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Original Articles and Clinical Cases.

ON THE SPINAL CORD DEGENERATIONS IN ANÆMIA.

BY J. MICHELL CLARKE, M.A., M.D., F.R.C.P.

Professor of Pathology, University College, Bristol; Physician to the Bristol General Hospital.

THE exact relationship of anæmia to the degenerations in the spinal cord which are comprised under the various terms, "diffuse degeneration," "combined sclerosis," and "subacute combined sclerosis" of the cord, is still a matter about which there is considerable difference of opinion. From a clinical standpoint, anæmia may be associated with degeneration of the spinal cord in at least three ways: (1) it may distinctly precede the spinal changes for a longer or shorter time; (2) it may accompany them from the first, and proceed *pari passu* with them; or (3) it may appear late in the course of the cord affection, just as it often occurs in the later stages of any chronic illness. In the last instance, the anæmia is not as a rule so profound as in the other two. It should be added that in any case the anæmia may from time to time undergo considerable remissions, and occasionally be cured.

Although the subject is not a new one, many cases having been published, as it is still to a certain extent

sub judice, the following cases, which belong entirely to the first group, where anæmia predominates over and precedes the spinal symptoms, and which illustrate both the early stages of the degeneration in the posterior columns of the cord and also their later development, have seemed to me not unworthy of record. I wish to emphasise that this paper deals only with cases in which the cord changes were, so far as one could judge, secondary to antecedent severe anæmia. In two of them disease of the cord was not suspected during life, and in all the anæmia was of considerable duration. It is not, therefore, a question in these cases of anæmia appearing in the course of primary chronic spinal cord disease. The second case is of especial interest, as I was enabled to watch it throughout the whole course of the illness; it presents the cord affection in an early stage, and is further interesting in that the anæmia was cured, and the cord changes had apparently ceased to advance.

With regard to the form of anæmia present in these and similar instances it is now established that it is by no means only, nor even most often, pernicious anæmia. In the published cases there is a lack of exact observations on the blood, and I regret that this fault unavoidably attaches to one of two of the following reports.

The first case was the first example in which the slighter changes in the cord came under my observation, and appeared to represent the earliest stage in the cord affection of anæmia, but as the patient was only under observation during a short and fatal illness this was not certain. The correspondence of the lesion, though in a less advanced form, with that in Case 2, in which, as will be seen, there is no doubt that the degeneration is in the early stage, proves, however, that this first case shows the commencement of the cord lesion of anæmia.

Case 1.—The patient was a man, aged 26, who was admitted into the Bristol General Hospital, under Dr. Harrison, for pneumonia, and died a few days later. He was profoundly anæmic; examination of the blood gave red cells 660,000 to c.m., irregular in size and shape; hemoglobin, 16 per cent.; blood decimal about $\frac{1}{13}$.

Besides the ordinary lesions of pneumonia and general anæmia of all the organs the chief changes found *post mortem* were as follows. The non-consolidated areas of the lungs were rusty in colour; the heart small, but not fatty; the pancreas somewhat indurated; the mucous membrane of the small intestines thin, and in parts atrophic; Peyer's patches inconspicuous; the intestinal mucosa nowhere gave a pink colour with mercuric chloride solution; no iron reaction in liver, spleen, or kidney.

The brain and spinal cord were apparently healthy, except that they were very anæmic.

Microscopic examination of the organs showed no noteworthy changes, except in the spinal cord. Sections were made of all parts of the cord, and exhibited partial degeneration of the posterior columns, entirely confined to the cervical portion, and not quite extending to the lower limit of that region.

The extent of the degeneration is shown in figs. 1 and 2. It was most extensive at the level of the third and fourth cervical roots, occupying the greater portion of the central parts of the posterior columns, not affecting, however, the anterior and posterior extremities of the column of Goll, and leaving an unaffected zone of varying width on the dorsal surface of the cord, and lining the posterior commissure and posterior cornua. At the level of the fifth and sixth cervical the degeneration formed on each side a narrow truncated area, the broad end dorsally, in the lateral border of the posterior median, and mesial part of the postero-external, columns. The posterior roots were normal, and there was no evidence of the entrance of degenerated fibres from them into the cord. Sections stained by Marchi's method showed a few scattered degenerated fibres in those parts of the posterior columns which, by the Pal-Weigert stain, appeared healthy, and also a very few in the lateral columns; both sets in the cervical region only.

