

## TOXIC DEGENERATION OF THE LOWER NEURONES SIMULATING PERIPHERAL NEURITIS.

BY STANLEY BARNES, M.D., B.Sc., M.R.C.P.,

*Senior House Physician to the National Hospital for the Paralysed and Epileptic, Queen Square.*

THE cases recorded in this paper present a clinical picture similar in many respects to what is met with in peripheral neuritis, and yet in other ways resembling progressive muscular atrophy. I have been able to collect together seven instances<sup>1</sup> of this condition which have recently come under observation at the National Hospital, and I am indebted to Dr. Buzzard, Dr. Bastian, Sir William Gowers, and Dr. Ferrier, for their kind permission to publish these cases.

*Case 1.*—Lizzie B., a domestic servant, aged 21, was admitted to the National Hospital, Queen Square, on December 18, 1892, complaining of difficulty in walking and weakness of the hands for three and a half years. The family history was unimportant. Although she said she had always been a delicate child, her only previous illnesses had been measles in childhood, and anæmia since the age of 14; the latter had persisted with varying severity up to the onset of the present illness.

In the spring of 1899 she was in bed for a fortnight with rheumatic fever; the attack was a slight one, and in a few days she was about again doing light house work. A week after getting about, she found that the right hand was beginning to get weak, and that the fingers would go blue and cold. The weakness slowly increased, and shortly afterwards began to appear in the left hand, whilst her walking also became impaired. By June, 1899, she had to give up her work, and by July, 1899, the weakness had become so great that she was obliged to take to her bed. The weakness still increased, and for four or five weeks (August, 1899) she lay in bed unable to feed herself, with difficulty in

<sup>1</sup> Whilst this communication was in the press, Case 3 died in hospital; the results of the autopsy are reported in the appendix to this paper.

swallowing and in speaking. Bed-sores and incontinence of urine and faeces came on, and a hectic temperature was recorded; delirium was present at times. From this point forwards (September, 1899) she began steadily to improve. She recovered control over her sphincters, swallowing and speech became natural and the bedsores healed. By May, 1900, she had sufficiently recovered to be able to walk with assistance, and to feed herself; since then she has slowly but steadily improved. Whilst at her worst the limbs were absolutely helpless, and very tender, although quite numb; the subjective sensory signs had been absent for about a year before coming into hospital.

On admission she was a fairly well-built healthy looking girl, with no sign of visceral disease. Her memory was good and she was not emotional. There was no impairment of function of any of the cranial nerves, and the pupils reacted well to light. The muscles as a whole were well developed, especially the trunk and proximal limb muscles. In the arms the extensors and flexors of the elbows were of fair strength, but the extensors of the wrist were markedly weak and atrophic; the flexors of the wrist were also weak, but not so weak as the extensors. Most marked, however, was the great atrophy and weakness of the small hand muscles, especially on the right side; the thenar and hypothenar eminences had almost disappeared, and no faradic or galvanic excitability could be obtained here or in the lumbricales or interossei. The hands adopted the *main en griffe* position, but this could easily be reduced on manipulation.

In the lower extremities, the small muscles of the feet and the anterior tibial muscles were considerably atrophied and almost powerless; no reaction to faradism could be obtained in either set of muscles; the calf muscles were of only moderate power, not nearly so strong as they should have been in a girl of her build; the extensors and flexors of the knee were stronger but probably deficient, whilst hip movements were well performed. The weakness was almost completely symmetrical in both upper and lower extremities, but in both the right limbs tended to be more severely affected.

Slight tenderness of the calves on pressure was the only sensory sign present. Both feet were purplish-blue in colour and were usually very cold; the toe-nails were ribbed and atrophic (since the illness). The skin over the fingers was glossy and smooth, and usually moist with perspiration.

The jerks in the arms were normal; the knee-jerks were present, but diminished; the ankle-jerks were absent on both

sides, and the plantar reflexes were difficult to obtain, but of the flexor type. Romberg's sign was absent. The gait was of the "dropped foot" type, without any ataxia.

There was a slight bluish line on the gums opposite several teeth, and of the kind usually seen in cases of lead poisoning; but no history of any lead poisoning could be obtained, nor had she ever suffered from colic. Alcoholism and diphtheria were also definitely excluded.

Under treatment she slowly improved, the forearms and legs especially recovering; the hand and foot muscles showed only slight recovery after a five months' course of massage and galvanism.

*Case 2.*—Emily G., a single woman, aged 28, was admitted to the National Hospital on August 10, 1900, complaining of weakness of the hands and of the left foot since April, 1900. Her family history was unimportant. She had been a laundress for several years, and had suffered much from indigestion, but had never suffered from any acute disease. Alcoholism was denied.

For a month before the onset of the weakness she had suffered from a moderately severe attack of rheumatism in both feet—pain and swelling at the ankle-joints being the most marked signs. One morning, as the rheumatism was subsiding, she woke up to find her right ankle and left hand weak, and the weakness continued to increase for a few days, until it was as severe as when she was admitted.

On admission she was a well-built woman of good intelligence, and presenting no signs of alcoholism. The cranial nerves, viscera, and sphincters were all normal.

*Motor system.*—The trunk muscles were well developed and of good power. There was great weakness of the movements of the upper extremities, chiefly in the hands and wrists (extensor movement being weaker than flexion); the elbow movements were weak, and the shoulder movements, though stronger, were evidently below their normal strength. The arms were affected almost symmetrically, but the right was throughout a little the weaker. In the lower extremities there was great weakness of all movements at the right ankle, where dorsiflexion was almost nil. The left leg was affected, but to a much slighter degree. All the limb muscles were flabby and wasted; the small muscles of both hands were almost completely atrophied, the hand adopting the *main en griffe* position; there was much wasting of the extensor group of the forearms and of the anterior tibial group of the right leg. There were no contractures.

