

of the broth with the bodies of the bacilli was performed in different animals. In the first experiment 4 c.c. of clear broth were injected into the marginal vein of a rabbit weighing 720 grammes. In  $2\frac{1}{2}$  hours the temperature had fallen  $2^{\circ}$  and there was slight diarrhoea. In  $4\frac{1}{2}$  hours there was a further fall of  $2.5^{\circ}$  and the temperature altogether remained subnormal for over five hours. On the next day it had regained its normal limit, though the animal continued to lose weight. In the second animal a similar dose of 4 c.c. of the broth containing the bodies of the bacillus were injected into the marginal vein. The temperature fell about  $1.5^{\circ}$  in two and a half hours, after which it began to rise slightly, and during the whole of the next day the temperature of the animal was febrile. In one and a half hours after the injection there was slight diarrhoea and the animal lost 70 grammes in twenty-four hours. The temperature remained at about the normal level till the fifth day. On the seventh day it had fallen and there was slight diarrhoea. On the eighth day there was a fall to  $98^{\circ}$  F. and on the ninth day when death occurred the temperature was below  $95^{\circ}$ . The total loss of weight was 210 grammes. These results were compared with the results of injecting a similar dose of the same stock of broth containing the bodies of the bacillus but which had been subjected to heat. In the first of these experiments the mixture of broth and bodies was heated at  $60^{\circ}$  C. for ten minutes. The result of the injection was the cause in a very short time of a febrile rise of temperature which lasted the whole of the day and was present in the morning of the following day, the temperature then gradually falling to the normal. In one and a quarter hours after the injection there was profuse diarrhoea and the animal lost somewhat in weight during the first two days of experiment. In another experiment a similar dose was given after being heated to the boiling point of water for ten minutes. In less than an hour after the injection profuse diarrhoea was observed and the temperature rapidly fell, the total fall being  $7^{\circ}$  F. The animal died in six hours.

It is seen from these experiments that the clear broth—that is, the broth not containing the bodies of the bacillus—produces a fall of temperature and loss of weight with some diarrhoea and that a similar dose of the broth with the bodies of the bacillus causes some lowering of temperature and a reactionary febrile rise and that the effect of heating the mixture of broth with the bodies of the bacillus is to increase the poisonous activity of the solution, so that when the mixture was heated to  $100^{\circ}$  C. it proved fatal to the animal in six hours with great lowering of temperature. The explanation of this appears to be that the action of the heat causes the discharge of the poison which is present in the bodies of the bacillus. 1. The type of action of the poison of the bacillus coli appears to be the same as that of the other two bacilli investigated, in some cases producing a great fall of temperature and in other cases a rise of temperature. 2. Heating the dead bodies of the bacillus suspended in the broth culture fluid increases the toxicity of the solution, as in the case of the two other bacilli, but in the case of the bacillus coli it requires a temperature of the boiling point of water to effect this, whereas with the other two micro-organisms such a temperature rather diminishes than increases the toxic action. Altogether, the mode of action of the poisonous products of the bacillus coli is more irregular than with the other two bacilli, not only as regards its lethal but also as regards the irregular kind of fever and after-fever produced.

*Growth of the bacillus in proteid solutions.*—As with the other bacilli, very different forms of proteid solution were used as culture medium—liquid serum, serum diluted with salt solution, serum diluted with broth, alkali albumin in broth, and Marmorek's fluid. The general result obtained in these culture media was that the bacillus coli digested the proteids present and produced an abundance of albumoses (a much greater quantity than the typhoid bacillus and Gärtner's bacillus), so that at the end of a month's incubation of such a culture a brilliant biuret reaction was obtained. The digestion of proteids by the bacillus coli is not nearly so marked as it is with the anthrax bacillus or the diphtheria bacillus. A more remarkable effect was observed in the fact that after the bacillus had been growing in a proteid solution for some time it precipitated the proteid in the form of a clot, and this occurred more particularly in the solutions of diluted serum and in Marmorek's fluid. The results were compared with a control flask which was not inoculated and which was kept in the incubator

alongside the cultures. The precipitation of the proteid in the form of a gelatinous clot was not constant although it occurred in the majority of cases. It did not appear to be due to any increased acidity of the culture medium produced by the growth of the bacillus in it, inasmuch as no such increase of acidity was present, the liquid remaining alkaline. The phenomenon appears to be a special action of the growth of the bacillus coli. In some solutions Gärtner's bacillus produced the same result. Thus five flasks were prepared containing about 100 c.c. of Marmorek's fluid, which is a mixture of one part of ascitic fluid with two parts of broth. Two flasks were inoculated with the bacillus coli, two were inoculated with Gärtner's bacillus, and one was kept as a control. In fourteen days a copious and soft clot had formed at the bottom of all the four flasks, the liquid in the control flask remaining limpid and unclotted. In none of the similar experiments with the typhoid bacillus was any clot or precipitation of the proteid observed, so that this serves as another distinction between the typhoid bacillus and the two other bacilli. The clotting of the proteid solution is of interest in connexion with the experiments of Stillmark, who found that the substance called ricin, which is obtained from the seeds of the castor-oil plant and which will be discussed later, also produces a clotting in proteid solutions, especially serum. Stillmark used it as an argument in favour of the ferment nature of the toxic body, ricin.

## THE RELATIONSHIP OF SOME FORMS OF COMBINED DEGENERATIONS OF THE SPINAL CORD TO ONE ANOTHER AND TO ANÆMIA.

By J. S. RISIEN RUSSELL, M.D. EDIN., F.R.C.P. LOND.,  
ASSISTANT PHYSICIAN TO UNIVERSITY COLLEGE HOSPITAL AND  
PATHOLOGIST TO THE NATIONAL HOSPITAL FOR THE  
PARALYSED AND EPILEPTIC, QUEEN-SQUARE.

### INTRODUCTION.

THOUGH the writings of Lichtheim<sup>1</sup> ten years ago first called general attention to the association of symptoms indicating affection of the spinal cord with those of pernicious anæmia, Leichtenstern<sup>2</sup> in 1884 described two cases of what was evidently the same condition, as tabes associated with anæmia. During the decade which has elapsed since Lichtheim's first paper many important communications on the subject have been made which have greatly advanced our knowledge not only of the clinical characteristics of this affection of the spinal cord but also in regard to its etiology and pathology. Among the earlier contributions to the subject two emanated from the National Hospital for the Paralysed and Epileptic, the first by Dr. H. M. Bowman,<sup>3</sup> whose promising career was so early terminated by death, and the second by Dr. James Taylor,<sup>4</sup> whose important communication holds a leading place in the history of the disease. I feel it in a measure my duty, therefore, to record our further experience of the affection at the hospital since the second of these papers appeared in 1895, and I am greatly indebted to Dr. Charlton Bastian, Sir William Gowers, and Dr. Ferrier for allowing me to make use of the cases which form the subject of the present communication. Although a large number of papers have appeared on the subject of the changes found in the spinal cord in cases of pronounced anæmia, and although a few writers have suggested a possible connexion between this condition and that described by Gowers under the title of ataxic paraplegia, no serious attempt has been made to discuss the relationship fully or to establish a connexion between the two affections, if we except an important paper by Rothmann<sup>5</sup> which deals with the whole subject of the primary combined tract affections of the spinal cord. Besides presenting other features of interest the following cases appear to me to afford a good opportunity of discussing

<sup>1</sup> Neurologisches Centralblatt, 1887, p. 236.

<sup>2</sup> Deutsche Medicinische Wochenschrift, 1884.

<sup>3</sup> Brain, 1894, vol. xvii., p. 198.

<sup>4</sup> Transactions of the Royal Medical and Chirurgical Society, 1896, vol. lxxviii., p. 151.

<sup>5</sup> Deutsche Zeitschrift für Nervenheilkunde, 1895, Band vii., p. 171.

the possibility of such a relationship with a reasonable prospect of adding to our knowledge on this subject. I propose therefore to relate briefly the clinical histories of the three cases, to deal much more fully with the morbid changes met with in the spinal cords post mortem, to discuss the etiology and pathology of these and similar cases, and finally to adduce reasons for considering that the affection is the same as that which has been described as ataxic paraplegia.

