Original Papers.

LANDRY'S PARALYSIS: A CLINICAL AND PATHOLOGICAL STUDY.

By

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INTRODUCTION.

In 1859 Landry described the first case of a kind of acute or subacute paralysis which since then has become associated with his name. In their clinical features these cases are sufficiently dramatic to attract attention, and in their incidence sufficiently rare to merit individual publication, so that the subsequent literature has been plentifully supplied with reports of cases and discussions concerning them. Landry himself described a clinical syndrome which was fairly definite, but which was associated in the cases described by him with a remarkable lack of post-mortem findings. With more modern technique for examining the nervous system it is likely that changes would have been found which he failed to find, but even by these methods it is probable that they would be remarkably slight. Without entering upon a discussion of the nature of disease, it may be said that diseases have traditionally been described as entities on the basis of a common etiology, a common syndrome or complex of symptoms and physical signs, and a common pathology. With Landry's paralysis little or nothing is known of a common etiology, and the pathological findings, in so far as they are not negative, have been variable; consequently a diagnosis of 'Landry's paralysis' must rest upon the most unsatisfactory and variable member of the triad, viz., upon a complex of symptoms and physical signs. The essentials of this complex, in its typical form, are an acute or subacute paralysis of lower motor neurone type ascending from the feet upwards, symmetrically on both sides of the body. There is no objective sensory disturbance, and no loss of function of the sphincters of bladder or rectum. There is little or no febrile reaction, and no considerable muscular atrophy. The common result is death from paralysis of the motor nuclei of the bulb. It is proposed in this paper to describe three hitherto unreported cases which corresponded in their clinical features more or less closely with this picture, together with the post-mortem findings in two of them; further,
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to compare them with the reports of 52 cases collected from the literature, in the hope of answering the question whether there is such a disease as Landry's paralysis with a uniform etiology, symptomatology and pathology, or, if not, what the relation of this particular symptom-complex is to etiological and pathological factors, and how far it can be related to other and more strictly defined diseases.

Before passing to an actual description of cases, some mention must be made of the criteria which have been used in judging whether a case should be included in this series or not. Practically any case which has been reported under the name of Landry's paralysis or acute ascending paralysis and which shows no evidence of involvement of the upper motor neurone, and no, or very slight, objective sensory disturbance has been included, provided any atrophy of muscles which occurs is insignificant compared with the paralysis. With a few notable exceptions all the cases have been collected from English or American literature on account of its greater accessibility.

I have to thank Dr. S. A. Kinnier Wilson for permission to make use of the first case, W. A., and Dr. D. Firth for the other two, R. T. D. and J. L. W.

PERSONAL CASES.

Case 1. W. A., age 50, male. Admitted to King's College Hospital, April 8, 1928, under the care of Dr. Kinnier Wilson.

A spare man, with rather poorly developed musculature, of temperate habits. No significant past history of disease. He had been for a fairly long walk on the day before the onset of symptoms.

He first noticed a dull aching pain in his left foot, which extended to the calf and, on the second day, up to the level of the navel and thence to the right arm. On the third day pain of a similar character was felt in the right foot, and he found that his legs gave way under him. Later in the same day his left arm became useless and his right arm weak. He remained in much the same condition till towards evening on the fourth day, when he had great difficulty in breathing and was particularly troubled by some phlegm in his throat which he was unable to cough up. He was admitted to hospital that same evening.

His respirations were shallow, and at the rate of about 40 to the minute; the pulse was 140, regular, and of poor volume and tension, the radial artery being tortuous and easily palpable. Temperature 99° F. Examination of the lungs revealed very poor air entry on the right side, but no adventitious sounds or impairment of note. Breathing was diaphragmatic. The area of cardiac dulness was almost completely obscured by emphysema; the sounds were normal but distant. B.P. 120/90. The abdomen was lax and slightly distended, but not otherwise abnormal. The urine was normal, and there was no disturbance of function of the sphincters of the bladder or rectum.

With the exception of the diaphragm there was almost complete flaccid paralysis from the pectoral muscles downwards. Slight flexion and extension of the toes was possible. Deep and superficial reflexes were all absent except that the plantar responses were both feebly flexor. The left arm was completely paralyzed, with loss of deep reflexes; the right arm was very weak, but feeble movements of the fingers were possible. The
biceps jerk was just present, the triceps jerk very doubtful and the supinator jerk absent. All movements of the neck could be performed weakly; he could just raise his head from the bed. The cranial nerves showed no abnormality. The fundi were normal, and mastication, deglutition and articulation were all normally performed. No sensory changes could be detected.

On the fifth day there was no notable change. The temperature was, morning 98.4°F., evening 101.6°F., the pulse 140, and respiration 40. Air entry on the right side of the chest had improved a little.

Lumbar puncture was performed. The fluid issued under what appeared to be slightly increased pressure. It was clear and contained 4 lymphocytes per c.mm. Total protein .06 per cent. (by Mestrezat’s diaphanometric method); globulin test (Ross-Jones’ modification of the Nonne-Apelt reaction) negative. Sugar and chlorides were both within normal limits, and the Wassermann reaction was negative. No organisms were found.

In the evening of that day (the fifth) it was found that he could move the terminal phalanx of his left thumb, which he could not do before, and he thought the movements of his right arm and toes were stronger. They were not obviously so. Coarse râles could be heard over the right lower lobe.