Of sensory changes, numbness of the hands and fingers and tenderness of the calves and legs were well marked; there was also slight but definite anæsthesia to light touches and to pin-pricks on both hands. There was well-marked sweating and congestion of the hands and feet.

*Electrically*, no faradic response could be obtained in the severely atrophied muscles, which required a strong galvanic current to produce a contraction; there was no polar change.

The knee-jerks were present, the left being brisk and the right considerably diminished. There was no ankle clonus, and the plantar reflexes were absent.

She was treated by massage and galvanism to the limbs, and strychnine hypodermically.

During her six months' stay in hospital she improved greatly in every respect, the hand atrophy and some weakness of flexion of the right ankle alone remaining on her discharge.

*Case 3.*—Elizabeth A., aged 34, was admitted to the National Hospital on September 8, 1902, complaining of weakness of hands and legs for thirteen months. She is unmarried and her family history is good. In childhood she suffered from scarlet fever and whooping cough, and at the age of 29 she had an attack of "jaundice." Shortly afterwards she went to South Africa, and remained there till a few weeks ago. In July, 1901, she was taken ill with mumps, which ran a fairly usual course; before she was fully convalescent jaundice with headache and vomiting came on, and it was as the jaundice was clearing up that she first noticed weakness of the legs with pain and tenderness of the feet, calves and knees. This got steadily worse, so that in about a month (September) she was unable to stand, and again took to her bed. The condition now began to improve, but a relapse occurred early in November, in which the hands as well as the legs got steadily weaker. She was at her worst about Christmas, 1901, and then had great weakness of the hands with much atrophy of their muscles, considerable weakness of the forearms and some of the upper arm groups; foot movements, especially flexion of the ankle, were much weakened, and all other leg muscles were affected, whilst the trunk muscles became so weak that she was unable to sit up in bed without support. There were no ocular, bulbar, or sphincter troubles.

From that time she slowly began to recover, the trunk muscles first, and then the proximal limb muscles; but the hands and feet have recovered very slightly if at all.

She is a life-long total abstainer, has never had ague, and has

PLATE I.



CASE 3.—Very severe atrophy of all the small muscles of the hands on both sides; tendency to the "claw-hand."



never been exposed to lead poisoning. There was no beri-beri in the district.

On admission she was a thin, pale, well-educated woman of 34; her memory was good, and she was not at all emotional. An enlarged movable kidney on the left side was the only visceral abnormality found. The cranial nerves were normal, and there was no optic atrophy or neuritis.

Her muscles as a rule were poorly developed, and could be easily examined owing to the small amount of subcutaneous fat present. The trunk and proximal limb muscles were of normal power and size, but the forearms and legs showed great muscle wasting and weakness, especially marked in the extensors of the wrists and the flexors of the ankles. The wasting here, however, was quite over-shadowed by that of the hands and feet, where hardly any muscle tissue seemed to remain. The hands adopted a *main en griffe* position, but were quite easily passively moved; the only muscle that could be felt to contract in either hand was the abductor transversus pollicis.

The feet were "dropped" but flaccid, not contractured; they could just be flexed against gravity; all the intrinsic foot muscles seemed to have disappeared; no faradic excitability could be obtained in the feet or hand muscles.

There was a sense of numbness of the hands and fingers and of the feet and toes, but no objective sensory change could be demonstrated here. The skin of the hands and feet was smooth, glossy and perspired freely, but the nails were normal. She could only walk with assistance—a typical "dropped foot" gait.

Up to the present (September 28) no material change has occurred in the condition.<sup>1</sup>

*Case 4.*—Ellen H., a domestic servant, aged 36, was admitted to the National Hospital on April 1, 1902. She complained of weakness of hands and legs of eight months' duration. The family history was good, and her own health had been good except for an attack of rheumatic fever at the age of 14.

In September, 1901, she had an attack of diphtheria; the attack was of moderate severity, and the local signs soon passed off. About three weeks after the onset of the diphtheria, she noticed her speech was becoming nasal, although she never had regurgitation of fluids through her nose; at the same time double vision and considerable difficulty in reading came on, quickly followed by a sense of heaviness of the hands and feet, the right hand and the left foot being chiefly affected.

<sup>1</sup> See Appendix.

There was at no time any sphincter trouble. As far as can be ascertained, the weakness of the hands and legs progressed for about eight weeks; certainly no improvement began to occur until March, 1902, or about four months after the onset of the paralysis.

Thenceforth a slow but steady improvement occurred, the left hand and the right leg especially improving.

With the paralysis had come on pain and great tenderness of the legs, and to a less extent of the forearms; whilst numbness and difficulty in distinguishing objects touched by her hands had also been very marked, but were considerably improved.