**CASE 1.**—A married woman, aged forty-four years, was admitted into the National Hospital for the Paralysed and Epileptic on May 11th, 1896, under the care of Dr. Bastian, complaining of loss of power and impairment of sensation in both inferior extremities and the right hand, violent intermittent pain in the stomach and chest, and loss of control over the sphincters. A brother, aged thirty-two years, is the subject of locomotor ataxy, two sisters died in youth from concussion of the brain, and a third from convulsions when teething. She had had seven children, of whom two had died within twenty-four hours of birth, and a third at the age of thirteen months from (?) rickets. She had been a teetotaler for thirty years. Thirteen years before her admission she suffered from a severe hæmorrhage after a confinement and had never regained her strength since. Her catamenia had been regular until the last two or three years when it had become very scanty. She had never had miscarriages and there was no history of syphilis. About a year before she came into hospital she began to suffer from tingling and numbness of her hands and feet, which lasted for two months and then passed off. Since Christmas, 1895, she had gradually become weaker, with shortness of breath on exertion, and about the end of January she began to be clumsy in the use of her feet. She took to her bed in the middle of February and about the end of that month, when she tried to get up, she found that she could not stand. About the beginning of March she began to suffer from cramps in her legs, which at the time of her admission were almost constant when she was awake. She suffered from constipation for a time and this was followed by diarrhoea a week ago, since which the motions had been passed involuntarily. A day or two before she came under observation she noticed some difficulty in using the right hand, which became numb and began to tingle. On admission she was found to be emaciated, her skin and mucous membranes were very pale, and there was marked œdema of her ankles, feet and tissues over the sacrum. She was only able to move her lower extremities feebly and was much troubled by twitchings and cramps, the latter extending up into the abdomen. The power of movement of the right arm was also impaired. The muscles of the limbs were much wasted, but no tenderness was elicited on pressure. There was partial loss of sensibility of the lower extremities and right arm, and she was not often able to detect touches on the right side of the trunk. Painful impressions were not felt on the legs and thighs and there was an inability to appreciate heat and cold below the level of the umbilicus on the right side and below the pelvis on the left. The knee-jerks were brisk, there was ankle clonus on both sides, and the plantar reflexes were very brisk. There was absolute incontinence of urine and fæces, with inability to feel when the evacuations were passing. There were no cerebral symptoms and the cranial nerves were intact. Hæmic murmurs were heard over the precordia and in the neck. Hæmoglobin was 28 per cent., the red cells were much diminished, and nucleated red cells were present in relatively large numbers. The pulse was 78, the respiration was 16, the morning temperature was 98.6° F. and the evening temperature was 99°. Subsequently the knee-jerks became abolished, there was œdema of the conjunctivæ, diarrhoea set in, she developed a bedsore on the sacrum, began to be delirious, and eventually died on June 11th, 1896—i.e., one month after admission, and a little more than a year from the commencement of her illness.

**Necropsy.**—I made the post-mortem examination nineteen hours after death and found the body extremely emaciated, of a yellowish-white colour, with no abnormal pigmentation, and with œdema of the lower part of the back, ankles, and feet, and a large bedsore on the sacrum. The subcutaneous fat was exceedingly small in amount and the marrow of the long bones was natural. The skull and dura mater were natural, but the cerebral convolutions were shrunken, with compensatory œdema of the pia-arachnoid. The brain was otherwise natural on macroscopic examination, as were the cerebellum, pons, and medulla. The cranial nerves were natural and there were no retinal hæmorrhages. The bones

and meninges of the spinal canal were natural, as was the appearance of the spinal cord even on section, no sclerosis or other change being obvious to the unaided eye in the fresh condition. There was a slight excess of bright yellow clear fluid in the pericardium; the left pleural cavity contained about half a pint and the right a few ounces of similar fluid. There was no tabby striation of the heart and there were no hæmorrhages anywhere. Both lungs were emphysematous, with œdema and hypostatic congestion more pronounced on the right side. The liver was slightly fatty and did not give the iron reaction. The spleen was natural; the capsules and the kidneys were adherent, but there was no obvious reduction of the cortex. There were no enlarged glands in the abdomen and no malignant disease was discovered anywhere. A small fibroma existed in the uterus.

**Microscopic examination.**—The changes met with in the central nervous system on microscopical examination were limited to the spinal cord and caudal part of the medulla oblongata. The regions affected in the medulla oblongata were those occupied by the posterior columns and the direct cerebellar tracts, but the degeneration appeared to extend far beyond the limits of the latter tract in the lateral region of the medulla. The degeneration in the posterior columns was more pronounced in the funiculus gracilis than in the funiculus cuneatus, and the cells of both were intact. Next to no recent degeneration existed in the former, while there was considerable degeneration of this kind in the funiculus cuneatus and direct cerebellar tracts. The restiform body showed no obvious change in sections prepared by the Pal-Weigert method, but in those prepared by the Marchi method an extensive amount of recent degeneration was seen in these structures passing to the cerebellum. The pyramids were intact with the exception of a few scattered fibres in a recent state of degeneration which were seen in these structures both before they decussated and among the decussating fibres. The arcuate fibres passing from the posterior column nuclei were intact and the emergent fibres of the hypoglossal nerves showed no degeneration, though there was marked pigmentation of the cells of their nuclei. The essential changes in the spinal cord consisted in a degeneration of the nerve elements, thickening of the neuroglia, and marked vascular changes. In the cervical region of the cord the degeneration was most pronounced in the postero-internal columns and the cornu commissural and posterior root zones on both sides. Some of the postero-external column was preserved, though there were only scattered fibres, the degeneration being very marked even in this part of the posterior columns. A band of healthy fibres, however, separated the grey matter from the more altered parts of the posterior columns, this being especially well marked at the cornu commissural region and posterior horn; but even in these parts there were many fibres in a recent state of degeneration. Indeed, the fibres showing early degenerative changes were more numerous in these better preserved parts of the posterior columns, and in the areas bordering on them, rather than in parts where the degenerative changes were more pronounced and obviously of longer standing. The lateral region of the spinal cord on each side was similarly affected to the posterior columns; here diffuse degenerative changes existed in both crossed pyramidal tracts and in the direct cerebellar and posterior part of the antero-lateral ascending tracts. Healthy fibres in the lateral limiting layer separated the grey matter from the profoundly altered lateral columns, but even among these fibres there were many in a recent state of degeneration, a condition which, as in the posterior columns, was most marked in the areas of junction between the obviously pronouncedly degenerated and the apparently healthy fibres of this part of the cord. There was marked degeneration of one direct pyramidal tract and slight of the other; there were also two islets of degeneration in the region of the ground bundles on the side of the more affected direct pyramidal tract, and one small islet in the position of the anterior part of the ascending antero-lateral tract a little ventral to the anterior horn. The precise degree of degeneration and its distribution varied at different levels; thus sections from another part of the cervical cord showed only slight affection of the direct pyramidal tracts, though the one was more affected than the other, as was the case in the other section described; but the islets of degeneration in the ground bundles only existed on the side of the more affected direct pyramidal tract. In the thoracic region of the cord, as in the cervical, the precise distribution of the degeneration varied but the main characteristics were

constant (see Fig. 1). Thus there was marked degeneration of the posterior columns with a zone of healthy fibres separating the degenerated areas from the grey matter. Intermingled with the healthy fibres were many in a state of recent degeneration, this being markedly the case in the cornu-commissural zone also. The degeneration in the lateral region of the cord occupied the crossed pyramidal and direct cerebellar tracts, and in the lateral limiting layer where the fibres were in the

FIG. 1.



Transverse section of the thoracic region of the spinal cord in Case 1.

main preserved there were many in a condition of recent degeneration, a state of things common to the margins of all the areas of healthy fibres bordering on the pronouncedly degenerated parts. In the anterior columns the morbid change extended beyond the confines of the ventral portion of the direct pyramidal tract on each side and to a lesser degree on one side in that part of the tract immediately ventral to the anterior commissure, while this part of the direct tract

FIG. 2.



Transverse section of the lumbar region of the spinal cord in Case 1.

on the opposite side was free from any change. In no part of the transverse area of the cord did the distribution of the degeneration vary so much as in its ventral portion; thus in other sections from the thoracic cord while the amount of change was different in the two anterior columns as before, in neither was that part of the tract immediately ventral to

the anterior commissure affected. In other sections, again, not only the ventral portions of the direct pyramidal tracts were degenerated, but also the antero-lateral margin of the cord and the ground bundles to a point opposite the outer limit of the anterior horn.

In the lumbar cord (see Fig. 2) the postero-internal column was markedly degenerated with the exception of that part of it occupied by fibres of the septo-marginal tract and the fibres of the cornu-commissural zone, both of which had escaped. A marginal area of healthy fibres also existed in the dorsal portion of the posterior columns, but was less marked in the postero-internal than in the postero-external column, considerable portions of other parts of which tract had also escaped. A wide band of healthy fibres separated the grey matter from the more altered parts of the postero-external tract. Fibres in a state of recent degeneration existed in fair numbers in all parts of the posterior columns except the most changed parts of the postero-internal tracts. Such fibres undergoing degeneration were evident in the septo-marginal tracts, but were less so in the band of healthy fibres bordering on the grey matter, while the cornu-commissural zone had escaped in great part even from such early degeneration. In the lateral region of the cord the degeneration was limited to the crossed pyramidal tracts, all parts of the transverse area of the cord ventral to this being free from degeneration, with the exception of the tip of the anterior column on one side where it abutted on the anterior fissure; here there was slight degeneration. A considerable number of recently degenerated fibres existed in the crossed pyramidal tracts, and some in the ventral part of the direct tract, which showed no obvious change when treated by the Pal-Weigert method. There was also a considerable amount of recent degeneration present in the apparently healthy parts of both direct tracts, but more marked on one side than on the other. Similar variations were met with as in other regions of the cord; thus the degree of affection of the cornu-commissural zone was more marked in some sections than in others; the amount of the septo-marginal tract which escaped also varied as did the degree of affection of the ventral tip of the anterior column. The lower lumbar region of the cord was the seat of pronounced degeneration of the posterior columns, though this was not complete in any part of them, healthy fibres being scattered among the degenerated. There were, however, certain parts of these columns which had largely escaped degeneration, an occasional degenerate fibre being alone found in them; these areas comprised the cornu-commissural zone, the septo-marginal tract, the external part of the posterior columns bordering on the grey matter of the posterior horn, the posterior root zone, and a very narrow band of fibres extending along the periphery of the dorsal part of the posterior columns except that part of them close to the posterior median septum. Only a few scattered degenerated fibres were seen in the lateral columns and in the antero-lateral region of the cord. The lower sacral region was free from degeneration with the exception of a few scattered fibres in the posterior columns, while the upper part of this region was similarly spared with the exception of a few small areas of degeneration in the posterior columns. On both sides there was a limited area of such degeneration abutting on the inner border of the posterior root zone and a more pronounced band occupying the dorsal third of the posterior column on one side, situated a little internal to a line which, if extended to this region of the columns, would represent the inner border of the gelatinous substance of Rolando and a similar, though less extensive, band than the last, situated in the ventral half of the dorsal fifth of the posterior columns, close to the posterior median septum, from which it was separated by an area of normal fibres no broader than the degenerated band itself. A degenerate fibre here and there in other regions of the transverse area of the sacral cord was all that was to be seen. The neuroglia was much thickened in the affected areas of white matter. The vessels had thickened walls and were engorged, these conditions characterising both those in the affected areas of white matter and in the grey. In the sacral region of the cord, where the degeneration of the white matter was so limited in distribution, the thickening of the neuroglia was equally limited and vascular changes were by no means conspicuous. Though some of the vessel walls were thickened there was little engorgement and no obvious increase in the number of vessels in the grey or white matter. The nerve cells of the anterior horns were scarce in most parts of the cord



