SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD.

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INTRODUCTION.

MUCH as we feel the need of some other name under which to describe the affection, seven cases of which we are about to record, most of the papers that have appeared on the subject have borne the above or some similar title, so that to introduce a new name for the affection now would probably lead to confusion, however much it might serve to obtain for our own cases recognition that they are examples of a distinct morbid entity.

By combined degeneration of the spinal cord is meant an affection in which tracts of different function are concomitantly affected. It is, therefore, obvious that under such a title might legitimately be included a variety of different affections, each of which is characterised by the concomitant implication of tracts of different function. Examples of such affections are to be found in the "Ataxic Paraplegia" of Gowers, if there be such an affection distinct from the class of case with which we are more immediately concerned in our present paper; "Friedreich's Ataxy," "Cerebellar Heredo-Ataxy," such cases of "General

Paralysis of the Insane" as present degeneration in the posterior columns of the cord in conjunction with similar change in the lateral columns, and the like.

It therefore follows that there is need for a name that would serve to distinguish the class of case we are about to describe, from the affections that have just been enumerated, for it possesses a very definite clinical picture, not as a rule difficult of recognition, and a morbid anatomy which is as characteristic as that of tabes or any other disease of the spinal cord, with as distinctive a morbid picture as that possessed by the disease just mentioned. A name other than "Combined Degeneration," would undoubtedly do much to establish the affection as a separate and distinct morbid entity, would facilitate its study, and free it from the entanglements by which it is at present hampered, in consequence of the fact that so many different diseases of the spinal cord are characterised by combined degeneration of tracts of different function. We however, feel, that at present we shall probably be serving a more useful purpose by retaining the term "Combined Degeneration," and must trust to the "Subacute" as being sufficient to exclude most other forms of combined degenerations of the spinal cord, such as are likely to be confused with the affection now under consideration.

Its present name is, however, not the only entanglement from which it would be well to free the malady. The cases that were first recorded, and which led to the recognition of this disease as a distinct morbid entity, were described by Lichtheim as instances of cord changes associated with anæmia. Leichtenstern, the records of whose cases were next to appear, described the affection as "Progressive pernicious Anæmia in Tabetic Patients." In this way it has come about that the affection has become intimately bound up with anæmia, which has been variously described as "profound," "pernicious," "grave," "fatal," and so on. As a consequence of this, two totally distinct conditions have been confused, and in the literature that has grown up around the publications of Lichtheim and Leichtenstern we find cases of each recorded in a manner that suggests that

the authors regard the affections as belonging to the same category, or, indeed, as if they are identical. Anæmia, in its relation to the subacute combined degeneration of the spinal cord, has to be considered from three points of view, in so far as the publications on the subject are concerned. There are the cases of subacute combined degeneration of the spinal cord with which we have to deal more directly in this paper, in some of which cases anæmia is a feature in the symptomatology; secondly, cases of anæmia in which certain symptoms arise which point to some disturbance of nerve function and in which certain changes are found in the spinal cord after death; and, lastly, cases of severe anæmia in which there have been no clinical phenomena pointing to disturbance of nerve function, but in which, nevertheless, histological examinations have revealed certain definite morbid changes in the spinal cord.

Cases of the first group are readily recognised clinically in consequence of the very definite symptomatology which they present, the phenomena pointing to serious structural defects in the nervous system; and the morbid changes found on necropsy serve to distinguish them from any other affection of the nervous system. In some of the cases anæmia is a striking feature in the symptomatology, while in others, if present at all, it is slight and unobtrusive.

The second class comprises a group of cases in which vague symptoms of a more or less indefinite character arise in the course of severe anæmia, which may or may not be characterised by the features which are supposed to be diagnostic of the so-called pernicious variety. The majority of the symptoms indicating implication of the nervous system point to interference of function consequent on molecular changes in the nerve elements rather than to gross structural changes in these parts. Histological examination, nevertheless, reveals gross changes in some such cases, and while these cannot be said to be identical with the changes found in the subacute combined degenerations, there is sufficient to make it impossible to deny that the changes found in these cases may represent an earlier stage of the affection which, when fully developed, presents so

characteristic a morbid picture as that which we propose to lay before our readers.

The third group is composed of cases in which, though structural changes are found in the spinal cord on necropsy, there have been no symptoms during life which have pointed to affection of the nervous system. Nonne, Minnich, Burr and others have devoted attention to such cases, and all that can be said in this connection is that although they prove that structural changes may occur in the spinal cord in cases of anæmia, they do not admit of the interpretation that these defects are the earliest changes the full development of which are seen in the subacute combined degenerations, on examples of which our present paper is based.

All the cases like our own that have been published from the National Hospital for the Paralysed and Epileptic belong to the first category, and in all of them there has been the characteristic clinical picture supported by the equally typical morbid appearances found after death.

The first paper from this source was by the late Dr. Bowman and dealt with a single case; a paper by Dr. James Taylor dealt with two cases, and one by one of us (J. S. R. R.) was based on three such cases.

We are indebted to Dr. Hughlings Jackson, Dr. Buzzard, Dr. Bastian, Sir William Gowers and Dr. Ferrier for permission to publish the following cases, which were under their care in the National Hospital, and we take this opportunity of thanking them for their kindness.

Clinical Aspect.

The following account of the clinical features of this disease is based upon nine cases in the wards of the National Hospital during the last three years. A *post-mortem* examination was made in seven of the cases. In the remaining two the diagnosis, although not established by pathological investigation, appears certain. One of these patients died shortly after leaving the hospital, but there was no opportunity for examination, and the other still remains in the hospital.

Added to the detailed clinical and pathological account in the appendix are three other cases, two of which are at present in the National Hospital, and the diagnosis of an early stage of combined degeneration seems highly probable, and a third, probably of the same nature, in which recovery has taken place.

In the first of these series of cases (No. 1) which came under our observation the symptoms were peculiar and striking, and the correct diagnosis was not made during life. In the remaining cases the aspect and course of the disease were so similar to those of the first case that a definite diagnosis was made and was confirmed by subsequent *post-mortem* examination.

So far as we may argue from these nine cases the clinical picture of the disease except in its earliest stage is very definite, and presents features which distinguish it from other affections of the spinal cord. The course of the disease almost always tends to a fatal issue. The changes in the clinical features which occur in the course of the malady are striking, and may be divided into three stages, separated the one from the other by abrupt transitions and by a marked change in the symptom complex; this constituting perhaps one of the most striking clinical features of the affection.

The three stages of the disease indicated may be summarised as follows:—

(1) A stage of slight spastic paraplegia with slight ataxy and marked subjective sensations in the lower limbs.

(2) A stage of severe spastic paraplegia with marked anæsthesia of legs and trunk.

(3) A stage of complete flaccid paraplegia; absent knee-jerks; absolute anæsthesia; rapid wasting and loss of faradic excitability in the muscles of the paraplegic region; increase of superficial reflex excitability; absolute incontinence of both sphincters and œdema of the lower extremities and trunk.

Though an anæmic state has hitherto held an important place in the symptomatology of this disease, and by some authors has been placed in important causal relation with

the spinal cord lesions, we have not included this symptom in the foregoing summary of important symptoms, for the reasons that some of the most typical cases presented no anæmia throughout the whole course of the disease; others presented anæmia only late in the disease, when great general emaciation came on; while in other cases anæmia was an obtrusive symptom from the first, and preceded the manifestation of nervous symptoms by many months.

Repeated examination of the blood in the anæmic cases failed to reveal the alterations found in pernicious anæmia. The changes found were such as occur in cases of secondary anæmia. As regards the causal relation of this disease with pernicious anæmia it may be pointed out that according to the recent opinions of the highest authorities on the subject,[1] a diagnosis of pernicious anæmia arrived at from the character of the blood elements alone is quite unjustifiable.

Etiology based upon the Observation of Seven Cases.

Age.—The disease appears in the fourth and fifth decades of life. The average age of the patients was forty years, the youngest being thirty years old, and the eldest being forty-nine years old.

Sex.—Women seem to be rather more commonly affected than men. Four of the seven cases were females, and three were males.

Heredity.—A slight family history of nervous disease was present in two cases. A marked tubercular family history was present in four cases. Acute rheumatism in three cases, and a history of cancer in two.

Other Factors.

These patients had been, without exception, strong and healthy till a short time before the symptoms became

[1] S. Coupland, "Pernicious Anæmia," Allbutt's "System of Medicine," vol. v., p. 504.

manifest. Four of them had a definite history of syphilis, and in two only could this be excluded with comparative certainty. There had been alcoholic excess in three of the cases, and prolonged suppuration in three others (pyonephrosis, chronic cystitis, and chronic bronchitis). In two cases the symptoms first appeared after pregnancy. Two of the patients lived in adjoining houses in the same street. All the patients were in comfortable circumstances, and no connection could be traced between the disease and acute illness or emotional disturbances.

The onset of the disease was in most cases slow and insidious, and could not be attributed to any immediate exciting cause. In the most acute cases, however, the symptoms came on rapidly, and were ushered in by headache, vomiting, pyrexia, and malaise. Where anæmia had preceded the appearance of nervous symptoms, faintness, languor, palpitation, and irregular pyrexia were the symptoms which brought the patient under the notice of the physician.

The earliest manifestations of implication of the nervous system were subjective sensations in the lower extremities; numbness, a feeling of stiffness, and sometimes tingling. These symptoms were often so slight that it was many months before the patient sought medical advice, but once having appeared they were constant, and showed no tendency to disappear. Soon after these sensory manifestations, signs of slight spasticity and ataxy developed; the legs were clumsy and felt stiff and cold, and there was generally some dragging of the feet in walking. There was at this period of the disease no involvement of the cranial nerves, no girdle sensation, and no sphincter trouble. The signs present at this time were simply an increase of the deep reflexes in the lower extremities, the extensor response in the plantar reflex, and very slight loss of sense of passive position in the lower extremities. Similar symptoms and signs appeared in the upper extremities, generally at a later date than in the lower limbs, but sometimes coincidently, and the clumsiness of the upper limbs was first noticed by the patients in the act of writing.

The clinical picture was one of slight ataxic-paraplegia, and this constituted the first stage of the disease.

Whether the course of the disease was rapid, as in Cases Nos. 2 and 6, where the duration of the illness was four and three months respectively, or chronic, as in Cases Nos. 5 and 9, this stage usually occupied from a half to three-quarters of the whole duration of the illness.

The transition from the first to the second stage was usually abrupt, and was marked by the loss of ability to stand or walk, and by considerable loss of sensibility, to all forms, in the legs and lower part of the trunk. In five of the cases the change occurred in the course of a single night, and the patients, having gone to bed able to walk fairly well, found themselves unable to stand on getting out of bed in the morning. The inability to stand and walk was owing to loss of sense of position, and not to any marked loss of motor power, for this was quite good in some cases. Throughout the second stage the power of movement, as a rule, steadily declined, but was not completely lost in any muscle until the third stage—that of flaccidity—was reached. There were, however, two cases in which there was no marked loss of power until the stage of flaccidity was reached, and one in which the legs became completely paralysed, though still spastic. The muscles were rigid, and exhibited no marked wasting, and their electrical excitability remained normal. The most characteristic sign of the second stage was the rapid development of anæsthesia. Sense of passive position was absolutely lost in the lower limbs, and much impaired in the hands, which usually presented tabetic athetosis. Other forms of sensibility were impaired equally and in an increasing degree. The anæsthesia of the skin was always of peripheral distribution at first, appearing over the feet and hands; but as it gradually extended upwards it became segmental in distribution, and its upper limit upon the trunk was always a segmental limit, sharply defined. The highest level to which the anæsthesia has reached in any of the cases has been the upper limit of the sixth cervical root area (plates i. and ii.). In its progress upwards it may be limited for a

PLATE I.

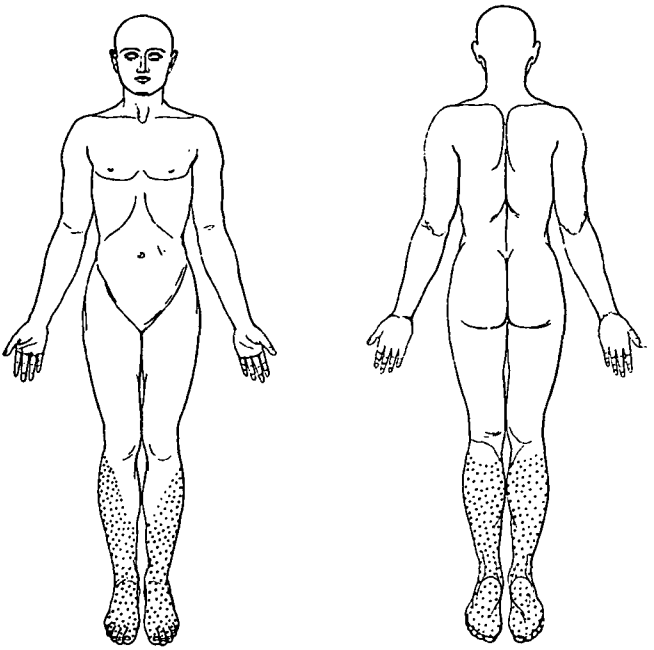


FIG. 1.

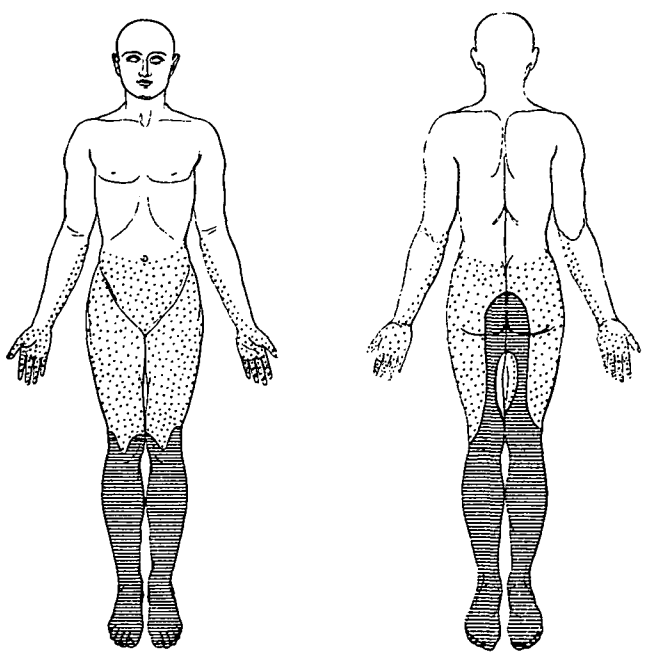


FIG. 2.

FIG. 1.—An early stage in the anæsthesia. Case No. 8.
FIG. 2.—Anæsthesia early in the flaccid stage. Case No. 4.

(The dotted areas represent partial, the lined areas complete, loss to all forms.)

PLATE II.

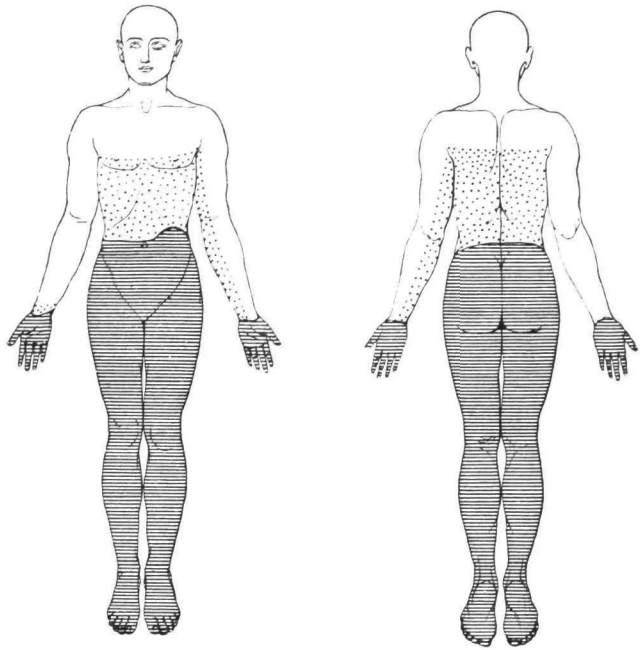


FIG. 1.

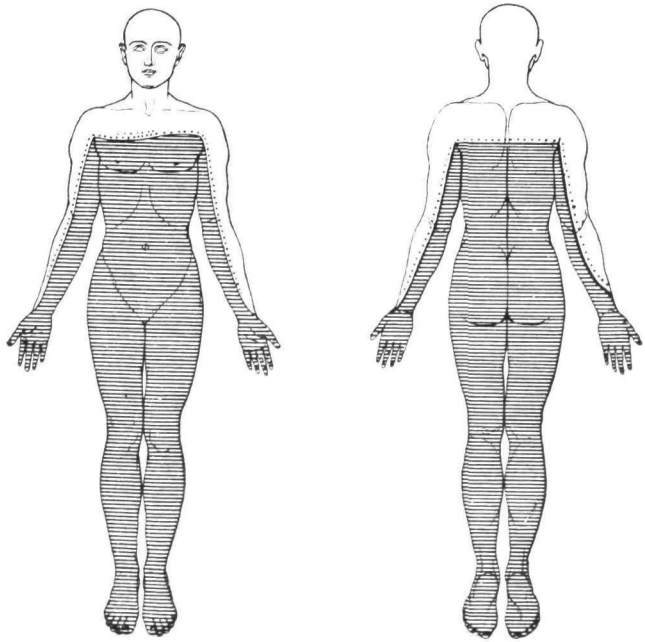


FIG. 2.

FIGS. 1 & 2.—Two late stages in the anæsthesia of Case No. 1.
(The dotted areas represent partial, the lined areas complete, loss to all forms.)

long time to a certain segmental level, and then suddenly encroach for several segments higher, and over the newly-involved area may show marked remissions and exacerbations in its progress to complete anæsthesia. Anæsthesia dolorosa and delay amounting to as much as fifteen seconds has been met with.