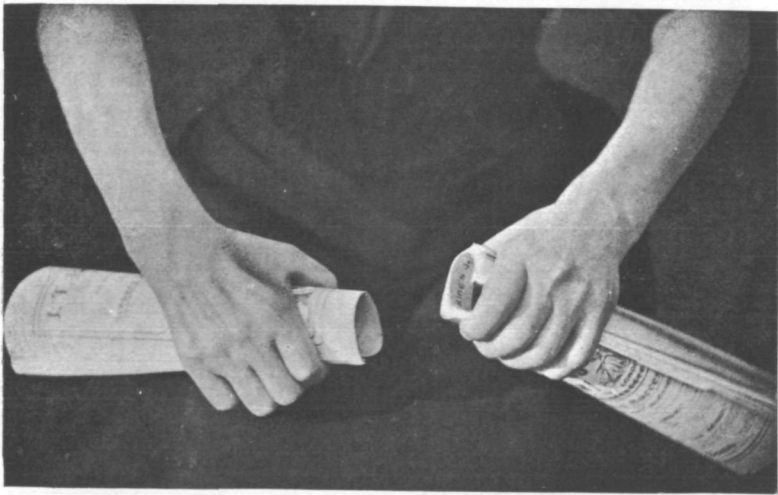
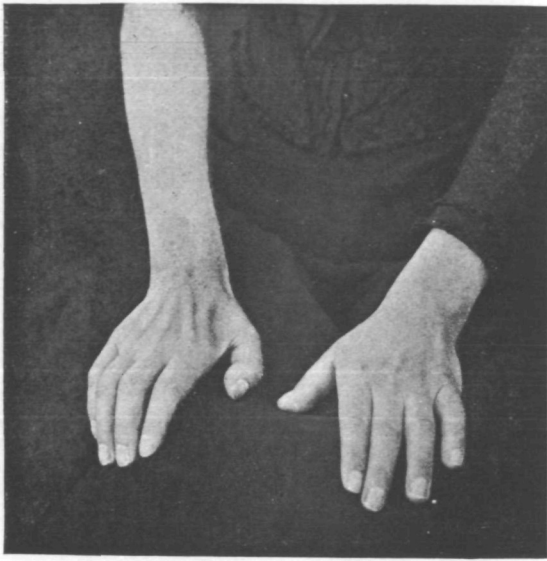
Atrophy of muscles began to come on shortly after the onset of the paralysis, and became progressively worse until Christmas, 1901. By this time the small muscles of the right hand were extremely atrophic, those of the left being less so, but still markedly smaller than normal. The forearm and legs were also much wasted, and some general emaciation had also occurred.

The atrophy remained unchanged till March, 1902, since which a steady filling out of the muscles had occurred, only the right hand muscles now being severely wasted.

On admission, she was a fairly well-built woman of healthy appearance; no abnormality was detected in the thoracic or abdominal viscera. The muscles generally were of good size and power, but there was considerable wasting of the forearm and legs (below the knees especially), and the small muscles of the right hand were extremely atrophic; the left hand muscles were also atrophic, but to a much less extent than those of the right hand. In the latter the interossei, abductor pollicis, flexor brevis pollicis and opponens had almost disappeared, and no faradic or galvanic irritability could be found in them. In each forearm the extensors were weaker than the flexors, but both sets of muscles reacted to faradism; it was also noticeable that the wasting was greater on the ulnar than on the radial side of the forearm, and that in firmly grasping an object with her right hand, the hand was not only slightly flexed on the forearm, but was also deflected to the radial side (see photograph, Plate I.). In the left forearm and hand similar changes were also visible, but were much slighter. By September 25, 1902, when the photograph was taken, the left forearm and hand were practically normal, and contrasted markedly with the still atrophic, though also improved, right forearm and hand.

In the lower extremities "foot-drop" was well marked, especially on the left side, and there was corresponding wasting and diminution of faradic excitability of the extensor groups of the

PLATE II.



CASE 4.—The upper figure shows the marked atrophy of the right hand muscles as compared with the left. The lower figure shows the position of the hand in grasping, *i.e.*, slight flexion at wrist with deflection to the radial side.



legs; the small muscles of the feet were very atrophic, especially on the left side; there was very slight contraction of the calf muscles.

Movements at the elbows and knees were all of moderate power, whilst those of the shoulders and hips, as well as all trunk movements, were of normal strength. The ocular, facial, palatal, mandibular and lingual muscles all appeared to act perfectly.

*Anæsthesia* to all forms of sensation existed markedly on the right hand and wrist and upon the left foot and outer side of the leg below the knee. None could be made out on the left hand and right foot, although in these members also the patient had a subjective sense of numbness. Of the reflexes the supinator jerk was diminished on the right side, but normal on the left; both knee-jerks were rather brisk, but no ankle-jerk could be obtained on either side; the right plantar reflex was of the flexor type, but the left was absent. All the other reflexes were normal. Both hands and both feet were nearly always blue and cold, and sweated profusely.

Under treatment by massage and galvanism, slow but steady improvement has occurred, so that now (September 28) the left upper extremity is almost normal, and much improvement has taken place in the right arm and hand; foot-drop is still present to a slight extent on the left side, but is far less marked. The objective anæsthesia has almost entirely disappeared.

*Case 5.*—Mary H., a single woman, aged 39, was admitted to the National Hospital in September, 1899, complaining of general weakness and loss of power. There was a strong neurotic history on her father's side, one uncle having suffered from alcoholic insanity and two others from neurasthenia; her mother was suffering from Bright's disease. The patient had always been of a "nervous temperament," and had had much domestic worry of recent years. For a considerable time before admission she had been a housekeeper, and had taken two bottles of stout a day; recently she had had frequent toothache, for the relief of which she took whisky, sometimes as much as eight glasses a day.

About Christmas, 1898, she took a long drive and caught a chill; she found that on her return home her hands were weak and her legs were less steady than usual. Since then the weakness had steadily increased, and slight numbness had come on in the extremities. Cramp pains in arms and legs had been frequent, but no other pain was complained about.