and of those present many were obviously atrophied and others though of good size stained badly. These cells were better preserved in the sacral region of the cord than elsewhere, but even here some groups were wanting and others showed evidences of atrophy. In sections prepared by the Marchi method the anterior horn cells throughout the cord were characterised by marked pigmentation and granularity, a condition of things also seen in the cells of Clarke's columns.

*Remarks.*—We have in this case a typical example of the spinal cord changes which have been described as occurring in association with pernicious anæmia. Clinically the case conformed to this type and the results of the microscopical examination are strictly in accord with those which are regarded as characteristic of this affection. The case, however, serves to emphasise what has already been shown by certain previous observations—viz., that such changes in the spinal cord and their resulting symptoms may occur in all forms of profound anæmia even though they do not conform absolutely, either clinically or as regards the changes found post mortem, to the rules laid down for the diagnosis of the so-called pernicious variety of anæmia. Thus among other signs wanting in this case were the absence of retinal or other hæmorrhages (apart from those in the spinal cord), the normal condition of the marrow of the long bones, and the failure of the liver to give the iron reaction. The special features which call for comment as regards the changes found in the spinal cord on microscopical examination, in that they have not been constantly met with in all cases of the kind previously recorded, are the changes in the grey matter, there being both altered condition of some of the cells and the existence of small hæmorrhages. It is also worthy of note that no hæmorrhages or the remains of these were met with in the white matter, where the degenerative changes of the nerve elements are so pronounced, and that small areas of degeneration in otherwise healthy parts occur quite independently of the presence of any vessel with altered walls in their neighbourhood. One other point alone calls for comment in this case and that is that in the lower lumbar and sacral regions of the cord the posterior columns are almost exclusively affected. This is not a little curious when we remember how profoundly affected the lateral and antero-lateral tracts were in other regions of the cord, for with such affection of these tracts we are at least justified in expecting to find evidences of descending degeneration in the crossed pyramidal tracts and the efferent antero-lateral tracts, including the direct pyramidal, instead of which there is no evidence of such degeneration, an occasional degenerated fibre being alone found in these tracts in the lower lumbar and the sacral regions of the cord.

CASE 2.—A man, aged fifty-three years, was admitted to the National Hospital for the Paralysed and Epileptic under the care of Dr. Ferrier, on Oct. 16th, 1896, complaining of inability to walk, difficulty in commencing the act of micturition, and girdle sensation. His father died from "consumption of the bowels" and his mother had been paraplegic for five years, the condition having been gradual in onset. A sister had died from phthisis, another from dropsy, and a third with wasting. The patient had been much exposed to wet and cold. Twenty years before his admission to the hospital he suffered from gleet, but never had a sore. He had always been temperate. At the age of twenty-six years he had pains in his calves for three or four days and then woke up one morning quite blind and unable to sit up or move his head, arms, or legs. He could swallow and had no difficulty in passing urine. His limbs were flaccid. By the end of the same day he could move his head and by the end of the second day could see with his left eye and was practically well, except that he could not see with the right eye and was unable to stand for about seven weeks. After this he got quite well, though blind in the right eye, and remained so until a year and nine months before he came under observation, when he began to notice that he was unable to bear the heat of a fire on his legs. The bedclothes and the lining of his trousers felt damp, whereas in reality they were quite dry. These subjective feelings at first got worse and then disappeared about seven months ago; but at this time he had a sensation as if walking on wool, his legs became uncertain in their movements, and he had to use sticks in walking. His walking had become gradually worse and he had been quite unable to do so at all for three months. A month before this he developed a girdle sensation which had persisted

and at the same time micturition became precipitate. On admission he was found to be the subject of advanced spastic paraplegia. Both legs were extremely stiff, but he could lift them off the bed, could flex and extend at the hip fairly, and he could draw up the legs and move the toes and feet at the ankles well. By far the weakest movement was flexion at the knees. The left leg was possibly slightly the stronger. A girdle sensation was present and there was some pain complained of in the lower dorsal and lumbar regions of the back. There was slight blunting of sensibility for tactile and painful impressions up to the level of the umbilicus. The knee-jerks were increased but there was no ankle clonus. The arms were normal. There was divergent strabismus of the right eye due to blindness from simple optic atrophy, there being only just perception of light with this eye and the pupil only just reacting to light. The ocular movements were normal, there was no nystagmus, and the other cranial nerves were intact. About five weeks later he was much weaker and apparently very anæmic; he suffered a great deal from pain about the lower ribs and in the abdomen, and there was almost complete retention of urine. The great rigidity of the inferior extremities had now altogether disappeared, the limbs became flaccid at all the joints, and there was slight wasting of the calves and thighs on both sides, with great diminution of Faradaic irritability of the muscles of the buttocks, thighs, and legs. To galvanism K.C.C. > A.C.C. The knee-jerks were completely absent, there was no ankle clonus, the plantar and cremasteric reflexes could not be obtained, and the reflex of the sphincter ani was also absent. The epigastric and abdominal reflexes were, however, present. There was complete loss of sensibility for touch and pain up to the knees and marked impairment to two inches above the groins. The skin over the buttocks and sacrum became acutely inflamed, with superficial points of ulceration. The heart was dilated and a slight systolic murmur was heard at its apex. The temperature was 100.4° F. Two days after this he was slightly weaker and the temperature was subnormal, but the bed-sore was slightly better. Four days later he died.

*Necropsy.*—I made the post-mortem examination nine hours after death and found the bones of the skull natural but the dura mater unduly adherent to the inner surface of the skull-cap. The pia-arachnoid presented old patches of thickening, but the convolutions were natural, as were the rest of the brain, the cerebellum, pons, and medulla oblongata, on macroscopic examination. All the cranial nerves appeared natural with the exception of the right optic nerve, which was much atrophied and grey in colour. The spinal canal was natural, as were the meninges and cord, both on external examination and on section. No sclerosis or other defect was evident to the unaided eye in the fresh state. The heart was dilated, the lower lobes of the lungs were in a condition of hypostatic congestion, with old caseous and pleuritic thickening with adhesions at the apex of the right lung. The abdominal viscera were natural, with the exception of very slight adhesion of the capsules of the kidneys, without any obvious reduction in the width of the cortex, and there was hæmorrhagic cystitis.

*Microscopical examination.*—Subsequent microscopical examination of the central nervous system revealed the following changes. In the medulla oblongata the degenerations were limited to the caudal end. There was pronounced degeneration of the fibres of the funiculus gracilis and cuneatus, the cells of which were intact, as were the emergent arciform fibres. The lateral region of the medulla occupied by the direct cerebellar tract was greatly altered, and extending dorsally and ventrally along the margin of the medulla from the most changed part were a few scattered degenerate fibres with a little patch of them opposite the commencement of the anterior horn on one side and a larger patch just external to the pyramid on the opposite side. There was some degeneration in both pyramids at the level of the decussation; in one it was the part bordering on the anterior median fissure which was chiefly affected, while in the other there were two patches of degeneration separated from each other and from the anterior median fissure by healthy fibres. Degenerated fibres could also be seen among those decussating. Some small foci of degeneration and scattered altered fibres were present in the pyramids for a short distance above the decussation; otherwise the medulla was free from obvious change after the upper limits of the funiculus gracilis and cuneatus were reached and after the direct cerebellar tract had passed into the restiform body. In the

cervical region of the spinal cord there was marked degeneration of the postero-internal columns, having all the appearance of being complete, as seen with a low power lens, and separated from the degenerated part of the postero-external column by a narrow band of more or less normal fibres. The postero-external column was much less degenerated and only about the inner half of the tract was affected, the outer part bordering on the grey matter of the posterior horn being preserved. There was, however, a limited area of this outer zone of the postero-external column which was profoundly degenerated near the periphery of the cord in the region of the posterior root zone. The cornu-commissural zone was fairly preserved, but in this as well as in the best preserved parts of the postero-external column many degenerate fibres and spaces from which such swollen degenerate fibres had evidently fallen out were to be seen. The direct cerebellar tract on one side was considerably degenerated about its middle, while the ventral portion was less altered. Dorsal to the more altered part was a less degenerate area, while immediately external to the posterior root was an area of more intense degeneration at the periphery of the cord. On the other side of the cord the ventral part of the direct cerebellar tract was most altered, the middle less so, while the dorsal part of it was as much affected as was the area immediately external to the posterior root. There was degeneration of a patchy and scattered character in the crossed pyramidal tracts; this was less evident in the deeper parts of these tracts and the lateral limiting layer was in the main well preserved. Both direct pyramidal tracts were markedly degenerated in their ventral two-thirds, while only isolated degenerate fibres were dotted about in the portion of the tract immediately ventral to the anterior commissure. The degeneration overstepped the limits of these tracts and extended into the ground bundles and antero-lateral descending tract region at the periphery of the cord; but in both these regions the degeneration outside the area of the direct pyramidal tracts was in the shape of scattered fibres rather than of any compact cluster of these. A few minute islets of scattered degenerate fibres were also seen at the periphery of the cord to about midway between this and the grey matter of the anterior horn.

