require to be extremely extensive to give this clinical picture, and if it were so extensive would probably cause death at once. Syphilitic epiphysitis with pseudo-paralysis would give rise to non-movement of the limbs only, the intercostals being unaffected. In Oppenheim's disease, if this does exist as a separate entity, the similarity would be striking. The author, however, has not seen a case of true Oppenheim's
disease, although he has had a fairly wide clinical experience.

**Prognosis.**

This is uniformly bad. All cases of true Werdnig-Hoffmann paralysis succumb, those of infancy especially rapidly.

**General Conclusions.**

The author feels that these six cases are clinically and pathologically similar to those described by Werdnig and Hoffmann. Seen at an early age, there is little doubt that clinically they might have been diagnosed as
Oppenheim's disease. The author is inclined to agree with Greenfield, Stern and others that Werdnig-Hoffmann paralysis and Oppenheim's disease are one and the same condition with widely differing clinical manifestations, but the same pathological basis.
Case I.  Josephine O'Leary.

Admitted to Hospital 5.12.19.

Died 1.2.20.
Aged eight months,

Complaint.  The child's back was weak, her head fell forward, and she did not move her arms or legs well.

Duration.  About two months, since the child was six months old.

Family History.  This was the first child, and the father, aged 41, and the mother, aged 31, were alive and well.  There was no history of deformities or paralysis on either side of the family, and there had been no miscarriages.

Previous Health.  She was a full-term child and the mother had been very well during the
pregnancy. No instruments were used at birth, but the labour was long (36 hours). The child was breast-fed up to the time of admission. She had never made any attempt to sit up and had not cut any teeth. She was weak, but otherwise healthy. She had had bronchitis three months previously.

Present Illness. When about six months old it was noticed that when the child was picked up she dropped her head forward. When a younger baby, she had held her head up quite well. At the same time it was noticed that she had a kyphosis when she sat up. The child did not kick about much or use her arms. All her limbs were very weak.

On examination, the patient seemed well nourished, but her muscles were flabby. Her cheeks were red and healthy-looking, the head was well formed.
(circumference 16 9/16 ins., fontanelle the size of 6d.) She lay on her back with her forearms flexed on her chest. She moved her forearms quite freely. The legs lay perfectly flaccid, with the left one slightly rotated out at the hip. She could move her leg very slightly. The feet were small and ill-formed, tending to show talipes. When the child was lifted the head dropped forward or backward, owing to weakness in the neck. A marked kyphosis was present when she sat up. The muscles everywhere were soft and flabby. There was a slight beading at the costo-chondral junction. There was marked over-action of the diaphragm and paralysis of the intercostals. Lungs, heart, and digestive organs normal.

Nervous System. The pupils reacted equally
to light, the knee-jerks and all other reflexes were absent. There were no evident sensory changes.

10.12.19. The baby was bright and intelligent, very flaccid, taking well.


19.1.20. Difficulty in swallowing. Temperature up.

1.2.20. Died of pneumonia.

Post-Mortem Examination.

The body was that of a well-developed and well-nourished female child. Rigor mortis was not present.

Brain. The meninges were very oedematous and congested, especially along the vertex. No excess of cerebro-spinal fluid was apparent. The brain was hardened before sectioning.

Cord. This showed no macroscopic signs of
inflammation or degeneration.

Abdomen. The liver, spleen, and kidneys were apparently normal.

Thorax. Right Lung: The whole lower lobe and the posterior part of the middle and upper lobe showed marked consolidation. Parts sank in water. This lung was in the stage of hepatization, and on pressure pus appeared in the larger bronchi.

Left Lung: No pathological changes.

Heart. The right side was filled with ante-mortem clot. No valvular changes. The muscle was flabby and muscular development was everywhere poor.

Microscopical Examination.

Sections of the calf muscle showed a tendency for some of the fibres to be swollen
and to appear unduly enlarged. The majority, however, showed marked atrophy. There appeared to be an increase in the nuclei, but this was probably an apparent increase only, not real.

A section of the cord showed the characteristic features of Werdnig-Hoffmann paralysis, namely, a decrease in both the number and size of the anterior horn cells. Prolongations, that is, dendrons and axons of the cells, were not present. The peripheral nerves were not stained to show myeline and appeared normal with the ordinary stain.
ILLUSTRATIONS.

Figure I. Showing large, normal, well-formed anterior horn cells from a case about the same age as those being studied.