The limbs wasted considerably, especially the upper extremities, so that by September, 1899, although she could still walk, she was unable to button her clothes, &c.

There was a history of some mental enfeeblement and occasional hallucinations during the two months prior to entering the hospital.

On admission she was a moderately wasted woman of good colour. Vision was good and the optic discs were normal. The pupils reacted well to light and on convergence the other cranial nerves were also normal. The muscles as a rule were of poor size, more especially those of the limbs. Trunk movements were of good power and those at the shoulders, elbows, hips and knees were also fairly good. The forearms were considerably weakened and wasted, the extensors of the wrist and fingers having suffered more than the corresponding flexor muscles, although the latter were obviously weak. The small muscles of the hands were greatly weakened and wasted, and were by far the most atrophic muscles found; the lumbricales and interossei had been affected as much as the thenar and hypothenar groups; some fibrillary twitching was to be seen in the thenar muscles. The affection of the legs was comparatively slight, the flexors of the ankle not being markedly more weakened than the extensors. The gait was feeble and shuffling, but not of the "steppage" type. There were no rigid contractures.

Of sensory changes, numbness in the hands and feet were present to a slight degree only, but no definite loss of sensibility to light touches or pin-pricks could be found.

The muscles of the legs and arms were slightly tender if squeezed. There was no sphincter defect. The tendon jerks were present in about the normal degree in the upper and lower extremities and were equal on the two sides. The jaw-jerk was present, and the plantar reflexes were of the flexor type.

The only electrical changes found were in the small muscles of the hand, where a well marked reaction of degeneration was present.

The patient was treated in hospital for about six weeks by massage and galvanism, but no material change in the condition had occurred on her discharge.

*Case 6.*—Henry N., a sea captain, aged 50, was admitted to the National Hospital on November 1, 1897, complaining of weakness of the hands and legs.

His previous history was good, except that he had been constantly exposed to cold and wet (once having been shipwrecked)

and had suffered from erysipelas of the scalp eleven years previous to admission. He was a total abstainer from alcohol, and had never had malaria or any other fever.

About March 1897, he had an acute febrile attack with a temperature of  $103^{\circ}$ , for which he was admitted to hospital. He was at first supposed to be suffering from enteric fever, but in three or four days the temperature fell to normal and remained so. He was kept in bed for five weeks, and during this time the left leg became gradually weak, quickly followed by a progressive weakening of the hands and right leg; some general wasting also occurred, but there was at no time any difficulty with swallowing or with speaking; the sphincters were unaffected. There was no loss of feeling anywhere.

On admission six months after the onset, he was a powerfully-built man, of good memory. There was no defect of any of the cranial nerves.

There was a great wasting of the interossei, thenar and hypothenar eminences of both hands, more marked in the right than the left; there was also considerable wasting and corresponding weakness of the muscles on the ulnar side of the forearms. The long extensors and flexors of the fingers were weak, but all other muscles in the upper extremities were of good size and power. In the lower extremities there was some atrophy of all the muscles below the knees, and considerable weakness of the calf and anterior muscle groups. The gait was feeble and of the "dropped-foot" type.

The electrical reaction showed nowhere a full reaction of degeneration, but in the weakened muscles there was a diminished excitability to faradism. The supinator-jerks and knee-jerks were equal on both sides and normally brisk; but no plantar reflex or ankle-jerk was noted. No objective sensory changes could be made out.

The patient remained in hospital for three months, during which time no further progress of the disease occurred. He was discharged on February 1, 1898, in a slightly improved condition.

*Case 7.*—George G., an engineer, aged 22, was admitted to the National Hospital on April 18, 1899, complaining of weakness in the arms and legs of nine months' duration. The family history and previous history were good; he had never taken alcohol, nor had he suffered from ague or tropical fever.

The onset was rather acute whilst he was apparently in good health, and off the Coast of Mauritius. His first symptom was weakness in the right hand, and this was quickly followed by

weakness in the left hand and difficulty in walking. The weakness rapidly increased, and in a few days both upper extremities were weak in all their movements, and he became unable to stand. There was severe pain and tenderness in the legs, especially at night-time, there was never any feeling of numbness, nor any sphincter trouble. He was taken into hospital a few months later and improved whilst there, but on his discharge the weakness again increased until he was admitted to the National Hospital six months after the first sign had occurred.

On admission, he was a well-built young man of fair education. The abdominal and thoracic viscera appeared to be healthy, and no defect was found in the cranial nerves. Motor power was good in the trunk and shoulder muscles, but extension and flexion of the elbows were below normal strength. Flexion of the wrist was weakened, but not so much as extension; all the movements of the hands were very weak, but none were lost. There was marked atrophy of the thenar, hypothenar and interosseous muscles in both hands, and to a less extent there was wasting of the forearm muscles.

In the lower extremities dorsiflexion of the ankle was his weakest movement, and the calf muscles were also considerably weakened; other movements were of good power. There was considerable tenderness of the calves on pressure, and great pain was caused by pressure over the nerve-trunks. There was no objective anæsthesia. The knee-jerks were normal, and the plantar reflexes were present and of the flexor type.

He remained in hospital for three months, being treated by massage and galvanism; he steadily improved, and on his discharge he had almost completely recovered, only a little weakness and atrophy of the hand muscles remaining.