In the thoracic cord (see Fig. 3) the postero-external

FIG. 3.

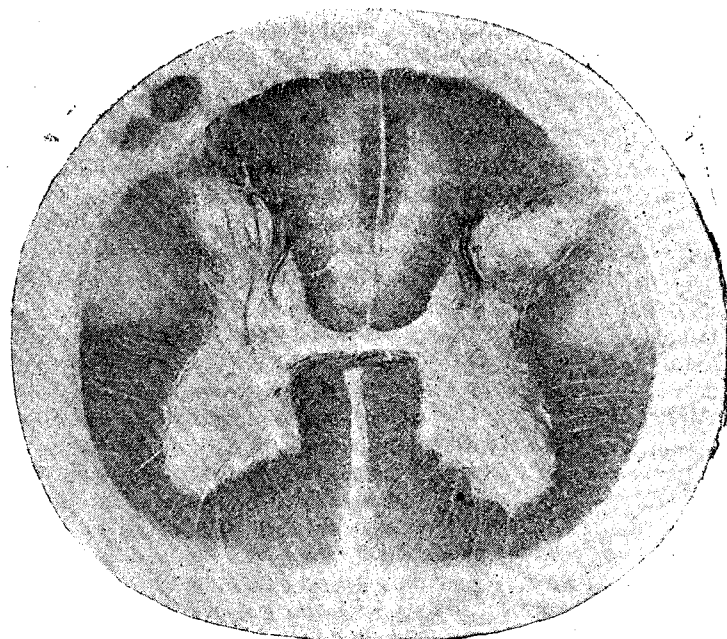


Transverse section of the thoracic region of the spinal cord in Case 2.

and internal columns were more equally affected, and the degeneration was less pronounced than it was in the latter tract in the cervical region, being, indeed, more comparable to that seen in the former tract in that region of the cord. Very little of the cornu-commissural zone was preserved at the ventral extremity of the postero-internal column, but at the dorsal end of the tract at the periphery of the cord was a small zone of more or less healthy fibres. A similar condition existed to a lesser degree in the contiguous part of the postero-external column, the whole of the outer half of which tract was also preserved, with the exception of the posterior root zone which was

markedly degenerated. The change in the direct cerebellar tracts was considerable, and the crossed pyramidal tracts were more profoundly altered than in the cervical region of the cord, the degeneration being rather more extensive in area on one side than on the other. The lateral limiting layer was fairly preserved. There was marked degeneration of the ventral three-fourths of the direct pyramidal tracts and degenerate fibres in the other fourth, more especially on one side. An extensive overflow of degeneration into the antero-lateral descending tract region and ground bundles was seen, the area of the ventral portion of the cord thus occupied by degeneration being very much more extensive than in the cervical cord. A few scattered degenerated fibres were seen in the white matter between this ventral area of degeneration and that of the crossed pyramidal and direct cerebellar tracts. In the lumbar region of the cord (see Fig. 4)

FIG. 4.



Transverse section of the lumbar region of the spinal cord in Case 2.

there was marked degeneration of only a part of the posterior columns. The septo-marginal descending tract was well preserved, as were the cornu-commissural zone and the outer part of the postero-external column bordering on the posterior horn and root. The whole of the periphery of the cord between the posterior root and posterior median septum, including the posterior root zone, was fairly preserved. There was marked degeneration of the crossed pyramidal tracts and the change was limited to their confines. A patchy and scattered degeneration existed in the direct pyramidal tracts and antero-lateral region at the periphery of the cord, with some scattered degenerated fibres in the ground bundles. Here and there a degenerate fibre was seen between the ventral area of degeneration and the lateral columns. In the sacral cord the septo-marginal descending tracts in the posterior columns were well preserved, while a limited narrow strip of marked degeneration existed on each side just external to them, somewhat patchy and of different extent and distribution on the two sides. A little scattered degeneration was also seen external to this more altered area. The cornu-commissural zone was intact on both sides. The crossed pyramidal tracts were degenerated but there was no evidence of degeneration in the direct pyramidal tracts or antero-lateral region of the cord. In addition to the degeneration of the various tracts of nerve fibres there were pronounced changes in the grey matter, consisting in destructive changes in the cells, diminution in the number of the fine nerve fibres which coursed through it, and increased vascularity. The degree of destruction of the nerve cells of the anterior horns varied at different levels. Some sections of the cervical cord showed that a large number of the cells had disappeared, others were markedly atrophied, while here and there small groups of apparently unaffected cells were seen. In other sections the groups of intact cells were much larger, while in some while there was a marked diminution in the number of cells of one anterior horn in the other the changes were much less pronounced. The same may be said of the thoracic region of the cord, where there was a great sparsity of cells and a great many of those present were atrophied. Similar

changes were seen in the lumbar cord but fewer cells were atrophied, while many of those present appeared to be swollen. The cells were plentiful in the sacral cord but many appeared to be somewhat swollen, while the pericellular space in some cases was so large as to suggest a certain amount of shrinking of the swollen cells. There was an increase in the number of vessels in the affected areas of white matter, especially the posterior columns; the majority of the vessels had greatly thickened walls with multiplication of nuclei, some appeared to be hyaline, and all were intensely engorged. Pronounced as were these vascular changes throughout the cord in no other part was there so great an increase in the number of capillaries met with as in the lumbar region, where there was a perfect meshwork of small thin-walled engorged vessels in addition to larger vessels with thickened walls. The neuroglia was thickened in the affected area but there was no infiltration of the tissues with round cells, nor were there any perivascular collections of these, and though the vessels were so engorged no hæmorrhages could be detected.

*Remarks.*—It would serve no useful purpose if we were to speculate as to the nature of the past illness which resulted in the patient's losing the sight of his right eye. A sufficiently long interval elapsed to justify our assuming that there was no direct connexion between that illness and the condition which resulted in his death. The earlier part of the clinical history of the last illness conformed to what we regard as more or less characteristic of ataxic paraplegia, while the subsequent development of anæmia and muscular flaccidity and abolition of the reflexes, together with the rapidly fatal issue, were in keeping with one class of cases of combined cord changes associated with anæmia in which the anæmia only becomes obvious late in the course of the illness. The changes met with in the spinal cord post mortem are such as are seen in ataxic paraplegia and in the cases of spinal cord changes associated with anæmia. It is obvious, therefore, that this case goes far to prove that there is a very close relationship between these two forms of affection of the spinal cord, if, indeed, they be not eventually proved to be identical. It is interesting to note that in contrast to the first case the changes in the sacral region of the cord are most pronounced in the crossed pyramidal tracts and are only slight in the posterior columns, the reverse of that which obtained in the other case.

CASE 3.—A married woman, aged fifty years, was admitted into the National Hospital for the Paralysed and Epileptic on Dec. 19th, 1894, under the care of Sir William Gowers, complaining of weakness in her arms and legs, numbness and tingling in her hands and feet, girdle sensation, and loss of control over the sphincters. Her father died from apoplexy at the age of sixty-three years; one brother had died from variola and another from rheumatism but otherwise the family history was good. She had been married thirty years and had had two sons and one daughter who had survived, while eight children had died in infancy, and she had had one miscarriage. The patient had not suffered from any previous illness, had always been temperate, and had lived in comfortable circumstances; but for six months she had nursed her husband, who died from phthisis five months before she came into hospital. She became ill after her husband's death, feeling great weakness in the lower limbs which caused her to fall about, and in a fortnight's time she was obliged to take to her bed and had not been up for more than a few hours since. At the commencement of her illness she noticed numbness and tingling in her hands and feet, and she had since suffered from girdle pains at the level of the umbilicus but had never had any cramps or lightning pains in the limbs. For three months she had been unconscious of passing her evacuations and both urine and fæces had been passed in her bed; the former did not dribble but passed in a stream; she was not, however, conscious of any desire to pass urine. There had never been any diplopia. On admission there was no loss of power noted in the lower extremities as she lay in bed, and the upper extremities, though relatively not so strong as the lower, presented no definite loss of power. She was unable to raise herself from the horizontal to the sitting posture and was unable to stand alone, and when supported she lifted her feet rather high and stamped them down in walking. There were no contractures, the knee-jerks were equal, there was no ankle clonus, the elbow-jerks were absent, and it was doubtful if any jerks could be elicited at the wrists. The inferior extremities felt cold and stiff, there were tingling and numbness in the fingers and feet, pain