On the sixth day it appeared as if he could raise his head a little more easily from the bed, and slight flickering contractions of the pectoral and left biceps muscles could be obtained. There was still no objective sensory change, and no sphincter trouble.

The patient died that evening of broncho-pneumonia.

Post-mortem examination (No. 75, 1928, in hospital records).


Unfortunately only the spinal cord with its membranes and nerve roots was preserved for sectioning.

The membranes were in all sections normal. Their blood-vessels were perhaps over-filled with blood but there was no evidence of inflammatory infiltration. The blood-vessels in the cord itself were also very full of blood, but again there was no evidence of inflammatory infiltration.

The nerve tracts in the cord and the spinal nerve roots had a normal appearance in sections stained with hematoxylin and eosin, but Marchi’s method was not used.

The nerve cells were examined after staining with Nissl’s methylene blue. About one-third of them were normal in appearance. The rest showed changes which varied from complete disappearance of granules, with eccentricity of the nucleus and a rounding and blurring of cell outlines, to cells which showed only some diminution in size of the granules. This gave them a fine dust-like appearance, often only at one pole of the cell, or immediately round the nucleus. The extreme change was not very common, nor could it be said that such chromatolysis as there was, was predominantly perinuclear. In the lumbar and sacral parts of the cord the process was most advanced; in these parts it was difficult to find a completely normal nerve cell, whether in the anterior or posterior horns. In the thoracic region chromatolysis was still well-marked but normal cells were commoner. The cells of Clarke’s column and those at the base of the posterior horns seemed more affected that those in the anterior horns themselves. In the cervical region changes were slight, and again most easily found in the intermediolateral parts of the grey matter.

The neuroglia showed no change, but special neuroglial stains were not used. The central canal of the cord was patent down to the sacral region.
CASE II. R. T. D., age 25, male. Admitted to King's College Hospital, November 26, 1927, under the care of Dr. Firth. Nothing is known of the past history of this patient. He was a well-developed muscular young man.

His illness started with headache and pain in the back. He vomited once. The pain and headache continued and on about the tenth day his legs rapidly became paralysed. Two days later he was admitted to hospital, when a complete flaccid paralysis of the arms, lower intercostals, diaphragm, abdominal muscles, and legs had supervened. A little feeble movement of the toes was possible, and the plantar reflexes were flexor. Slight early papilloedema was noted in both fundi, but otherwise the cranial nerves were normal. Pain persisted in the back, and he vomited once after admission. There was no objective sensory change and no loss of sphincter control.

A lumbar puncture was performed. Unfortunately the report on the fluid obtained has been lost, and it is only known that a pleocytosis, mainly (? wholly) of lymphocytes was present.

He died about 12 hours after admission to hospital. His temperature during this time was in the neighbourhood of 101° F.

Post-mortem examination (No. 239, 1927, in hospital records).

Lungs: Collapse of both lower and the posterior parts of both upper lobes, more complete on the right than on the left. Tuberculous scars at both spicis. Heart: Right side engorged. Aorta: Slight early atheroma. Intestines: Distended with gas. Brain: Basal ganglia rather pink in colour. Otherwise normal. Cord: The veins on the posterior aspect were engorged, and the cord itself very soft and slightly pink. The other organs were all normal.

Microscopic sections showed the following pathological changes.

The meninges of the cord and round the brainstem showed slight general infiltration chiefly with lymphocytes, but also with a few plasma-cells and an occasional polymorph. This infiltration was much more marked in the immediate neighbourhood of the blood-vessels, which were engorged with blood. It was most conspicuous in the lumbar region, less so round the brainstem, and least of all in the thoracic region. Perivascular infiltration with small round cells was also very marked round the blood-vessels of the cord and brainstem. It was most conspicuous round the medium-sized vessels, the Virchow-Robin spaces being packed with lymphocytes, but, particularly in the lumbar region, it extended to the small vessels and capillaries. All the vessels were engorged, but there was no evidence of thrombosis or hemorrhage; nor was there any evidence of inflammatory infiltration in the nerve-roots.

The nerve-cells. In the lumbar region Nissl's stain showed an almost complete chromatolysis of all the nerve-cells, both in the anterior and in the posterior horns. A few cells still preserved a few granules in the peripheral parts of their cytoplasm. Many were swollen and rounded, with nuclei excentric and badly stained. In the thoracic region these changes were even more advanced. Most of the cells were rounded and had lost their processes; some were vacuolated, and many showed excentricity and poor staining of the nuclei. Only a very few retained any Nissl's granules. The changes were again general, but more marked in the anterior horns. The section through the brainstem was made at just below the upper limit of the gracile and cuneate nuclei. The nerve cells of the hypoglossal nucleus were practically normal in appearance, as were those of the eleventh nerve nucleus, although the latter did show some signs of perinuclear chromatolysis. The cells of the gracile and cuneate nuclei and of the olives showed rather more definite perinuclear chromatolysis, and those granules which were present seemed smaller and less definite than usual. On the whole, however, degenerative changes in the cells in this region were slight, and nowhere so marked as in the cord.

There was some neuroglial proliferation in the cord, especially in the anterior horns of the thoracic part. The central canal was patent in all the sections examined,
Sections of the motor cortex and of the ulnar, posterior tibial and external popliteal nerves, stained with haematoxylin and eosin, showed no abnormality. Marchi’s method was not used.

