mentation). While, therefore, we study and admire the insight and patient labour of the great Austrian psychologist, Professor Freud of Vienna, let us at the same time pay homage to the great English father of neurology, who taught us to understand the nervous system, Dr. Hughlings Jackson.

(*To be continued.*)

CLINICAL STUDIES. II.—ON THE ASSOCIATION OF PERNICIOUS ANÆMIA WITH SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD.

By BYROM BRAMWELL, M.D., F.R.C.P.E., LL.D., F.R.S.E., Consulting Physician, Royal Infirmary, Edinburgh; Physician, Chalmers Hospital, Edinburgh.

THE object of this paper is to suggest that the anæmia associated with subacute combined degeneration of the spinal cord is much more frequently the pernicious form of anæmia than is usually supposed.

Subacute combined degeneration of the spinal cord is, in my experience, a rare condition. I have notes of five cases; in all of them the anæmia was, I believe, pernicious anæmia. (I have probably seen other cases which I did not recognise.) In two of the cases the diagnosis was confirmed by post-mortem examination; in both, appearances typical and characteristic of pernicious anæmia were present in the liver, bone-marrow, and other organs.

In his admirable article on "Subacute Combined Degeneration of the Spinal Cord" in Allbutt and Rolleston's *System of Medicine* (p. 791), Dr. James Collier makes the following statement with regard to the condition of the blood in cases of subacute combined degeneration:—"In a few instances anæmia has been absent throughout, the hæmoglobin and the cytology being normal; this occurs in cases which have run an acute and fatal course in a few months. Usually the blood shows a secondary anæmia of varying severity; the hæmoglobin ranges from 35 to 75 per cent., the lower of these figures being common; the colour-index is usually above the normal, and may be as high as 1·6. Anisocytosis, poikilocytosis, and polychromatophilia are common. Normoblasts are sometimes numerous, but megaloblasts have not been found. The leucocyte count is normal, unless some suppurative complication supervenes. The reaction for free iron in the liver has not been obtained in any case."

The impression made on my mind by this statement is that

the anæmia associated with subacute combined degeneration of the spinal cord is not usually, in Dr. James Collier's opinion, pernicious anæmia. It is certainly remarkable that in no case of subacute combined degeneration with which he was acquainted, when his article was written, was the reaction for free iron in the liver, which is such a characteristic pathological feature of pernicious anæmia, found on post-mortem examination. There can, I think, be no doubt that in many of the recorded cases of subacute combined degeneration of the spinal cord the anæmia was pernicious anæmia. The findings—both clinical and post mortem—of many of the published cases seem to me to be quite conclusive on this point. This opinion appears to me to be corroborated by Dr. Collier's statement—"that the colour-index is usually above the normal, and may be as high as 1·6." This statement is very suggestive that the anæmia was in reality pernicious anæmia. A high colour-index, in my experience, though not *per se* conclusive, is very strongly suggestive of pernicious anæmia. A high colour-index is seen in some cases of leukæmia, more especially the lymphatic form, but, so far as I know, and as my experience enables me to judge, is not met with in secondary anæmia or in cases in which the anæmia is apparently idiopathic (for which there is no discoverable cause) unless the anæmia is of the pernicious type.

The age-period at which subacute combined degeneration is most frequent seems to be corroborative of this view. Dr. Collier states as regards the age of patients affected with subacute combined degeneration of the spinal cord (p. 787):—"The extremes at which the onset of the disease has been recorded are thirty-five and sixty-five years of age. A few cases have occurred between thirty and forty, but during the succeeding decade they become increasingly numerous, and the highest incidence is reached between the ages of fifty-five and sixty years."

Now, profound and persistent anæmia in patients, especially in male patients, over forty years of age, which is actually and really "*idiopathic*" (*i.e.* for which there is no discernible cause, such as malignant disease, especially malignant disease of the body of the stomach; hæmorrhage from piles; insidious bleeding from a duodenal or gastric ulcer; Bright's disease, etc.), is usually, in my experience, pernicious anæmia.

The age-period at which pernicious anæmia and subacute combined degeneration of the spinal cord occur is practically the same. In 140 cases of pernicious anæmia of which I have notes,

107 cases (or 76·4 per cent.) were between the ages of 35 and 65 (inclusive) when the patients came under observation; that is to say, at the same age-period at which subacute combined degeneration of the spinal cord most frequently occurs (see Fig. 6, p. 271).