The gray matter and other parts of the cord were normal.

Case 2.—Profound anæmia, three and a half years' duration; paræsthesiæ and paresis of legs after two years; recovery from anæmia; death from gangrene of lung following pneumonia; post mortem, stationary changes in cord.

J. S., aged 28, gardener. First admitted to hospital March 29, 1900. Family history good, both parents alive and well, and two brothers and three sisters are in good health.

He has never had any bad illness, nor suffered from anæmia previously. He has not had syphilis.

In 1898 he had a severe scalp wound which bled profusely, and about a year later he had profuse epistaxis from a blow from a stone.

For nine months he had been gradually losing strength, and had become anæmic. On exertion he had a sensation of tightness across the epigastrium, and pains in the back and legs. The feet and ankles became swollen towards night. For a week previous to admission he had been obliged to take to bed.

He was very pale in appearance; there was no jaundice. The pulse, 92, was soft and compressible, the tongue red and clean. Many of the teeth were carious.

The lungs were normal; systolic murmurs were audible at the base and apex of the heart, and over the great vessels. The lower edge of the liver could be felt, and the tip of the spleen came just below the costal margin.

The pulsations of the abdominal aorta were very plainly felt.

The urine was acid; Sp. gr. 1021; it contained a trace of albumen, no sugar, and showed a faint band of urobilin.

He was given iron and arsenic, and kept at rest in bed, and on this treatment he steadily improved. In June he left the hospital much better, but with still a trace of albumen in the urine, and tendency to œdema of the feet.

He returned and was re-admitted on April 25, 1901. He said that he had kept fairly well during the year, but had failed very much in the last six weeks. Since the beginning of the illness the slightest exertion had given him palpitation. Additional symptoms now were: twitching of the muscles of the legs at night, defective smell and taste, vomiting in the morning, a feeling of numbness in the fingers and toes, and loss of flesh. On examination he was well nourished; he was anæmic, but had not the lemon tint of pernicious anæmia; the pulse was 84, very compressible. The organs were in the same condition as previously. The tip of the spleen could just be felt. The knee-jerks and other reflexes were normal. The colon again contained scybala. The twitching of the leg muscles sometimes prevented sleep. The amount of urine passed daily was from twenty to forty ounces, it still contained a trace of albumin, and showed a moderately well-marked but diffuse urobilin band. Specific gravity 1025. There were no hæmorrhages in the fundus oculi, which was anæmic, but otherwise normal in both eyes.

From June 7 to 17 he was not so well, the temperature was raised to 100° with slight diurnal variations, and he was very weak, not being able to wash himself or get out of bed. There

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

was also an increase of the urobilin in the urine, and the spleen became slightly larger.

From June 17 the condition of the blood gradually improved, he looked better, the spleen diminished in size, and the urobilin band practically disappeared from the urine. The skin was somewhat dark and pigmented. The muscles of the legs were weak and flabby, but not tender or distinctly wasted. Sensation was unaffected; the plantar reflexes were flexor in type, and feeble.

He now left the hospital, and was next admitted on April 3, 1902. He had kept in fair health until the beginning of the year, when he began to get very weak and to suffer from shortness of breath, palpitation, and giddiness.

He had a red flush on the cheeks, but the mucous membranes and the rest of the skin were pale. Over the chest, back, and limbs small round pigmented spots and petechiæ were fairly numerous. The pulse was regular, 76, full, and somewhat tense. The tongue was red and clean.

Physical examination showed that the condition of the organs was the same as on previous occasions, except that the liver was not felt. The spleen was slightly enlarged. The urine sometimes contained a faint trace of albumin. By Jaffé's test it appeared to contain a large quantity of indican, and with the spectroscope it showed a diffuse, but not intense or sharply-defined urobilin, band. There were also crystals of oxalates and phosphates.

During April and May his condition remained much the same; he was very weak and had no appetite. The temperature rose occasionally to 100° F. at night, falling a degree or so in the morning. He complained of numbness and tingling in the feet, especially in the right foot. Both optic discs and fundi were very pale, but there were no signs of past or present hæmorrhages. Towards the end of May he had a very bad attack of diarrhœa, after this he improved, and left the hospital at the end of June without any fresh symptoms. It should be added that at the beginning of June he was not so well, suffering much from pains in the back, abdomen, and limbs, and there was a rise of temperature to over 100° F. on several successive nights. The tingling and numbness in the legs and feet continued, but without objective loss of sensation, except that he had some difficulty in feeling a hot test-tube as hot. He was seen as an out-patient in October, and was then keeping well, though not very strong. His cheeks were red and his face generally a good colour; his chief complaint was of tingling and numbness in the feet and legs, and of some weakness. He attended as an out-patient

for about two months. He could walk a fair distance, and there was nothing remarkable about his gait. The knee-jerks were present, not very active; there was no wasting of muscles and no rigidity. Plantar reflexes weak and flexor in type. Very slight defect of sensibility to touch and prick over the lower extremities, especially on the feet.