The lower lumbar and first sacral areas were always affected before the lower sacral and upper lumbar areas, and the lower cervical segments before the upper thoracic segments.

A girdle sensation in the lower thoracic region was common at this stage, and severe lightning pains in the lower extremities were frequent. A prominent feature of all the cases has been a severe constant dragging pain beneath the lower costal margin, always unilateral; in some cases on the right side and in others on the left.

Attacks of severe intercostal pain on one side were followed by herpes in two cases and in a third by a cutaneous hæmorrhage exactly limited to a nerve root distribution (plate ix., fig. 1). Similar cutaneous hæmorrhages have been observed in cases of tabes dorsalis by Strauss [1] and others.

In this stage the mental faculties were not affected, and the special senses were found to be normal. Optic neuritis was not present, but in two of the anæmic cases multiple retinal hæmorrhages were found.

The cranial nerves were affected in some cases. Reflex iridoplegia was never present. Many of the cases presented slight nystagmus on extreme lateral deviation of the eyes. Weakness of the external rectus muscle with corresponding diplopia was present in two cases, and in one of them it was bilateral. Slight unilateral facial paresis was present in one case, and marked unilateral paresis and ataxy of the larynx, with alteration of voice, was present in one case.

The sphincters were in this stage often unaffected; in some cases there was slight incontinence, and in one case only complete incontinence. Considering the depth of the

[1] Strauss. "Des ecchymoses tabétique à la suite des corses de douleurs fulgurantes," *Acad. de Neurologie*, 1881.

anæsthesia, this condition of the sphincters was remarkable, and contrasted very strongly with the absolute incontinence always present in the third stage.

Trophic changes were not observed.

Both the superficial and deep reflexes were increased and the jaw-jerk and foot clonus were obtainable. A marked extensor plantar response was present in every case.

During this stage the general condition of nutrition may be good. In the patients with anæmia there were superadded the symptoms of that condition. Both the anæmic and the non-anæmic patients were subject to irregular elevations of temperature and symptoms of dyspepsia.

The length of this stage of the disease has varied in the different cases from three weeks to six months, but it was usually short, and occupied less than one-sixth of the whole time of illness. The average duration of this stage in the cases which have up to the present time proved fatal was five weeks.

The transition from the second stage—that of spastic paraplegia—to the third stage—that of flaccid paraplegia—occurred rapidly in the course of a few days, and was marked by the development of its following succession of symptoms in the lower extremities:—Absolute flaccid motor paralysis; absolute anæsthesia; complete incontinence of the sphincters; loss of the deep reflexes; rapid wasting of the muscles, with loss of faradic excitability; and œdema of the legs and trunk.

This change in the clinical picture occurred in most of the cases while they were under observation in hospital, and it was accompanied by a marked change in the general condition, malaise, drowsiness, anorexia, and general asthenia, becoming evident, and when anæmia was present, it became much increased. Pyrexia was always associated with the event. The accompanying temperature chart from Case 3 shows the behaviour of the temperature in all the cases in which the transition from the second to the third stage was observed.

The lower extremities, which before had been spastic

PLATE III.

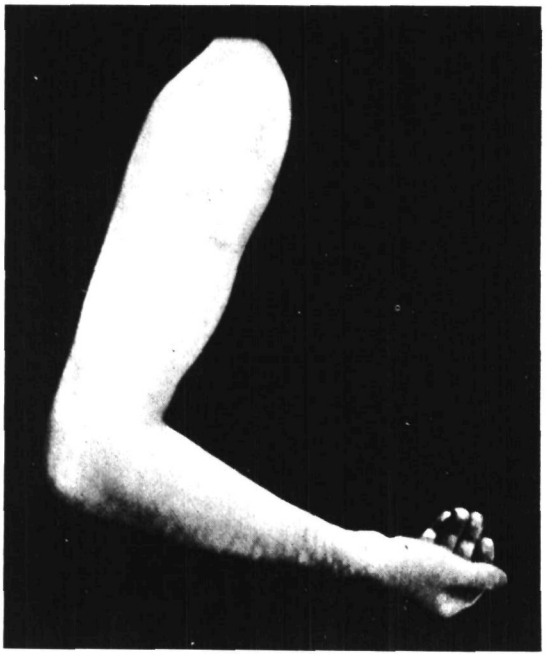


FIG. 1.—The right upper extremity of Case No. 7 when admitted.

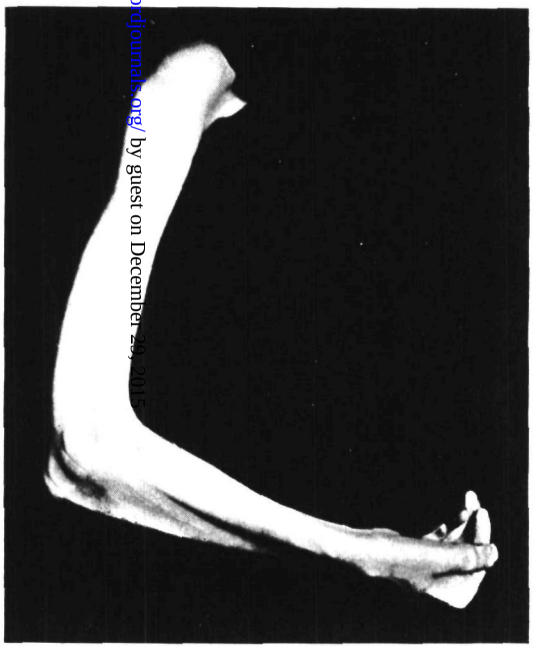
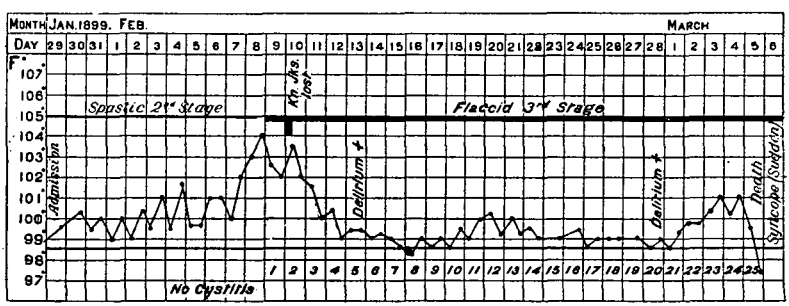


FIG. 2.—The same limb three days before death, showing the extreme muscular wasting.

with reflex spasms, epileptoid spasms, and increase of the deep reflexes, in the course of twenty-four hours became absolutely paralysed, the spasticity giving place to complete flaccidity with marked hypotonicity. The foot clonus was no longer obtainable, and the knee-jerks gradually becoming reduced to mere flickers upon reinforcement, were finally lost about four days after flaccidity had set in. Accompanying this flaccidity was the most striking alteration of the electric excitability, the faradic excitability rapidly falling almost to zero, and the galvanic excitability being much reduced, sometimes with and sometimes without a polar change. The diminution of faradic excitability was observed directly



Temperature Chart of Case 3.

the flaccid condition had set in. That the early change in the electric excitability was not due to the severe œdema of the subcutaneous tissues having insulated the deeper tissues was proved by the employment of sterilised needle electrodes plunged deep into the muscle, the condition of complete anæsthesia of the part allowing of this procedure. The muscles wasted rapidly. In the lower limbs and trunk the wasting was general, but in the upper extremities the wasting, which generally appeared later than in the lower extremities, affected first the intrinsic hand muscles and then the ulnar flexors, radial flexors, extensors of wrist, extensors of elbow, supinati, and fifth cervical group, in that order. This wasting continued throughout the third stage

progressively affecting fresh muscles in an upward direction until, in the cases where the third stage was prolonged, there was extreme atrophy of all the observable muscles of the body, except those supplied by the cranial nerves (see plates 3 and 4).

The trunk muscles, with the onset of the third stage show complete paralysis below a segmental area, usually the ninth dorsal. Beevor's sign was well marked in all the cases (*i.e.*, the shifting upwards of the umbilicus in the attempt to sit up). Subsequently the upper abdominal and spinal muscles, the lower intercostals, and, in some cases, the diaphragm became completely paralysed.

With the exception of single instances in which paresis of the external recti, or of the face on one side, or of the larynx on one side, were met with, no paralysis of muscles supplied by the cranial nerves was noticed, nor were the neck muscles or the infrahyoid muscles affected.

The anæsthesia of the lower extremities and lower trunk rapidly became absolute, and the anæsthesia rose segment after segment; first relative, then slowly becoming absolute. In most cases the anæsthesia reached as high as the first dorsal segment before death, and in two cases it reached the sixth cervical segment (see plate ii.). Girdle pains, lightning pains, and paræsthesia were no longer complained of, but the heavy pain beneath the costal margin persisted to the end. With the onset of the flaccid stage the sphincters became in every case completely incontinent, but showed some reflex contraction to the usual tests. Cystitis occurred in several cases, but it was readily amenable to treatment, except in the cases with a long final stage. In these cases pyelonephrosis occurred. One of the most prominent symptoms following the change to the flaccid stage was the rapid appearance of much soft translucent œdema in the lower extremities and lumbar region. The œdema was much influenced by gravity, and could be readily removed from the feet by raising the legs. Becoming most marked on the fourth day of the flaccid stage, it showed remissions and exacerbations, and disappeared finally after about fourteen days.

PLATE IV.

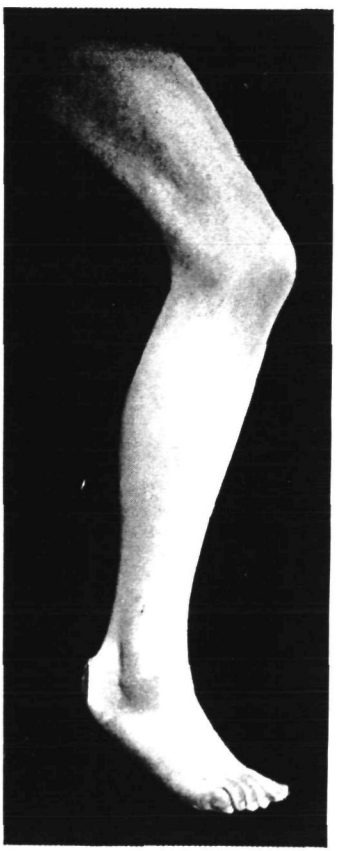


FIG. 1.—The right lower extremity of Case No. 7 when admitted.

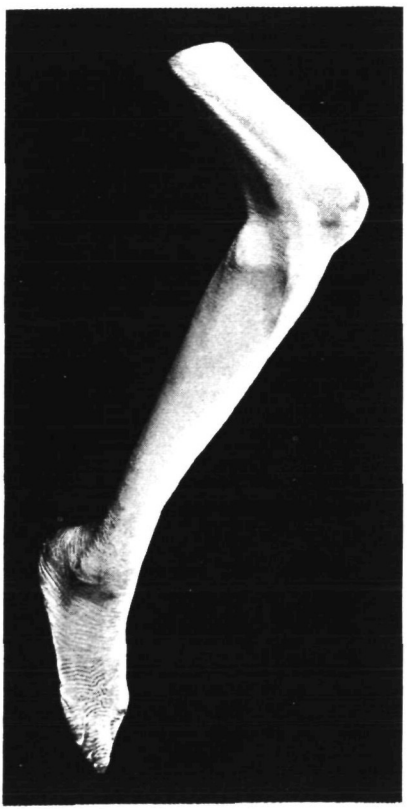


FIG. 2.—The same limb three days before death, showing the extreme muscular wasting.

Acute œdema of one arm, preceded by intense pain and lasting three hours, was observed twice in one case; but with this exception, no œdema was observed above the lumbar cushion. This symptom was present to a marked degree in every case. At this period signs of mental deterioration and disturbance appeared; drowsiness, childishness, nocturnal delirium, and varied delusions were common, and in one case there was prolonged maniacal delirium. Repeated convulsive attacks were noticed in three cases. The spasms were of a fine clonic nature, and affected the limbs only, and chiefly the periphery of the limbs. One of the patients (who only had two attacks) lost consciousness during the attacks, but in the other cases this did not occur.

The convulsions were strikingly like those produced in some people by the administration of chloralose.

The condition of the cranial nerves did not alter during this stage. In some of the patients, towards the end of the illness, the pupils were small, with loss of the cocaine reaction (paralysis of cervical sympathetic).

The abdomen was invariably retracted.

Trophic changes in the skin, similar to those seen in neuritis, occurred in the extremities, and the patients, notwithstanding the utmost care, developed severe bedsores.

The deep reflexes were lost with the onset of the third stage, while the extensor response in the plantar reflex remained marked, and this combination of the signs of posterior and lateral tract involvement was found most valuable in the diagnosis of cases seen for the first time in the third stage of the disease. Case No. 8 came to the hospital at the beginning of the third stage, with incomplete flaccid paralysis of the legs, extreme ataxy, absent knee-jerks, and anæmia. There was a history of syphilis, and the case had been diagnosed as "tabes." The presence of the extensor response was not in accord with the diagnosis of tabes. This case was published in "An Investigation upon the Plantar Reflex," BRAIN, vol. lxxxvii., and it was then submitted that this alteration of the plantar reflex justified a diagnosis of postero-lateral sclerosis. Though there was no pathological verification in this case, the fact

that she died three weeks later, with all the symptoms here described as typical of the third stage of combined degeneration, and that her own medical attendant subsequently furnished us with her earlier clinical history—one of spasticity and ataxy, foot clonus being present to within a few days of admission—places the value of this sign in this case beyond doubt.

A most remarkable fact, considering the wasting of the lower extremities, is that the general superficial reflex excitability of the skin of the lower extremities remains greatly exaggerated till quite late in the third stage.

The third stage, as a rule, lasted about six weeks, three weeks being the shortest period, and death occurred either from sudden syncope or respiratory failure. Two cases, however, lived five months and nine months respectively after the onset of the flaccid stage; but in these cases the onset of the flaccid stage was just as severe and the symptoms for the first few weeks quite similar to those in the more rapidly fatal cases. After reaching a condition in which death was hourly expected, these patients rallied a little and lingered a long time in a drowsy state of low vitality, with no fresh development of symptoms except progression of the muscular wasting and general emaciation. One of these patients would certainly have died in the eighth week of flaccidity of an attack of respiratory failure but for the use of artificial respiration and stimulants. The other case was aroused from a severe syncopal attack by powerful stimulants, without which it seemed probable that he would have died at a similar period. In the condition of mental and physical paralysis, profound anæmia, general emaciation, and sepsis in which these patients lingered for many weeks, it was difficult to conceive how life was maintained from day to day.

A remarkable feature of the cases was the absence of any improvement of the nervous symptoms under treatment. From the first appearance of the disease to the fatal event, the tendency was for the symptoms to increase, sometimes halting, sometimes progressing rapidly, but never showing any remission. Under treatment the general health and the

anæmia improved markedly in some cases, but the nervous symptoms never.

All the patients, in whatever stage they came under observation, showed irregular pyrexia, and this entirely apart from any anæmic state; for the non-anæmic cases presented it markedly, and apart from the presence of any obvious cause, such as cystitis, bedsores, &c. The temperature was often subnormal, and the range of upward excursion did not exceed 102·5° F., and was usually about 100·5°F.; with the transition from the spastic to the flaccid stage there was always a marked increase in the pyrexia, lasting several days (see chart).

Though the passage from the first to the second stage was not actually observed in any case, it was ascertained with certainty in two of the cases from the private medical attendant of the patients that marked pyrexia had been present at that time.

In the clinical picture of this disease there remains to be discussed the anæmia, which may be considered under the following headings :—

(1) The anæmia preceded the appearance of the nervous symptoms, and was marked throughout Cases Nos. 3 and 4.

(2) Its date of appearance was coincident with that of the nerve symptoms, and increased with them. Case No. 7.

(3) It was only present at the end of a prolonged third stage, when emaciation became extreme. It was then profound. Case No. 1.

(4) There was no anæmia during the whole course of the illness. Cases 2 and 5.

(5) The blood was not examined. Case No. 6.

The characters of the blood were those of a secondary anæmia. The red blood-corpuscles were well shapen, except in Case No. 4, when the anæmia was most profound. A few small dark-coloured cells were generally present. Nucleated red blood-cells were only found in one case, and then in very small numbers. Gigantoblasts and microblasts were not found.

The number of leucocytes were increased both relatively to the red-cells and absolutely. The number of lymphocytes

were relatively increased in all cases, and that of the coarse oxyphile-cells diminished. In three cases large oval-cells with reniform nuclei were found in small numbers.

The hæmoglobin was diminished in greater proportion than were the corpuscles. The diminution in number of corpuscles was most marked towards the end of the illness; for an instance in Case 4.

Two months before death—Hb. 56 per cent., R.B.C.'s 4,000,000.

Three days before death—Hb. 18 per cent., R.B.C.'s 800,000.

There was nothing in the blood of any of the cases in which it was examined to suggest "pernicious anæmia."

Neither the spleen nor lymph glands were palpably enlarged in any case.

Hæmorrhage was uncommon except from the bladder in connection with cystitis, when it was common. It was met with in the retina in two cases, and in the skin in one case, and in these cases it was not repeated. Thrombosis was not met with.

The usual symptoms of anæmia, air hunger, lassitude, syncopal attacks, &c., were marked.

In several cases the anæmia showed marked temporary improvement under treatment with iron and arsenic, but the improvement lasted only a short time.

The other organs of the body presented nothing worthy of special notice.

The clinical picture in three tableaux here set forth has been followed by all of these cases up to the present time fatal. The cases varied as regards the anæmia and the length of the illness. But if the slightness of the symptoms in those patients presenting a long first stage, and the conditions under which the third stage was prolonged in Cases 1 and 7, the regularity of the course of the disease as regards time is most striking.

Most of the patients have died within four months of losing ability to walk. The duration of the illness varying between three months and thirty months averages under nine months.