#### CLINICAL CONDITION.

At the stage when they came under observation the cases recorded above all showed a well-marked atrophy of the small muscles of the hands, together with weakness of the extensors of the wrist and of the flexors of the ankle. The atrophy of the small muscles of the hand in five of the cases reached a severe degree, and especially in Case 3, where only the slightest contractions were possible in the interossei, lumbricales, thenar, or hypothenar muscles. In the more severe cases there was no reaction to the faradic

current in the hand muscles, and diminished reaction in the extensor group of the forearms and in the flexor group of the ankle. In other words, there was an atrophic paralysis of the peripheral type, a paralysis in which the most distal muscles had suffered severely, and in which the proximal muscles were only slightly or not at all affected. In none of the cases did the muscles particularly affected correspond to particular peripheral nerves; the distribution of atrophy corresponded rather to the segments of the cord, the first dorsal supply being especially picked out.

A marked feature of these cases was the absence of rigid contractures. The reason for this appeared to be twofold: firstly, because there was little or no pain on active or passive movement, so that the limbs were kept constantly supple; and secondly, because with the severe atrophy and loss of power of particular muscles there always occurred weakening of the neighbouring muscles.

In all the cases sensory changes, though present, were comparatively slight. They were most marked in Case 4, in which patient definite objective anæsthesias could be made out. All but one of the patients complained of *numbness* in the extremities at some period of the disease, but, as a rule, this sensation was only temporary, and was not noted after admission to hospital. The most prominent sensory sign in all the cases was *muscle tenderness* and tenderness on pressure over the nerve-trunks in the limbs; this persisted in every case until admission, although in Case 1 the most severe grade of the disease had occurred some three years previously. The sensory changes found were thus similar in all respects to those seen in ordinary alcoholic neuritis, but were much less severe at all periods of the disease. In none of the cases was any change found in the fundus oculi.

Case 1 was the only case in which sphincter trouble had occurred; bulbar signs also only occurred in this case at its worst stage and in the case which followed diphtheria, so that, apart from the well-known selective action of the diphtheria toxine in paralysing the palate and ocular muscles, it might be said that cases of the kind recorded here do not show signs of involvement of the cranial nerves, except in

those instances in which a severe and widespread paralysis exists.

*Diagnosis.*

None of the cases were seen during the progress of the acute symptoms in the early stages. Had they been seen then, there is little doubt that the diagnosis would have been very difficult and that they would have been called multiple neuritis, Landry's acute ascending paralysis, or possibly polio-myelitis. The rapidity of onset of the nervous symptoms was extremely variable, varying from a few days (as in Case 7), to nearly seven months (as in Case 1). With regard to the acute cases, the resemblance to Landry's paralysis, must have been extremely striking—the rapid spread of paralysis from the periphery to the central muscle groups, the slight sensory signs, the slight involvement of the sphincters and the absence of tendency to the formation of bed-sores. In none of the cases recorded was I able to get any account of the electrical excitability of the muscles in the early stages. From the histories given, atrophy of muscle appeared only to come on late in the disease and would not, therefore, assist in the diagnosis at an early stage.

The diagnosis from pure acute or sub-acute polio-myelitis would have been less difficult in the early stages, owing to the sensory signs present. All the cases gave a history of muscle tenderness, and in most of them numbness of the extremities, a sensation of tingling or (spontaneous) pain in the limbs were present, and from the patients' accounts were much more severe and persistent than is usually seen in acute anterior polio-myelitis. The distribution of the paralysis would also have given a clue to the character of the disease in most cases, for although the signs were as a rule mainly motor, there was a well-marked symmetry of affection both in the upper and lower extremities, which would strongly suggest rather a general toxic or inflammatory condition than a focal polio-myelitis. The fact of the disease occurring in adults would not of course of itself negative a diagnosis of acute polio-myelitis.

Later in the disease, particularly at the stage when the

cases were seen in hospital, the diagnosis was in several cases a matter of considerable difficulty at first. It looked as though we had to deal with a patient who had suffered from some acute paralytic condition upon which had been grafted as it were a chronic progressive muscular atrophy. Certainly the resemblance to the Aran-Duchenne type of the latter disease was very striking—the claw hand with atrophy of hand muscles which showed the electrical changes of degeneration, with more or less definite atrophy of other muscles, almost exactly resembled what is seen in progressive muscular atrophy; but the diagnosis of this disease in association with an old neuritic condition was clearly negatived by the course of the affection and the regularity with which one or both of the knee-jerks was found impaired or lost. It is almost unknown in the Aran-Duchenne form of progressive muscular atrophy, to meet with a patient whose knee-jerks are not brisk, except in association with definite atrophy of the quadriceps muscle. In none of the recorded cases was there such a definite atrophy, and in none was there any exaltation of the tendon jerks in the lower limbs; ankle clonus was never found, and the plantar reflex was usually deficient or absent, and when present was always of the flexor type. In only one case also was there any contracture of the calf muscle, and even here (as in the other cases), the lower limbs were quite flaccid. The course of the disease was even more certain evidence that the condition was not one of progressive muscular atrophy. Despite the great wasting of muscles that had occurred in some of the cases, all the patients under observation tended gradually but constantly to improve. Even the hand muscles have filled out again after appearing almost absent, as has been especially noticed in Case 4, during the six months she has been under observation.

The diagnosis of multiple neuritis could not be excluded in any of the cases. In each of them there was the same type of atrophy and weakness with muscle-tenderness, largely symmetrical in distribution and with diminished tendon-jerks. The most marked differences from the usual

form of polyneuritis were—(1) the great atrophy of the intrinsic muscles of the hands; (2) the comparative slightness of sensory changes; (3) the absence as a rule of contractures and (4) the integrity of the psychical condition.