It is noteworthy that in the thoracic part of the cord, where the degeneration of nerve cells and neuroglial proliferation were most marked, there was least inflammatory infiltration. It was confined almost exclusively to the sheaths of the vessels dipping into the cord, and to their larger branches.

Case III. J. L. W., age 16, male. A case seen privately by Dr. Firth, to whom I am indebted for the following details.

Past history. Whooping cough, catarrh of the stomach, an abscess in the neck, and measles, all before the age of ten years.

On November 5, 1927, the patient complained of headache and general malaise.

On the second day of his illness he still felt vaguely unwell, but a little better, and on the third day went to work as usual. He complained of nothing further till the sixth day when headache became more intense, and he took to his bed. He was very restless. On the seventh day he was unable to hold his head up and complained of pain in his neck. This pain moved downwards later between his shoulders and to the level of his waist. He was sleepless, but was still able to get out of bed. On the eighth day he was worse, but got up. There were pains in the back of the neck, shoulders, knees and ankles. He had to go back to bed. His head was retracted and he was unable to raise it from the pillow. He vomited once, and had some difficulty in swallowing. The temperature was 103° F.

On the ninth day his temperature was still 103° F. He vomited several times, and the difficulty in swallowing increased. His left arm became completely paralysed. During the night he was delirious, and his temperature rose to 104° F. On the tenth day he was seen by Dr. Firth. He was lying in bed with an anxious expression, breathing rapidly and feebly. The cranial nerves were normal, and articulation was normal. There was complete paralysis of the left arm, lower intercostal muscles, diaphragm and abdominal muscles, and of the legs. Slight movement of the right hand and forearm was possible. No deep reflexes could be obtained. There was no objective sensory disturbance. He died on the evening of the same day.

There is no mention of sphincter trouble, or of any other physical sign in either chest or abdomen.

A post-mortem examination was not allowed.

Analysis of Cases.

Fifty-four cases in all have been collected and tabulated. They all show a paralysis of the lower motor neurone type affecting both sides of the body and of wide distribution. None shows any considerable objective sensory disturbance, and only two of the recovered cases wasting that was at all marked. In none was there any clinical evidence of pyramidal involvement. The mortality of the whole series is high—70 per cent. These features alone are enough to separate it fairly definitely from typical cases of anterior poliomyelitis, polyneuritis, myelitis, or the described muscular atrophies. It is obvious, however, that it is not sufficiently homogeneous for a detailed analysis of clinical and pathological findings to be of value without subdivision into groups, but one or two general observations may be of use.
The series, as remarked, shows a mortality of 70 per cent. Males constitute 80 per cent of the cases. The age-incidence is as follows:

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<th>Age in years</th>
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<th>20—30</th>
<th>30—40</th>
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<tr>
<td>No. of cases</td>
<td>3</td>
<td>10</td>
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<td>8</td>
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The youngest was two and a half years, and the oldest 64, so that, though practically no age is exempt, by far the heaviest incidence is during young adult life, chiefly in the third decade. With regard to occupation it can be said only that men of the labouring class, and those most exposed to cold and poor conditions generally seem to be affected chiefly, and town dwellers more than countrymen. This is more an impression gained while reading the literature than a conclusion drawn from a comparison of records, which were too often incomplete for anything more to be possible.

In reviewing the series it became clear that several of the cases were too incompletely reported to be of value in a detailed analysis. For this reason 13 were rejected, and the following analysis has been made on the remaining 41. Even these were often not described in the detail one could have wished, so that for some of them classification has of necessity been speculative, and any conclusions drawn from it cannot be more than provisional.

A preliminary grouping was made as follows:

I. Cases with post-mortem findings.
   Further divided into:
   (a) Those without evidence of inflammatory infiltration of the nervous system.
   (b) Those with inflammatory infiltration of the nervous system.

II. Fatal cases reported without post-mortem findings.

III. Cases which recovered.

Each group was analysed separately and it was found that in each (including the two subdivisions of Group I) three roughly distinct types could be differentiated, and further that in each group these three types were approximately the same. To give the analysis of each of these groups in full and separately would obviously involve a great deal of needless repetition, so that the plan adopted here has been to analyse the series as a whole, using the three types mentioned as a basis. Before proceeding, however, something must be said about the constitution of the three types. As will be seen little help can be obtained from considerations of etiology since too little is known of it; subdivision will have to depend on clinical and post-mortem findings. These findings are no more or less than the evidence that can be found of damage to the organism, and reaction on the part of the organism, not only to the
noxious agent directly, but to the presence of tissue already damaged by that agent. Such a classification therefore will simply be a classification of types of injury and reaction, none of which is necessarily specific for any single noxious agent. It has been found further, that no one factor, whether clinical or pathological, could be used to differentiate any two types absolutely, without, as judged by other factors which one has no reason to look upon as less important, making obviously forced and artificial subdivisions. This point was brought out particularly clearly when the attempt was made to classify on the basis of the presence or absence of inflammatory infiltration. Both inflammatory and non-inflammatory groups fell roughly into three types, six in all. Calling these for the moment Types a, b, c, and Types d, e, f, it became clear that e, for instance, might have more in common with, say, a, than with d or f, and was more naturally grouped with it. It follows that a classification, to be of any value, must be based on as many factors as possible taken together; in other words that it must be a classification of groups of factors, although it may be justifiable at times to lay more stress on one factor than on another. The result of applying this method here has been to reduce the series to three groups, in which the following distinguishing factors seem to be of preponderating importance.