The following cases, which are included in the appendix, presented the clinical picture of the malady, but have not been verified.

Case No. 9, at the present time under the care of one of us (J. S. R. R.) at the National Hospital, we regard as an instance of the disease, and it suggests that in some cases the latter stages of the disease may be more chronic, especially the second stage, which in the other cases has been short, and in this case complete anæsthesia, complete incontinence and complete paralysis, with wasting of the muscles and diminution of faradic excitability are present, while the legs are very spastic and the knee-jerks increased with double foot clonus, that is, in the second stage, whereas, in the other cases, such symptoms only appeared with the onset of flaccidity and the loss of the deep reflexes.

Three other cases are recorded in the appendix. The first, No. 10, is submitted as a case of combined degeneration during a prolonged second stage, and the second, No. 11, as a case slowly passing from the second to the third stage. It is suggested that Case No. 12, in which recovery took place, was also of this nature—at all events, it could not be clinically distinguished.

Diagnosis.

The differential diagnosis of combined degeneration, while it is simple in the later stages, presents great difficulty in the early stages. Since few of the cases in which the diagnosis has been verified after death were seen in the first stage, and since the clinical picture of that stage has been drawn almost entirely from the accounts of the patients and their friends (collected with every possible precaution to avoid error), and from the medical attendants of the patients at their own homes, and since no diagnosis of combined degeneration was made at the stage in any of these cases verified after death, we can do no more than point out the probable features that may lead to a correct diagnosis in the first stage.

The importance of early diagnosis is obvious from a point

of view of prognosis, and it is possible that the disease may then be amenable to treatment.

The early clinical picture of combined degeneration, that of slight ataxy and spasticity, resembles closely that of the common paraplegic form of disseminated sclerosis in an early stage. Three of the cases here recorded were examined by competent authorities soon after their symptoms commenced and the diagnoses made by them, were :—

Case No. 3. Slight spastic paraplegia. Anæmia. ? cause.

Case No. 5. Early disseminated sclerosis.

Case No. 6. ? Early disseminated sclerosis.

In attempting to distinguish these two diseases, careful attention should be paid to the history. The age at which combined degeneration occurs is not the most common for the appearance of symptoms of disseminated sclerosis. The preponderance of subjective sensations in the legs, the absence of the functional manifestations, of exacerbations and remissions of the symptoms, of nystagmus, and of sphincter trouble which are so usual in disseminated sclerosis, and the presence of irregular pyrexia are probably of great importance in the early diagnosis of combined degenerations.

The presence of anæmia in an early case of spastic paraplegia should give rise to a suspicion, but the possibility of chlorosis, associated with disseminated sclerosis in young women, must be borne in mind. A symmetrical affection of all limbs, with slight ataxy and spasticity, preponderating in the legs, is a most important distinguishing symptom of combined degeneration.

In the second stage the diagnosis is more certain. The history of slight symptoms preceding a sudden complete and lasting helplessness of the legs ; the preponderance at first of ataxy over loss of power ; the rapidly-increasing anæsthesia, paresis, and spasticity ; the severe lightning pains ; the absence of sphincter trouble as a rule ; the pyrexia and the ænemia, if present, serve to separate the disease from other forms of paraplegia.

In the third stage the diagnosis is easily made from the only diseases which present a symptomatology in any

way resembling that of combined degenerations. These diseases are tabes dorsalis, acute myelitis, polyneuritis, and spinal tumour.

Most of the cases were sent to the hospital for the first time in this stage labelled "Tabes," on account of the flaccidity, anæsthesia, loss of deep reflexes, and complete incontinence. A history of spasticity changing rapidly to flaccidity, the completeness of paralysis and anæsthesia, the pyrexia, the œdema of the legs, the rapid muscular wasting and loss of faradic excitability, and that sure sign of involvement of the pyramidal system—Babinski's extensor response in the plantar reflex—at once excludes tabes dorsalis. Moreover, the Argyll-Robertson pupil was never present. In one case bilateral sympathetic paralysis had been described as "slight bilateral ptosis, marked myosis, and reflex iridoplegia." The sudden onset of complete paralysis and œdema resembles the onset of acute myelitis, but the preceding history will at once distinguish the two conditions.

A tumour pressing on the spinal cord, and giving rise in order to slight and severe spastic paraplegia, and finally to flaccid paraplegia, in some cases produces the picture most nearly approaching that of combined degenerations. The absence of severe root pains preceding the paralysis and the distribution of the physical signs in very unequal degree, in the upper and lower limbs, together with the absence of other distinctive signs of spinal tumour, should prevent an error in diagnosis.

The involvement of all the limbs, with flaccid paralysis, wasting, diminution of faradic excitability, anæsthesia, and loss of the deep reflexes are not unlike the symptoms of peripheral neuritis, but the resemblance is superficial only. The history of a preceding spastic state is incompatible with the diagnosis of polyneuritis. Total incontinence of the sphincters, paralysis of the trunk muscles, anæsthesia upon the trunk, following a root distribution, girdle sensations, and the presence of the extensor response in the plantar reflex are symptoms quite incompatible with a diagnosis of polyneuritis.

Prognosis.

So far as these cases are concerned the certain diagnosis of combined degeneration passes a short sentence upon the patient.

It may be, however, justifiable here to note that a patient of Dr. Ferrier's, at the National Hospital, suffered with a short illness associated with pyrexia, in which he suffered successively with slight ataxic paraplegia, severe ataxic paraplegia, and flaccid paraplegia, with wasting, œdema, and complete incontinence. After remaining flaccid for five days, he rallied from an apparently moribund state, and made a rapid recovery.

This patient is still under observation, and is at work. (Case No. 12.)

Treatment.

It has been already mentioned that under treatment with iron and arsenic the anæmia may improve greatly for a time.

No drugs have been found to influence the nervous symptoms in any way. Mercury, iron, iodide of potassium, arsenic, strychnine, quinine, salicylates, and various animal extracts have been given with no benefit.

Morbid Anatomy.

The condition of the body at the time of death varied with the duration of the last stage of the disease. When this had been long, the limbs and especially the lower extremities were wasted, and in some cases this was extreme, and the legs had become contracted in the flexed position. In those cases in which the last stage of the disease was of shorter duration, the wasting was not so marked, and in these cases there was often a good deal of adipose tissue, not only over the trunk, but also over the extremities. Bedsores have always been present.

The brain, cerebellum, and pons in most cases appeared perfectly normal, but there was occasionally some wasting of the cortex, with slight thickening of the membranes and

compensatory œdema. The vessels at the base of the brain appeared perfectly normal.

The spinal cord, apart from being slightly wasted (a condition, however, by no means always present) appeared perfectly normal, so far as its external aspect was concerned. There was, however, in one case slight opacity of the arachnoid membrane. On section of the cord, the gray appearance of the degenerated parts was at once obvious, and this became more marked after the cord had been hardened in Müller's fluid, when the sclerosed areas stood out of a lighter colour than the neighbouring healthy tissue.

The lungs have shown various degrees of œdema and patchy pneumonia, but otherwise have appeared normal.

The heart, both in regard to its valves and the condition of its walls, has appeared normal; in one case it was described as fatty. The pericardium has in all cases appeared normal.

The liver was generally enlarged to a slight degree, but showed no marked change; no free iron reaction has been obtained.

The spleen was found enlarged and soft, but the condition seemed to depend on the condition of the bladder and kidneys; for when these were normal the spleen did not manifest the above changes.

The kidneys often showed some change secondary to the condition of the bladder, either septic infarcts or pyonephrosis; in other cases they were either normal or showed slight granular change.

The bladder showed varying degrees of cystitis.

The bone marrow was examined in two cases from the femur, and in the first appeared red and almost diffluent, resembling the condition of the softened spleen; and this was a case in which the bladder appeared fairly healthy; in the second case it was of a more normal appearance, being pale and of the usual consistency. The muscles of the leg showed various degrees of atrophy, in most cases being flabby and very œdematous, but in others being simply wasted. The muscles of the upper extremity were much less affected than those of the lower.

Plate V.

Series of sections from the medulla and spinal cord of Case No. 1.

The last stage of the disease in this case was of long duration, and consequently the amount of sclerosis is greater.

The sections have been stained by the Weigert-Pal method, and show the most marked change in the mid-dorsal region, where the whole of the periphery of the cord is affected, leaving the gray matter and a few medullated fibres in the immediate neighbourhood intact (figs. 4, 5, 6, 7). In the lowest of these, however, the whole of the periphery is not destroyed, a portion of the antero-lateral tract remaining intact (fig. 7).

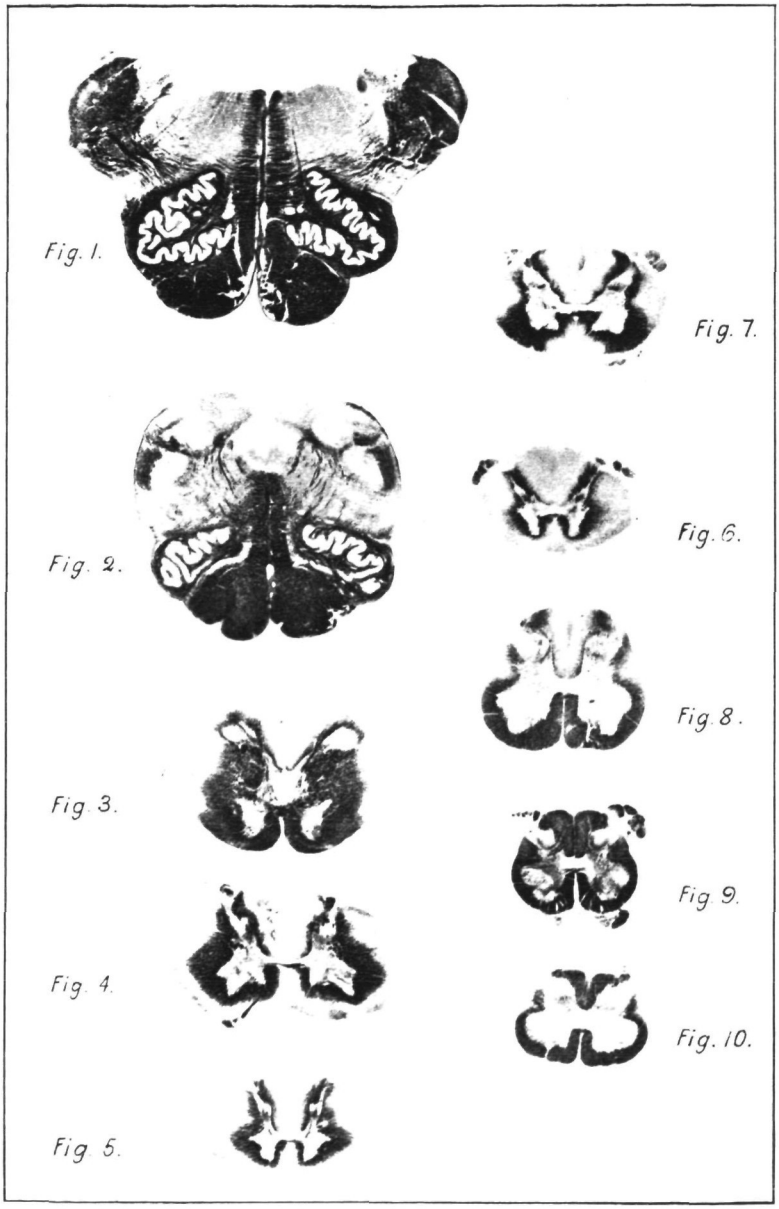
In the lumbar region the disease tends to be limited to the posterior columns and the crossed pyramidal tracts, while in the sacral region, except for some slight affection of the crossed pyramidal tracts, the cord appears normal (figs. 8, 9, 10).

In the lower cervical region the destruction of the cord is still extensive, involving the periphery, but leaving a wider area of normal medullated fibres round the gray matter (fig. 4).

At the level of the first cervical segment (fig. 3) the most marked degeneration of the cord exists in the posterior columns and direct cerebellar tracts, but it is not limited to these.

In the medulla (figs. 1 and 2) the pyramids appear normal, but there is obvious degeneration in the region of the direct cerebellar tract and of the posterior column nuclei.

PLATE V.



CASE NO. 1.

Microscopical Appearances.

The stress of the disease fell upon the mid-dorsal region of the cord, and therefore it will be convenient to commence with a description of the condition found in this region, and subsequently to pass to other portions of the cord. On examining a section of the cord taken from about the level of the sixth or seventh dorsal nerves stained by the Weigert-Pal method, it was at once apparent that there had been very marked destruction of the white matter of the cord all round the periphery, leaving the gray matter and a small area of white matter immediately surrounding it perfectly normal (see plate v., figs. 5 and 6, and plate vi., figs. 6 and 7); and it was apparent also that the destruction was not in any way limited to the long tracts of the cord, but affected the endogenous and exogenous fibres alike—in fact, all that was not in close proximity to the gray matter.

The posterior columns, which are generally most affected, may be completely sclerosed except for a small area in immediate contact with the middle third of the posterior horns.

If from this point in the mid-dorsal region the process was traced up the cord, it was found that the general destruction gradually became less, and, instead of affecting all tracts alike, tended to limit itself to the posterior columns (the columns of Goll being more affected than those of Burdach), the dorsal and ventral cerebellar tracts; and to the crossed pyramidal tracts (plate v., figs. 3 and 4, plate vi., fig. 3). But even in the cervical region, although these may be the most affected areas of the cord, yet the disease was by no means limited to them, for scattered degenerate areas were also present, a favourite situation for these being in the ventral region of the cord in the position occupied by the direct pyramidal tracts and the neighbouring ground bundles (plate v., fig. 4).

The destructive lesion was found as high as the upper portion of the medulla, but degenerate fibres could be seen by the Marchi method in the pyramidal tracts as high as the mid-region of the pons, and in the upper portion of the ventral cerebellar tract in the velum.

Plate VI.

Series of sections from the medulla and spinal cord of Case No. 2.

The last stage of the disease in this case was comparatively short, lasting only about three weeks.

The sections have been stained by the Weigert-Pal method, and show the most marked degeneration in the mid-dorsal region. In this region (figs. 5, 6, 7, 8) there is degeneration both of the posterior and antero-lateral tracts, leaving the ventral portion of the cord unaffected except for a few scattered patches.

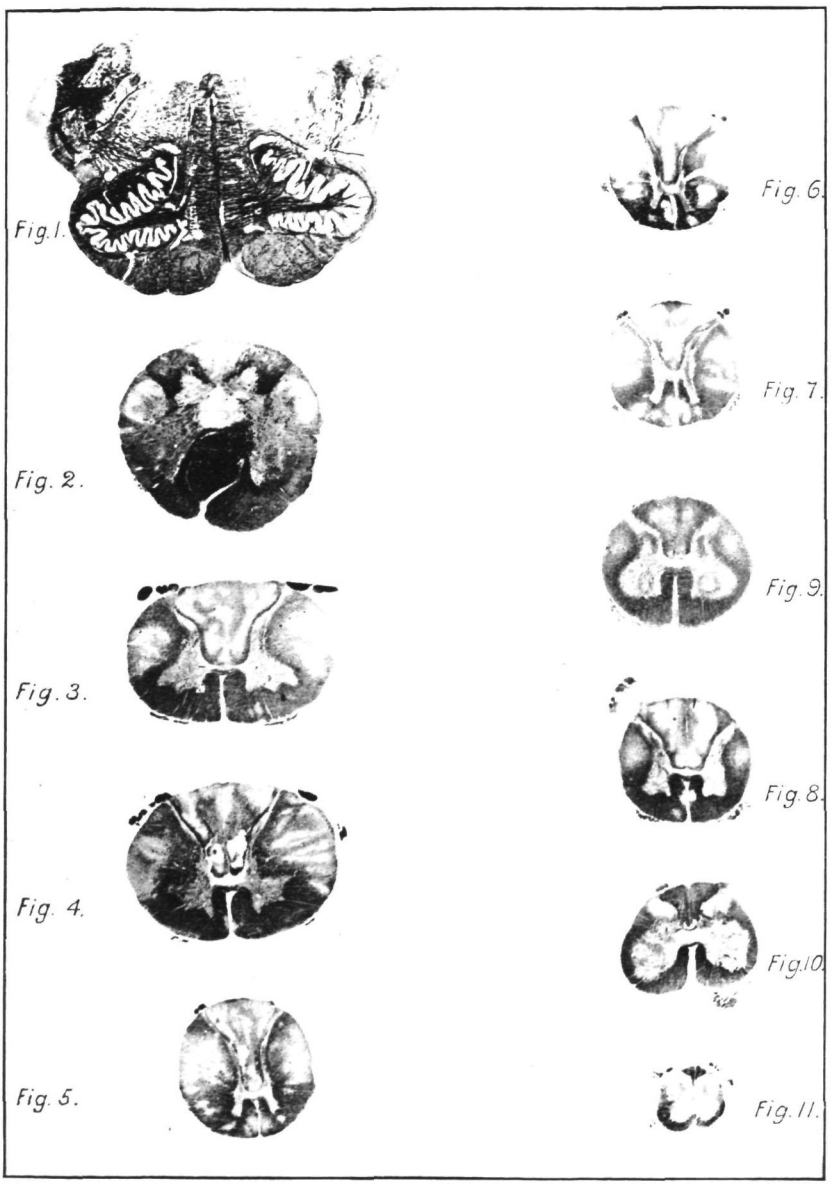
In the lumbar region (fig. 9) the degeneration is almost limited to the posterior columns and the crossed pyramidal tracts, while in the sacral region (fig. 10), except for some slight change in the crossed pyramidal tracts, the cord appears normal.

In the cervical region (figs. 3 and 4) there is marked degeneration in the neighbourhood of the crossed pyramidal tract and the posterior columns, leaving the ventral portion of the cord almost normal.