The condition of the blood at this date showed very marked improvement.

He was not seen again until May 14, 1903, when he was brought up to the hospital in an almost collapsed condition. He was very drowsy, and at first refused to take any nourishment.

There were signs of consolidation of the lower lobe of the left lung, and the breath and sputum were horribly offensive. The pulse was 120, very feeble, and the heart's sounds almost inaudible.

The temperature was irregular, soon after admission it rose to 103°, and for some days afterwards varied between 100° and 104°. He was very dusky in colour. The abdomen was retracted, the spleen was not felt. The urine was retained, a specimen withdrawn by catheter was acid, Sp. gr. 1.030, with much albumin and many hyaline casts.

The lung symptoms steadily developed, and he died from heart failure ten days after admission.

During this last stay in hospital he was too ill to make a satisfactory examination of the nervous system possible; he came in with a sacral bed-sore (he was very ill at home for three weeks before admission), and one developed on the right heel shortly afterwards. So far as could be made out there was no decided loss of sensation to touch or prick over the lower extremities, no spastic contracture of them, and he could move them well. There was general wasting.

The following table gives the condition of the blood at intervals during the whole course of the illness:—

Chart of Blood.

	Red blood corpuscles.	Hæmoglobin.	Blood decimal.	White cells.	
March 27, 1900..	2,800,000 ..	50 per cent. ..	1 ..	10,000 ..	Slight increase in eosinophiles, in lymphocytes and mononuclear cells.
June 11, 1900 ..	3,000,000 ..	55 per cent. ..	$1\frac{1}{2}$..	7,000	
May, 1901 ..	2,240,000 ..	32 per cent. ..	$\frac{1}{2}$..	8,000 ..	Lymphocytes and mononuclears increased somewhat. Eosinophiles in normal proportion.
June 3, 1901 ..	2,000,000 ..	38 per cent. ..	$\frac{1}{2}$..		
June 20, 1901 ..	1,700,000 ..	34 per cent. ..	1		
July 15, 1901 ..	3,800,000 ..	52 per cent. ..	$1\frac{5}{8}$..	5,000	

	Red blood corpuscles.	Hæmoglobin.	Blood decimal.	White cells.	
{ May 23, 1902	.. 2,000,000	.. 30 per cent.	.. $\frac{3}{4}$	.. 4,000	Differential count showed normal proportion between kinds of white cells.
{ Oct. 16, 1902	.. 3,420,000	.. 48 per cent.	.. $\frac{1}{2}$	.. 4,000	
{ May 15, 1903	.. 4,100,000	.. 80 per cent.	.. 1	.. 20,000	Specific gravity 1,061. A polymorphonuclear leucocytosis due to pneumonic changes.
{ May 20, 1903	.. 4,100,000	.. 75 per cent.	.. —	.. 20,000	

With regard to the red cells, at the beginning of the illness, and at each subsequent relapse, there were numerous microcytes, macrocytes, and poikilocytes, with a small number of normoblasts. As the condition improved on each occasion, the red cells tended to return to the normal shape and size. No megaloblasts were seen at any stage. The *post-mortem* appearances were briefly: gangrene of lower lobe of left lung; general bronchitis; congestion of base of right lung; heart muscle pale and flabby, but not fatty; congestion of liver and spleen; kidneys intensely congested and indurated; marrow in ribs, sternum, and shaft of one tibia red in colour.

Sections of the various organs were stained with hæmatoxylin and eosin, hæmatoxylin and rubin and rosin, and osmic acid and carmine.

The following is a short summary of the microscopical changes:—

Heart.—No fatty change; increase of pigment round nuclei of muscle fibres.

Liver.—Congestion; cloudy swelling of liver cells, many of which showed vacuolation.

Spleen.—Intense injection; some excess of large pale cells in sinuses, apparently due to proliferation of cells lining them.