in the lumbar region of the spine and in the hypogastrium, with a girdle sensation just above the pubes. There was a loss of tactile sensibility over the right inferior extremity up to the level of the brim of the pelvis in front and to the fold of the buttock behind, with inability to recognise pin-pricks below the knee in front and up to the middle of the thigh behind. In the left leg there was slight blunting of sensibility for tactile impressions up to the middle of the thigh in front and to just below the fold of the buttock behind and there was blunting to pin-pricks over the same area. The plantar reflexes were equal and brisk, while the abdominal reflexes were not obtained. The fundi were normal, the pupils responded normally, there was no nystagmus or ocular paralysis, and the other cranial nerves were also intact. Ten days later the patient complained of bearing-down pain in the abdomen and back; there was retention of urine and incontinence of fæces, and from this time her urine had always to be drawn off by means of a catheter. She was unconscious of the passage of urine and occasionally of the passage of fæces also. A fortnight after this the knee-jerks became extremely feeble and in about two months from the time of her admission they were abolished. The lower limbs were drawn up, flexed at all the joints, and rigid, resisting attempts at passive movement. There was absolute loss of power in the lower extremities, with loss of muscular sense, inability to sit up in bed, and great weakness, unsteadiness, incoördination and loss of muscular sense in the upper extremities, while the intercostals and diaphragm acted fairly well. There was loss of sensibility for tactile and painful impressions up to the brim of the pelvis in front and up to the tenth dorsal spine behind, except the back of the left thigh where there was only blunting and over the lower third of this thigh in front where there was loss of sensibility for painful impressions but where tactile sensibility was only blunted. On the trunk tactile sensibility was blunted up to the level of the fourth rib on the right side and the third rib on the left side. The patient's replies were not to be relied on when the arms were tested, except that she always felt a pin-prick. As regards tactile impressions she sometimes said she could feel while at other times she said she could not. Her urine had always to be drawn off, there was complete loss of control over the sphincter ani, and she was unconscious of the act of defecation. Her general condition was very bad: there was marked general wasting, not limited to any parts specially, with marked tendency to trophic disturbance in the shape of a sacral bed sore and a small black patch on the right heel. So, too, two drops of hot water dropped on the chest gave rise to sores, which at first sloughed, but afterwards healed. The sacral bed sore also improved under treatment. About this time she developed general bronchitis. A week or two later the patient began to wander and to suffer from delusions at night; but during the day, though dull and slow, she remained fairly clear mentally. Her fundi were examined the day before she died and were found to be normal. The fatal termination of the case resulted on March 10th, 1895—i.e., about eight months after the commencement of her illness.

*Necropsy.*—At the post-mortem examination, performed by Dr. W. S. Colman fourteen hours after death, the body was found to be very thin, with a bed sore over the sacrum. The brain was found to be much wasted, with a large amount of compensatory fluid beneath the arachnoid, but the organ was otherwise natural to the unaided eye, as were the cerebellum and pons, but the medulla low down showed some degeneration in the posterior columns. The cranial bones and meninges were natural, as were those of the spinal cavity. The external appearance of the spinal cord was natural, but on section some discolouration was noticed in the posterior columns down to the lumbar enlargement, while none could be seen in the sacral region of the fresh cord. There was nothing else noteworthy beyond the fact that the liver was enlarged and tough, its capsule thick and opaque, and its lobules very distinct (no iodine reaction). The spleen was enlarged and soft and the kidneys were very tough, with a little thinning of the cortex.

*Microscopical examination.*—I subsequently made the following microscopical examination. The medulla oblongata only showed changes towards its caudal end, and these consisted in marked degeneration of the fibres of the funiculus gracilis and cuneatus on each side and similar degeneration of both direct pyramidal tracts, all of which changes were obvious in sections stained by Pal-Weigert method. Specimens prepared by Marchi's method showed



more recently degenerated fibres in the funiculus cuneatus than in the funiculus gracilis, and in both nearly all such fibres were seen in the deeper parts bordering on the grey matter, though some also were seen at the dorsal periphery of the funiculus cuneatus. Fibres in a recent state of degeneration were also seen throughout both direct cerebellar tracts, but most in the deeper parts of both tracts bordering on the formatio reticularis. This method further revealed recently degenerated fibres in large numbers in the restiform body on each side and a few scattered degenerated fibres in the pyramids, which fibres could be seen crossing at the decussation of these structures. Examination of the spinal cord showed that in the cervical region, as seen with a lens of low magnification, there appeared to be a complete absence of normal fibres in the postero-internal column, even the cornu-commissural zone sharing this fate. The postero-external column was also degenerated, though less markedly than the postero-internal, and a band of healthy fibres separated the grey matter from the altered part of the postero-external column. This zone of healthy fibres was most marked in the ventral part of the tract and existed only as a very thin band in the dorsal part of it. Fibres in a recent state of degeneration were conspicuous by their absence, very few being seen except in the zone between the grey matter and the ventral part of the more pronouncedly degenerated area of the postero-external column. There was marked degeneration in the lateral region of the cord, occupying chiefly the confines of the crossed pyramidal, direct cerebellar, and posterior part of the antero-lateral ascending tracts. In parts there was almost as complete a disappearance of nerve fibres as in the postero-internal columns, but on the whole the change was less pronounced than in these tracts. The lateral limiting layer was preserved. Recently degenerated fibres were scattered throughout the lateral columns, in some parts of which they were numerous while in others they were scarce. There were a considerable number in the ventral part of one crossed pyramidal tract and they were also numerous in the lateral limiting layer. The ventral part of the direct cerebellar tract and the dorsal part of the ascending antero-lateral tract were similarly occupied by a considerable number of such fibres in a recent state of degeneration. There was a moderate amount of degeneration in the direct pyramidal tracts and, as seen in the specimens prepared by the Pal-Weigert method, the change was most marked in the ventral part of these tracts, though slight throughout along the margin of the anterior median fissure. Ventrally the area of degeneration tended to encroach on the antero-lateral

FIG. 5.

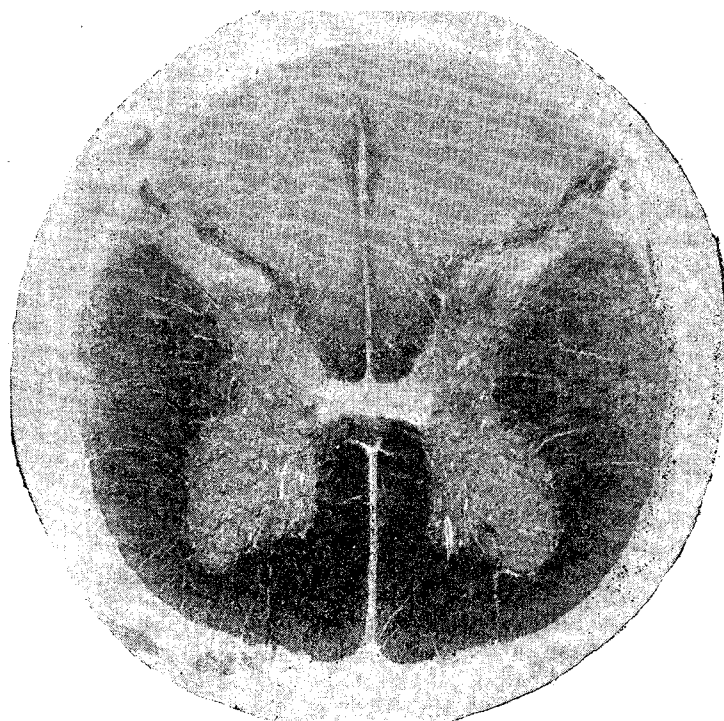


Transverse section of the thoracic region of the spinal cord in Case 3.

descending tract region of the cord and two islets of degeneration were present in the course of this tract on one side, one opposite the anterior angle of the anterior horn and the other opposite a point midway between this and the lateral horn. A few fibres in a recent state of degeneration were scattered through the direct pyramidal tracts.

Sections from the thoracic cord (see Fig. 5) showed that the postero-internal columns were as markedly changed as in the cervical region, and that the degeneration of the postero-external columns was more pronounced than in the upper regions of the cord, being in great part as advanced as that seen in the postero-internal columns. The cornu-commissural zone was, however, more preserved than in the cervical cord and the band of healthy fibres separating the grey matter from the degenerated part of the postero-external column was more extensive. Fibres in a recent state of degeneration were present in both these zones of apparently healthy fibres, the number of these varying at different levels. The amount of degeneration of the lateral tracts of the cord was more extensive in area, as was that of the ventral portion of it, so that a smaller amount of apparently normal white matter separated the lateral degenerated area from that in the ventral portion of the cord. Less of the lateral limiting layer was preserved on one side than on the other, [and recently-degenerated fibres were seen in these better-preserved parts. Such fibres in a recent state of degeneration were also present in the crossed pyramidal tracts and chiefly in one direct cerebellar tract, though they were present in the other also. The precise distribution of these fibres varied at different levels, so that in some sections they were much more scattered and irregularly distributed in the lateral columns than in others. The anterior columns were only affected in their ventral half as seen in specimens prepared by the Pal-Weigert method, with marked extension of the degeneration into the adjacent ground bundles and antero-lateral marginal tract to opposite the external limit of the anterior horn, but even in the healthy part there was evidently a sparseness of normal fibres in the region between the anterior and lateral columns of the cord, especially a short distance from the periphery. Exceedingly few recently-degenerated fibres were, however, seen in the changed and unchanged parts of the anterior columns. In the lumbar region of the cord]

FIG. 6.