### *Prognosis.*

In all the cases at the stage at which they first came under observation, the prognosis was good in that they tended constantly to lose their sensory signs and to gain power in the affected muscle groups. The hand muscles appeared to be the last to recover, and as far as it has been yet possible to trace the cases, it would seem that years may elapse without full recovery occurring. Nevertheless in all the cases a steady if slow improvement was the rule. In only two of the seven cases was there a history of anything approaching a relapse; all improved under hospital treatment.

### *Etiology.*

Five of the cases gave a history of some febrile condition preceding the onset of the disease, viz., rheumatism (in two cases), diphtheria, mumps, and some pyrexial disease of unknown origin in one case each. In one a definite history of alcoholism was found; in the last case no etiological factor could be made out. As compared with the peripheral neuritis usually seen, it is remarkable that only one of the seven cases might be of alcoholic origin; it is also worthy of note that all of the above factors have also been recorded as antecedents of Landry's paralysis. The severity of the antecedent disease does not seem to have been at all commensurate with the degree of weakness following; for example, in Case 1 the attack of rheumatism was extremely slight, whilst the paralysis ultimately became very severe.

### *Pathology.*

In none of the cases did a fatal termination ensue,<sup>1</sup> so that the morbid anatomy and pathology can only be inferred from clinical considerations, and from a comparison with

<sup>1</sup> See Appendix.

what has been found in similar but fatal cases. Regarded from a purely clinical standpoint it is difficult not to conclude that we are here dealing with a disease which has affected not only the peripheral nerves but the spinal cord. Referring to progressive muscular atrophy, Gowers (1) states that "cases are met with (although not frequently) that present every gradation to subacute polio-myelitis in one direction, and perhaps also to polyneuritis in another." Clinically, the cases reported here appear to be of this intermediate form. If the severe atrophy of the hand muscles (as shown in the photographs) is to be considered as solely a peripheral nerve lesion, then it must be that particular parts only of peripheral nerves are involved, for the atrophy is as severe in those hand muscles supplied by the median as in those supplied by the ulnar nerve, whilst many muscles of the forearm supplied by the median have remained of fair power. It seems much more rational to suppose that we have here to deal with a toxic affection of the lower neurones, the motor neurones being much more severely affected than the sensory.

On this hypothesis it would be comparatively easy to understand why a mixed motor and sensory nerve like the median should have lost some of its functions whilst others remain. For we should then be dealing with a kind of system degeneration, in which the fibres supplying the muscles subserving the more highly organised movements in the upper extremities are the ones which suffer first and most. We are, however, bound to assume also that the toxine, or more probably toxins, do not act solely on the lower motor neurones, but also upon the lower sensory neurones, although to a much slighter degree; otherwise it is impossible to explain the symptoms of persistent muscle-tenderness, numbness, and anæsthesia which have been noted. This view of the pathology of these cases accords well with the findings of Batten (2) in cases of diphtheritic paralysis; he found "that the dominant lesion in diphtheritic paralysis is a parenchymatous degeneration of the myelin sheath of the nerves. . . . It seems almost certain that a general poison like that of diphtheria must

act on the whole neurone, and . . . that the effect of the poison manifests itself at least in fatal cases in the myelin sheath, and not in the cell-body." However true it may be that in ordinary forms of diphtheritic paralysis there is no change in the cell-bodies, yet it is difficult to believe that cases like those recorded here with long persistent local atrophies are due purely to peripheral nerve affections.

A case very similar to these was published this year by Luzzetto (3), in which malaria appeared to be the cause of the paralysis. The patient rapidly developed paralysis of the hand muscles and of the extensor groups of the forearms, with muscle-tenderness, but no objective sensory change; marked atrophy of the thenar and hypothenar muscles followed, and the patient died of pneumonia about two months after the onset of the nervous symptoms. Marked degenerative changes were found in the nerves and in the anterior horn-cells, and Luzzetto concluded that the cord changes were not secondary to the nerve changes, but that the whole neurone was involved simultaneously.

Another case in many respects resembling those under discussion has been published by Stewart (4). The patient was a woman of 33 years of age, and seven months pregnant at the time of the onset of the disease. No febrile attack preceded the illness, and no other toxic cause could be discovered. The symptoms were numbness of the hands and feet, much tenderness of the calves, and some anæsthesia with atrophy of muscles in the upper and lower extremities. The disease progressed for about six months, the patient dying of pneumonia. The nerves here showed both parenchymatous and interstitial changes, evidently a true neuritis. There was also a doubtful inflammatory condition in the capsule around the anterior horn-cells of the cord, and undoubted chromolytic changes, and in places atrophy of many of the cells.

The cases recorded here appear to correspond clinically rather to the first than to the second of these cases, in that, in Stewart's case, sensory changes were very marked, almost if not quite as marked as in cases of alcoholic neuritis. Possibly the reason for this difference in the clinical symp-

toms is that the first recorded (malarial) case, was one of toxic degeneration and not of true neuritis; whereas in the second case there was a marked inflammatory condition of the peripheral nerves. I think the distinction is an important one, although it is quite likely that the two conditions may be present in a single case. It would appear probable that when the nervous system is suddenly flooded by toxins the full effects of the poison may be developed, and a true neuritis ensue; whereas if the same toxin were only administered in small doses over a longer period, a selective action might ensue, and cause a degenerative as opposed to an inflammatory reaction. It must also be true that certain of the toxins causing flaccid palsies tend rather to produce inflammatory than degenerative results and *vice versa*; for instance, diphtheria only rarely causes any interstitial inflammation of peripheral nerves, whereas it is almost the rule in the alcoholic palsies to get an interstitial neuritis developed. Toxins like those of influenza, rheumatism, mumps, &c., would appear to approach more closely to the diphtheritic type, *i.e.*, to cause parenchymatous degeneration rather than interstitial neuritis, and it is not surprising to find the symptoms of the "neuritis" following these diseases differing in a more or less marked degree from those seen in the more common (alcoholic) form of multiple neuritis.