Kidney.—Chronic glomerular nephritis of moderate extent, affecting the convoluted tubes but slightly.

Marrow.—Excess of polymorphonuclear cells.

No iron reaction given by any organ.

The brain was normal.

Spinal cord.—By the Pal-Weigert stain the posterior columns showed a degeneration which, beginning in the upper dorsal region (see fig. 7) as a small area of degeneration in the posterior and central parts of Goll's column, extended throughout the cervical portion of the cord. In the cervical region the degeneration was almost entirely one of Goll's column, except that it extended a little on the dorsal surface of the cord to involve the posterior end of the postero-external columns (fig. 6). The

degenerated areas gave no reaction with Marchi's stain, most probably because the degeneration was of old standing, but in them were minute areas or cavities, from which the nerve fibres had disappeared. This same appearance was also noticed to a very small degree in the crossed pyramidal tracts for the extent of two or three segments in the upper dorsal region of cord only. The other parts of the cord were normal, as were also the gray matter, the anterior horn cells, and both anterior and posterior roots at all levels.

The interest of this case lies in the circumstance that the patient had recovered from his long continued anæmia, and died from an accidental lung affection. Further, the changes in the cord had not advanced very far, and apparently had ceased to extend; I think this is also the reason of the slight affection of the postero-external columns. The microscopic appearances and the clinical symptoms both point to the stationary character of the cord lesion. If this inference is correct, then the case illustrates the close connection of the cord changes with anæmia, and their dependence upon the latter. As showing the completeness of the recovery from anæmia the fact that the hæmato-poietic organs were able to cope with the strain of the fatal illness is important. Although in some respects, especially in the recurring episodes of blood destruction, the illness resembled pernicious anæmia, yet in most of its features, and notably in the fact of such complete recovery, it did not correspond with the latter condition. The state of the blood fairly corresponds to Cabot's third grade of secondary anæmia, the leucocytosis, which accompanies this form in the severer cases, not being very pronounced.

Case 3.—John C., aged 45, admitted under Dr. Harrison. The clinical notes of this case were very brief; it appears to have been entered in the hospital records as pernicious anæmia, but the notes, blood changes, and *post-mortem* appearances hardly bear out this diagnosis. The illness began nine months previously to admission with an attack of pneumonia, followed by severe anæmia, and for the last four months of this time he had had various paræsthesiæ, numbness and tingling in the hands and feet, with weakness of the limbs. There was no absolute paralysis, nor anæsthesia. He died of bronchitis, for which he came into the hospital, nine days after admission.

The blood examination gave 2,600,000 red cells; hæmoglobin 30 per cent.; blood decimal $\frac{3}{8}$. No increase of white cells. Red corpuscles varied in size; many poikilocytes; no megaloblasts or normoblasts.

FIG. 5.

FIG. 6.

FIG. 7.

Post mortem.—The fat was bright yellow; some yellow transudate in serous cavities gave no urobilin band; general bronchitis; œdema of bases of lungs; no fatty changes present in the heart or other organs; kidneys very pale but not fatty; the liver and kidney gave a faint iron reaction, but not the spleen; the latter weighed 4 ozs., and appeared healthy; marrow healthy; small intestine showed patches of catarrh, no pink colour was obtained by treatment of mucous membrane with mercuric chloride solution; brain and cord healthy in appearance, except for the general anæmia, which affected every organ.

The above findings were confirmed by microscopical examination. The cord showed a more advanced degeneration of the posterior columns than in the two preceding cases, though here also the columns of Goll were most affected. The degeneration extended regularly, though slightly patchy in character, from the medulla to the level of the first lumbar roots, but not below this, being most intense in the cervical and upper dorsal regions. In the former the most intense degeneration occurred along the boundary between the postero-median and postero-external columns (fig. 8); it affected the greater part of these columns, leaving a marginal zone of varying extent, lining the posterior commissure and cornua and the dorsal surface of cord, free from disease. In the dorsal region the degeneration is rather less extensive, the marginal area being broader; the diseased part gradually diminished in passing down the cord until it became a very small patch on each side at the first lumbar segment, below which it could not be traced (figs. 10, 11).

In sections stained by Marchi's method a few scattered degenerated fibres were seen, as in case 1, in the lateral columns, (position of pyramidal tracts) and in the postero-external columns, in areas which by the Pal-Weigert stain appeared normal.