In the medulla (fig. 2) the pyramids appear normal, and the only degeneration visible by this method is that seen in the funiculus gracilis.

Although the degeneration has been described in certain tracts, it will be noticed that it is by no means limited to the strict margins of the tracts, and also that the degeneration occurs in patches, but that the margins of these never have the sharp edge that is commonly seen in disseminated sclerosis.

PLATE VI.



CASE No. 2.

The upper portion of the pons, the internal capsule, and the cortex of the brain appeared perfectly normal.

On passing to the condition of the cord below the mid-dorsal region, it was found that the diffuse destructive process steadily tended to diminish as the lumbar region was reached, and here it was usually found that the degeneration was limited to the crossed pyramidal tracts with some patchy destruction in the posterior columns, and possibly also in the ventral region of the cord (plate vi., fig. 8). In the sacral region the degeneration was almost entirely limited to the crossed pyramidal tracts, though in some instances patchy degeneration was present in the posterior columns also.

With regard to the condition as seen by the Marchi method, the same features as above described were observable, but it was found that the areas in which degenerate fibres could be seen were considerably wider than those which the Weigert-Pal method had indicated, and these recently degenerate fibres were present in largest numbers in that part of the affected area which bordered on the healthy white matter interposed between this and the vacuolated area to be described below. Degenerate fibres were also found scattered in the otherwise healthy white matter, in the vacuolated region, and to a much less extent or not at all in the sclerosed areas (plate vii.).

Lissauer's tract appeared, for the most part, normal on examination both by the Weigert-Pal and Marchi methods. In some cases it was rather pale as seen in sections prepared by the former method, but when compared with the normal tract the difference was not striking, and the absence of any recently degenerated fibres also seemed to support this view. Even in the mid-dorsal region, where the periphery of the cord was extensively affected, this tract, together with the apex of the posterior horn, escaped destruction.

There were obviously two distinct processes at work in relation to the alteration found in the spinal cords of these cases.

(1) A focal destructive lesion.

(2) A system lesion.

PLATE VII.

Series of sections from the medulla and spinal cord of Case No. 5 stained by the Marchi method. The sections have been drawn under an Edinger's projection apparatus.

In the medulla the most marked degeneration is seen in the direct cerebellar tracts and to a less extent in the pyramids (fig. 1).

In the cervical region (figs. 2, 3, 4) the areas of most marked degeneration appear to be the columns of Burdach, the pyramidal and direct cerebellar tracts, although the degeneration is by no means limited to these. The apparent absence of degeneration in the columns of Goll is accounted for by their complete sclerosis. The areas of degeneration are wider than those seen when similar sections are stained by the Weigert-Pal method.

In the dorsal region (figs. 5, 6, 7) the area of degeneration is wider, leaving only a small band without any degenerated fibres in the antero-lateral tracts.

In the lumbar and sacral regions (figs. 8 and 9) of the cord, degenerated fibres can be seen in the posterior columns, in the situation of the crossed pyramidal tracts, and in the ventral region of the cord.

PLATE VII.

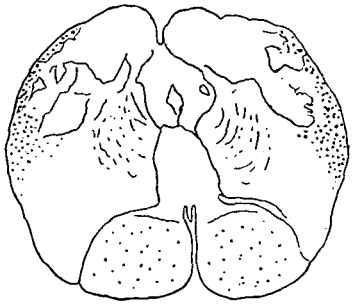


Fig. 1.

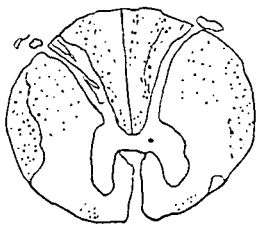


Fig. 2.

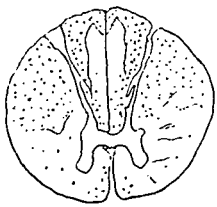


Fig. 5.

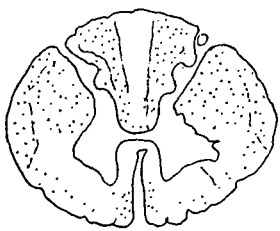


Fig. 3.

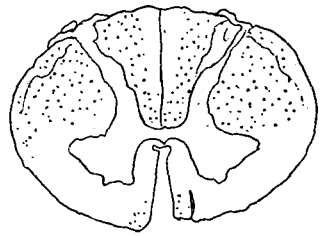


Fig. 4.

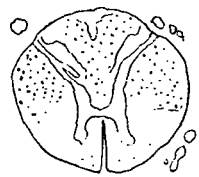


Fig. 6.

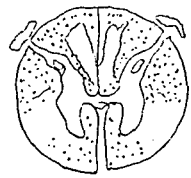


Fig. 7.

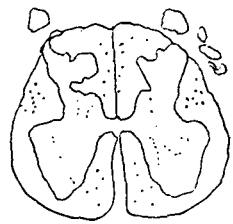


Fig 8.

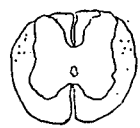
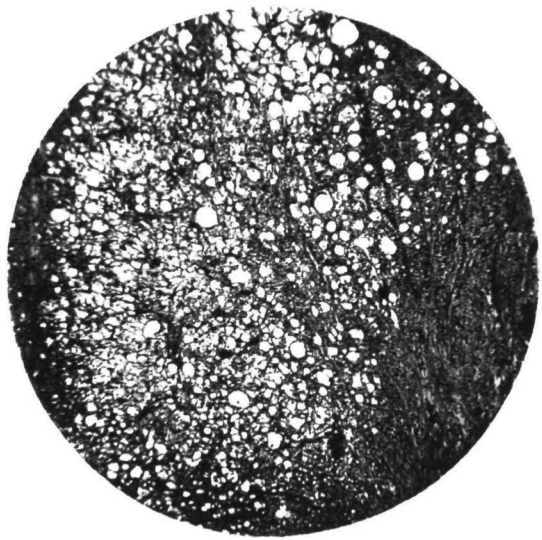


Fig. 9.

CASE NO. 5.

PLATE VIII.



Transverse section of the spinal cord from the mid-dorsal region to show the vacuolated condition which occurs in these cases from the swelling of the medullated sheath and subsequent absorption of the products of degeneration.

The normal gray matter and some healthy fibres are seen to the left of the field, and some vessels with thickened walls can be seen in the vacuolated area. Magnified 43 diameters. The largest space seen in the centre of the field measures ·07 mm. in diameter. The normal medullated fibres in the same field measure rather less than ·01 mm.

With regard to the first, on examining the margin of the patches of degeneration, it was found that the earliest process that took place was swelling of the medullated sheaths, the axis-cylinders remaining apparently unaltered. The next step was that the swollen sheath underwent fatty degeneration, and this in turn became absorbed, and at the same time the axis cylinders disappeared, a space being thus formed, simply surrounded by the connective tissue of the cord. This space was often of considerable size from the fact that the individual spaces became fused into one another, and in those portions of the cord where the destruction had been most acute nothing was left but the connective tissue which formerly supported the now atrophied fibres forming the vacuolated areas above alluded to and figured in plate viii. In certain cases in which the condition had existed for a considerable time, or in those portions of the cord in which the disease was of longest standing, a considerable amount of fibrous tissue had become deposited in and about the loose meshwork, and a dense sclerosis of the cord had occurred in which neither spaces, medullated sheaths, nor axis cylinders could be seen.

As to the second process, viz., the system degeneration, it was found that the long tracts of the cord exhibited a degeneration similar to that which is found after transverse lesions of the cord, that is to say, there was degeneration of the medullated sheaths and axis cylinders and a gradual replacement by connective tissue giving rise to a definite sclerosis of the cord. The two processes merged into one another so closely that it was often impossible to say which was the focal lesion and which the system lesion, but as a general rule the farther from the mid-dorsal region the more easy it was to distinguish what appeared to be system degeneration from that due to focal changes, so that in the cervical region the system degeneration became more apparent in the afferent tracts, while in the lumbar region it was more evident in the efferent tracts, but it is not to be supposed that the change was limited to afferent or efferent tracts in either region, for extensive degeneration was found in the pyramidal tracts even as high up as the medulla,

while, on the other hand, similar changes were found in the posterior columns in the lumbar region.

The gray matter was practically normal. There were no degenerate areas present, nor were there any hæmorrhages, and, moreover, the vessels were neither thickened nor engorged.

The cells of the anterior horns and of Clarke's columns were for the most part normal; in certain sections of the cord, however, there were possibly rather fewer cells than normal, but those that remained were well stained. The nucleus and nucleolus were normal, as were the cell processes and the chromophilic granules, both as regards their arrangement and their staining; many of the cells were however extensively pigmented, this pigment being apparent not only by the Marchi method, but also by the Nissl method.

The anterior nerve-roots appeared normal both to the Marchi and Weigert-Pal methods, and this even in the dorsal region, where they lay in close contact with the degenerated areas within the cord.

The posterior nerve-roots and the posterior root ganglia appeared normal, although here again the cells contained a considerable amount of pigment. In one case, however—No. 7—in which a subcutaneous hæmorrhage had occurred in the area of skin supplied by the seventh left posterior root (plate ix., fig. 1), a cyst measuring 3 mm. in diameter and filled with clear fluid was found (plate viii., fig. 2). Many of the cells of this ganglion had undergone considerable atrophy, although others appeared perfectly normal. There was also an incision of the connective tissue between the cells. The vessels of the cord in the affected areas were engorged and their walls thickened, but there was no actual thrombosis. In the unaffected areas, however, the vessels were neither engorged nor thickened. An exceptional condition was, however, met with in one case in which the middle coat of the vessel appeared to have undergone a hyaline change. There was no obvious thickening of the membranes even over the areas in which the sclerosis of the cord was most marked.

PLATE IX.

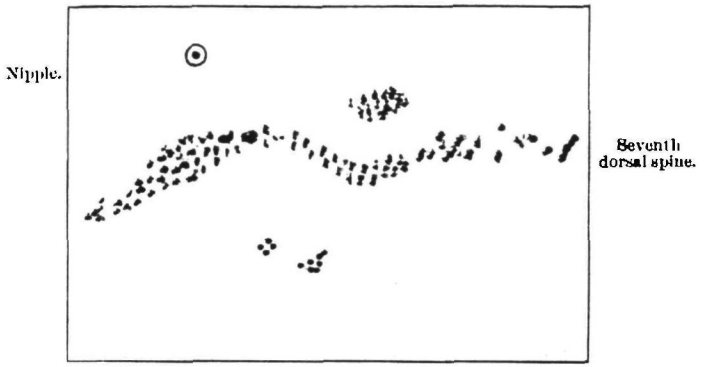


FIG. 1.

Subcutaneous hæmorrhage over chiefly the seventh left thoracic root area. The left limit of the figure is the middle line of the body in front, the right limit is the posterior mid-line. The seventh dorsal spine and nipple are indicated.

(*Traced from the body upon paper and reduced.*)

FIG. 2.

Section through the seventh left thoracic posterior root ganglion showing a cyst occupying the centre of the ganglion (case 7). The cyst measured 3 mm. by 4 mm. and was filled with a clear fluid. The walls of the cyst are composed of two coats, an outer of closely packed and an inner of loose connective tissue. Many of the cells of the ganglion are normal; altered and shrivelled cells are also present. Magnified six diameters.

Nerves.—Various peripheral nerves have been examined, and in most of the cases they were found to be normal or showed only very slight changes, either by the Marchi or Weigert-Pal methods. In one case (No. 1), however, there was very considerable degeneration of the nerve-fibres —a change that not only occurred in the larger nerve-fibres, but which also involved the finer branches of the nerves within the muscles, and which appeared to affect not only the motor nerves but also those of sensory origin within the muscle-spindle. The degeneration of the nerves would seem to be a late manifestation of the disease, as this patient lived a long time after the disease was far advanced.

Muscles.—The condition of the muscle-fibres in these cases varied considerably, although they all showed atrophy; the degree to which this had taken place differed to a very great extent. In the most extreme case the fibres had become so reduced in size that they had lost their striation, and measured only ·004 mm. in diameter, and there was in this case a corresponding increase of the connective tissue (plate x., fig. 1). It was interesting to note that although the atrophy of the muscle-fibres had become so extreme, yet many of the finer nerve-fibres in the immediate neighbourhood were, to all appearances, perfectly normal. On the other hand, in the cases in which the atrophy was not so marked (and these form the greater proportion of the cases) it was found that the extent to which the muscle-fibres were reduced in size was such, that instead of measuring from ·06 to ·08 mm. in diameter, they measured on the average less than ·04 mm., and assumed a rounded instead of the polygonal shape commonly seen in muscle cut in transverse section after hardening (plate x., fig. 2). In a small number fat could be seen within the muscle-fibres; these were always fibres of small size, and usually measured from ·03 to ·02 mm. in diameter. This fatty degeneration of the fibres was rather the exception than the rule. There was no evidence of any inflammatory process, unless we accept the increase of connective tissue as having this significance; whereas, as above stated, this was sufficiently accounted for by the extreme atrophy which the muscle-fibres had undergone.

Muscle-spindles.—These organs appeared remarkably well preserved, especially when the atrophic condition of the muscle in which they lay was taken into account. The capsule and general appearance of the spindle was normal; the intrafusal muscle-fibres were of normal size, retained their striation, and only a few of them exhibited slight fatty degeneration. With regard to the nerves passing to the muscle-spindle, many appeared normal, and all those examined contained at least one normal fibre; when, however, we consider the large number of nerve-fibres which are normally present in the muscle-spindle, it seemed probable that there had been a certain amount of atrophy of the nerve-fibres even within the muscle-spindle.

The muscle-fibres of the diaphragm appeared normal.

The heart muscle appeared fairly normal; there was no fatty degeneration, but there was brown pigmentation of the fibres, extending from either pole of the nucleus of the fibre; the muscle-fibres did not appear much atrophied, and measured about ·02 mm.

The liver in the cases examined did not give the free iron reaction. There was some fat in the periphery of the lobules of the liver, but not in such amount as to be considered pathological.

The kidneys in those cases in which there had been infection from the bladder showed areas of small cell infiltration; in other cases they appeared normal, or showed slight fatty degeneration in the epithelium of the tubules.

Pathology.

Various views have been advanced as to the ætiology and pathology of the affection; but as these have been fully discussed in a former paper by one of us (J. S. R. R.), we do not propose to do more than epitomise the salient points brought out in that discussion. The spinal cord changes have been variously attributed by different writers to one or other of the following causes :—

PLATE X.

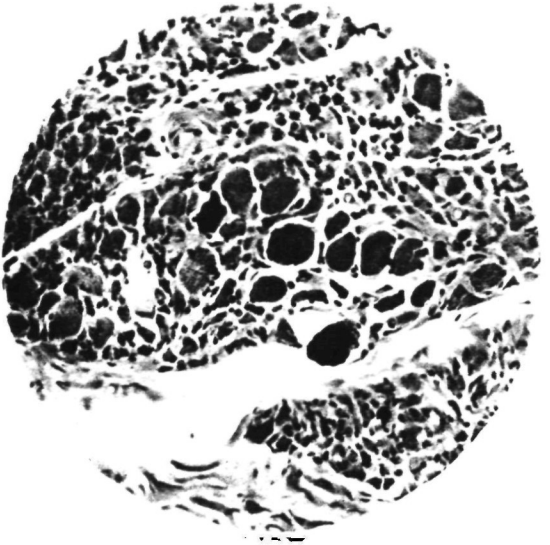


FIG. 1.—Transverse section from the vastus internus muscle of case No. 1, showing the extreme degree to which atrophy may take place. A portion of the muscle has been selected in which some comparatively large fibres remain, but the majority are atrophied to such a degree that they measure less than ·004 mm. The large muscle fibre in the centre of the field measures ·03 mm., *i.e.*, about one-half the diameter of a normal fibre.

There is a very considerable increase in the nuclei between the muscle fibres, but not more than can be accounted for by the fact that the normal connective tissue nuclei are approximated owing to the atrophy of the muscle fibres. Magnified 160 diameters.

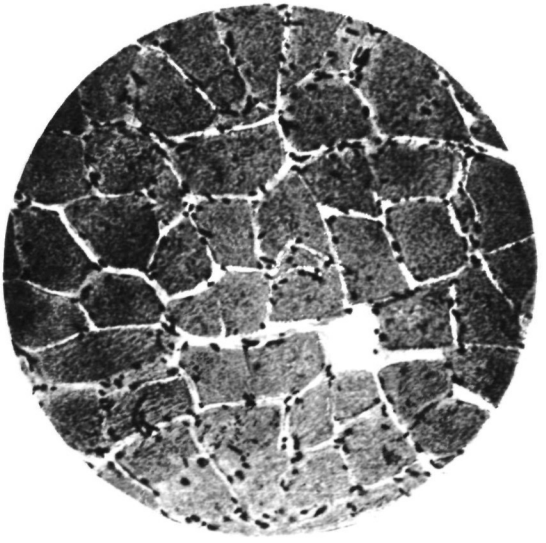


FIG. 2.—Transverse section from a normal vastus internus muscle for comparison with the above. The normal muscle fibres measure about ·06 mm. in diameter. Magnified 160 diameters.

(1) The anæmia frequently found in association with the spinal cord symptoms in these cases.

(2) Multiple hæmorrhages in the spinal cord occurring in association with the anæmia.

(3) Thickening of the walls of the blood-vessels, the vascular change being primary and that in the nerve elements secondary in origin.

(4) An acute myelitis occurring in the earlier stages of the disease, or a disseminated myelitis having a predilection for certain tracts of the spinal cord.

(5) The affection of the white matter secondary to a primary change in the gray matter of the cord.

(6) A toxic agent, which is jointly responsible for the changes in the spinal cord and for the anæmia in those cases in which this symptom is present.