I. An acute ascending paralysis with little or no febrile reaction and a remarkable slightness of post-mortem findings.

II. An acute ascending paralysis not uncommonly associated with sensory changes suggestive of peripheral neuritis, and with the signs of general toxæmia but little febrile reaction; with post-mortem findings, which, though variable, generally show both parenchymatous and interstitial changes in the central nervous system and peripheral nerves.

III. An acute ascending paralysis preceded or accompanied by an acute febrile illness and with post-mortem findings resembling those of anterior poliomyelitis.

How far this grouping is justifiable will be seen from the detailed analysis of the 41 cases which follows. The cases have been tabulated as shortly as possible. It was difficult in many of them to estimate the duration accurately, since the onset was often insidious. The rule followed has been to date the illness from the first day when any paralysis or weakness was noted. This, of course, is purely arbitrary. The paralysis, except where it showed abnormal features, has not been described in detail; where not otherwise stated it may be taken that it was of the flaccid ascending type, and approximately symmetrical.

I. There are 11 cases in this group four of which recovered, giving a mortality of 60 per cent. There was only one female, so that roughly 90 per cent. are males.

Age distribution lay between 10 and 60 years, with some preponderance between the ages of 20 and 30. The average age of the whole group was 30
years; of the fatal cases alone, 33 years, and of the non-fatal alone, 25 years.

The duration of the illness in fatal cases varied between 4 and 40 days, with an average of 15 days. The paralysis was in all cases of the ascending type except in one, where it began in the arm. Bulbar involvement was mentioned in 75 per cent. of the cases, usually before the twelfth day. Wasting, or change in the electrical responses, was not reported in any case, although the latter point was investigated in only a few of them. In 3 cases (25 per cent.) paralysis seemed rather less complete in the distal than in the proximal segments of the limbs. This may well be due to the greater mechanical advantage at which the distal muscles act. Slight sphincter disturbance occurred in two cases, where it was almost certainly due to profound general weakness. In one, however, it is stated that the bladder was paralysed before the skeletal muscles.

*Sensory changes.—Subjective:* Paræsthesiae, pains, numbness, heaviness, or aching were reported in 75 per cent. of cases. Objective: Very slight changes in three. These consisted in slight blunting of sensation on the soles or legs, or slight tenderness of calves and arms. It would seem quite justifiable to say that for all practical purposes there is no objective sensory change reported in this group. Febrile reaction was negligible in all cases but two: in one case it was undoubtedly due to a terminal broncho-pneumonia, and in another it is of doubtful significance. This case was atypical also in the early bladder paralysis, and one had some hesitation in including it in this group.

The cerebrospinal fluid was examined in only one case, and was then found to be normal.

*Pathology.—*Chromatolysis, more or less advanced, was found in the nerve cells of the cord in all cases. The three cases reported by Buzzard (1907) showed some diffuse fatty change in the peripheral nerves and in the nerve fibres of the central nervous system. He himself points out that this change is not specific and may be found as a result of any profound toxæmia, and that it is not associated with any loss of function. It is probable that similar changes would have been found in the other cases had they been looked for carefully enough.

An enlarged spleen was mentioned twice, both times in association with tubercle; in one, old pulmonary tubercle, and in the other, with an area of tuberculous meningitis in the mid-dorsal region.

Except for the possibility of tubercle in the two above mentioned cases, and a very speculative connection with syphilis in two others and with wetting in one more, no etiological factors can be suggested for any of these cases.

In the non-fatal cases recovery was apparently complete, the whole duration of the illness varying between approximately six weeks and one year.

II. This group contains 20 cases of which 9 recovered, giving a mortality of about 50 per cent. The age varied between about 5 and 60 years with an average over all of 28 years. The fatal cases alone gave an average of 30 years the others an average of 26. Women constituted about 25 per cent.
of the cases. In the fatal cases the duration varied between 4 and 42 days, with an average of 15 days.

It is in this group that differences from the classical Landry type were most marked, although the paralysis was ascending in all but one case.

Bulbar involvement was mentioned in about 75 per cent. of cases; a conspicuous feature was the occurrence of ophthalmoplegias with or without paralysis of one or both seventh nerves, particularly in the non-fatal cases. Ophthalmoplegia, as evidenced by squint, diplopia or ptosis, was noted in six (25 per cent.), and weakness of one or both seventh nerves in about the same proportion. Ophthalmoplegia and facial weakness were each mentioned only once among the 11 fatal cases.

Changed electrical reactions were mentioned five times. In one case the muscles reacted badly to faradism, and in another the nerves were less excitable than the muscles to faradism. In a third, a definite reaction of degeneration developed five weeks from the onset; in a fourth, there was diminished response, but no reaction of degeneration, and in a fifth, reaction of degeneration in the anterior tibial muscles. As would be expected, these changes seem rather more definite among the recovered than among the fatal cases.

Wasting of muscles was mentioned in four cases (20 per cent.). In one fatal case of rather long duration the wasting was most marked in the shoulder muscles; it was slight and general in two others, and in a fourth confined to the extensors of the wrists, the small muscles of the hands and the anterior tibial muscles, but came on a considerable time after the onset of the illness.

Sphincter disturbance was mentioned in five cases (25 per cent.). In all but one (where there was definite double incontinence) it was slight in degree and probably unimportant.