The degenerated fibres, as in the other cases, could be traced upwards to the posterior nuclei, chiefly nucleus gracilis, in the medulla, in which they ended (see figs. 3 & 4). The gray matter, posterior roots and other parts of the cord were healthy. For vessels, see general description.

Case 4.—This patient was one who died of anæmia in the hospital; but, unfortunately, I have no notes of the case, nor of the condition of the blood.

A complete examination was made of the spinal cord, brain, and some of the peripheral nerves. The brain and the nerves were healthy. In the cord degeneration of the posterior columns was found, extending through the cervical and dorsal regions, and

through the lumbar as low as the level of the fourth lumbar roots, where it ended, not involving the sacral region. The degeneration in this case is more extensive than in the foregoing cases (see figs. 12, 13, 14), and corresponds in this respect more to case 5. It was, however, as in the milder cases, most extensive in the cervical region and upper dorsal regions, in which the whole of the posterior columns were affected, except a very narrow bounding rim of healthy tissue. In the lower dorsal and lumbar regions this margin is larger.

In the lateral columns in the upper and mid-dorsal regions of the cord there was a small area of degeneration on each side (not shown in the figures) in the position of the pyramidal tracts, but this did not extend into the other parts of the cord.

Case 5 is published in full in the *British Medical Journal*, vol. ii., p. 325, with figures of the spinal cord degenerations. In this case the condition was apparently one of pernicious anæmia. She died nine days after admission to the hospital. The duration of illness was 12 months, during the *last four months* of which she had suffered from increasing weakness of the legs, with a feeling of deadness in them; when admitted there was some loss of motor power, no affection of sensation, and the plantar and deep reflexes were active.

The blood examination on admission gave red corpuscles 870,000, many poikilocytes, macrocytes, microcytes, and some normoblasts. White corpuscles 10,000, the increase being due almost entirely to polymorphonuclear cells. Hæmoglobin 30 per cent.; blood decimal .6. Seven days later red cells 830,000; whites 30,000; hæmoglobin 25 per cent. The changes in the cord were most advanced in this case, as a reference to the figures will show; briefly they consisted in a fairly complete degeneration, though somewhat patchy in distribution, of the posterior columns extending the whole length of the cord, ending above in the nuclei of the posterior columns in the medulla, and in the lower dorsal and upper lumbar region of a small area of degeneration in the posterior part of the left lateral column.

This series of cases, I think, shows that the spinal degeneration which occurs as a secondary change in profound anæmia, and has been found and described by many observers, begins in the posterior columns and first in the cervical and upper dorsal regions of the cord. Further, that in cases which die from some cause in an early stage of the

cord disease, the affection may be unsuspected during life, and will be found limited to this region after death. In more advanced cases the posterior columns are involved almost throughout the cord, and the disease is then most extensive in the region in which it first begins, affecting here the whole of the posterior columns except a narrow rim of tissue on the dorsal surface and lining the posterior commissure and posterior horns: in the lumbar and sacral regions rarely spreading to so great an extent. These changes, though fairly regular, and possibly indicating that the fibres of the posterior columns which run the longest course are earliest degenerated, do not exactly map out special tracts, but are somewhat patchy in distribution, often varying at different levels for no obvious reason. The posterior roots do not seem to be affected. The appearances in some instances suggest some relation to the vessels, as the degeneration often seems to begin in the terminal distribution of the small artery that runs into the cord along the septum between the column of Goll and the postero-external column, that is to say, a small area about midway between the anterior and posterior ends of Goll's columns, involving slightly the postero-external columns. This relation is, however, though suggestive, not constant, and therefore no undue stress can be laid upon it.

In the cases in which the posterior column changes are most marked a patch of degeneration is also to be seen, either on one side or both, in the lateral columns in the position of the crossed pyramidal tract; this, again, is most evident in the cervico-dorsal or upper dorsal regions, but in one case appeared in the dorsi-lumbar region. It is more patchy and less regular even than the degeneration in the posterior columns, and does not extend over so great a length of the cord, in mild cases being limited to a few segments.¹

It must be added to this that though the Pal-Weigert stain may indicate degeneration limited to the above situations, sections stained by the Marchi method often show a few

¹ A typical example of the affection of the pyramidal tract in these cases is figured in my paper in *Brit. Med. Journ.*, 1897. Vol. ii., p. 326, fig. 3.

scattered degenerated fibres occurring singly in a much wider distribution in the posterior, lateral, and occasionally a very few in the anterior, columns. Fibres stained black by this method also appear, if the case is a recent one, in the areas which by the Pal-Weigert stain appear to be already degenerated (see fig. 4). As regards the finer changes they may be said briefly to be practically identical with those described by Dr. Risien Russell in cases of "subacute combined degeneration" of the cord. The vacuolation resulting from the destruction and dropping out of nerve fibres is generally well seen.