The existence of so many different views on this question must, in part at any rate, be due to the opinions of writers being based on the particular conditions found in the cases which have come under their individual observation, and in greater part probably owing to the confusion that has already been alluded to, and in consequence of which cord changes occurring in the course of severe anæmia have been regarded as identical with the subacute combined degeneration of the cord in which anæmia may be a prominent symptom. A study of our own cases, in conjunction with all the recorded cases that strictly come within the same category does not, it appears to us, admit of such diversity of opinion.

The first point to be considered is what justification there is for regarding the cord changes as due to anæmia; but the objections to this hypothesis are so strong that we do not propose to devote much space to its discussion. Though a marked feature in many of the cases of the disease under consideration, anæmia has not been present, at any rate, to any notable degree in some, while in others in which it has been a prominent feature, the anæmia has not become obvious until some time after the spinal cord affection has manifested its presence by such clinical phenomena as we know indicate disturbance of this part of the central nervous

system. Moreover, although cases of profound anæmia commonly occur, and although a large number of such cases which present the features of the pernicious and other varieties of anæmia have been examined by competent observers, in none of them have there been either clinically or after death the phenomena which characterise the class of case whose pathology we are now considering. Morbid changes have been found in the spinal cord in some cases of fatal anæmia, but in none of them have the changes been in any way comparable to those so characteristic of the group of cases of sub-acute combined degeneration. While dissenting from the view of those who hold that anæmia is responsible for the morbid changes present in the cases of combined degenerations, we are, nevertheless, prepared to admit the possibility that anæmia may play a part in reducing the resistive powers of the nerve elements, thus rendering them less able to withstand the baneful influence of toxins, a property which anæmia may be supposed to share with other debilitating influences and cachectic states. Thus it may happen that anæmia or other impoverished states of the system, themselves dependent on the action of some toxin, may in their turn render the nerve elements more susceptible to the action of the same, or, it may be, some other poison.

The view which supposes the degenerative changes in the various affected tracts of the cord to be due to small hæmorrhages is equally untenable, for no hæmorrhages were present in any of the cases included in our present series, nor could the slightest traces of former extravasations be detected. Even when hæmorrhages have been described as present, they have been too few, too small, and too scattered to possibly account for degenerations affecting tracts symmetrically and in their entirety throughout so large a part of the spinal cord, and producing so profound an alteration as to result in the complete degeneration of certain of them in parts of their course. Moreover, did larger hæmorrhages occur at certain points in the cord so as to interrupt the greater parts of the same tracts on both sides, we should find some evidence of ascending degenerations of certain tracts above such lesions

with their escape, at any rate in part, below them, and of descending degenerations of other tracts below such hæmorrhages with partial or complete escape of the same tracts above them. Not only have no such hæmorrhages ever been met with, but the distribution of the degenerations in the cord quite precludes such a possibility. It is only necessary to remember that in most of these cases the degeneration both in the posterior and lateral columns is most pronounced in the mid-thoracic region of the cord, and that it diminishes in degree and extent in both pairs of tracts as we pass towards the cephalic and caudal extremities respectively.

The hypothesis which, while not regarding the degenerations in the cord as secondary to hæmorrhages, nevertheless assumes that they are of vascular origin in the sense that the degeneration commences in the immediate vicinity of vessels with altered walls, owes its origin to the observations of Nonne and Minnich, who both found areas of degeneration surrounding vessels with altered walls, but who were not dealing with the class of case whose pathology we are now discussing, but with cases of anæmia in which patches of degeneration were met with in the spinal cord. We have found nothing in the appearances of the morbid changes in the cords of our cases to justify the belief that the affection is vascular in origin in the sense that alterations occur primarily in the walls of the blood-vessels, and that the changes in the nerve elements are secondarily induced. That the topographical distribution of the degeneration of the white matter of the cord depends on the vascular distribution, however, there seems to be little question. This will be obvious if it be borne in mind that the blood supply of a given transverse area of the cord is mainly derived from two sources, the anterior median arteries in the anterior median fissure and the peripheral arteries derived from the vessels of the pia mater. The former supply the gray matter of the anterior horns and the white matter bordering on them, and the neck of the posterior horns, including Clarke's columns, while the latter supply nearly the whole of the rest of the white matter of the cord. The distribution of the affection in the white

matter of the cord in these cases of combined degeneration is precisely that of these peripheral vessels. Why there should be the escape of the area of supply of the anterior median arteries is not clear, but this much seems certain, viz., that the affection of regions supplied by the peripheral vessels does not depend on pachymeningitis in these cases, for no such change has been found in any of our present series. This admission that the morbid condition owes its topographical distribution to the vascular supply must not be interpreted as meaning that we are of opinion that the degenerations of the spinal cord are vascular in the sense that they depend on changes in the vessel walls, whose impermeability leads to impoverishment of the nerve elements. That such thickening of vessels occurs, and that when it occurs it cannot fail to affect the nutrition of the parts supplied by such vessels is admitted; but that this is the primary cause of the degeneration of the nerve element is far from our belief. We regard such changes in the vessel walls as have been found as depending on the same cause as the parenchymatous degeneration of the nerve elements, or as resulting from irritative disturbance consequent on the degenerative changes in these; and that the only part played by the vessels in the initiation of the morbid changes in the nerve elements is that of bringing the toxic material to them.

The question of the vascular supply of the cord and its influence on the topographical distribution of the morbid changes is, however, of interest from another point of view. It is tempting to assume that the fact that the most extensive changes are met with in the mid-thoracic cord is due to the fact that this portion of the cord is less well supplied with blood than any other part, a view that would appear to receive some support from the fact that it is in this region that we most commonly meet with transverse softening, presumably due to vascular thrombosis and unfortunately and erroneously designated transverse "myelitis." On searching for anatomical evidence, however, in support of the view that the mid-thoracic region of the spinal cord is least well supplied with blood, we can find little to justify the

assumption, most of the evidence from this standpoint indicating rather that it is the lowest part of the thoracic cord and the lumbo-sacral region that is least well supplied with blood, both because this part of the cord is farthest from the origin of the anterior and posterior spinal arteries which are derived from the vertebrals in their course within the cranial cavity, and because the reinforcing arteries which reach the spinal cord by way of the nerve-roots have both a longer and a more vertical course from below up to this part of the cord, in addition to which of all the reinforcing arteries these are farthest away from the heart. Some observations conducted by Dr. Carrington, and referred to by the late Dr. Moxon in one of his suggestive Croonian Lectures (*Lancet*, 1881, i., p. 530), are worthy of attention in this connection. Injections were made into the femoral arteries in seven dead bodies, and in spite of its being *a priori* more probable that the vessels at the lower end of the spinal cord would be better injected than those at the upper end, the reverse obtained. In all the subjects the spinal arteries filled from above down, the injection either ceasing at the lower end of the cord or above that part, and while it was obviously reinforced by vessels which entered along the nerves, in no case were the reinforcing vessels of the nerves of the cauda equina found injected.

Much as all this bears against the possibility that the part of the cord most affected in the combined degenerations is that least well supplied with blood, it has to be remembered that it is not in the region of supply of either the anterior or posterior spinal arteries, or of the reinforcing arteries that enter the spinal cord by the nerve-roots that the degenerations occur, but that the degeneration is in the area of supply of the pial vessels.

We have next to consider the view that the spinal cord affection in the sub-acute combined degenerations is the result of myelitis. The objection which has been advanced against considering the degenerations as the result of hæmorrhages, to the effect that parts of certain tracts should be affected above such lesions and should escape below, while others should be affected below and escape above, is equally

applicable in the case of myelitis. Then, again, although we see all stages, including what appears to be the earliest of the changes in the spinal cord, we never meet with a round cell infiltration of the tissues so characteristic of changes of inflammatory origin.

The view that attributes the changes in the white columns of the cord to a primary affection of the gray matter appears to us to be erroneous in that in no small proportion of the total number of recorded cases, including all those of our present series, the gray matter has been found intact, while in a large number of cases in which changes have been found in the gray matter they have been slight and insignificant compared to the degeneration of the white matter, so that the latter could not possibly depend on the former changes. Moreover, there is a wonderful symmetry in the affection of the white matter, while changes in the gray matter when present are, as a rule, irregularly distributed. A further argument against this view is to be found in the fact that the parts of the white matter which chiefly escape are largely those the fibres of which are of endogenous origin.

There only remains for our consideration the view that a toxic agent is jointly responsible for the changes in the spinal cord and for the anæmia in those cases in which this symptom exists; and to this view we strongly incline. Although no poison has been determined in these cases, both the clinical picture and the morbid changes suggest that some toxin is responsible for the production of the disease. This toxic body (whatever may be its chemical nature) may reasonably be supposed to produce a parenchymatous degeneration by its action on the nerve elements of the spinal cord. Such a theory accords best with the changes found and with their distribution. The most reasonable explanation that can be offered as to why some parts of the cord are affected and others are not is that all parts of the central nervous system are not equally prone to be deleteriously affected by one and the same toxic agent, and that while certain parts are exceedingly easily damaged by one poison, others have a peculiar power of resistance to

the action of such a toxin, while it may be that these very parts are much less able to resist the action of some other toxin which may have little or no effect on the parts so susceptible to a poison having different properties.

Appendix of Clinical Cases and Pathological Results.

Case 1.—M. M., a stevedore, aged 27 years, was admitted into the National Hospital under the care of Dr. Bastian on October 27, 1897, complaining of numbness and loss of power in the legs and dysuria. He had always had the best of health previous to this illness. He denied venereal disease, and no fact was elicited suggesting that he had had syphilis. He had never taken excess of alcohol. He had suffered from a winter cough for many years.

Five months before admission he began to notice that his legs were numb and stiff, that he dragged his feet in walking, and caught his toes in the ground. A tight feeling round the lower chest troubled him greatly at times. A few weeks later he became unsteady when walking in the dark, and fell into his basin on several occasions when washing himself. He was treated at the London Hospital, where his condition was described as one of spastic paraplegia with ataxy and much anæsthesia of the legs. For three months before admission he had been losing his memory, and had become dull mentally.

Ten days before admission he became unable to stand or walk, and for the first time in his illness became unable to hold his urine. The legs which had been stiff till this time became quite flaccid. He had never had any shooting pains or "crises."

When admitted he was a powerfully built, ruddy faced man. He was not anæmic. Mental state dull and drowsy. Memory bad. Special senses normal. Pupils equal and reacted normally. Divergent strabismus due to weakness of the right internal rectus; otherwise the cranial nerves were normal. Erectores spinæ and respiratory muscles normal. Great weakness of the lower half of the abdominal muscles, the umbilicus shifting upwards an inch on the attempt to sit up. All the movements of the upper extremities were very weak and were accompanied by tremulous incoordinate movements. The intrinsic hand muscles were wasted, and he could not approximate the thumb and little finger of either hand. There was marked hypotonia of the upper extremities. The electrical reactions of the muscles were normal.

Table of all the Physical Signs and Symptoms that have occurred in the Cases 1-9.

	First Stage.	Second Stage.	Third Stage.
Mental symptoms	—	—	Puerility; Delusions; Mania; Coma
Convulsions	—	rare	occasionally present
Speech and articulation...	—	—	—
Special senses	—	—	—
Cranial nerves	—	sometimes affected	—
Nystagmoid movements...	—	present	present
Pupils	equal and react	equal and react	equal and react
Palsy of trunk muscles	—	spastic palsy	flaccid palsy
Palsy of diaphragm	—	—	sometimes present
Upper extremities :—			
Paralysis	? slight	slight or marked	spastic or flaccid
Wasting	—	sometimes present	marked
Ataxy	present	marked	severe
Lower extremities :—			
Paralysis	slight spastic	severe spastic	complete flaccid
Wasting	—	sometimes present	severe
Ataxy	present	severe	extreme
Subjective sensations	present	present	present
Shooting pains	—	present	present
Girdle sensation	—	present	often present
Pain beneath costal margin	—	—	present
Herpes	—	present	present
Anæsthesia	—	partial loss	complete loss
Sphincters...	—	usually normal	incontinence
Superficial reflex excitability	+	+ +	+ +
Plantar reflexes	? extensor	extensor	extensor
Deep reflexes	increased	increased	lost
Pyrexia	present	present	present
Anæmia	present	present	present
Hæmorrhages	—	—	present

All movements of the lower extremities were performed feebly. The muscles were hypotonic, but were not wasted, and the electrical reactions were normal. When supported on either side he could just stand. The attempt to walk produced the most wildly incoordinate movements. There was complete loss of sensibility to all forms below the ninth dorsal root level and impairment to all forms as high as the fourth dorsal root level, and over both hands and the ulnar border of the left forearm. There was a marked girdle sensation immediately below the ensiform cartilage, and he complained of a constant heavy pain in the hepatic region. Reflex incontinence of urine with a considerable amount of residual urine. Severe cystitis. Cranium and spine normal.

Reflexes.—Wrist and elbow-jerks absent; knee-jerks only just obtained with double reinforcement; no foot clonus. Superficial reflex excitability of the lower limbs much increased. The plantar reflexes showed the extensor response. Some chronic bronchitis and emphysema. Temperature 101° F. No palpable enlargement of the spleen. The other organs were examined and found healthy.

A few days after admission the knee-jerks were lost and were never again obtained. The legs rapidly became completely paralysed. The muscles of the legs, forearms, and hands wasted rapidly, and their faradic excitability was lost early. Severe œdema of the legs and trunk appeared and lasted about a month, subsequently disappearing. He was twice seized with an attack of fine clonic spasm in all four extremities, without loss of consciousness. The anæsthesia became absolute everywhere below the sixth cervical root level. He became generally much emaciated, and died of asthenia on June 8, 1898. The blood examined two months before death showed hæmoglobin 25 per cent., R.B.C.'s 1,500,000 per cm. No nucleated red cells present.

Duration of illness—fifteen months; stage of slight ataxic paraplegia with anæsthesia—five months; stage of severe paraplegia with + knee-jerks—one month; stage of flaccid paralysis with absent knee-jerks, wasting, loss of faradic excitability, and œdema—nine months.

Post-mortem Examination.

The body was extremely wasted, the wasting being most marked about the lower extremities, which were fixed in a position of partial flexion at the hips and knee-joints. There

were several bedsores, both healed and open. There was an abscess in the left groin. Brain and membranes were normal. Spinal cord in external appearance was natural, but on section showed distinct sclerosis of the posterior and lateral columns. Heart and pericardium were normal. Lungs showed some patchy pneumonia. Liver was natural. Spleen was enlarged and friable. Kidneys were both enlarged, and showed a condition of pyonephrosis. Bladder showed evidence of chronic cystitis.

In sections prepared by the Weigert-Pal method all that was obviously wrong with the medulla above the level of the posterior column nuclei was degeneration in both lateral regions in the area occupied by the ventral cerebellar tract. More caudally there was, in addition to the degeneration in this situation, marked degeneration of the fibres of the posterior column nuclei and of the restiform body to a much slighter extent. Nothing obviously abnormal could be determined in the pyramids. In the upper cervical region there was complete degeneration of the posterior columns, the parts bounding the gray matter alone escaping. There was also marginal degeneration affecting the direct cerebellar and posterior part of the afferent antero-lateral tract, encroaching slightly on the crossed pyramidal tracts. The ventral part of the cord was preserved, with the exception of a very slight symmetrical degeneration in a very limited area in the efferent antero-lateral tract area. Lower in the cervical region some more of the postero-external column was preserved, the degeneration being on the whole less intense in this tract than in the postero-internal. There was in addition marginal degeneration, which affected the whole of the periphery of the remaining parts of the cord, including the direct pyramidal down to the anterior commissure. The crossed pyramidal tracts were considerably encroached upon, while the degeneration was rather less marked in the position of the efferent antero-lateral tracts than elsewhere in the affected parts. The same topographical distribution of the degeneration obtained in the thoracic region, though the extent of the area affected was greater; a smaller unaffected boundary separated the gray matter from the degenerated parts in the lateral and ventral regions of the cord, so that the crossed pyramidal tracts, for instance, were wholly involved while the lateral limiting layer escaped. In the lumbar cord the degeneration was less extensive in distribution; a considerable area in the antero-lateral region escaped, and there was no marginal degeneration at this point. In the posterior columns the fibres of the efferent septo-marginal tracts were seen to be unaffected. In the

lower lumbar and sacral regions the ventral portion of the cord was quite normal, the degeneration being limited to the crossed pyramidal tracts.

Sections prepared by the Marchi method confirmed what was shown by the Weigert-Pal method, and added the following information :—In the medulla, scattered recently degenerate fibres existed in both pyramids, and the areas of degeneration were more extensive than would be supposed from a study of the sections prepared by the other method alone. The same applies to the cord, for recently degenerate fibres were seen in areas which otherwise appeared normal. This method made it clear that in the affected parts three zones existed—(1) of advanced change, in which there was thick-set sclerosis, and little if any recent degeneration; (2) in which the bulk of the fibres was normal, but recently degenerate fibres were scattered throughout them; (3) an intermediate zone, in which the marked feature was the large clear spaces from which the products of degeneration had escaped. Thickened septa separated these spaces and scattered recently degenerate fibres, fewer than in the better preserved parts and more than in the sclerosed parts, lay among them.

The Nissl method revealed no abnormality in the cells of the gray matter of the cord, nor in those of the posterior root ganglia, nor could any change be determined in these parts by other methods of staining.

The nerve to the vastus internus muscle showed very considerable degeneration both by the Marchi and Weigert-Pal methods; by the Strœbe method many normal axis-cylinders could be seen, but it was noted that the medullated sheath of the nerve also tended to take the blue stain in an irregular manner, and a similar appearance was seen in the nerves of dogs in whom recent degeneration had been experimentally induced.

Muscles.—In the vastus internus there was extreme atrophy of the muscle-fibres, with a corresponding increase in the interstitial tissue between the fibres (plate v., fig. 1). There was also a considerable amount of fat within the individual muscle-fibres, and the transverse striation had disappeared from almost all, except a few of moderate size; but it is extraordinary to note how many apparently healthy well-medullated nerve-fibres lie in an area of muscle which is absolutely degenerate. Some of the atrophied muscle-fibres measured only ·004 mm., and even the largest measured only ·036 mm. The finer intermuscular nerve-fibres showed degeneration.