Sensation.—Subjective disturbance was mentioned in all but three cases, i.e., in more than 80 per cent. These consisted of pains, paraesthesiae, and a feeling of numbness or heaviness in the limbs. Aching and backache were not commonly mentioned. Objective changes of a minor degree were common, being mentioned in nearly 50 per cent. In three cases this consisted in tenderness over nerve trunks, in four, muscle tenderness; hyperæsthesia was mentioned twice and impairment of sensation on arms and thighs, and indefinite impairment on the legs, once each.

Febrile reaction and toxæmia.—Febrile reaction was mentioned in only two cases, in one of which it was probably due to coexisting bronchitis. In 11 cases (about 50 per cent.), there was more or less marked general toxæmia. This varied from simple constipation to constipation with colic and definite hæmatoporphyrinuria. In other cases the evidence was very varied; vomiting and headache with septic teeth; fever following vaccination; delirium, labial herpes, stomatitis and coryza; Grave's disease. Reddish or claret-coloured urine was mentioned in three cases; plumbism and chronic nephritis in one. One may speculate that in those cases where the urine was noted to
be reddish or claret-coloured the condition has been haematoporphyrinuria, the more so that in one of them there was a history that trional and sulphonal had been taken.

Examinations of blood and cerebrospinal fluid were too few to justify any general conclusions.

Pathology.—The changes found in the nervous system were very variable, but in all cases both spinal cord and peripheral nerves were affected. They varied from chromatolysis of the nerve-cells of the cord combined with more or less parenchymatous degeneration in the peripheral nerves, to advanced degenerative changes in the nerve-cells of the cord, with degeneration in the tracts and perivascular round-celled infiltration, and, in the peripheral nerves, marked parenchymatous and interstitial change. The latter consisted in swelling and fragmentation of myelin, swelling of the axis-cylinder, proliferation of the cells of Schwann and inflammatory infiltration. Simple interstitial neuritis was mentioned in one case. In another, changes in the peripheral nerves were very marked, while in the cord the tracts were normal and the nerve-cells showed only a low degree of chromatolysis.

There was nothing notable in the other organs, except that the spleen was enlarged in two cases.

Etiology.—Clearly any of the toxæmic conditions already mentioned may have been factors in the etiology. In addition there were three cases in which syphilis was possibly a factor, in one combined with alcohol. Alcohol and exposure in one, and exposure alone in another complete the list of observed etiological factors for this group.

Recovery.—This was practically complete in five cases. In one of them the pupil light reflex had not returned after eight weeks, and on this account the possibility of syphilis was considered. The whole duration in these cases varied from six to eleven weeks. In four others there were more or less definite sequelæ; in one the knee jerks were still absent after two years; in another, reaction of degeneration appeared after five weeks, but the further progress of the case is not reported. In a third there was some general wasting, and, in a fourth, wrist and foot drop. These two cases were followed up for nine weeks and 13 months respectively.

III. The third group contains 10 cases; only two of these, unfortunately, were reported with post-mortem findings, so that, for the most part, they have been grouped together on clinical grounds. There were only two recoveries, giving a mortality of 80 per cent. The average age was 18 years. No patient was younger than 10, and none older than 30 years. There were no females. The duration of the fatal cases varied between three and 12 days, with an average of seven.

Paralysis.—This was fairly typically ascending except in three cases (33 per cent.). In two the arm was first affected and in the third the shoulders and neck. Bulbar involvement was mentioned in 50 per cent. There was
no report of the electrical reactions. Wasting was mentioned in only one case. Here the legs were markedly wasted and the knee jerks lost after 20 days. Sphincter disturbance was relatively frequent. It was reported in 60 per cent. Usually slight in degree, there was nevertheless complete double incontinence in one instance. It is probable that in these cases incontinence is due rather to the severe constitutional illness than to actual nervous lesions of the centres or tracts controlling the bladder and rectum.

Sensation.—Subjective changes such as paraesthesiae, numbness, etc., were remarkable from their rarity. On the other hand such symptoms as backache, headache, and general malaise were common. Apart from slight hyperaesthesia, no objective changes were mentioned.

Febrile reaction.—Fever was marked in all cases but two, in which it did not rise above 100° F. The first of these was an unusual case in that the condition was apparently associated with B. anthracis. The fever was very commonly associated with headache, vomiting, and other signs of an acute febrile illness, and in three cases with stiff neck or head retraction.

The cerebrospinal fluid in one case showed a pleocytosis.

Pathology.—As was said above, there are only two post-mortem reports in this series. One of these (Case 2 above) has already been described among my personal cases. The other showed hemorrhagic softening of the anterior horns with marked degeneration of nerve cells and perivascular infiltration. Many organisms resembling B. anthracis were present.

Etiology.—Apart from the anthrax mentioned above, severe wetting and chill in one case, and previous recent vaccination in another, no possible factors could be suggested.

Recovery.—In the two non-fatal cases, wasting of the legs and absent knee-jerks were noted in one, which was followed up for only 20 days, and in the other, weakness of the left leg, persisting six months later.

It will be well at this point to recapitulate as shortly as possible the main points which have been brought out in this analysis, laying especial stress on those which serve to distinguish the different groups one from another.