Figure II. To contrast with Figure I, showing the paucity and small size of the anterior horn cells.
Case II. Elsie Bristow.

Admitted to Hospital 4.5.20. Died 8.5.20. 
Aged 6 weeks.

Complaint. Pneumonia. Duration. Five days.

Family History. The father, aged 27, and the mother, aged 26, were alive and well, and there was one other child, a boy aged five years, alive and well. There had been no miscarriages and the home surroundings were good. There was no history of paralysis in the family. Another child, a girl, was born in 1927, and is now nine months old, quite healthy.

Previous Health. She was a full-term child, and the labour was normal (12 hours). She was born black, with the cord round her neck. The mother was healthy during the pregnancy. The child was breast-fed, but had always been weak from birth.

Present Illness. Five days ago her breathing became quickened. No vomiting or diarrhoea was present. Since birth the child had always
been quiet, had a weak cry and never moved her arms or legs much. There had been no movement which the mother had noticed, even of the hands or feet, and certainly not of the upper arms or legs. The child had always been limp, as she was on examination. She had made no attempt to move her head from side to side or to hold it stiffly. Her cry had always been small and weak. The child's weight at birth was 10 pounds, and she had wasted steadily every since.

On Examination, the child's temperature was 97.4°, her pulse was 126 and her respirations 48. She was a well-developed and fairly well nourished baby, and was propped up in bed. Her fontanelle was open $\frac{4}{8}$in. x $\frac{3}{4}$ in. There was marked in-drawing of the lower ribs and dyspnoea. The back and limbs were straight and the abdomen
Her circulatory and digestive systems were normal.

Respiratory system. There were crepitations over the right middle lobe.

Central nervous system. The knee-jerks were absent, the plantars flexor, the abdominal reflexes absent. The pupils reacted to light. She liked to hold her hands freely pronated. The movement with the upper arm and legs was extremely small. Her forearms and legs (calves and feet) moved. She had a definite grip with her hands and had the power to flex her limbs slightly at the hips. Her movements at the ankles were good. Her muscles everywhere were flabby and poor, but the child had the appearance of being fairly well nourished. On respiration there was great indrawing of the lower ribs. There did not seem to be any true
action of the intercostal muscles at all, and the breathing seemed to be purely diaphragmatic. The child's colour seemed improved during the 24 hours after examination. She had a small cry like a kitten. In handling the baby there seemed to be an absolute absence of strength in the back muscles, and the child took up the position she would assume if she were anaesthetized. There was no paresis of the facial muscles.


Post-Mortem Examination.

The body was that of a fairly well developed, but ill-nourished child. The muscles were extremely flabby. The weight of the child was $8\frac{1}{2}$ pounds and the length 23 inches. The brain and cord appeared normal macroscopically. The brain weighed 1 pound, 3 ounces, 2 drachms.

Lungs. There were areas of collapse in both
lungs, with a small area of purulent bronchopneumonia at the left base. The pleural and pericardial cavities were normal. The heart weighed 11 ounces, the liver 6 ounces, the spleen 10 drachms, the kidneys 14 drachms, the thymus 11 drachms, and were all normal. There was nothing in the peritoneum. The muscles everywhere were pale, atrophied, and deficient. The pectoral muscles could not be seen and the intercostals were very thin and wasted. The diaphragm was thin. The recti were widely separated and much atrophied. The muscles of the thigh seemed more deficient than those of the calf, but both were wasted. There was a large amount of subcutaneous fat everywhere.

**Microscopical Examination.**

Sections of the cord at various levels
showed marked diminution of the number of anterior horn cells, with complete or partial atrophy of many, leaving a ghost space only where one had existed.

The muscles gave the appearance of that of a disused muscle. Many fibres were diminished in size and showed a tendency for fibrous tissue to be laid down between the bundles. The nuclei appeared to be increased in number.
ILLUSTRATIONS.

Figures III, IV and V.  Showing the degree of hypotonia present. In Figure IV one might have expected more hypotonia to be shown at the wrist.
Case III.  

Joan Bowman.

Admitted to Hospital 11.3.21.
Died 12.4.21.    Aged 3½ months.


Family History.  The mother, aged 26, was alive
and well.  The father, aged 30, had an abscess in
his thigh.  They had been married three years; this
was the first child and there had been no miscarriages.