This case was examined also especially with regard to the muscle-spindle; it was found that the spindle, not only when teased out but also on transverse section, appeared normal, except for the fact that the nerves did not in every case stain well; the striation of the muscle-fibres within the spindle was well preserved, and apart from some fat within the fibres, they were normal. When stained by the Weigert-Pal method the nerve-bundles passing to the spindle stained badly, and comparatively few fibres were seen within the spindle; when, however, we consider the advanced degeneration of the muscle, the condition of the spindle was well preserved, although the nerve supplying it would seem to have undergone considerable degeneration.

Case 2.—J. S., a police constable, aged 36 years, was admitted into the National Hospital, under the care of Dr. Ferrier, on January 4, 1899, complaining of numbness and loss of power in all four limbs and loss of control over the sphincters.

His family history was unimportant. He had suffered with rheumatic fever and typhoid fever in childhood. He denied venereal disease. He had never indulged in excess of alcohol. He had always enjoyed good health, but had been much exposed to the weather.

The history of the illness was as follows:—On September 14, 1898, while at drill, he suddenly felt faint, and on reaching home vomited and had severe headache, which lasted three days. At the end of this time, on getting out of bed one morning, his ankles gave way under him, and from this time he suffered with a dull heavy pain in the loins and with a tight feeling round the stomach. The legs became numb and stiff, and he dragged them in walking. He was very ill generally, and frequently vomited.

In November, 1898, he rapidly lost power of standing, and suffered with severe shooting pains in the legs.

A month later the legs became completely flaccid, and he lost control over the sphincters. He suffered greatly with dyspnœa at this time.

When admitted he was a well-built healthy-looking man, with a flushed face and a distressed expression. He lay in bed breathing rapidly, and was unable to sit, stand, or walk. There was much soft œdema of the legs and trunk, and a large superficial sacral bedsore. The temperature ranged between 99° F. and 101° F.

His mental state was intelligent. He was delirious at night. The special senses, optic discs, and cranial nerves were normal. The pupils were equal and reacted normally.

The abdominal muscles, lower part of the erectores spinæ, and diaphragm were very weak, breathing being almost entirely thoracic.

The upper extremities were weak, but all movements could be performed against some resistance; no rigidity nor wasting. There was extreme incoordination and tabetic athetosis in both upper limbs.

The lower extremities were completely flaccid, and hypotonus was extreme. He could just move all the joints of the legs, but not against the least resistance. All the muscles of the limbs responded normally to both faradism and galvanism.

He complained of an intense heavy pain in the left hypochondriac region and of a broad girdle-sensation between the umbilicus and the ensiform process. Severe shooting pains in the legs. There was marked loss of sensibility to all forms below the twelfth dorsal root level, and generally ten seconds' delay in the perception of severe painful stimuli. There was complete loss of sense of passive movement in arms and legs. There was complete incontinence of sphincters, and there was cystitis.

Reflexes.—Wrist, elbow and knee-jerks absent; no foot clonus. Superficial reflex excitability of the lower limbs greatly increased. Plantar reflexes showed extensor responses.

Heart and lungs normal. Spleen not felt. No anæmia.

After admission the lower extremities rapidly became completely paralysed; the muscles wasted and lost their faradic excitability. The same event happened somewhat later in the hands and forearms. The diaphragm and lower intercostals became paralysed, and respiration became much embarrassed.

The anæsthesia gradually became complete, first over the sacral root areas and then step by step upwards till it reached the upper limit of the fourth dorsal root area.

The muscular wasting increased, and the galvanic excitability became much reduced. The knee-jerks were always absent. The superficial reflex excitability of the legs remained excessive. The extensor responses remained marked.

The patient died of respiratory failure twenty days after admission. Blood count two days before death: hæmoglobin 90 per cent.; red corpuscles 4,500,000 per c.mm.; no nucleated red cells.

Duration of symptoms—four months; stage of slight ataxic paraplegia—nine weeks; stage of severe palsy with rigidity—four weeks; stage of flaccidity, wasting, loss of faradic excitability, absent knee-jerks, and complete anæsthesia—three weeks.

Post-mortem Examination.

The body was poorly nourished, the wasting of the lower extremities being out of all proportion to that of the rest of the body; a bedsore was present over the sacrum. There was some patchy consolidation of the lungs. The spleen was enlarged, but the other organs of the body appeared healthy. The spinal cord, so far as its external surface was concerned, appeared to be healthy, but on section degeneration in the posterior and lateral columns was apparent.

Microscopical Examination.

Cortex.—The cells of the cerebral cortex and the tangential fibres appeared normal; no degeneration could be seen by the Marchi method. The cerebellum and pons appeared perfectly normal.

Medulla.—The upper portion of the medulla appeared perfectly normal both by the Marchi and Weigert-Pal methods. At the level of the posterior column nuclei there was by the Marchi method degeneration in the funiculus gracilis and cuneatus and in the direct cerebellar tracts, but only a few degenerate fibres could be seen in the pyramids. By the Weigert-Pal method degeneration could only be seen in the funiculus gracilis.

Spinal cord.—The brunt of the disease had fallen on the mid-dorsal region, and had affected the posterior columns and the region occupied by the crossed pyramidal tracts more than the ventral region of the cord, although there were numerous patches of degeneration even in this area. In the cervical region the degeneration was limited to the posterior columns, the crossed pyramidal and the direct cerebellar tracts, and had left the ventral portion of the cord even less affected than in the dorsal region. The degeneration was much more scattered and patchy than in some of the other cases, and did not affect the whole periphery of the cord in the mid-dorsal region to so marked an extent.

By the Marchi method there was considerable degeneration both in the regions above described and also around them. There was considerable vacuolation in the mid-dorsal region of the cord, but the recent degeneration, as shown by the Marchi method, was most marked in the long tracts of the cord.

By the Nissl method the cells of the anterior horn, although somewhat pigmented, appeared perfectly normal; the cells of Clarke's column also were normal.

By van Gieson's method there was considerable thickening of the walls of the vessels in those areas of the cord where the degeneration was most marked, while in the region of the cord where there was no change there was no engorgement or thickening of the vessels. In the gray matter of the cord in the mid-dorsal region the vessels appeared full and engorged, although there was no actual exudation round them. The posterior nerve-roots appeared normal. The cells of the posterior root ganglia also appeared normal but were considerably pigmented. The Marchi method showed no degeneration.

Peripheral nerves.—By the Marchi method there was some degeneration in the left sciatic and left anterior crural nerves, and more in the left than the right phrenic nerve. In the corresponding nerves of the right side the degeneration was equally marked, and by the Weigert-Pal method some atrophy of the nerve fibres could be seen.

Muscles.—The fibres of the left vastus internus muscle were fairly uniform in size, but were below the average of the normal muscle, measuring about ·04 mm. The transverse striation was well marked and there was no fatty change. The right vastus internus was in the same condition, the fibres measuring ·04 mm. in diameter. The striation was well marked and there was no fatty change.

Case 3.—S. D., a married woman aged 48 years, was admitted into the National Hospital under the care of Dr. Bastian on January 20, 1899, complaining of stiffness and numbness of the legs.

Three years before admission she began to suffer with a tumour in the left loin, and two years later the left kidney was excised for pyonephrosis. She recovered completely from this operation. With this exception her health had always been good. Several facts were elicited suggesting that she had had syphilis. She had not taken excess of alcohol.

Her illness began in September, 1898, when she first noticed weakness and stiffness and numbness in the legs. Shortly afterwards she fell downstairs, and subsequently had great difficulty in walking and had slight incontinence of urine. The legs gradually got worse and she became very pale. A girdle sensation appeared just above the umbilicus.

When admitted she was a very anæmic, sallow-complexioned woman. She was well nourished. Her mental state was reduced and her memory was poor. Speech, articulation, special senses,

optic discs and cranial nerves were normal. The pupils were equal and reacted normally. The abdominal muscles below the umbilicus were very weak, and the umbilicus shifted upwards an inch in the attempt to sit up. All movements of the upper extremities were performed strongly. There was slight ataxy of the hands. All movements of the lower extremities were performed very feebly and were very ataxic. The legs were slightly rigid at all joints. There was no wasting. There was marked blunting of sensibility to all forms below the ninth dorsal root area. Complete loss of sense of passive position in the legs. She complained of shooting pains in the legs and of a girdle sensation just above the umbilicus. Slight incontinence of urine.

Reflexes.—Wrist, elbow, and jaw-jerks were brisk. Knee-jerks exaggerated. Double foot clonus. Superficial reflex excitability of the lower limbs much increased. Plantar reflexes were extensor responses.

Urine normal. Temperature ranged between 98° F. and 102·5° F. The spleen could not be felt. There was a loud hæmic murmur to be heard in the neck. No hæmorrhages were found. Blood count: Hæmoglobin 20 per cent., R.B.C.'s 1,800,000 per cm. Red cells all sizes and irregular in shape. No nucleated forms. Some Eichhorst's cells seen. There was a marked lymphocyte leucocytosis and no hyaline cells were seen.

A week after admission the legs became quite flaccid, the knee-jerks were lost, the anæsthesia and incontinence became complete, the muscles began to waste and to lose their faradic excitability, and œdema of the legs and trunk appeared, the extensor plantar reflexes remaining.

Under treatment with iron and arsenic the anæmia improved considerably, the hæmoglobin reaching as high as 50 per cent., but it gradually fell again to 20 per cent. The œdema disappeared. The lower extremities became extremely wasted, the muscles entirely losing their excitability to faradism; the diaphragm became paralysed. Bedsores developed. The patient died suddenly of syncope five weeks after admission.

Duration of illness—six months; stage of ataxic spastic paraplegia—four months; stage of flaccid paraplegia—two months.

Post-mortem Examination.

The body was fat, the limbs were flaccid. The brain showed some shrinking of the convolutions on the right side about the upper part of the ascending parietal convolution, but otherwise

was normal. The spinal cord was somewhat shrunken and firmer than normal, and on section showed changes in the posterior and lateral columns. There was some fluid in both pluræ, and the bases of both lungs were considerably collapsed. The heart appeared normal. The liver was enlarged and weighed 60 ozs. Spleen was large and soft and weighed 12 ozs. The left kidney was absent (removed by operation). The right weighed 8 ozs. and was covered by small raised nodules (septic infarcts). The bladder showed cystitis. The muscles of the lower extremity were pale, flabby, and very watery; the biceps cubitis was of normal appearance.

Cortex.—Microscopical examination of the cerebral cortex both with regard to the cells, the medullated fibres, and the tangential fibres, showed no change in these structures.

Cerebellum and pons.—Both these appeared normal by the Weigert-Pal and Nissl methods, but by the Marchi method degenerate fibres could be seen in the ventral cerebellar tract and in the velum, but no other degeneration could be seen at this level.

Upper level of the medulla.—This region appeared normal by the Weigert-Pal method, but by the Marchi method degeneration could be seen in the restiform bodies and in the ventral cerebellar tracts, and there was also scattered degeneration throughout both pyramids. In the medulla the degeneration first became marked at the level of the posterior column nuclei by the Weigert-Pal method and was present in the pyramids, in the direct cerebellar tract, and in the funiculus gracilis and cuneatus. The same section stained by Marchi shows very considerable degeneration of a recent character in the direct cerebellar tracts and older change leading to vacuolation in the pyramids.

Spinal cord.—By the Weigert-Pal method the degeneration was most marked in the dorsal region of the cord, where it affected almost the whole of the white matter except a small zone immediately surrounding the gray matter. The sclerosis was rather more marked in the crossed pyramidal tracts than in the other parts of the cord in this region. In the cervical region of the cord the degeneration was less extensive and was more patchy in distribution—for instance, there were numerous irregular patches of sclerosis in the region of the direct pyramidal tract, while the portions of the cord external to this were less affected. In the upper cervical region the destruction wa smost marked in the posterior columns and in the cerebellar tracts. Passing then to the lower dorsal and

lumbar region, it was found that there was some affection of the posterior columns down to the lower lumbar region, but the sacral was quite free. There was degeneration corresponding to the crossed pyramidal tracts in the lower dorsal, lumbar and sacral regions, and in the latter region it was the only degeneration present. By the Marchi method all the features as above described were present, but it was very striking how little recent degeneration, as evidenced by the presence of fat granules, was present, while the vacuolation and sclerosis of the cord were marked features, and it was only in the areas that appeared normal by the Weigert-Pal method that any number of recently degenerated fibres could be seen. The gray matter of the cord and the cells of the anterior horn and the cells of Clarke's column appeared normal. It could not be positively asserted that there was no change, nor that there was no diminution in the number of the cells of the anterior horns, but it could be asserted that there were numerous perfectly normal cells in the anterior horns in every region of the cord.

Sections stained by van Gieson's method showed that there was no inflammatory condition in the gray matter. In the areas in which the sclerosis of the cord was most marked the vessels were full and engorged and their walls were thickened, but there was no evidence of thrombosis, and in the normal regions of the cord the vessels were neither dilated nor thickened. There was no change in the pia-arachnoid membranes of the cord.

Anterior nerve-roots appeared normal both by the Weigert-Pal and by the Marchi method. The posterior nerve-roots also appeared normal by both methods.

Posterior root ganglia.—No change could be found in these either by the Nissl or Marchi methods. The cells were, however, extensively pigmented.

Peripheral nerves.—No change could be found in any of the following peripheral nerves which were examined by the Marchi and Weigert-Pal methods—right and left sciatic, median, anterior crural, and phrenics.

Muscles.—Right rectus femoris: The fibres of this muscle varied very greatly in size, the largest measuring only ·04 mm. in diameter and the average less than ·02 mm. The striation was well preserved. Left vastus internus: The description given above of the right rectus femoris will apply to this muscle. There was no fatty change within the muscle fibre. Right biceps: The fibres of this muscle were much less atrophied than those above described and were far more uniform in size.

Case 4.—M. D., a married woman, aged 39 years, was admitted into the National Hospital, under the care of Dr. Bastian, on August 16, 1899, complaining of general loss of strength and anæmia of two years' duration and of loss of power and feeling in the legs of six weeks' duration. Until this illness her health had always been good. No facts were elicited suggesting that she had had syphilis. She had indulged freely in alcohol. She lived in the same street as the patient S. D., in Case 3 just described.

Two years before admission, without any assignable cause, she lost her strength, and became very pale and breathless. Her medical attendant found that she was suffering from severe anæmia and irregular pyrexia. She remained confined to bed for six months, and then slowly got better, but never regained her original strength.

Three months before admission she first noticed numbness, weakness, and unsteadiness in the legs. These symptoms increased, but she was able to get about and to do her housework till a week before admission. During this time she had severe shooting-pains in the legs and had a constant heavy pain beneath the left costal margin, and a girdle sensation just below the ensiform process.

A week before admission she became unable to stand, the legs and hands became very numb; she had incontinence of urine, œdema of the legs, and several fainting attacks. The legs at this time became very stiff.

When admitted she was a well-nourished woman. The skin was very pale and sallow. Her mental state was one of extreme exhaustion, and she was delirious at night. Temperature from 98° F. to 101° F. Speech, articulation, special senses, optic discs, and cranial nerves were normal. The pupils were equal, and reacted normally. The abdominal muscles and lower part of the erectores spinæ were very weak. She could not sit up in bed or maintain the sitting posture when raised. The movements of the upper extremities were feeble, and there was marked incoordination. There was some fine tremor of the fingers. The lower extremities were flaccid, and all movements were extremely feeble; great incoordination and marked hypotonia; some general wasting. All the muscles of the lower extremities showed great diminution of excitability to faradism and galvanism; A. C. C. > K. C. C. She complained of occasional shooting-pains in the legs and of a severe dull pain beneath the left costal margin. There was a tight girdle sensation at the level of the ensiform process.

There was distinct diminution of sensibility to all forms, evenly distributed below the fourth dorsal root level and over the eighth cervical and first dorsal root areas. There was complete loss of sense of passive position in the lower extremities, and marked loss in the hands. There was reflex incontinence of both sphincters.

Reflexes.—Wrist, elbow, and knee-jerks absent. The plantar reflexes showed the extensor response. The superficial reflex excitability of the lower limbs was much exaggerated.

Heart.—There was a soft apical systolic murmur and a loud venous hum in the neck. The pulse was regular and of low tension. Blood count, August 20: Hæmoglobin, 56 per cent.; red blood cells, 4,000,000 per cm.; no poikilocystosis; no nucleated red cells; a few Eichhorst's cells; white cells normal. There were no hæmorrhages. She was treated with arsenic, strychnine, and iron.

On August 21 she had a syncopal attack, and in the course of the next half-hour the right upper extremity became very œdematous as high as midway between the elbow and shoulder. Four hours later the œdema of the arm had completely disappeared.

She left the hospital against advice on August 24, but was readmitted on September 16 profoundly anæmic and with a large sacral bedsore.

Blood count on October 2: Hæmoglobin, under 20 per cent.; red blood cells, 800,000 per cm.; marked poikilocystosis; no nucleated red blood cells; no Eichhorst's cells; ratio of white cells to red, 1 to 40. There was marked increase in the number of lymphocytes. No coarse oxyphile or hyaline cells were seen in stained specimens.

There was then marked œdema of the lower extremities and of the hands. The upper extremities were almost completely paralysed, and the muscles only reacted to strong faradic stimulation. There was complete flaccid palsy, with great wasting, loss of faradic excitability, and polar change in the muscles of the lower extremities. There was almost complete anæsthesia to all forms below the seventh cervical root area, and absolute anæsthesia below the fourth dorsal root level. There was complete incontinence of both sphincters. The deep reflexes were absent; the plantar reflexes were still extensor responses. She was constantly delirious; the temperature remained above normal; and she died of respiratory failure on October 19.