In the degenerated areas there is an increase of the neuroglial framework, the vessels often show greatly thickened walls, and sometimes hyaline degeneration of them. In some of my sections the overgrowth of neuroglia seems to have been more extensive than was met with by Drs. Putnam and Taylor.¹ The older the patch the greater seems to be the sclerosis, the denser the structure of the part, and the less marked the vacuolated spaces, as if the tissues had contracted. In such cases the increased connective tissue may appear to spread directly from the vessel walls, and sometimes a leucocytal infiltration is seen around the latter. These changes seem to me to be entirely secondary to the parenchymatous degeneration of nerve fibres, and although, as alluded to above, this degeneration shows an apparent relation to vascular distribution, I should not attach further weight to this than that it may possibly indicate the route of conveyance of a toxin.

In favour of the secondary nature of the vascular changes is the fact that they are not evident in regions where the nerve degeneration is slight (and recent), and, further, are not present in areas of the cord where the only evidence of disease lies in the presence of a few scattered degenerated fibres. I found no patches of myelitis in my cases. The gray matter and its contained cells showed no important changes, the only noticeable one being the not infrequent presence in the cells of the anterior horn and of Clarke's

¹ "Diffuse Degeneration of the Spinal Cord." *J. Nerv. and Mental Dis.*, 1901.

FIG. 8.

FIG. 9.

FIG. 10.

FIG. 11.

column of an unusual amount of pigment. This pigmentation is also mentioned by Putnam and Taylor. The meninges were in all cases unaffected, and the peripheral nerves, where examined, normal.

To turn to the clinical features of these cases, clinical symptoms may certainly be absent, and the lesions in the cord not even visible at the *post mortem*, but only found after hardening and staining it. It is probable, therefore, that such degenerations in the cord are of more frequent occurrence in patients dying from anæmia than is generally supposed. As these changes are secondary and subsidiary to the general symptoms of severe anæmia, they may easily be overlooked, but my more recent experience is that a careful investigation will generally elicit some signs of the affection of the cord.

The most prominent clinical symptoms are certainly paræsthesiæ of various kinds, such as numbness, tingling, feelings of pricking, or of pins and needles, first appearing in the feet and legs. Later the hands and forearms may be affected, when a common complaint is, that numbness or deadness of the fingers renders fine movements difficult. These paræsthesiæ vary much in intensity during the course of the illness. Objective disturbance of sensation is not marked, but in the late stages may consist of some deficient appreciation of all forms of sensation over the lower extremities. After these sensory symptoms weakness in the legs may follow, often in the sense that they feel heavy, and later still both arms and legs may be weak. A frequent and often troublesome symptom, is twitching of the muscles, especially of the legs, and at night. The deep reflexes are present, ankle clonus is not obtained, and the plantar reflex, flexor in type, is sometimes difficult to get. The knee-jerk was absent towards the end of life in case 2, but he could only be examined as he lay in bed.

There is no ataxy, and no incontinence of urine.

In relation to the clinical symptoms, I should like to briefly mention another case, though the diagnosis was not confirmed by a pathological examination.

The patient was a middle-aged man who suffered from a.

form of rhinitis, with a spongy condition of the nasal mucous membrane, which gave rise to recurrent attacks of profuse epistaxis. Under treatment in Hospital he was invariably relieved, but after an interval, generally of considerable duration, six months to two years, he relapsed, and the attacks of epistaxis returned. This epistaxis led to moderately severe anæmia of the chlorotic type, as regards the ratio of red blood cells to hæmoglobin. He was thus under observation for anæmia at intervals for over five years. The following is the chart of the blood, which indicates a progressive deterioration of it :—