Transverse section of the lumbar region of the spinal cord in Case 3.

(see Fig. 6) the most pronounced degeneration of the posterior columns was in the middle third of the postero-internal tract, with the exception of that part of it occupied by the fibres of the septo-marginal tract which was preserved. The cornu-commissural zone and a band of fibres between the grey matter and the degenerated part of the postero-external columns were also preserved. Otherwise a scattered degeneration was present in the posterior columns. Recently-degenerated fibres were also scattered through these tracts, but were most marked in the better preserved parts, such as the cornu-commissural zone, the septo-marginal tract, and the band of fibres bordering on the grey matter. Next to no recently-degenerated fibres were seen in the most altered parts of

the posterior columns. The caudal end of the lumbar region was characterised by marked degeneration of the posterior two-thirds of the postero-internal column, the anterior third of the posterior columns, including the cornu-commissural zone, being intact. The septo-marginal tract was only fairly preserved, there being scattered degenerated fibres in it. The postero-external column was less degenerated than the postero-internal, and the zone of fibres bordering on the grey matter was preserved, as was also a very narrow peripheral zone at the dorsal end of both posterior columns. There was marked degeneration of Lissauer's tract, while the crossed pyramidal tracts were only slightly degenerated and the other tracts of the cord were practically intact. In the sacral region a little scattered patchy degeneration was to be seen in the posterior columns, especially in the dorsal part of the postero-external column, where there was a fairly well-defined patch of degeneration on one side. At the caudal end of the sacral cord, however, there was practically no degeneration except of Lissauer's tract, which was considerably degenerated, though to a less extent than in parts less caudally situated.

As in the two other cases so here there were changes in the grey matter, vessels, and interstitial tissue of a pronounced character. The anterior horn cells had largely disappeared in the cervical region, a few atrophied ones remaining in places, while other small groups of cells were fairly preserved, though even these stained badly as a rule. Similar changes were seen in the thoracic cord, where the cells were even more scarce. Few cells were preserved in the cephalic end of the lumbar cord, but towards the caudal end of this region of the cord it was chiefly the ventral part of the anterior horn that was poor in cells, and those remaining here were markedly atrophied. In contrast to other parts of the cord the anterior horns in the sacral region were rich in cells. In some sections, however, there was a sparseness of them, while others were obviously atrophied. Throughout the cord sections stained by Marchi's method showed the cells to be markedly granular and the majority stained black. Many of the fine fibres in the grey matter stained badly, while others were obviously degenerated. The vascular changes consisted in thickening of the vessel walls, some to such an extent as to almost occlude their lumina, marked engorgement of them, and a large increase in the number of capillaries in some parts. The grey matter of the sacral cord was crowded with engorged capillaries, while vessels with thickened walls were only seen here and there. In the lumbar cord the capillaries were fewer than in the sacral, while vessels with thickened walls were more plentiful. The latter form one of the chief features of the vascular changes in the thoracic and cervical regions of the cord, and such vessels were seen in the affected tracts of white matter as well as in the grey. Indeed, another feature of the thoracic, and more especially of the cervical, cord was the great increase in the number of vessels in the affected parts of the posterior columns. No hæmorrhages were to be seen either in the affected grey or white matter. There was much thickening of the neuroglia in the affected areas of the cord, and this change was most pronounced where the degeneration of the nerve elements was most intense—viz., the posterior columns, especially the postero-internal tracts.

*Remarks.*—This case is an admirable instance of the occurrence of the clinical features and morbid changes which characterise cases of spinal cord changes in anæmia in a patient in whom if anæmia was present it was not sufficient to attract attention and in whom neither during life nor after death were the signs by which we recognise pernicious anæmia detected. It is noteworthy, however, that although there was no obvious anæmia a condition of profound marasmus existed. Like the other two cases subjective sensory disturbances and inability to coördinate the movements of the inferior extremities were among the earliest manifestations of the disease. Spasticity was never a prominent feature during the time that the patient was under observation, sensory defects, muscular enfeeblement, and ataxy being the leading symptoms pointing to affection of the nervous system. But, as in the other cases, the final stages of the disease were characterised by abolition of the reflexes, flaccidity, and loss of control over the sphincters. As regards the degenerations in the spinal cord, it is noteworthy that their distribution in the lower lumbar and sacral regions of the cord was rather intermediate in type as compared with what was

met with in the other two cases, but that it conformed more to the condition met with in the first case than to that met with in the second in that the changes were more pronounced in the posterior columns than in the lateral tracts in these regions of the cord.

#### GENERAL REMARKS.

A comparison of the clinical histories of the foregoing three cases is alone sufficient to convince one that they belong to the same category of affections of the spinal cord, and any doubt which may have existed on this point could not reasonably be entertained after comparing the morbid changes met with and their distribution in the three cords. It is equally evident that the clinical manifestations and the nature and distribution of the morbid processes are such as have been described as typical of a group of cases in which symptoms indicating the existence of disease of the spinal cord are associated with profound anæmia. But the character of the nervous symptoms, their mode of onset, progress, and termination, harmonise fairly well with what is met with in ataxic paraplegia, the rate at which one event succeeds another and eventually terminates in death within one or two years from the commencement of the illness being alone contrary to what we have been in the habit of regarding as characteristic of this affection. This rapid progress to a fatal termination corresponds rather to what we would expect in some more or less chronic slowly progressive form of myelitis. The morbid changes met with on post-mortem examination, however, exclude this possibility, while they are quite in keeping with what we are in the habit of finding in cases which clinically present the features of ataxic paraplegia. While there is this general resemblance of the three cases to each other, and they collectively present features characteristic of a certain group of diseases which form a clinical and pathological entity, they individually serve to throw light on certain side issues with regard to the etiology and pathology of the disease of which they are examples. The first case is one in which the association of profound anæmia with the spinal cord changes is unquestionable, but in that the anæmia did not conform either clinically or post mortem to the rules which have been laid down for the diagnosis of the pernicious variety the case serves to emphasise the fact that such spinal cord changes may occur in profound anæmias not having all the characteristics of so-called pernicious anæmia. The second case furnishes an example of the fact that the symptoms of the spinal cord affection may precede any evidence of anæmia and that for a very considerable period of time, in this case about a year and ten months. Of the three cases perhaps this serves more than any of the others, at any rate clinically, to show how close is the association between the cases of combined sclerosis occurring in anæmia with those of so-called ataxic paraplegia or postero-lateral sclerosis. The third case makes it clear that cord changes indistinguishable from those which have been described in profound anæmia may occur without any obvious anæmia throughout the short clinical course of the affection. The patient was, however, markedly debilitated and in a condition of extreme marasmus and it is quite possible that had she lived longer anæmia might have been a late feature in this case as in the second here recorded.

That a close association exists between the changes in the spinal cord and profound anæmia in some cases is beyond question, but it appears equally certain that the cord changes cannot be attributed directly to the anæmia from an etiological point of view, as has been supposed to be the case by some writers. The fact that cases occur, like the third here recorded, in which anæmia, if present, has at any rate not been sufficiently prominent to attract attention argues strongly against the view that the spinal cord changes depend on the anæmia. So, too, instances have been recorded by Nonne,<sup>6</sup> Minnich,<sup>7</sup> Arning,<sup>8</sup> Teichmüller,<sup>9</sup> and Bödeker and Juliusberger<sup>10</sup> where, like the second case, the clinical manifestations of the spinal cord affection preceded any obvious signs of anæmia, which further argues against this view. Another consideration which is opposed to this hypothesis and to which sufficient weight has not been given is the fact that the number of cases of spinal cord changes of this kind is small compared with the large numbers of profound anæmias met with from

<sup>6</sup> Archiv für Psychiatrie, 1893, Band xxv.

<sup>7</sup> Zeitschrift für Klinische Medizin, 1892, Band xxi.

<sup>8</sup> Inaugural Dissertation, Leipzig, 1895.

<sup>9</sup> Deutsche Zeitschrift für Nervenheilkunde, 1896, Band viii.