Duration of illness: Anæmia—two years; nervous symptoms —five months; stage of spastic paraplegia—ten weeks; stage of flaccid paraplegia—ten weeks.

Post-mortem Examination.

Body well nourished and fat; the limbs were flaccid. There was a bedsore over the sacrum. The brain was normal; the spinal cord appeared normal on its external surface, but on section showed degeneration of the lateral and posterior columns. The heart was flabby and appeared fatty, but the valves were normal. The lungs were very œdematous. The liver was large, weighed 67 ozs., and was friable and fatty. On testing it for free iron a reaction developed which was inconclusive, but subsequent microscopical examination showed that none was present. The spleen weighed 16 ozs., and was diffluent. The kidneys were slightly granular, but were otherwise normal. The bladder appeared fairly normal. The bone marrow of the femur was of a dark red colour, almost diffluent, and very like the spleen in consistency. The muscles were pale, flabby, and very watery.

Microscopical Examination.

Cortex cerebri.—This was normal both as regards the cells, medullated fibres, tangential fibres, and the Marchi method revealed no degeneration. Cerebellum and pons appeared normal.

Medulla.—The upper portion of the medulla appeared normal by the Weigert-Pal method. By the Marchi method, however, degenerated fibres could be seen in both direct cerebellar tracts and in the restiform bodies. At the level of the decussation there was considerable degeneration in both cerebellar tracts, in both the funiculus gracilis and cuneatus, and in the pyramids, as shown both by the Marchi and Weigert-Pal methods.

Spinal cord.—By the Weigert-Pal method there was degeneration of the posterior columns from the lumbar to the cervical region; the destruction was most marked in the dorsal region, somewhat less in the cervical, still less in the lumbar, while the sacral region escaped altogether. The areas of degeneration were rather patchy, but in the cervical region the degeneration was more marked in the column of Goll than in the column of Burdach. There was degeneration in both lateral columns of the cord especially marked in the peripheral portions of the cord in dorsal region. The degeneration in the pyramids could be traced from the cervical to the sacral region, but below the mid-dorsal region it assumed the character of a descending degeneration. The direct cerebellar tract was degenerated, and could be traced up to the restiform body. The fibres in immediate relation with the gray matter appeared fairly normal. The recent degeneration

as shown by the Marchi method was very slight, and the areas which showed most fatty granules were those belonging to the long tracts of the cord. The cells of the anterior horn were somewhat pigmented, but otherwise appeared normal; and the cells of Clarke's columns also were normal.

Vessels.—In the regions of the cord where the sclerosis was most marked there was thickening of the walls of the vessels which affected chiefly the middle coat. In the normal portions of the cord the vessels appeared normal.

Posterior roots.—These appeared perfectly normal.

Posterior root ganglia.—The cells of these ganglia were well formed and appeared normal, though there was rather a large amount of pigment present.

Peripheral nerves.—The following nerves were examined and appeared normal:—The right anterior crural and the branch to the right vastus internus muscle, the nerve to the left rectus femoris, and the left sciatic.

Muscles.—The muscle fibres of the right vastus internus were considerably atrophied, the average diameter being somewhat under ·04 mm.; there was no fatty change within the muscle fibres, and the striation was well marked. The muscle fibres of the left rectus femoris were of irregular size, and averaged about ·032 mm. in diameter, and the striation was well marked.

Liver.—No free iron could be detected in the liver. There was a good deal of fat, but not more than is often found in the livers of persons dying of wasting diseases.

Kidneys.—These appeared normal.

Case 5.—E. F., a married woman aged 49 years, was admitted into the National Hospital under the care of Dr. Hughlings Jackson on December 23, 1898, complaining of loss of power in both legs, sphincter trouble and bedsores.

The family history was unimportant. Previous to this illness her health had been good; there was no history of syphilis and she had always been most abstemious as regards alcohol.

The history of the illness was as follows:—A year before admission the legs became numb and weak and were easily tired. Soon after she dragged the legs in walking and was unsteady when standing, and had occasional diplopia. For ten months she remained able to do her work, but at the end of this time she rapidly became quite unable to stand, and had severe shooting pains in the legs.

A month before admission the legs, which up to this time had

been stiff, became quite flaccid, she completely lost control of the sphincters and developed œdema of the legs and trunk, and a large bedsore made its appearance.

When admitted she was a well-nourished, healthy-looking woman. She was not in the least anæmic. She was quite unable to move the legs and trunk, she was completely incontinent, and there was a large sacral bedsore. She had severe cystitis, and the temperature was 102° F. By day she was mentally clear, but at night there was noisy restless delirium. Speech, articulation, special senses and optic discs were normal. The pupils were equal and reacted normally. There was marked weakness of both external recti. The abdominal muscles were completely paralysed below the umbilicus. The upper extremities were slightly tremulous, but were otherwise normal. There was complete flaccid palsy of the lower extremities. All the muscles were much wasted. None of the muscles of the lower extremities reacted to faradism and the reaction to galvanism was very feeble. There was absolute loss of sensibility to all forms below the first lumbar root level, and marked impairment to all forms as high as the tenth dorsal root level. There was complete loss of sense of passive position in the lower extremities and some impairment in the hands and fingers. There were some trophic changes in the skin of the feet. There was complete incontinence of both sphincters and severe hemorrhagic cystitis.

Reflexes.—The wrist and elbow-jerks were exaggerated. The knee-jerks were totally absent; there was no foot clonus, but two months before admission she had been seen by Dr. Tooth, and he had made a note that at that time the knee-jerks were exaggerated and that there was double foot clonus. There was much soft œdema of the legs and lower part of the trunk. The spleen was not palpably enlarged. There was no anæmia. The other organs were examined and found healthy. She died comatose thirteen days after admission.

Duration of symptoms—thirteen months; stage of slight ataxic paraplegia—ten months; stage of severe paraplegia—one month; stage of flaccid paraplegia, absent knee-jerks and œdema —six weeks.

Post-mortem Examination.

Body well nourished, excess of adipose tissue, bedsore over sacrum. All the organs of the body appeared normal except the spinal cord, which showed on section distinct changes in the posterior, antero-lateral and anterior columns.

Microscopical Examination.

Cerebral cortex appeared normal both as regards its cells and the tangential fibres, and no degeneration could be seen by the Marchi method. Cerebellum was normal.

Pons.—There were scattered degenerate fibres in both pyramids in the pons and in the superior cerebellar peduncles. By the Weigert-Pal method the pons appeared normal.

Medulla.—There were scattered degenerate fibres throughout both pyramids and both restiform bodies as seen by the Marchi method.

Lower level of the medulla.—Degeneration of both direct cerebellar tracts was most marked, there was scattered degeneration in both pyramids and also in the funiculus gracilis and funiculus cuneatus, but more marked in the former than in the latter. By the Weigert-Pal method some change could be seen in the direct cerebellar tracts and in the posterior columns, but the pyramids appeared normal.

Spinal cord.—By the Weigert-Pal method the degeneration was most marked in the dorsal region of the cord, affecting the posterior and crossed pyramidal tracts to the greatest extent, leaving the ventral portion less affected. In the cervical region the posterior columns were more affected than the lateral, while in the lumbar region the lateral columns were more affected than the posterior. The process in this case would seem to be much less destructive than in some of the other cases, there being more recent degeneration and more sclerosis, but less vacuolation ; the distribution of the degeneration is, however, the same. By the Marchi method there was in the cervical region marked degeneration in the posterior columns, especially in Burdach ; the columns of Goll were so sclerosed that they showed little recent degeneration. Degeneration was also present in the pyramidal and direct cerebellar tracts, and in a few fibres in the ventral columns of the cord, while in the lumbar region some degenerate fibres could also be seen in the posterior column and in the ventral region of the cord. In the sacral region there was degeneration in the crossed pyramidal tracts alone.

Van Gieson's method: The gray matter appeared normal. The vessels in the affected areas were thickened and engorged, but were not thrombosed ; in the unaffected areas of the cord they appeared normal.

Nissl method : The cells of the cervical and dorsal region of the cord were possibly fewer in number than normal, but those remaining were well stained and appeared normal. The cells in

the lumbar region appeared perfectly normal. The cells were considerably pigmented.

Peripheral nerves.—The following peripheral nerves were examined and were found to be perfectly normal both by the Marchi and Weigert-Pal methods—the right and left sciatic, left anterior tibial, the nerves to the right and left vastus internus muscles, and the nerves to the right and left vastus externus muscles.

Muscles.—Right rectus femoris: The fibres of this muscle are somewhat atrophic, averaging about ·04mm. in diameter; they are well striated and show but slight fatty change within the fibres. Right vastus externus muscle: The fibres vary greatly in size, having a rounded instead of polygonal outline; there were several degenerate fibres scattered throughout the muscle, which showed black granules when stained by osmic acid; these fibres are not numerous, and are always of small size, ·02—·03mm. Right vastus internus muscle exhibited the same condition as the above two muscles. It is very noticeable, however, how few nerve-fibres there are in the muscle tissue when stained by Pal's method when compared to the normal. When, on the other hand, one compares the condition with that found in case No. 1, in which, in spite of the extreme atrophy of the muscle, the nerve-fibres are well preserved, one cannot but think that the absence of nerve-fibre in this portion of the muscle is a fortuitous condition.

Case 6.—Ruth M., aged 45 years, was admitted into the National Hospital under the care of Dr. Hughlings Jackson on June 30, 1897, complaining of paralysis of the legs and sphincter trouble. There was a history of epilepsy, cancer, and of phthisis in the family. She had been a strong, healthy woman, and she had probably had syphilis. She had been addicted to alcohol. A very incomplete history of the illness was obtained owing to the patient's mental state and the absence of any friends who were in a position to give a detailed history.

Her illness dated from six weeks before admission, when she began to complain of numbness of the hands and feet, stiffness of the legs, and difficulty in walking.

A fortnight later she became unable to stand, developed a girdle sensation and sphincter trouble. She had frequent fainting attacks, and several attacks of general convulsions, in which she lost consciousness and passed urine.

When admitted she was a poorly nourished woman, unable to stand or walk. There was some mental obfuscation. Speech,

special senses, optic discs, and cranial nerves were normal. The pupils were irregular, and there were anterior synechiæ in both eyes. The upper extremities showed some slight incoordination, but were otherwise normal. The respiratory muscles and erectores spinæ were normal; the lower half of the abdominal muscles were weak. Both lower limbs were rigidly extended and were completely paralysed. There was diminution of sensibility to all forms below the ninth dorsal root level, and a tight girdle sensation at this level. There was distension of the bladder with overflow.

Reflexes.—Wrist and elbow-jerks increased; knee-jerks exaggerated. Double foot clonus. Superficial reflex excitability increased in the legs. Plantar reflexes brisk. Marked anæmia. Blood not examined. Liver and spleen not palpably enlarged.

After admission the temperature remained above 101° F. She was constantly delirious. The legs became flaccid, the knee-jerks disappeared, and slight œdema of the lower extremities appeared. The anæsthesia became absolute, the sphincters completely incontinent, and she died much emaciated seven weeks after admission.

Duration of illness—fourteen weeks; stage of spasticity—eleven weeks; stage of flaccidity—three weeks.

Body much emaciated. Brain: the convolutions were somewhat shrunken and there was slight compensatory œdema, otherwise normal. Spinal cord was normal to external appearances, but on section showed sclerosis of the posterior and lateral columns. The heart was natural. The lungs were œdematous. Liver was large and firm, and there was evidence of old perihepatitis. The kidneys were normal.

Microscopical Examination.

Sections of the medulla and spinal cord showed by the Weigert-Pal method that at the level of the pyramidal decussation there was extensive degeneration of the fibres of the posterior column nuclei and of the lateral region of the medulla in the area occupied by the cerebellar tracts, in addition to which there were two small areas symmetrically placed in the antero-lateral region of the medulla. Moreover, a patchy degeneration was evident in the pyramidal fibres at the decussation. The upper cervical cord was the seat of complete degeneration of the posterior columns except the part bordering on the gray matter. There was extensive degeneration of the lateral columns, but the ventral portion

of the cord was preserved. In the lower cervical cord a similar condition was present but to a less marked degree, in the dorsal portion of the posterior external column, while the lateral column degeneration was more extensive, and there was here patchy degeneration in the region of the direct cerebellar tracts, though not confined to these. In the thoracic cord the posterior degeneration was as extensive as in the upper cervical region, and in the lateral areas of the cord more extensive than at the higher levels, as was also the degeneration of the direct pyramidal tracts, which obviously extended beyond the strict limits of these. The only parts of white matter preserved were those bordering on the gray. In the lower thoracic region some fibres in Goll's column were preserved, and there was less extensive degeneration in the ventral parts of the cord. In the lumbar region there was no degeneration in Goll's column, but some in Burdach, especially in the peripheral portion, while the whole of the ventral portion of the cord was preserved.

The Marchi method revealed scattered degenerated fibres in the pyramids, in the lateral region of the medulla in the parts occupied by the cerebellar tracts, and also in the restiform body, but not confined to the area normally occupied by these tracts. There were degenerate fibres in the posterior column nuclei. The condition found in the spinal cord confirmed the findings by the Weigert-Pal method. The great feature of the Marchi specimens was not so much the bringing into evidence of recently degenerated fibres, of which there are comparatively few, but the making e ident of spaces by the falling out or absorption of the destroyed fibres. Fibres that still stain black are seen in the less affected parts, *e.g.*, in the white matter bordering on the gray. The parts of the cord most destroyed were the postero-lateral and ventral, the part between these two areas in the antero-lateral region being less affected. In the upper sacral region there was some falling out of the fibres in the neighbourhood of the ground bundles, but there were scarcely any black fibres. In the lower sacral region no change was found except a few black fibres on each side of the posterior median septum. No descending degeneration was evident, in spite of the lateral columns being extensively destroyed in the lumbar region of the cord.

Case 7.—S. W., aged 38 years, was admitted into the National Hospital, under the care of Dr. Bastian, on November 23, 1899, complaining of paralysis and numbness of the legs, swelling of the legs, and loss of control over the sphincters. There was a strong

family history of tubercular disease. He had been a strong healthy man. He had had syphilis when 22 years old, and had been a heavy beer drinker. A year before this illness commenced he suffered with inflammation of the bladder.

Three years before admission he caught a chill, and directly afterwards noticed that his feet felt numb and stiff. During the next two years the numbness gradually crept up the legs and invaded the trunk, and he was unsteady and dragged his legs in walking, but he kept at his work without much difficulty.

Six months before admission he suffered with severe shooting-pains in the legs. His legs became very stiff, and he became much more unsteady, could not walk in the dark, and fell into his basin when washing. At this time he was a patient at Charing Cross Hospital, where the presence of double foot clonus and increased knee-jerks was noticed.

He remained in this condition without the development of further symptoms till six weeks before admission, when in the course of a few hours he became unable to stand, and for the first time during his illness lost control of the sphincters; this loss remained complete. The loss of sensibility of the legs and trunk became much more severe; he became very pale in the face, and œdema of the legs appeared. He developed cystitis, and became delirious at night.

When admitted he was a pale, sallow-faced, sparely-nourished man. The skin had a waxy-yellow appearance. He lay on his back in bed, unable to move the legs or trunk. He was delirious at night, and his temperature was 102·5°. He had severe cystitis and much hæmorrhage from the bladder. His mental state was facile, and he had varied delusions. On two occasions he had an attack of general convulsions lasting ten minutes, during which time he was comatose. The special senses and cranial nerves were normal. The retinal fundi were yellow in colour, and there were a few small hæmorrhages. The pupils were small and equal; they reacted normally. The erectores spinæ and abdominal muscles did not contract on attempting to sit up or on the attempt to move the trunk. The lower intercostals moved badly in respiration; the diaphragm acted well. All movements of the upper extremities were performed feebly and with marked ataxy. The weakness was more marked in the periphery and the intrinsic muscles of the hands, and the ulnar flexors were markedly wasted. In these muscles faradic excitability was much diminished; to galvanism, K. C. C. > A. C. C. There was absolute paralysis of the lower extremities, with slight flexor and

adductor spasm. There was some rigidity at all joints, but the muscles hung loosely on the bones and were flabby. There was no wasting. There was some diminution to faradism below the knees. There was a severe girdle pain round the lower part of the chest and some shooting pains in the legs. There was complete analgesia to all forms of moderate stimuli from the upper limit of the first lumbar root distribution. Light touches and pricks were not felt below the fifth dorsal root level. There was complete loss of sense of passive position in the lower extremities and marked loss in the joints of fingers and hands. Absolute incontinence of both sphincters. Severe cystitis. Cranium and spine normal. Severe bedsore on left hip. The knee-jerks were exaggerated; no foot clonus; wrist and elbow-jerks brisk. The plantar reflexes were brisk extensor responses, and there was some dorsal retraction of the great toes. The reflex excitability of the lower extremities was greatly exaggerated. There was marked breathlessness on slight exertion; loud basic systolic murmur and *bruit de diable*. Pulse, very low tension. Blood count: Hæmoglobin, 30 per cent.; red blood cells, 1,600,000 per cm.; white blood cells; a marked lymphocyte leucocytosis; very few hyaline cells seen; all other normal forms seen; no poikilocytosis; no microblasts, normablasts, and no gigantoblasts; no Eichhorst's cells found. There was no palpable enlargement of the spleen or of the lymphatic glands. No œdema was present at the time of admission. No abnormality was found in the other organs.

During the first week after admission the clinical picture changed remarkably; the deep reflexes disappeared, and were never again obtained. The spastic condition of the lower limbs gave place to one of complete flaccidity. The muscles of the legs and hands wasted rapidly and lost their faradic excitability within a few days. The excitability to galvanism and to percussion were almost abolished. Much soft œdema of the legs and back appeared, and lasted about three weeks. A heavy constant pain was complained of in the left hypochrondriac region. The cystitis was soon cured with appropriate treatment, and the bedsore healed. Following a severe attack of pain in the left side, a cutaneous hæmorrhage, precisely limited to the area of distribution of the seventh left dorsal root, appeared with two smaller patches over the tenth and eleventh left dorsal root areas. Trophic changes in the skin, similar to those seen in neuritis, occurred in the four extremities. The wasting of the muscles was progressive, and the diaphragm became paralysed.