Previous Health.  She was a full-term child,
ever able to take the breast, and fed on Half-Cream
Glaxo.  She was a good baby, cried weakly and was
quite intelligent.  Her birth weight was seven pounds.

Present Illness.  From birth on the child had not
moved well, but her weakness had become much more
marked lately.  She had never cried loudly, her cry
being small and weak.  Mentally she seemed normal.

On Examination, she was a well-covered, bright,
intelligent child.  Her fontanelle measured
1½ x 2 finger's breadths.  The muscles of her
arms and legs were flaccid.  Her abdomen was
prominent and she had a tendency to umbilical hernia. There was very marked depression at the lower end of her sternum and projection at the angle of Ludwig. On lifting her arms and legs and letting them go they fell back immediately. Pronation of the arms and movements of the hands and feet were noticed to be still possible.

Nervous System. Her knee-jerks and all other reflexes were absent. No fibrillary twitchings were noticed. There was marked hypotonia.

Respiratory System. Her breathing was abdominal and her chest was normal.

Her discs were normal. She had no strength in her back muscles.

4.4.21. The intercostals were certainly improved.

5.4.21. Her movements were improved.
6.4.21. Her movements were as bad as ever.

12.4.21. She developed broncho-pneumonia lasting twelve hours, and died.

**Post-Mortem Examination.**

The body was that of a fairly well nourished child, the length being 24 inches and the weight 7 pounds, 12 ounces. The sternum was depressed and the abdomen prominent. The brain and cord weighed 19½ ounces. Nothing abnormal was seen in them. The trachea and larynx, pleura and pericardium were normal.

**Lungs.** There was a small patch of broncho-pneumonia at the right base. The left lung appeared normal.

The heart weighed ¾ ounce, the liver 3¼ ounces, the spleen ¾ ounce, the kidneys ¼ ounce, and were all normal.

The intestines showed slight colitis.

The thymus was definitely larger than normal.
On throwing back the skin from the ribs there was very little muscle to be seen, but there was a great increase in the subcutaneous fat. The pectoralis major had almost disappeared. The quadriceps in the thigh were small, pale and poorly formed. The thyroid and suprarenal appeared quite normal.

**Microscopical Examination.**

There was an increase in the nuclei and the muscle fibres were atrophied. The diaphragm was normal. The cord showed gross diminution of the anterior horn cells at all levels both in number and size. Very few cells were even approximately normal. Many of the cells showed much vacuolation.
ILLUSTRATIONS.

Figures VI and VII. Showing the normal bundles of muscle fibres, which appear somewhat swollen. Near the normal fibres atrophied bundles are shown, the nuclei of which appear very numerous. This is probably an artefact. Disused muscle presents a similar appearance to this.
Case IV. Ian Bull.

Admitted to Hospital and died 15.2.22.
Aged 7½ weeks.

Complaint. Paralysis.

Duration. Since three days old.

Family History. The mother was alive, well and healthy, but the father had nervous trouble. There had been four children, but no miscarriages. The first child, a boy, was seen by Dr. Hutchison at the age of nine months, and died of Werdnig-Hoffmann paralysis. Next came two girls, who were, at the time the patient was examined, alive and well. Finally came the patient.

Previous Health. He was a full-term child and the labour was normal. He was fed on Glaxo from a few days old.

Present Illness. Nothing abnormal was noted until the child was three days old, when the
left arm was seen to be turned out. On the fourth day the right arm was seen to show contractures. The child was not able to roll his head, nor to lift or move his limbs for some days. He gradually regained power, and now his cry, which was small and weak, was stronger. He could pull his limbs up and he seemed to be doing very well indeed. His chest had been collapsed from the first week and he had been breathing with the aid of his diaphragm only. Lately he had developed diarrhoea and bronchitis.

On Examination, he was a collapsed, pale child, obviously ill with pneumonia. His diaphragm alone was working. He died shortly after admission.

Note. This child attended the Medical Registrar several times in the Out-Patient Department.
He could certainly move his legs well, the arms were paralysed in the proximal parts and there was a definite ulnar-nerve type of paralysis to the right arm, with contractures. The left arm showed flaccid paralysis and slight movement of the hand muscles. The child could roll his head slightly and could cry loudly.

**Post-Mortem Examination.**

The body was that of a wasted child, the length being 25 inches and the weight nine pounds.

The thorax was thin and much depressed.