Further, I am disposed to think that in many cases of subacute combined degeneration of the spinal cord in which the anæmia does not at first conform to the pernicious type, the anæmia is probably in reality pernicious anæmia. Case III. is very important and instructive in this respect. The patient, a man of 31, suffered from nervous symptoms suggestive of disseminated sclerosis; in the earlier stages of this case there was slight anæmia, but no blood examination was made. A fortnight before his death (11th November 1907) a blood-count showed no features suggestive of pernicious anæmia; the condition of the blood at that date was as follows: red corpuscles 4,200,000 per c.mm., hæmoglobin 70 per cent., colour-index 0·8. During the next fortnight very rapid deterioration of the blood took place without loss of blood or other obvious cause (evidently the result of an acute intoxication), and the stage of rigidity passed into the stage of flaccidity. On 25th November the condition of the blood was: red corpuscles 600,000 per c.mm., hæmoglobin 28 per cent., colour-index 2·3. Some normoblasts and megaloblasts were present in the blood, which presented all the characteristic features of pernicious anæmia. On 27th November the patient died. Post-mortem examination showed (1) all the characteristic appearances of pernicious anæmia—the liver gave a very marked Prussian-blue reaction, the marrow of the bones was typical; and (2) the typical appearances in the spinal cord of subacute combined degeneration.

In this case, then, there was for *three years* no marked anæmia while nervous symptoms due to subacute combined sclerosis of the spinal cord were present; then all of a sudden, apparently as the result of acute intoxication, rapid destruction of the blood took place, and the characteristic clinical features (confirmed by post-mortem examination) of pernicious anæmia developed.

Now, this case seems to suggest that in cases of subacute combined degeneration associated with anæmia, which is thought to be secondary in nature, but in which the colour-index is above the normal (such cases as Dr. Collier mentions), the anæmia is in reality pernicious anæmia. The same statement perhaps applies to some of the cases of subacute combined

degeneration in which the anæmia is thought to be secondary and in which the colour-index is normal or below the normal.

I submit that the cases recorded below and the arguments which I have just advanced suggest that the anæmia associated with subacute combined degeneration of the spinal cord is much more frequently pernicious anæmia than is usually supposed—indeed I almost feel inclined to suggest, looking at the course which Case III. pursued, that if the condition were to last long enough, the anæmia associated with subacute combined degeneration of the spinal cord would in many, possibly in all, cases prove to be pernicious anæmia. Or, to put it another way, when the nervous symptoms indicate the presence of subacute combined degeneration of the spinal cord, the physician should strongly suspect that the anæmia associated with the condition is pernicious anæmia, for, even if the blood condition is not at first indicative of pernicious anæmia, the characteristic features of pernicious anæmia will, if the patient lives long enough, be developed in some (possibly in all) cases.

It will be noted that in this case, and also in Case V., the development of the flaccid stage of subacute combined degeneration and the acute blood destruction were coincident. This fact has also been noted by Collier; he states (*ibid.*, p. 794):—"The change from the spastic to the flaccid type sometimes coincides with the appearance of severe anæmia." The coincident occurrence of rapid blood destruction and the development of the flaccid paralysis is suggestive that both are due to acute intoxication. It will be interesting to observe whether in other cases of subacute combined degeneration rapid deterioration of the blood, deeply pigmented urine, and fever accompany or immediately precede the development of the flaccid stage of the disease.

We are ignorant of the exact cause of pernicious anæmia. The facts at our disposal seem to suggest that it is probably a toxin, perhaps absorbed, as Dr. William Hunter has suggested, from the gastro-intestinal tract (though I differ from him in thinking that oral sepsis, due to bad teeth, is the cause, or a cause, of the disease; the glossitis and inflammatory spots on the buccal mucous membranes, which are so frequent in pernicious anæmia, are, I think, part and parcel, a feature of the disease, not a cause). But if this is so, we do not know whether the clinical condition which we term pernicious anæmia is always due to one and the same toxin, or whether it may not be due to more than one, possibly several, different toxins.

Dr. Collier argues that in cases of subacute combined degeneration the anæmia is not the cause of the spinal lesion, but that the anæmia and the spinal lesion are due to a common cause, probably a toxin or perhaps several different toxins. I agree with this view; it seems to me to be much more probable than Nonne's view, which suggests that the cord lesion is due to vascular changes, the result of the anæmia.