The plantar reflexes constantly were extensor responses, and the superficial reflex excitability of the lower limbs remained excessive.

Death occurred from exhaustion.

Post-mortem Examination.

The body was extremely thin and wasted, there was a sloughing bedsore over the sacrum, and the scar from an old hæmorrhage in the area corresponding to the seventh thoracic root of the left side. The skull and membranes of the brain were normal. The convolutions of the brain appeared normal, and the cranial nerves and the vessels were natural.

Spinal cord.—There was some purulent exudation on the outer surface of the dura mater in the lower part of the spinal canal arising from the bedsore over the sacrum. The external appearance of the cord was natural, there was no wasting, and the anterior and posterior roots appeared of normal size. There was no meningitis or thickening of the pia-arachnoid. On section the gray areas of degeneration were distinctly visible. The lungs were healthy except for some œdema at the bases. The heart was normal. The diaphragm was natural. The liver was slightly enlarged and gave no free iron reaction. The spleen was enlarged, soft and pulpy. The kidneys showed considerable pyelitis, and the infective infarcts were more numerous in the right than in the left. The bladder contained some purulent urine, and showed a condition of chronic cystitis. The bone marrow of the right femur was examined and appeared pale and of normal consistence. The muscles were wasted, but were not very pale nor œdematous. The right sciatic nerve was evidently very fatty. The posterior root ganglia appeared normal to the naked eye except the seventh left dorsal, and on making an incision into this, after it had been hardened in formalin it was found to contain a small cyst measuring about 3 mm. in diameter, and this contained a little clear fluid.

Microscopical Examination.

By the Weigert-Pal method the cortex appeared normal, the tangential fibres were well stained, the pons and upper levels of the medulla also appeared normal. In sections taken through the lower portion of the olive some change could be seen in the pyramidal tracts, and there was considerable vacuolation in this area; the direct cerebellar tract was similarly affected. In sections below the level of the posterior column nuclei degenera-

tion could be seen in the funiculus gracilis and funiculus cuneatus, the direct cerebellar tract, and in both pyramids. At the level of the decussation of the pyramids there was marked degeneration of the posterior columns, both internal and external, and also of the direct cerebellar tracts; both pyramids were also markedly affected. In the upper cervical region there was extensive sclerosis of the posterior columns, the direct cerebellar tract, and also very considerable affection of the pyramids, but though most marked in these is not limited to them. The nearer the sections examined to the mid-dorsal region the more extensive was the sclerosis, and it was no longer limited to the tracts above-mentioned but affected the whole of the periphery of the cord, leaving the gray matter and a small band of medullated fibres that immediately surrounded it alone normal. At the level of the twelfth dorsal the posterior columns were still markedly affected, but there was less degeneration in the ventral portion of the antero-lateral tracts, the degeneration of the pyramids was still marked. In the lumbar region the posterior columns still showed considerable degeneration, and there was degeneration both in the region of the direct and crossed pyramidal tracts, although it was not strictly limited to the tracts.

Marchi method.—In the cortex there were a few degenerate fibres in the white matter, and these could be traced down into the crura, being rather more numerous on the one side than the other. In the pons degenerate fibres could be seen in both pyramids and in the ventral cerebellar tract, and in addition to this there was a small area of softening with degenerate fibres just ventral to the posterior longitudinal bundle. In sections taken through the upper part of the medulla, scattered degenerate fibres could be seen in the pyramidal tracts, and in the direct cerebellar tracts these were more numerous and could be seen passing into the restiform bodies. Scattered degenerate fibres could also be seen in the region of the posterior column nuclei. In sections taken through the medulla at a lower level, scattered degenerate fibres could be seen in both pyramids, the direct cerebellar tract, and in the funiculus cuneatus, the degeneration being more marked in the last-named tract than in either of the other two. Very few recently-degenerate fibres could be seen in the funiculus gracilis, owing to it being extensively sclerosed. At the level of the decussation the same features as described in the above section were present. In the cervical region of the cord the recently-degenerate fibres were more scattered, and did not form such definite tracts as in the sections at higher levels. In the dorsal region

there was considerable degeneration all round the periphery of the cord, and the portions where the degeneration was of longest standing, viz., the columns of Goll, and the crossed pyramidal tracts showed fewer recently-degenerate fibres than the other portions of the cord. In the upper lumbar region the degeneration again became less, being most marked in the posterior columns and in the ventral region of the cord that lies on either side of the median fissure. In the sacral region the vacuolation, which had been a marked feature through the cervical and dorsal regions, had disappeared from all parts of the cord except the posterior columns, where it was still present to a slight degree; recently-degenerate fibres were still present both in the posterior and ventral region of the cord. In the coccygeal region a few degenerate fibres could be seen in the posterior columns at the most dorsal portion on either side of the median fissure.

Nissl method.—The cells of the cortex, pons, or medulla appeared for the most part normal; there were fairly numerous healthy cells in every region of the cord, but in the lumbar region, although they have a good nucleus and nucleolus, the cells were somewhat swollen and the chromophilic substance rather finely granular. Some of the cells were pigmented, but not to a marked degree. It is probable that there was some diminution in the number of cells in the anterior horn. The cells of Clarke's column were few in number, stained badly, and were markedly pigmented.

Van Gieson's method.—Sections stained by the above method taken at various levels in the medulla and spinal cord were examined with regard to the condition of the vessels and membranes. With regard to the latter no thickening could be found in any region of the cord; the vessels in the pia arachnoid were in some parts distended with blood, but there was no evidence either of recent or of old thrombosis. With regard to the vessels within the cord in those portions which were most affected, the vessels were often engorged, but there was no thickening of the walls or evidence of thrombosis. There was no small cell infiltration around the degenerate areas, whether recent or old.

Peripheral nerves.—The right sciatic showed marked degeneration by the Weigert-Pal method, more than one-half of its fibres having undergone degeneration. The same feature was apparent by the Marchi method, but the number of recently degenerate fibres was small, although in one bundle this was fairly marked. The right anterior crural nerve was very much better preserved

than the sciatic, comparatively little degeneration being visible by the Weigert-Pal method. By the Marchi method, however, although there was practically no recent degeneration the spacing of the fibres showed that a considerable number of fibres must have undergone atrophy. The right phrenic nerve appeared normal both to the Weigert-Pal and to the Marchi method.

Posterior root ganglion.—The cells of the posterior root ganglion were for the most part normal, although here again some were considerably pigmented, and others were shrivelled. The seventh left thoracic posterior root ganglion showed on section a small cyst measuring 3 mm. in diameter and filled with a clear fluid (plate ix., fig. 2). The walls of this cyst were laminated, the inner layer being formed of fine connective tissue and the outer layers of more closely packed fibrous tissue. Many of the cells of the ganglion appeared atrophied and pigmented, others, however, were normal. There was an increase of connective tissue between the cells. The anterior and posterior roots, both by the Weigert-Pal and Marchi methods, appeared normal.

(This case has not been examined with the completeness of the other cases owing to the fact that the patient only died shortly before the publication of this paper; but sufficient has been done to show that it was a typical case of the disease, and owing to the long third stage corresponded closely to Case No. 1 in its pathological aspect.)

Cases not Verified.

Case 8.—M. C., aged 38 years, a married woman, was admitted into the National Hospital under the care of Dr. Ferrier on September 23, 1898, complaining of weakness of the legs, numbness, and inability to walk. She had had syphilis ten years before admission, otherwise she had had good health. There was no history of alcoholic excess. Eighteen months before admission she first noticed numbness and stiffness in the calves of both legs. A few months later she dragged both feet in walking, the legs were stiff, and she had a tight girdle sensation round the waist. These symptoms gradually increased until six weeks before admission, when, in the course of one day, she became entirely unable to stand. With this she developed retention of urine (she had had slight precipitancy of micturition ever since the beginning of the illness).

Her doctor informed one of us (J. C.) that a month before admission he had examined her, and had found the knee-jerks brisk and double foot clonus present.

When admitted she was a very pale, sparely nourished woman; the mental state, speech, articulation, special senses, optic discs and cranial nerves were normal. There was slight lateral nystagmus. The upper extremities and trunk were normal as regards motion. The lower extremities were well nourished and were flaccid. She could execute all movements of the lower extremities against fair resistance as she lay in bed. On attempting to walk, supported on either side, the feet were poorly lifted, and she was wildly ataxic. When standing supported much *danse des tendons* appeared. She fell at once when unsupported. The electric excitability of the muscles was normal. There was slight blunting of sensibility to touch and temperature, but not to pain over the lower two lumbar and all the sacral areas. Sense of passive position was entirely lost in the lower extremities, and was very much impaired in the wrists and fingers. The sphincters showed alternating retention and precipitancy.

Reflexes.—Wrist and elbow-jerks brisk. Knee-jerks absent. General reflex excitability of the lower limbs increased. Plantar reflexes showed extensor responses.

Blood count: Hæmoglobin 60 per cent. of the normal; red blood-cells 4,900,000 per cm.; no nucleated red corpuscles; white blood-cells normal. Spleen not enlarged. Other organs healthy.

She left hospital a month later, her condition not having changed. A month after leaving hospital she developed complete anæsthesia and severe œdema of the lower extremities, which became completely paralysed. Bedsores developed, and she died a month later.

No autopsy was performed.

Duration of illness—twenty months; stage of slight ataxic paraplegia—sixteen months; stage of severe paraplegia—two months; stage of flaccid palsy, absent knee-jerks, and œdema—two months.

Case 9.—H. T., a dressmaker, aged 30 years, was admitted into the National Hospital under the care of one of us (J. S. R. R.) on October 31, 1899, complaining of numbness and weakness of the legs, sphincter trouble, and anæmia of one year's duration.

There was a family history of rheumatic fever. She had never been strong, and had frequently suffered with dyspepsia and anæmia. A year before admission she noticed that she was unsteady when walking in the dark, and she became very pale. This was followed by numbness in the legs, which became stiff

and dragged when she walked. She got about till nine months later, when she became much worse, and was unable to walk. Numbness in the tips of the fingers and a girdle sensation then appeared. She became very breathless and pale, but had no hæmorrhages. Ten days before admission she developed complete incontinence of both sphincters.

When admitted she was an extremely anæmic, sparely-nourished girl. Her mental state was weak and emotional. Speech was normal, but her voice was low pitched, and she did not control the blast of air properly. She had been deaf in the left ear for ten years and had tinnitus on that side; otherwise the special senses were normal. Optic discs and cranial nerves (except tenth and eleventh) normal; the pupils were normal; there was slight lateral nystagmus. There was general paresis of the left vocal cord. The trunk muscles were normal. Movement of the upper extremities was generally feeble, and there was distinct ataxy in both upper limbs. All movements of the lower extremities were very feeble. She could just stand when supported on both sides. Great rigidity of the legs and some general wasting. The faradic excitability was diminished. Marked flexor and adductor spasm. There was slight numbness in the finger tips of both hands and a tight girdle sensation round the lower part of the abdomen. There was marked impairment of sensibility to all forms below the root level—nowhere absolute. Severe dull pain in left hypochondrium.

Reflexes.—Jaw-jerk not obtained. Wrist and elbow-jerks exaggerated; knee-jerks exaggerated; double foot clonus. Superficial reflex excitability of the lower extremities much increased; plantar reflexes were brisk extensor responses; abdominal reflexes absent. Complete incontinence of both sphincters. Spine normal. Heart: Loud basic systolic murmur; *bruit de diable.* Liver and spleen not palpably enlarged. Some soft œdema of lower limbs and back. Blood count: Hæmoglobin, 68 per cent.; red blood cells, 4,700,000 per cm.; a few nucleated red cells present; no poikilocytosis; marked lymphocyte leucocytosis. The temperature ranged between 99° and 102° F.

This patient subsequently developed patches of herpes over the fifth left dorsal root area, and the anæsthesia crept up to the upper limit of the seventh cervical root area.

On November 17 the blood was again examined, with the following result:—Red blood cells, 3,708,000 per cm.; white blood cells, 7,000 per cm. No nucleated red cells. Differential leucocyte count:—(*a*) Polymorphonuclear cells, 71 per cent.; (*b*)

lymphocytes, 23 per cent.; (*c*) hyaline cells, 3 per cent.; (*d*) coarse oxyphile cells, 1·2 per cent.; (*e*) basophile cells, 0·6 per cent.; (*f*) cells with reniform nuclei, 1·2 per cent.

We are much indebted to Dr. A. G. Phear and to Dr. A. J. Whiting for valuable assistance in examining the blood of this patient.

Case 10.—A. T., a married woman, aged 37 years, was admitted into the National Hospital under the care of Dr. Buzzard on February 6, 1900. She complained of weakness and numbness in the legs and arms and inability to stand of seven months' duration. There was no history of syphilis or of alcoholism.

Seven months before admission she noticed that the feet were numb and slightly swollen. Soon afterwards the legs gradually became stiff and dragged when she walked, sometimes giving way at the knee. She did her work for five months. Two months before admission she became unable to stand and her arms became weak. She had had no ocular or sphincter trouble and no pain.

When admitted she was a well-nourished woman, not obviously anæmic. Mental state intelligent. Speech, special senses, optic discs and cranial nerves normal. There was slight incoordination in both hands, but no weakness or wasting. The trunk muscles were normal. All movements of the lower extremities were performed with considerable power, but with great incoordination. She could only stand when supported on both sides, and made the wildest excursions with her legs in attempting to walk. There was no wasting, and the electric excitability was normal. She complained of numbness in the legs and fingers. She could not recognise light touches below the fourth lumbar root level. There was no sphincter trouble. The wrist and elbow jerks were difficult to elicit; the left knee-jerk was obtained with double reinforcement; the right was absent. The plantar reflexes showed a brisk extensor response.

Case 11.—J. M., a married woman, aged 54 years, was admitted into the National Hospital under the care of Sir William Gowers on August 4, 1899, complaining of weakness of the legs and of tingling and numbness in all four extremities. Her health previous to this illness had always been good. She had led an irregular life as an actress.

Two years before admission she had an attack of inflammation of the eyes, and herpes appeared all around the right eye. Shortly after this the legs and the fingers became numb; she had burning

pain in the feet and a feeling as if she was walking on cotton wool. The legs slowly became stiff and she dragged them. The numbness spread slowly upwards, and she had a tight girdle feeling at the level of the umbilicus. She became very unsteady in walking.

Four months before admission she developed ptosis on the right side which passed off in a few weeks.

A month before admission she began to have difficulty in passing urine.

On admission she was a well-nourished, pale, sallow-complexioned woman. Mental state and speech normal. Smell was very defective in both nostrils, but otherwise the special senses were normal. The pupils were equal and reacted normally. The cranial nerves were normal to objective tests, but she stated that her voice in speaking and in singing had deteriorated very much during the year preceding admission. All movements of the upper extremities were powerfully performed, but with some incoordination, and there was some tabetic athetosis when the hands were held out and the eyes shut. The lower extremities were weak in all movements and there was marked ataxy. She could only stand with support on both sides, and on the attempt to walk the feet were raised high and placed down forcibly and in any position. The abdominal muscles were very weak, and she could not raise herself into the sitting position without assistance. There was marked diminution of sensibility to all forms below the ensiform process. The same diminution was found over the hands and ulnar borders of the forearms. She complained of a sensation like iron bands round the pelvis and abdomen as high as the lower costal margin. There was complete loss of sense of passive position in the lower extremities and marked loss in the hands. There was occasional incontinence of urine and constant delayed micturition. Wrist and elbow-jerks present and equal; knee-jerks increased; double foot clonus and the plantar reflexes showed the extensor response. Blood count: red blood-cells 4,300,000 per cm.; hæmoglobin 80 per cent.

Case 12.—W. P., a scene-shifter, aged 45 years, was admitted into the National Hospital under the care of Dr. Ferrier on March 21, 1898, complaining of weakness of the legs and of the right hand. Family history and previous health good. He was a scene-shifter, and worked in an atmosphere laden with colour dust from the scenery. He denied venereal disease. He was in the habit of taking a good deal of alcohol.

Seven weeks before admission he noticed a numb cold feeling in both feet, which rapidly spread up to the waist. The legs

then became weak and stiff, and he dragged them in walking. Sudden flexor spasms in the legs troubled him at night. Six weeks later he was much worse, and the right hand became very weak. Sharp stabbing pains in all four limbs troubled him greatly.

On admission he was a strongly-built man; cranial nerves and special senses normal. Great weakness of both hands R. > L. Abdominal muscles so weak that he could not sit up in bed. Absolute paralysis of the right leg and almost absolute paralysis of the left leg. No wasting. Complete loss of sense of passive position in the lower extremities. Relative anæsthesia to all forms below the umbilicus. Sphincters normal.

Reflexes.—Knee, wrist, and elbow-jerks exaggerated; double foot clonus. Plantar reflexes brisk.

Skin of the feet thin and shiny. Temperature 98° F. to 100·5° F.

On the ninth day after admission the temperature rose to 103° F., and complete paralysis of the legs, complete incontinence and profound anæsthesia appeared. Two days later the knee-jerks were lost, and marked vaso-motor paralysis and œdema set in. He remained for a week in an apparently moribund state, with muttering delirium, and developed a right-sided pleurisy and a large sacral bedsore. At the end of this time he began to improve rapidly. The temperature fell. The anæsthesia and incontinence disappeared. The bedsore healed, and the spastic symptoms returned to slowly disappear in the course of the following two months.

At the time of writing this patient is at work, and the only sign of his illness that remains is the scar of the large bedsore.

During the acute stage of his illness he was treated with iodide of potassium and strychnine. During the last year he has had five epileptic attacks, never having previously had an attack.

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