I. This is a form of acute ascending paralysis, having its incidence almost exclusively on males and usually during the third decade of life. The case mortality is high, 60 per cent., but the prognosis appears to be slightly better under the age of 30 than above it. The paralysis is almost, but not quite always ascending in type; it is not associated with wasting, or, apparently, with changed electrical reactions. This last point needs more careful investigation. Slight sphincter disturbance is not uncommon, and is probably due to general weakness. Bulbar involvement is usual, but the nuclei of the third, fourth, fifth, sixth and seventh cranial nerves are not as a rule affected. Sensory changes are almost entirely subjective, and they take the form of paraesthesiae, pains, aching, numbness, etc., usually in the limbs and often preceding the onset of paralysis by a few days. They are present in nearly
all cases. Febrile reaction is conspicuous by its absence, nor are there any signs of meningeal irritation or of increased intracranial tension. The cerebrospinal fluid in one case was normal.

Post-mortem findings are limited to vascular engorgement of the meninges, chromatolysis of the nerve cells of the cord, and slight diffuse fatty change in nerve tracts and peripheral nerves, not of a specific nature. Recovery, when it occurs, is complete, but may take a year or more. When fatal, the whole duration is commonly about 15 days, and death usually results from respiratory paralysis or from bronchopneumonia. No points of prognostic significance can be suggested.

Nothing can be suggested with regard to etiology.

II. This group differs from Group I in that it has a smaller mortality, 50 per cent., and that the incidence is higher in females, although once more males predominate. The age incidence is not markedly different, and again the prognosis seems slightly better under than over the age of 30. Again the paralysis is almost always ascending in type. It differs from the paralysis in Group I in that motor cranial nerves are commonly involved, usually asymmetrically, and also in that changed electrical reactions and wasting are sometimes observed, although only in a minority of cases. Sphincter disturbance is rather more common, but generally of the same type. Sensory changes of a subjective nature do not differ appreciably from those in Group I. Objective sensory changes, often of the nature of tenderness over nerve trunks occur in half the cases, but are always slight; they are sufficiently definite, however, to constitute a point of distinction. Signs of a general toxæmia are common, so that, in spite of the absence of febrile reaction, there is more constitutional illness than in Group I.

Post-mortem changes in both cord and peripheral nerves are always present and of a parenchymatous nature, with or without inflammatory reaction. Recovery is often complete in two or three months; sequelæ, such as wasting and absent deep reflexes, are not uncommon. Fatal cases last usually about 15 days, and again no point of prognostic importance transpires.

Etiologically there seems to be some correlation with factors which are known to be of importance in causing a polyneuritis.

III. In this group the mortality is high, 80 per cent., and the age incidence definitely low—as a rule under 20 years. The preponderance of males is very marked. Paralysis is not always so typically ascending, and shows a tendency to start first in one limb and to become generalised later. Bulbar involvement is common, and is more like that of Group I than of Group II. Wasting is mentioned in one of the recovered cases; clearly most of these cases were of too short duration for wasting to have occurred. Sphincter disturbance is more frequent than in either of the other groups, and this is probably associated with the acute nature of the illness. The most characteristic feature of this group is the marked febrile reaction, often associated with signs of increased intra-
cranial tension and meningeal irritation. Sensory changes, both objective and subjective, are almost completely absent. The cerebrospinal fluid in one case showed a pleocytosis.

Post-mortem the changes are found to be strikingly like those of anterior poliomyelitis. Only two cases recovered, but in both of these recovery was not complete. There was wasting of the legs in one, and weakness of one leg in the other. The fatal cases have a duration on an average of only about half that in either of the other two groups.

The etiology remains obscure.

DISCUSSION.

It is fairly clear from this description of cases of acute ascending paralysis that it is the cases in Group I which correspond most closely with Landry's classical description. Before discussing them further the position of Groups II and III must be made clear, since they seem to have a more obvious connection with better known morbid conditions.

Group II appears to be fairly closely related to cases of multiple neuritis. Such cases form a very heterogeneous group. They have no single etiology but are related to a variety of toxic conditions, the toxin being sometimes exogenous, sometimes endogenous or metabolic, and sometimes the result of an infection, like diphtheria, or of an acute fever of unknown causation. In addition, there are a certain number of cases for which no known toxin can be suggested, or where the absorption of an unknown toxin from the gut is postulated. So far they correspond fairly closely with the cases in Group II, many of which showed evidence of toxæmia. It is significant that the group contained one case of acute hæmatoporphyrinuria, and three others in which hæmatoporphyrinuria was a possibility. It is said (Löffler, 1919), that of 14 recorded cases of acute hæmatoporphyrinuria no less than five have shown the syndrome of Landry's paralysis. Further, it is well known that hæmatoporphyrinuria, whether of the paroxysmal idiopathic variety, or following the administration of sulphonal, trional, etc., is commonly associated with multiple neuritis, and, as in other forms of multiple neuritis, this may affect either the sensory or motor nerves predominantly. According to Harris (1926) retention and even incontinence may occur, and also mental symptoms like nervousness and excitability and even epileptiform fits. Gastro-intestinal symptoms, such as colic, constipation and vomiting are almost the rule.