The abdomen was full and much distended.

The brain weighed 21\(\frac{1}{2}\) ounces and appeared normal. The trachea and larynx were normal.

Lungs. There was consolidation at the bases, broncho-pneumonia in the right lung.

The pleura and pericardium showed nothing.
The heart weighed 1½ ounces only.
The thymus was very large, weighing 14 drachms.
The liver weighed 7½ ounces, the spleen ½ ounce, and the kidneys 1 ounce.
The lymphoid tissue in the intestines was well marked.
The muscles everywhere were small and wasted, and the subcutaneous tissue was large in amount.

Microscopical Examination.
The cord. The anterior horn cells were small and degenerate or entirely absent. Sections from the cervical, dorsal, and lumbar regions showed the same changes in varying degrees. The muscles showed typical changes, large and small muscle groups being present. Fibres broken up into small groups were seen in places. The sciatic nerve showed no gross changes by this method of staining.
ILLUSTRATIONS.

Figure VIII. Shows marked flaccidity of the back muscles.

Figure IX. Shows the protruding abdomen, depressed sternum and contracture of the left arm.

Figure X. Illustrates also the markedly depressed sternum and over-acting diaphragm.

Figure XI. Shows the anterior horn cells with dendrons and axons in the cord of a normal infant.

Figure XII. Contrasts markedly with Figure XI, showing the decreases size of the anterior horn cells.

Figure XIII. From another portion of the anterior horn, showing even greater destruction of these cells.

Figure XIV. A drawing of a muscle in this same case, showing the diminution and variation in the size of the fibrils, the nuclei being disproportionately large.
Case V. Margaret Collinson.

Admitted to Hospital 20.3.22.
Died 22.3.22.
Aged 5½ months.
Complaint. Paralysis.
Duration. Since birth.

Family History. Father and mother alive and well and there was one other child, a girl aged six. There had been no deaths or miscarriages. Another girl was born in 1925, is now aged three years, and quite healthy.

Previous Health. The pregnancy was normal. She was a full-term child, well formed at birth.

Present Illness. She had never moved since birth, but had always stayed in whatever position she was put. She could move her feet and hands slightly, but not the upper part of her legs or arms. She had not apparently wasted. She had always
been inclined to gasp.

On Examination, she was a well-nourished, plump child, who was soft and flabby everywhere. None of her muscles could be palpated. Her respiration was entirely diaphragmatic. Her digestive and vascular systems showed nothing.

Respiratory system. There were signs of consolidation at both bases, especially the left. Her abdomen was very distended, and she kept her arms pronated. Her intercostals were not working and there was over-action of the diaphragm. She seemed to have difficulty in sucking, but was quiet and contented. She had much trouble in breathing. She died like a pneumonia.

Post-Mortem Examination.

The body was that of fairly well developed and moderately well nourished child, showing much subcutaneous fat everywhere.
The brain showed nothing macroscopically.

Lungs. The left lung showed early pneumonia and the right showed massive collapse. The pleura and pericardium were normal.
The heart weighed 1 ½ ounces, the liver 10 ounces, the spleen ½ ounce, the kidneys 1½ ounces, and the intestines were normal.

Microscopical Examination.
The pons and optic thalamus appeared normal.
The cord showed the typical Werdnig-Hoffmann paralysis changes and degeneration of the anterior horn cells.
The muscles showed atrophy of the fibres and fat replacing them.
ILLUSTRATIONS.

Figure XV. A drawing of a portion of muscle in Case V, showing the normal muscle fibre bundles. This contrasts sharply with Figure XVI.

Figure XVI. A microphotograph of muscle from the same child, showing both normal and abnormal fibres.

Figure XVII. Shows the majority of the fibres markedly atrophied. The bundles are interspaced with fat and some fibrous tissue is also present.
Case VI.  John Graham.

Admitted to Hospital 17.3.22.
Died 23.3.22.
Aged 9 weeks.

Complaint.  Paralysis.
Duration.  Since four weeks old.

Family History.  The father and mother were alive and well, but they had lost one child 11 years previously from a similar condition with similar symptoms, aged 4 months.

Previous Health.  The child was born on January 12th, 1922, and weighed 7½ pounds.  The labour was normal and no instruments were used, the child being apparently perfectly healthy.  He was taken off the breast at four weeks old because the mother's milk failed.  He had gained two pounds in the first two weeks.