	Red Cells.	Hæmoglobin.	White Cells.	
1896. Jan. ..	3,100,000..	31 per cent.		
(On leaving Hospital) } March	4,300,000..	62 per cent. ..		
1899. Feb. ..	2,400,000..	25 per cent. ..	10,250	Many poikilocytes, normoblasts, small and large red corpuscles.
			Polymorphonuclears	
			69 per cent.	
			Small lymphocytes	
			23 per cent.	Poikilocytes, normoblasts, micro- and macrocytes numerous.
			Large lymphocytes	
			4 per cent.	
			Eosinophiles 4 per cent.	
1900. July ..	2,750,000..	35 per cent. ..	9,000	As before.
			Differential count normal.	
1901. Feb. ..	2,400,000..	25 per cent. ..	12,000	
			Polymorphonuclears	
			67 per cent.	
			Small lymphocytes	
			23 per cent.	As before.
			Large lymphocytes	
			8 per cent.	
			Eosinophiles 2 per cent.	

On the last occasion the anæmia only slightly improved under treatment, but on previous ones recovery was satisfactory, as in 1896, but I have not thought it necessary to give the actual blood counts each time.

Whilst in the Hospital in July, 1900, he complained for the first time of various paræsthesiæ, especially tingling and numbness in the feet and legs; and on his subsequent admission in 1901 these symptoms had very much increased, and were the source of great discomfort. He now com-

plained of deadness or numbness of the hands and fingers, varying from time to time, and sometimes interfering with the performance of fine movements. There was no decided objective loss of sensation, although it was perhaps somewhat dull over the feet. He also complained of some weakness in the legs, so that he could not walk so far as formerly. There was no ataxy and no muscular wasting; the knee-jerks were slightly exaggerated.

I have not been able to trace this man, but I have no doubt that the case was one of the same kind, *i.e.*, of a spinal lesion developing secondarily to repeated attacks of severe anæmia.

Hæmorrhage as the cause of anæmia in such cases deserves special mention, and is probably of importance; it occurred in two of my cases as the prominent etiological factor, and has been noticed in several others.¹

The cases that I have described above form a fairly distinct group, and the changes in the cord occur in such a way as to show that they result from anæmia, and from forms of anæmia due to blood destruction. Though pernicious anæmia is one form which causes these cord lesions, it is by no means the only one. I am here taking pernicious anæmia in the ordinary sense of the term, though there is so much difference of opinion as to what actually constitutes pernicious anæmia that it is difficult to avoid confusion. In favour of the point that it is only when anæmia is due to blood destruction that these cord changes follow is the striking fact that they are not seen in chlorosis, of however long standing. A possible view of the pathology of these cases seems to me to be that of parenchymatous degeneration due to some toxin, possibly set free in the course of a pathological blood destruction, and therefore hæmolytic in origin. More extended observations on the blood, and on the precise character of the anæmia, would tend to elucidate the nature of the process.

In this particular group the cord changes often follow on so long a period of anæmia that it is difficult to suppose that

¹ *Vide* Dr. James Taylor, "A Case of Subacute Combined Sclerosis." *BRAIN*, 1904, p. 34.

the lesion is other than a secondary one, although it is possible that the cord changes might be due to the continued action of the same cause that has already produced anæmia, just as in those cases of cord degeneration and anæmia described by Dr. R. Russell and Dr. J. Taylor, they suppose that both conditions are due to the same toxin.

It may be mentioned, in passing, that in pernicious anæmia lesions in the spinal cord of quite another kind sometimes occur, namely, numerous small hæmorrhages, chiefly in the gray matter. Such cases are rare¹; the hæmorrhages are to be compared with those found in the retina in this disease, and seem to me to have nothing to do with the cases now under consideration. There was no evidence in my sections that the degeneration started from any lesions of this kind.

The question now arises: Is there sufficient reason to put cases such as are considered in this paper, in which the cord changes distinctly follow or are secondary to profound anæmia of some duration, into a separate group, and to distinguish them from those in which similar lesions of the spinal cord occur, apart from anæmia; and further, what is their relation to the cases described by Risien Russell, Batten, and Collier² under the title of "Subacute Combined Sclerosis," and by Putnam and Taylor³ and others, under the head of "Diffuse Degeneration of the Spinal Cord?" The latter writers say that "it seems to us too soon to make either clinical or pathological divisions in the general group of diffuse degenerations, and particularly to attempt the demonstrations of lesions peculiar to anæmia."

Such a division has been already attempted by Bastianelli in 1895, but his distinction, valuable as it is, is partly based on the acute or chronic course of the disease,⁴ and will hardly hold good, for, as three of my cases show, and as other writers have also pointed out, the anæmic cases which, according to his classification, fall into the

¹ For a case of this sort see *British Medical Journal*, 1897, vol. ii., p. 326.