The character of the paralysis in Group II differs from that which usually occurs in clear cases of multiple neuritis; it is on the whole more generalised, and usually ascending. Similarly sensory changes, although present in many cases, are minimal. There are not sufficient grounds for setting them apart as a separate disease. Irregular and indefinite areas of anæsthesia and hyper-anæsthesia, and tenderness over the nerve trunks and muscles are sufficiently common and characteristic to suggest multiple neuritis very strongly. Moreover, it is a feature of cases of multiple neuritis that sometimes the sensory
nerves and sometimes the motor nerves are affected almost exclusively; diabetic neuritis is usually mainly sensory, and lead neuritis is often mainly motor, while the two extreme types are sometimes the result of the same toxin in different patients. It would seem that the cases in Group II represent simply the extremes of a series, and not a distinct condition. The same argument applies to the fact that the paralysis is more than usually extensive in the cases in Group II, so that only its ascending nature remains to distinguish it from more ordinary cases of multiple neuritis. The frequency of the involvement of the eye and facial muscles is noteworthy; although similar involvement is well known in cases of multiple neuritis, it does not occur so often. The electrical reactions were not reported often enough for any useful discussion to be made about them. Sphincter disturbance was not uncommon, but then again this may occur in cases of multiple neuritis. The post-mortem findings were variable, but so they are in cases of multiple neuritis; parenchymatous and interstitial changes are both found, sometimes separately, and sometimes together. When they occur together it is possible that the one may be the result of the other; what the sequence is, is very difficult to say, although at times one may be able to make a more or less probable guess. After all, one would not expect that, in a group of cases with so varied an etiology, the post-mortem changes would be uniform.

They differ from the usual cases of multiple neuritis in that the central nervous system is far more affected than would be accounted for by a pure peripheral neuritis. It is possible that in some of the cases the changes in the central nervous system were secondary to those in the peripheral nerves, but this cannot be maintained for more than a minority of them. Nevertheless lead, for example, is known to affect the motor neurone inside as well as outside the nervous system; permanent atrophy of the intrinsic muscles of the hand may result from it, and even, rarely, a generalised progressive muscular atrophy. In other cases of multiple neuritis too, permanent atrophies may result which are probably evidence of damage to anterior horn cells. Consequently, once again, there is no evidence that Group II is more than a collection of extreme cases selected from the large and heterogeneous group called multiple neuritis. The position seems the more secure in that several cases intermediate in character between these cases and the more typical cases of multiple neuritis can be found reported in the literature. They have usually been reported as cases of Landry’s paralysis. For example, Stockton (quoted by Diller, 1902) describes the following case. A female, age 27, suffered with nervousness, insomnia and generalised pains for two weeks. The gluteal region was then noted to be anaesthetic and she was incontinent. Paralysis started in the legs and spread up to the arms, both arms and legs becoming anaesthetic at the same time. The patient had been given trional, and haematoporphyrinuria was present throughout her illness. This would appear to be a case of ascending polyneuritis which differs from those just described only in the extent of the anaesthesia. Diller (1902) reports the case of a man
aged 25, who, three weeks after he had developed a hard chancre, and while presenting typical signs of secondary syphilis, was seized with severe pains and general weakness and lassitude. Six weeks later he was admitted to hospital with much general emaciation, great weakness of his legs, and rather less of his arms. Knee-jerks, which at first were exaggerated, were soon lost. There were fibrillary twitchings in his muscles. One would have little hesitation in diagnosing this case as one of multiple neuritis due to syphilis, yet the neuritis is clearly very widespread and no mention is made of any objective sensory changes. Progressive muscular atrophy of syphilitic origin is a possible alternative diagnosis. An even clearer case is one reported by Green (1901). A boy aged 3 years and 10 months had an attack of diphtheria. Fourteen days later there was dysphagia, and paralysis of the soft palate and weakness of the legs. Later the pharyngeal muscles became paralysed and the left side of his neck weak; simultaneously the weakness of his legs increased, and finally spread up to involve the arms. He died of respiratory paralysis. In this case there appears to be a combination of paralysis of the palate and pharynx, probably due to local absorption of toxin by the perineural lymphatics, and an acute ascending paralysis due to the general diffusion of toxin throughout the body. The position then, of the cases in Group II as cases of ascending polyneuritis seems to be secure. On the grounds that they differ from the usual case of multiple neuritis in their generalised and ascending character, their high mortality, and their greater incidence on men than on women, there is some justification for placing them in a group by themselves.

Group III is in some ways a little more difficult to place, but many of its features suggest a connection with anterior poliomyelitis. The average age incidence is definitely lower than in either of the other groups. The paralysis tends to appear after a variable period during which the only signs are those of an acute febrile illness, sometimes with a suggestion of meningeal irritation. The paralysis is not quite so regularly ascending and shows a tendency to appear in one limb first; further, in the two cases which recovered it was associated with wasting of the legs in one and weakness of one leg six months later in the other. Sphincter disturbance was not uncommon, but neither is it in the acute stage of anterior poliomyelitis. Sensory changes were slight, as would be expected, but there seems to have been an absence of the pains and tenderness in the limbs which occur often in anterior poliomyelitis. The cerebrospinal fluid in one case showed a pleocytosis. The post-mortem findings in one case were not essentially different from those described for acute anterior poliomyelitis (Buzzard and Greenfield, 1921); those in the other case published with a post-mortem report will be discussed later. The main differences from acute anterior poliomyelitis are as follows. The age incidence, although lower than that in Groups I and II, is yet high. The mortality is very high, and the extent of paralysis greater than in typical anterior poliomyelitis. Nevertheless, these are only differences in degree. There is some doubt whether all cases of anterior poliomyelitis are really the same in their
etiology and fundamental pathology, and it is not suggested that this group is necessarily homogeneous. They do, however, suggest from their clinical course an acute febrile illness, due probably to an infection and further, from the pathological findings, to an infection via the blood stream. Buzzard (1907) brought forward reasons for supposing that the infective agent in anterior poliomyelitis was blood-borne, and, on account of the similarity of the post-mortem findings, the same would seem to hold good for these cases. The other case with a post-mortem report, besides showing changes very like those of anterior poliomyelitis, showed also the presence of a bacillus, probably \textit{B. anthracis}. Is it not possible that in this case, owing to some peculiar susceptibility obtaining at the time, the syndrome and post-mortem findings were caused by a septicæmia due to \textit{B. anthracis}?