Present Illness.  About the middle of February
he was noticed to be less active. On February 18th he had a collapsing turn; he became a bad colour and his limbs were noticed to hang limp. On March 6th "panting" was first noticed and for the few days prior to admission the child could not hold up his head. On Examination, the child was very pale and did not cry. There was no attempt at voluntary movement. There was no apparent wasting. No reflexes could be obtained, the face was cyanosed and the alae nasi were working. The breathing was purely diaphragmatic. The arms were slightly pronated. There was very slight movement in the right foot and flexion and extension of the fingers of the right hand. The eyes were normal and the facial movements good. The circumference of the abdomen is 15\(\frac{1}{2}\) inches and that of the chest 13\(\frac{3}{4}\) inches.
Post-Mortem Examination.

The body was that of a moderately well-developed and well-nourished child, the length being 24 inches and the weight 8 pounds. The brain, weighing 18½ ounces, and the cord were apparently normal. The muscles were wasted and pale and there was much subcutaneous fat present. The liver weighed 10½ ounces, the spleen ½ ounce, the kidneys ¾ ounce, and the heart 1 ounce. The lungs were collapsed, showing early pneumonia. The intestines were normal.

Microscopical Examination.

The pons crura and the cortex were normal. The cord and muscles showed the changes typical of Werdnig-Hoffmann paralysis, described in the other cases.
ILLUSTRATIONS.

Figure XVIII. Shows two normal anterior horn cells from a normal infant, with dendrons present. The shrinkage about the cells is an artefact.

Figure XIX. A drawing of normal anterior horn cells.

Figure XX. A drawing of the anterior horn cells in Case VI, showing a decrease in size, with loss of dendrons.

Figure XXI. A portion of an anterior horn from the same case, showing very gross destruction of the anterior horn cells, in some cases the nucleus only remaining. There is a tendency for vacuolation to be present.

Figure XXII. A drawing of a normal muscle-fibre with many small atrophied fibres also present.

Figure XXIII. A microphotograph of some normal and many abnormal atrophied muscle fibres.

Figure XXIV. Shows gross atrophy of muscle-fibres from Case VI.
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Figure I

Showing anterior horn cells from a normal infant of three months.
Anterior horn on left, showing paucity and small size of cells.

Case I  x20.
Elsie Bristow.  Case II.

Showing the flaccidity of the child's muscles and her inability to hold up her head.
Figure IV

Elsie Bristow. Case II.

Note the degree of hypotonia present at the wrist in this case.
Figure V

Elsie Bristow. Case II.

Note the flaccidity of this child. The back muscles and neck muscles do not act normally.
Muscle showing gross atrophy of the fibres and an apparent increase in the nuclei.

Case III × 450.
Longitudinal section of muscle fibres. Some of the muscle fibres are swollen and translucent. Atrophied muscle fibres seen in the upper region.

Case III  \( \times 450 \)
Figure VIII

Ian Bull. Case IV.

Showing the flaccidity of the muscles of the back and neck.
Figure IX

Ian Bull. Case IV.

Showing overaction of the diaphragm and in-drawing of the sternum at the attachment of the diaphragm.

Note the position of the left hand. The arm was paralysed and there was a tendency to early contractures.
Ian Bull. Case IV.

This also shows the overaction of the diaphragm and the sucking in of the sternum.
Anterior horn cells from the cord of a normal infant.
Anterior horn cells, showing the absence of dendrons and axons.

Case IV  X450
Figure XIII

Anterior horn cells, showing the gross diminution, both in size and number, of these cells.

Case IV  $\times 200$. 
Showing gross destruction of muscle fibres.

Case IV  X 550
Figure XV

Margaret Sullivan: Normal Muscle x 550

Normal Muscle fibres.

Case V x 550
Figure XVI

Showing normal and abnormal muscle fibres.

Case V  x150.
Normal and abnormal muscles fibres together.

Case V  x 150
Normal anterior horn cells from an infant.
Normal anterior horn cells.
Showing the decrease in size of the anterior horn cells, with loss of dendrons and vacuolation.

Case VI  x 400
Showing gross destruction of the anterior horn cells

Case VI
Muscle fibres, showing normal and abnormal fibres with atrophy.

Case VI  x400
Muscle fibres, showing normal bundles and also many atrophied fibres.

Case VI

×250.
Showing gross atrophy of muscle fibres.

Case VI  \times 100