At the present time it is impossible to discuss the pathological relationship between these cases and Landry's paralysis. The latter disease is a clinical symptom-complex, and its pathology is as yet uncertain. Raymond (5) considers that polyneuritis, poliomyelitis and Landry's paralysis are diseases that cannot be sharply distinguished from one another, and that they have the same etiology. Redlich, too, believes that polio-myelitis and polyneuritis are the same affection with different localisations. On the other hand, E. W. Taylor (6) denies that there is any certain evidence of a coincident inflammation of the ventral horn and the peripheral nerves.

I am inclined to think the balance of evidence is in favour of a coincident affection of the whole of the lower neurones, possibly more marked in one part of them than

another; that in these cases the motor neurone is more severely diseased than the sensory neurone; that in the cases recorded here, there is a parenchymatous degeneration rather than a true inflammation; and lastly, that although at some stages of the disease there is a lesion sufficiently severe to destroy for the time being the functions of the main mass of the nerve-fibres to the limbs, that in great part the lesion falls short of absolute destruction, so that a large amount of repair is possible in all cases, and that in some cases the repair of tissue and consequent recovery of function may be complete.

### CONCLUSIONS.

(1) There is a clinical type which is usually the sequel of acute specific fevers, which resembles the paralysis seen in multiple neuritis, but which is associated with great atrophy of the hand muscles. It usually begins about the second or third week after the febrile condition, and involves the muscles from the periphery to the trunk to a varying extent. It may progress for a few days only, or for several months. Sensory signs are present, but slight in degree. Although the condition somewhat resembles progressive muscular atrophy, the prognosis and etiology of the two conditions are probably widely different from one another.

(2) After a certain stage, when once definite improvement has begun, relapses are not common, and there is a constant tendency to improvement. Even years after the subsidence of the acute condition considerable improvement may still take place, the small muscles of the hands being the last to recover. Contractures are rarely developed.

(3) Probably the condition is one of toxic degeneration of the lower neurones, the motor neurones being more particularly affected.

### APPENDIX.

A further report of Case 3, with results of *post-mortem* examination.

On November 17, 1902, whilst still in hospital, the patient began to complain of obscure pain in the back and a general

sense of uneasiness. Nocturnal restlessness and insomnia came on, and the enlarged kidney became slightly more tender on pressure; there was a light cloud of albumen in the urine. This condition persisted for several days, and on November 24 she complained of feeling much weaker, and was unable to sit up in bed. It was then found that all the tendon-jerks had disappeared since the previous week. Numbness and tingling came on in the hands and feet, and next day there was incontinence of fæces and urine (although she was fully conscious) and respiration was embarrassed. No bulbar signs developed, but she died in the afternoon of November 25, of respiratory failure. The mode of death was almost identical with that which occurred in a case of Landry's paralysis which was in hospital shortly afterwards.

At the autopsy held next day, there was found congenital cystic disease of both kidneys of considerable severity; both kidneys were very much enlarged, but contained so much normal parenchyma that it is almost certain that this was not the direct cause of death. The other abdominal and thoracic viscera were normal. The spinal cord was smaller than usual, and most of the nerve-roots and peripheral nerves originating from the cervical and lumbo-sacral enlargement were thin and wasted.

Attempts to cultivate bacteria from the cerebro-spinal fluid and spinal cord, gave negative results (gelatin, agar-agar and bouillon). The central nervous system was removed and hardened partly in formalin and partly in absolute alcohol, and sections were prepared by the methods of Marchi, Weigert, Nissl and van Giesson; a few sections were also stained by hæmatoxylin and eosin. The peripheral nerves and posterior root ganglia were similarly treated, and parts of apparently normal and diseased muscles were stained by hæmatoxylin and eosin.

The following microscopic changes were found:—

*Muscles.*—The erector spinæ, infra-spinatus and flexor muscles of the forearm were normal. The pronator quadratus was moderately affected, as were the extensors of the wrist. The lumbricales, flexor brevis pollicis, abductor pollicis, opponens pollicis and hypothenar muscles all showed very marked changes from the normal.

In the diseased muscles there was found great thickening of the arteries and a proportional increase in the general fibrous tissue; in all probability there was no actual increase in the amount of fibrous tissue, the apparent increase being due to wasting of the muscle-tissue. There was no small-celled infiltration. The tendon appeared normal, and the muscle spindles

remaining completely unaffected side by side with atrophic muscle-fibres, were very prominent and proportionately numerous ; in every case the muscle-fibres contained in the muscle-spindles remained normal.

Atrophy of muscle-fibres has occurred very diffusely ; in some muscle-groups, it is true, nearly every fibre is atrophic, but the rule is for the degenerated fibres to lie side by side with normal ones. In those muscles which are only partly affected, only certain of the muscle prisms show any atrophic fibres ; in a severely affected muscle (the lumbricales for instance) every prism contains some degenerated fibres. The affected fibres are much reduced in size—to about one-sixth of their normal cross section ; they stain more darkly than usual but preserve their striation perfectly. They are not particularly granular, and contain no fat ; they have not lost their regularity of outline.