Except that the signs and symptoms are rather less variable, this group is of the same nature as Group II, the variable toxin being replaced by a variable infection, with corresponding changes in the post-mortem findings. On these grounds the name \textquoteleft acute infective ascending paralysis\righthere is suggested for this group.

The position of Group I must now be discussed. There is no doubt that in these cases there is a poisoning of the lower motor neurone, leading to rapid loss of function. Whether this poisoning affects only the cell body in the spinal cord, or whether it acts as well on the axon, or even on the axon alone, is in the present state of our knowledge no more than an idle speculation. Buzzard (1907) states that in cases of acute toxic polyneuritis changes may be found in the anterior horn cells before they are evident in the peripheral nerves; it cannot be concluded from this that these changes are necessarily secondary to an affection of the nerves which has not yet shown itself, although this is a possibility. Actually, the only point which distinguishes the cases in Group I from those in Groups II and III is the absence of reaction, whether constitutional or local. This cannot be explained by saying that the patients die before there is time for changes to become apparent; the average duration of the cases was approximately the same as in Group II and longer than in Group III. The presence or absence of reaction depends more on the peculiar condition of the patient than upon the actual cause of the disease, so that Landry's \textit{ascending} paralysis appears to belong to the group of diseases which depend chiefly on \textquoteleft diathesis\righthere or \textquoteleft idiosyncrasy.\righthere This is the conclusion reached by Grünwald in 1923. He further suggests that the condition may be an anaphylactic manifestation, brought about by the action of a toxin on a nervous system already sensitised by the previous action of the same or another toxin or infection. In this way he explains the common association of Landry's paralysis with a large number of different infective and toxic conditions. Exactly the same arguments would apply to cases of multiple neuritis, and at present the suggestion can be no more than a speculation. He also suggests the possibility of a constitutional diathesis, associated occasionally with the presence of such stigmata as hypertrophy of the thymus, an increase in the
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number of corpora amylacea, islands of myelin in the grey matter, asymmetry of the horns of the grey matter, an open central canal, etc. Apart from the fact that the central canal was certainly open in the two cases reported in this paper with post-mortem findings, no support for this suggestion can be found in this series. It, too, must remain in the realm of speculation.

Whatever predisposing cause there may be for the development of the syndrome of Landry's paralysis, there must be some immediate cause. No light has so far been thrown on its nature. Prima facie, a toxin would seem most probable, but one cannot exclude the possibility of an infection.

There is another group of cases which is certainly allied to the cases which have been described, viz. acute myelitis. Clinically they are distinct, in that they show invariably marked sensory loss, usually affecting deep as well as superficial sensibility, and usually signs of pyramidal involvement. They have a similar etiology, being associated with chill, exposure, and acute specific fevers and syphilis particularly. There is also a toxic variety sometimes associated with pregnancy; these have sometimes been reported as cases of Landry's paralysis, e.g., by Marinesco (1924), who describes a non-fatal case of acute ascending paralysis, occurring during the puerperium, and associated with marked sensory loss, exaggerations of knee- and ankle-jerks, and a double extensor response. There is no need to describe the post-mortem findings of such cases in detail; they can be found in Buzzard and Greenfield's book (1921) and in Buzzard's paper, 1907. Buzzard himself considers that these cases are due to an acute infection of the nervous system of lymphatic origin, contrasting them with cases of anterior poliomyelitis where the infection is carried by the blood stream. It is possible that in those cases where no infection can be traced, e.g., the cases associated with pregnancy, the toxin is brought to the nervous system by the lymphatics. One is tempted to contrast these cases with cases of Landry's paralysis, suggesting that in the latter the toxin is conveyed chiefly by the blood-stream, or at least exerts its influence by that route, and that the former are similar except that the toxin exerts its influence through the lymphatic channels. It is perhaps significant in this connection that in one case an area of tuberculous meningitis was associated with the development of the typical syndrome of Landry's paralysis. An area of meningitis of this kind is more commonly associated with the development of a tuberculous myelitis.

SUMMARY AND CONCLUSIONS.

Cases of acute ascending paralysis can be divided into three groups; a poliomyelitic group, a polineuritic group, and a group which shows little or no post-mortem change and no constitutional reaction. This grouping has already been suggested by Saltman, quoted by Pfeiffer, 1912.

These groups can be distinguished with more or less certainty on clinical and pathological grounds. A high mortality and a preponderating incidence on young adult males are characteristic of the whole series.
Although clinically and pathologically these cases fall into sufficiently distinct groups to be described as ‘diseases’ in the traditional manner, they have no common etiology. Landry’s paralysis is a syndrome probably caused by a toxin exerting its influence through the blood-stream, and more or less closely related on the one hand to a group of cases which are simply a variety of multiple neuritis, and on the other to a group which are best described as cases of infective poliomyelitis.

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