<sup>10</sup> Neurologisches Centralblatt, 1896.



various causes, even if we excluded the cases of chlorosis in young girls. Even in these Nonne would expect cord changes to occur, for in concluding that all anæmias of a progressive character may lead to degenerations in the spinal cord he asks if it is not possible for them to exist in cases of chlorosis also. It has been suggested that phenomena such as the absence of knee-jerks sometimes met with in cases of chlorosis may indicate a minor degree of a similar change which in the graver forms of anæmia becomes of so pronounced a character. I, however, venture to contend that the two conditions are not strictly comparable. Prévost<sup>11</sup> showed experimentally that depriving the lumbar centres of blood by compression of the abdominal aorta abolishes the knee-jerks, and I have shown<sup>12</sup> that the same thing occurs in general anæmia produced by bleeding and in cases in which asphyxia is artificially induced. So that if the spinal centres to which the knee-jerks are related be deprived of blood or supplied only with blood containing an excess of carbonic acid the knee-jerks are abolished. While the excess of carbonic acid may have something to do with this result in the case of asphyxia, reasons are given elsewhere<sup>13</sup> for regarding the want of oxygen as the more potent factor in both cases. My contention, therefore, is that in cases of chlorosis in which the knee-jerks are abolished or in which temporary paraplegia occurs such phenomena ought to be attributed to this starving of the spinal centres of oxygen leading to a condition of functional inactivity rather than to the action of an agent so powerful as that which is responsible for the profound changes met with in the spinal cord in cases of combined sclerosis whether associated with anæmia or not. The experiments of von Voss<sup>14</sup> are important in this connexion, for though he succeeded in inducing pernicious anæmia in animals by artificial means and in keeping them alive for periods up to twenty-four weeks, he could find no changes in their spinal cords such as have been found in these cases of combined degeneration in man.

A further argument which might be advanced against the view that anæmia is the cause of the combined degenerations of the spinal cord that have been met with in its association is that profound degenerations of the kind have not been met with in the severe anæmia which occurs in leucocythæmia, lymphadenoma, malignant disease, and the like. Too much cannot be made of this, however, for it is possible that the association has been missed through ignorance of the possibility of such an occurrence, and it may be that systematic examination of such cases in future with this object in view may reveal that such an association is very much more common than we supposed. A striking and instructive instance of the need for caution in this connexion is supplied by a case recorded by Michell Clarke<sup>15</sup> in which symptoms of spinal cord lesions were masked by those due to profound anæmia. Further, Eisenlohr<sup>16</sup> and Müller<sup>17</sup> have each found lesions of the peripheral cranial nerves in lymphatic leukæmia, and changes in the medulla oblongata have been found respectively by Kast<sup>18</sup> and Alt.<sup>19</sup> Then, again, Müller<sup>20</sup> observed a case of leukæmia with slight sclerosis of the postero-internal and to some extent of the postero-external columns, increasing in degree from the lumbar to the cervical part of the spinal cord with increase and thickening of the neuroglia and falling out of nerve fibres. Patches of degeneration were also found in the anterior and lateral tracts. And Nonne<sup>21</sup> has recorded two cases of leukæmia in which there were no nervous symptoms during life, but in which he found patches of degeneration in the anterior, lateral, and posterior columns non-symmetrically distributed. There was in addition in one of the cases sclerosis of the postero-internal columns throughout the cervical cord and slight symmetrical sclerosis of the outer part of this tract and median part of the postero-external column in the cephalic end of the thoracic cord. In spite of cases of this kind which appear to support the views of those who regard anæmia as the cause of the

spinal cord degenerations now under consideration the bulk of the evidence is opposed to this hypothesis. It appears to me to be more reasonable to suppose, as has been done by Lichtheim, Minnich, Taylor, and others, that the anæmia and spinal cord changes are the result of a common cause in the form of some toxic state of the blood. I do not, however, concur with Taylor, whose opinion is shared by Michell Clarke, in supposing that the degenerations may in part be the result of the hæmorrhages which take place in the spinal cord, and which are regarded as comparable to those which occur in the retina, brain, and other parts in pernicious anæmia. It may be that the presence of such hæmorrhages in the spinal cord is to be so accounted for; but in that they have also been found in cases of combined degenerations of the spinal cord in which anæmia was not a feature in the clinical history, the hæmorrhages may be the result of the action of a toxin on the walls of the spinal cord vessels whether the poison is or is not capable of inducing anæmia also. We are, of course, familiar with hæmorrhages of the kind in connexion with the action of various toxins on the central nervous system. That they form no essential part in the etiology and pathology of the spinal cord affection under consideration is proved by the fact that the most pronounced degeneration of the nerve elements may be met with in these cases throughout the spinal cord, without any hæmorrhages or their remains being detected. Further, in that such hæmorrhages have been commonly met with in the spinal cord in cases of severe anæmia without clinical manifestations of spinal cord symptoms, and without any change at all comparable to that of the combined degeneration type, it is reasonable to suppose that had they anything to do with the condition now under consideration they would be met with more frequently, in view of the large number of cases of severe anæmia which occur. Anæmia may play a part, and that a not unimportant one, in reducing the resistive power of the nerve elements so as to render them less able to withstand the baneful influence of some toxin, a property which anæmia would share with other debilitating influences and cachectic states. Thus it may come about 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.

In cases like the third, and one recorded by Rothmann, in which without obvious anæmia a condition of general malnutrition and marked cachexia was associated with the spinal cord affection, it is impossible to believe that the nervous system does not share in the general impoverishment, and whether the toxic agent had commenced its special action of destruction on the particular tracts affected in the combined sclerosis before or after the nervous system had commenced to share in the impoverished state of the body generally, the lowered state of nutrition of the nerve elements could not fail to facilitate the special action of the toxic agent on the particular tracts of the cord found degenerated, whether that degeneration is dependent on the action of the same poison which induced the general cachexia or whether some altogether different toxin is responsible for it.

The admission by most observers that the changes in the spinal cord are the result of the action of a toxin, though an important step in our knowledge of the etiology and pathology of these combined degenerations of the cord, leaves much to be further elicited. Thus Rothmann regards the affection of the white matter as endogenous in origin and the result of a primary affection of the grey matter. Teichmüller also regards the change in the grey matter as important and looks on both the tract affection and scattered areas of degeneration in the white matter as the result of small hæmorrhages. Pétion<sup>22</sup> similarly looks on the sclerosis as consequent on small hæmorrhages, while Nonne<sup>23</sup> attributes the changes in the white matter to patches of acute myelitis occurring in the earlier stages of the affection, and Bödeker and Juliusberger hold a similar view in that according to them the affection is to be regarded as a disseminated myelitis, which has a predilection for certain tracts of the spinal cord. 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

<sup>11</sup> *Revue Médicale de la Suisse Romande*, February, 1881.

<sup>12</sup> *Proceedings of the Royal Society*, vol. lvi., 1893.

<sup>13</sup> *Loc. cit.*

<sup>14</sup> *Deutsches Archiv für Klinische Medizin*, 1897, Band lxxviii., p. 489.

<sup>15</sup> *Brit. Med. Jour.*, 1897, ii., p. 325.

<sup>16</sup> *Virchow's Archiv*, 1878, Band lxxiii.

<sup>17</sup> *Inaugural Dissertation*, Berlin, 1895.

<sup>18</sup> *Deutsche Zeitschrift für Klinische Medizin*, 1895, No. 28.

<sup>19</sup> *Wiener Medicinische Wochenschrift*, 1896, No. 21.

<sup>20</sup> *Loc. cit.*

<sup>21</sup> *Deutsche Zeitschrift für Nervenheilkunde*, 1897, p. 165.

<sup>22</sup> *Norddeutsches Medicinisches Archiv*, 1896, N.F., Band vi., and *Neurologisches Centralblatt*, 1896, p. 747.

<sup>23</sup> *Neurologisches Centralblatt*, 1896, p. 137.

individual observations, for a general survey of the whole subject, giving due weight to the changes found in all the recorded cases, does not, it appears to me, admit of such diversity of opinion. Any view which attributes the changes in the white columns of the cord to a primary affection of the grey matter appears to me to be erroneous in that in no small proportion of the total number of recorded cases the grey matter has been found intact, while in a large number of cases in which changes have been found in the grey 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 grey matter when present are irregularly distributed as a rule. 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.

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 in many cases there are no hæmorrhages present nor can the slightest traces of former hæmorrhages be detected. Even when hæmorrhages are present they are 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 large 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 cervical and upper thoracic 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 such vessels with altered walls. But as von Voss has pointed out, and as I can fully confirm, such areas of degeneration are often seen in the neighbourhood of perfectly healthy vessels, while on the other hand vessels with markedly changed walls may be seen in parts of the cord free from degeneration, and, further, small areas of degeneration occur with no vessel of any kind in their immediate neighbourhood. Burr<sup>24</sup> rejects the vascular theory owing to the fact that he examined the spinal cords in seven cases of pernicious anæmia and in all but one found changes present although he scarcely ever found changes in the blood-vessels. That the topographical distribution of the degeneration of the white matter of the cord depends on the vascular distribution there can be little question. This will be obvious if it is borne in mind that the blood-supply of a given transverse area of the cord is derived from two sources, the anterior median arteries in the anterior median fissure and the peripheral arteries. The former supply the grey matter of the anterior horns and the white matter bordering on them and the neck of the posterior horn including Clarke's columns, while the latter supply the whole of the rest of the white matter of the cord. The distribution of the affection of the white matter of the cord in these cases of combined degeneration is precisely that of these peripheral vessels.

We have seen that cases occur in which there is affection of both regions of these different vascular supplies—viz., the grey as well as the white matter; but we have also seen that there are other cases in which the changes are limited to the area of supply of the peripheral vessels. Why there should be this escape of the area of supply of the

anterior median arteries in some cases 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, as has been supposed by Marie to account for certain forms of combined sclerosis. Difficult as these differences are of explanation they are no more curious than is the fact that in an admittedly infective disease like acute anterior poliomyelitis there should be affection of the area of supply of the anterior median artery alone, while that of the peripheral arteries escapes entirely. This belief that the morbid condition owes its topographical distribution to the vascular distribution must not be interpreted as meaning that I am 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 elements is far from my belief, in that cases have been recorded in which with extensive degeneration of the nerve elements no changes in the vessel walls have been detected. I regard the changes in the vessel walls as rather depending on the same cause as the parenchymatous degeneration of the nerve elements, 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.