*Nerves.*—The ulnar nerves were the most severely affected of the nerves examined. Hæmatoxylin stained sections showed marked thickening of the coats of the arteries, but no increase in the number of nuclei present nor any proliferation of interstitial tissue. By the Weigert method marked changes were found. Whole strands of fibres were degenerated and showed simply beads of unabsorbed myelin instead of a continuous medullary sheath. Many very finely medullated fibres were seen which showed fusiform swellings of myelin—probably regenerating fibres. About one-eighth of the fibres were of the normal size ; about one-third of the fibres were reduced to about half the normal diameter ; whilst the rest consisted of the very fine fibres with fusiform swellings. As in the case of the muscles, the fibres affected were scattered very diffusely throughout the nerve, and did not lie in special bundles. By the Marchi method no degenerative changes could be made out ; in all probability the fragmentation of myelin seen in some of the fibres by the Weigert method was an artefact.

*Posterior root ganglia.*—These all appeared to be normal in every respect.

*Medulla and spinal cord.*—All the sections of the medulla were normal ; no sign of any affection of the hypoglossal or vagus nuclei could be found.

In the spinal cord no abnormality could be detected by the Marchi or Weigert-Pal methods in any of the tracts. Sections stained by the van Giesson method showed an extremely marked change in the vessels of the whole spinal cord ; these changes were most marked in the cervical enlargement, but were also

present to a less extent in the lumbar enlargement and dorsal region. A section taken at the level of the eighth cervical segment (where the affection was severe) showed a great thickening of the walls of all the arteries, which appeared to be embedded in a faintly striated material with a peculiarly vitreous appearance; it stained faintly with basic dyes, and bright red with van Giesson's solution, but did not give the amyloid reaction. The septa seemed to be entirely composed of this material, and were greatly swollen; the pia mater immediately around the cord was similarly though less severely affected. Where vessels were cut in cross-section, this material was faintly laminated as it lay around them; a few nuclei were scattered irregularly through it, but otherwise it presented an almost homogeneous appearance. The vessels and supporting tissue of the nerve-roots at their points of exit from the cord were similarly affected. Throughout the endothelial coat of the blood-vessels was unaffected and none of the vessels appeared to be thrombosed.

The *cell changes* were almost entirely confined to the anterior horns, and were extremely marked in both the cervical and lumbar enlargements. A section taken at the level of the fourth cervical segment showed about a sixth of the anterior horn cells to be normal; a few cells were shrunken and deeply-staining, but there was no evidence of any cell having completely disappeared. The rest of the cells were in various stages of tigrolysis; they were swollen, stained homogeneously a faint blue colour (Nissl method), no tigroid bodies being visible; in most of the cells the nucleus was eccentric.

At the level of the seventh cervical segment the antero-lateral group was the one most markedly affected, only a few dark-staining, shrunken remnants remaining; in the other groups of cells a little acute change was present, but in the main they were normal. At the level of the first dorsal segment much atrophy of cells was apparent. In one section not a single cell was left in the entire anterior horn, and in most only a few ragged, broken remnants could be found to represent the horn-cells. In the second dorsal segment most of the anterior horn-cells were atrophic, but a few which had survived showed tigrolysis.

In the lumbar region there was no evidence of any cells having disappeared, and none were seen in an atrophic condition. Nearly every cell was much swollen, with excentration of the nucleus and marked tigrolysis; a few cells—not more than a tenth of the entire number—were apparently normal.

It was thus clear that as a whole two kinds of cell change

were present. In the first place, some of the cells had atrophied as a result of a long-standing process, whilst others were in a state of tigrolysis as a result of the morbid process which was the immediate cause of the patient's death.

The results of pathological investigation thus largely bear out what had previously been surmised. There can be little doubt that this patient succumbed to the third attack of a toxæmia which caused degeneration of the lower neurones. I would again emphasise the remarkable similarity between the terminal attack and the clinical condition seen in Landry's paralysis. If this patient had come into hospital for the first time during the final acute attack, and had shown no signs of previous nervous disease, there can be no doubt that a diagnosis of Landry's paralysis would have been made without hesitation. Whatever the pathological relationship between the two sets of conditions may be, it would seem that clinically one would have been justified in regarding this case as one of relapsing Landry's paralysis. The condition of the kidneys in this case may have been a factor predisposing to the disease by deficient elimination of toxins; but seeing that the amount of urine passed was never below the normal, I do not think they played any essential part in the production of the disease.

I am deeply indebted to Dr. Farquhar Buzzard for his care in the preparation of the specimens, and to Dr. J. S. Collier for his assistance in describing the pathological changes.

#### BIBLIOGRAPHY.

- (1) GOWERS. "Diseases of the Nervous System," 3rd edition, vol. i., p. 532.
- (2) BATTEN. "Diphtheritic Palsy." *Transactions of the Pathological Society of London*, 1899.
- (3) LUZZETTO. *Berlin Klinische Woch.*, April, 1902.
- (4) STEWART. *Philadelphia Medical Journal*, May, 1901.
- (5) RAYMOND. Oppenheim's "Lehrbuch der Nervenkrankheiten," 2nd edition, p. 394.
- (6) TAYLOR. "Poliomyelitis." *Journal of Mental and Nervous Diseases*, 1901.