² *BRAIN*, 1890, Spring.

³ *Journ. Nerv. and Ment. Dis.*, 1901.

⁴ See J. Taylor, "A Case of Subacute Combined Sclerosis," *BRAIN*, Spring, 1904.

FIG. 12.

FIG. 13.

FIG. 14.

acute class, are, on the contrary, often chronic in course. I believe, however, he is correct in the view that, as a general rule, in the cases secondary to anæmia the cord changes are slighter, and most often limited to the posterior columns.

Without laying undue stress on the anatomical characters of these cases, it seems to me that there are good grounds, both clinical and pathological, for separating them from similar forms of degeneration of the cord, and that these are :—(1) The presence of decided or severe anæmia as the first, or sometimes the only, sign of illness ; preceding any evidence of spinal cord lesion. (2) Clinically symptoms and signs of disease of the cord are never very pronounced, and may be absent, though, possibly, in most cases are present when looked for. (3) Anatomically the lesion is generally confined to the posterior columns, and, if it affects the lateral columns, only does so to a small extent. And (4) it differs in extent and distribution from *subacute combined sclerosis* or *diffuse degeneration of the cord* in the following ways, according as the disease in the latter case is slight or severe. (a) In the milder cases of diffuse degeneration the degenerations are more precisely limited to the neuronie systems of the cords ; thus, in two cases under my own observation the columns of Goll were diseased from the lumbar region upwards to the medulla, and the crossed pyramidal and dorsal cerebellar tracts were similarly affected ; whilst in (b) the more severe cases, the degeneration is both much more extensive than in the cases considered in this paper, and also affects the periphery of the cord most, and appears to spread thence inwards, at any rate in the lateral and anterior columns.

On the other hand, it must be admitted that the microscopical details of the degeneration process appear to be similar in both groups, and further that there are cases which occupy an intermediate position, in which the cord changes are associated with profound anæmia, and are also very extensive in distribution. It seems to me that the chief difficulty lies in the nature of these intermediate cases.

In conclusion, although the evidence is not sufficient for a final classification, I think that a step in advance

might be made by separating into two distinct groups (1) the cases of pronounced anæmia with lesions in the spinal cord of the character described in this paper, and with slight or absent clinical signs of this disease; and (2) those of sub-acute combined degeneration or diffuse degeneration of the cord in which there is no anæmia, or, if it is present, it is late and consecutive to the appearance of symptoms of cord disease, and in which also the pathological changes in the cord are more extensive and their symptoms pronounced, following more or less closely the course outlined by Drs. Russell, Batten, and Collier.

In support of this division it may be mentioned that in fifty cases of the latter kind collected by Drs. Putnam and Taylor, in only seven was there decided anæmia. Those cases which seem to combine the features of the two groups, in presenting both profound anæmia and widespread cord degeneration, I should propose to leave provisionally in a class by themselves pending further investigation.

I am much indebted to Mr. James Taylor, of Clifton, for his kindness in preparing the photographs for me.

ILLUSTRATIONS.

Photo-micrographs of Cord.

CASE 1.

Fig. 1.—Cord at level of third cervical.

Fig. 2.—Cord at level of fourth and fifth cervical.

These figures show the point of commencement of degeneration as described in the text.

CASE 2.

Figs. 5, 6, 7.—Sections of cord at level of second cervical, third and fourth cervical, second dorsal.

(In section of second dorsal there is a light streak across dorsal free edge of left lateral and posterior columns due to irregularity in thickness of section.)

CASE 3.

Sections of cord at level of :—*Fig. 8*, third cervical. *Fig. 9*, seventh cervical. *Fig. 10*, seventh dorsal. *Fig. 11*, first lumbar : This photograph is too light in the anterior and lateral columns which were perfectly healthy.

Fig. 3.—Marchi stain. To show degenerated fibres ending in nucleus gracilis.

Fig. 4.—Marchi stain. To show about the number of fibres which stain black by Marchi in a degenerated column of Goll, which is also shown stained by Pal-Weigert's method in *Fig. 8*.

CASE 4.

Fig. 12.—Cord at level of eighth cervical.

Fig. 13.—Cord at level of tenth dorsal.

Fig. 14.—Cord at level of second lumbar.

A similar degeneration extended through the cervical region to the medulla.