We have lastly to consider the view of Nonne and of Bödeker and Juliusberger, who regard the degeneration as the result of disseminated 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 tissue so characteristic of changes of inflammatory origin. What, then, are we to regard as the mode of origin of the changes met with in the various nerve tracts of the spinal cord? The answer appears to me to be simple. We have already admitted that a toxin is responsible for the production of the spinal cord changes, and nothing appears more natural than that this toxic body (whatever may be its chemical nature) should by its action on the nerve elements result in a parenchymatous degeneration of them. Such a theory accords best with the changes found and with their distribution. The most reasonable explanation which can be offered as to why some parts of the cords 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.

Another question which deserves fuller consideration than I have already given it in this paper is how far we are justified in regarding all the cases of combined sclerosis of the spinal cord as belonging to the same category. That there are many totally distinct diseases in which tracts of different function are simultaneously affected, or in which the affection of tracts of a certain function is followed by similar affections of other tracts of entirely different functions, is obvious; but there also appear to me to be conditions in which the tracts are so affected, and which are at present regarded as distinct from each other, which should be regarded as identical. As coming within the former category I would instance the following. 1. Cases of tabes with affection of the crossed pyramidal tracts, those with degeneration of the direct cerebellar tracts alone or in conjunction with the crossed pyramidal tracts. 2. Cases of primary lateral sclerosis in which the posterior columns become secondarily affected or in which the direct pyramidal and direct cerebellar tracts are involved and the posterior columns remain normal. (The only recorded cases of the latter are open to question in that the posterior columns may have been affected in the upper unexamined part of the cord in one case and in that Goll's columns were intensely stained by carmine in the

<sup>24</sup> University Medical Magazine, April, 1895.

cervical region in the other case.) 3. Combined sclerosis of the posterior and lateral columns in general paralysis of the insane. 4. Friedreich's hereditary ataxy. In the second category I would include all those cases in which, with or without the presence of anæmia, degeneration occurs in tracts of different function in the spinal cord simultaneously or in quick succession and in which, irrespective of the duration of the clinical history or the precise order of occurrence of the phenomena dependent on affection of the tracts, there is found post mortem degeneration of the posterior columns, the crossed and direct pyramidal tracts, and the direct cerebellar tract. But it will be obvious that further subdivision of this great group will be necessary if we are to include in it conditions with so wide a difference in length of clinical history as the cases which we have been considering and those described by Gowers as ataxic paraplegia. Let us consider what justification there is for including in this group those acute cases in which, without anæmia, there occur symptoms attributable to affection of the spinal cord indistinguishable from the symptoms which occur in the cases associated with anæmia, the anæmia cases and those which have been described under the title of ataxic paraplegia. Sir William Gowers's description of the clinical features of the last condition leads me to conclude that its course is essentially chronic. While true of many cases, however, exceptions certainly occur to the rule, if, indeed, the rule is still to hold good now that with a wider experience of the condition we find that so many cases presenting the clinical and pathological pictures of ataxic paraplegia differ from it only in one or two minor details, including a shorter clinical course. If we allow that cases of ataxic paraplegia may run a subacute or even an acute course, then there seems little or nothing to separate this class of cases from the cases of combined cord changes which have been described in anæmia. How closely similar the conditions are is well exemplified by two cases recorded by Wagner<sup>25</sup> as instances of postero-lateral sclerosis in the sense that we would regard them as cases of ataxic paraplegia, but which, if a distinction is to be drawn between ataxic paraplegia and the cord changes which occur in anæmia, must unquestionably be relegated to the latter category. Oddly enough, however, Wagner does not appear to have been struck by the similarity of his cases to those which have been described in association with anæmia, although the morbid changes met with are indistinguishable from those found in the cases of anæmia. Further, one of his cases was markedly anæmic and in one the duration of the illness was only six months, while in the other it was two years. To admit that these cases are examples of ataxic paraplegia is to admit that this affection may run a subacute course, and such an admission also involves the necessity of our regarding all these cases of combined sclerosis as belonging to the same class—that originally known as ataxic paraplegia—irrespective of the length of the clinical history and as to whether anæmia was a feature in the case or not. Such a view would not be out of keeping with what we know of other diseases of the nervous system which owe their origin to the action of poisons, whether these are generated in the body or introduced into the system from without, for all such affections present marked variations as regards acuteness and chronicity and as regards the extent and intensity of the resulting morbid process. That such should be the case is only what is to be expected in that the rate of progress and the amount of damage done must of necessity depend largely on the virulence of the poison, its amount, and the resistive or other antagonistic properties possessed by the tissues on which it acts. If, as seems highly probable, therefore, the combined degenerations of the spinal cord owe their origin to the action of some toxic substance, there is no reason why such degenerations should not present all degrees of variation in their rate of progress and why the same poison should not generate the more chronic process of "ataxic paraplegia" and the more acute changes in precisely the same tracts of the spinal cord in the cases of anæmia and of cachectic conditions in which the resistive powers of the nerve elements must of necessity be lessened, whether these states of the general system were in existence before the poison commenced its special destructive action on the nerve elements or only became pronounced subsequently to this. From what has been said it will be seen that there is much which suggests a

close relationship between ataxic paraplegia and the acuter forms of postero-lateral degeneration, but it would be premature to regard them as identical for there are some links in the chain of evidence which are still wanting.

Queen Anne-street, W.

## HÆMATURIA AS A SYMPTOM: METHODS EMPLOYED IN MAKING A DIFFERENTIAL DIAGNOSIS;

WITH 19 CASES ILLUSTRATING POINTS OF INTEREST IN THE DIAGNOSIS OF RENAL AFFECTIONS CHARACTERISED BY THE PRESENCE OF BLOOD IN THE URINE.

BY DAVID NEWMAN, M.D. GLASG.,  
SURGEON TO THE ROYAL INFIRMARY, GLASGOW.

THE appearance of blood in the urine during micturition is a symptom of a large number of different lesions and, as seen in surgical practice, may have its origin in any of the divisions of the urinary tract. Hæmaturia may be due to (a) lesions of the renal parenchyma or the pelvis; (b) disease of the ureters; (c) disease of the bladder; (d) disease of the prostate; (e) disease of the urethra; and (f) disease of the testicles. In this paper I shall endeavour in the first instance to discuss in a general way the characteristics of the urine in local lesions of the urinary tract in which hæmaturia is a prominent symptom and will describe in detail the exact methods which should be employed in making a differential diagnosis. Having done so, I shall classify the lesions of the urinary tract which are commonly associated with hæmorrhage and then describe in detail and illustrate fully by selected cases the etiology and symptomatology of renal hæmaturia. While in this communication only hæmaturia from lesions of the kidney will be illustrated by cases, I hope at a future time to publish a series of cases of disease of other portions of the tract in which the passage of blood in the urine was a prominent symptom and I shall then discuss the general question of treatment. I shall now refer to lesions of other portions of the urinary tract only in so far as it is necessary for differential diagnosis. We may classify the diseases of the kidney commonly associated with blood in the urine under the following heads:—(1) Traumatic lesions—(a) from injury and (b) from calculus; (2) Passive hyperæmia—(a) pressure on the renal veins, (b) torsion of the renal veins, and (c) reflex spasm of arterioles; (3) Inflammatory hyperæmia—(a) nephritis, acute and chronic, (b) tuberculous disease, and (c) cystic degeneration and hydatids; and (4) Tumours of the kidney. In the old nosological system of Vogel hæmaturia denotes a hæmorrhage from the kidney exclusively, but the name has been applied with different latitude of meaning by different writers. According to its etymological sense it should be restricted to cases in which blood is effused from the vessels in the kidney, ureters, or bladder and discharged along with urine, excluding from the definition urethral hæmorrhage in which the blood flows by drops or in a continuous stream from the orifice of the urethra and which is not properly a mictus cruentus. Every flow of blood from the urethra ought not to be considered a hæmaturia; a hæmorrhage having its starting-point in front of the muscle of Wilson ought to be distinguished from a true hæmaturia. The pathological conditions which are associated with the appearance of blood in the urine are very various and numerous, and while the great majority of these maladies are such that they naturally come under the cognisance of the surgeon many other cases of hæmaturia do not come under our consideration as they belong strictly to medical rather than to surgical practice. For example, hæmaturia may be an accompaniment of hæmophilia, septicæmia, typhus, enteric, or malarial fevers, small-pox, scurvy, or purpura; or it may be the direct consequence of poisonous agents, such as cantharides, alcohol, turpentine, phosphorus, and arsenic. Red urine is sometimes passed by patients who have taken sulphonal in large doses or for a long period. The Burgundy-red colouration is not due, however, to blood, but to the presence of abnormal pigments, urohæmatoporphyrin or its allies.

Eliminating such sources of hæmorrhage and considering

<sup>25</sup> Deutsche Zeitschrift für Nervenheilkunde, 1897, Band xi., p. 1.