In some cases of subacute combined degeneration the anæmia precedes, in others occurs coincidently with, and in others follows the spinal symptoms; in other words, the development and severity of the spinal symptoms do not depend upon the development and severity of the anæmia.

It seems reasonable to suppose, and clinical and pathological facts seem to support this view, that—

1. In some cases the toxin acts entirely on the blood, the result being pernicious anæmia without spinal symptoms. In this group are included the great majority of cases. Of 140 cases of pernicious anæmia of which I have kept detailed notes, there were only four cases of subacute combined degeneration. (Case II. recorded in this paper was not included in my cases of pernicious anæmia.)

2. In some cases the toxin acts entirely or chiefly upon the spinal cord; in these cases there is subacute combined degeneration without anæmia or with slight anæmia. These cases are rare.

In some of the cases included in this group in which the anæmia was at first slight, and in which the blood changes in the early stages were not suggestive of pernicious anæmia, profound pernicious anæmia is ultimately developed. Case III. is an illustration of this group.

3. In some cases the anæmia precedes the development of spinal symptoms. Cases IV. and V. are examples of this group. This seems to be the most frequent type of subacute combined degeneration.

4. In some cases the toxin from the first, or at all events at the time when the patient first comes under observation, acts both on the blood and the spinal cord, the result being typical pernicious anæmia with subacute combined degeneration of the spinal cord. Case I. seems to be an example of this group.

The notes of the cases are as follows:—

Case I.—Male, aged 72, seen in consultation on 28th August 1896, suffering from profound pernicious anæmia and spinal symptoms. The

condition (anæmia and spinal symptoms) had developed several months previously without apparent cause. The patient complained of numbness and loss of power in the legs; the knee-jerks were absent; there was considerable muscular atrophy and anæsthesia both in the legs and thighs. This stage of flaccid paralysis had been preceded by a condition of rigidity with increase of knee-jerks. At first the bladder and rectum were not affected.

Subsequent Progress of the Case.—Under gradually increasing doses of arsenic (maximum dose reached nine minims daily), strychnine, massage, and the faradic current, there was slight temporary improvement as regards the anæmia; no improvement in the spinal symptoms. Ultimately the bladder and rectum became involved, and the patient died three months later.

No post-mortem examination.

Case II.—Male, aged 72, seen in consultation on 18th May 1898. Duration, four years.

Symptoms.—Profound anæmia with spinal symptoms; numbness and anæsthesia in legs and arms; flaccid paralysis; loss of reflexes; incontinence of the bladder and rectum. In the earlier stages of this case shooting pains in the legs, loss of the deep reflexes, and an ataxic gait were the chief symptoms, and the case had been diagnosed by a distinguished London neurologist as tabes. It was, in its early stages, an example of the "tabetic" form of subacute combined paralysis. This form, though rare, is a well-recognised type of the disease; tabetic in its early stages, it passes like the ataxic-spastic or spastic type into the flaccid stage of paralysis, usually in association with profound anæmia, in the later stages.

The patient died a year later. There was no post-mortem examination.

Note.—I have not included this case in my cases of pernicious anæmia as no examination of the blood was made. I am, however, disposed to think it was a case of pernicious anæmia. With this opinion Dr. Aldren Turner, who joined in the consultation, agrees.

Case III.—Male, aged 33, admitted to Edinburgh Royal Infirmary on 18th September 1906 suffering from ataxic-spastic paraplegia, vertical nystagmus, derangements of the bladder and rectum, and optic atrophy exactly resembling that characteristic of disseminated sclerosis.* The mucous membranes were slightly anæmic. No examination of the blood was made at this date. The condition seemed to be indicative of disseminated sclerosis.

* On 25th February 1907 Dr. W. G. Sym's report on the eye condition was: —"Vision is $\frac{6}{18}$ in the right eye and $\frac{6}{24}$ in the left. The optic discs are definitely paler than normal, especially at the outer side. The vessels are slightly reduced in size."

The illness had commenced at the age of 31 ; the patient had been previously healthy, and had not suffered from syphilis.

Under treatment (5 minims of Fowler's solution, thrice daily, with rest in bed and massage) rapid improvement took place; the patient's walking quickly improved, and the bladder derangement disappeared. He was discharged from hospital on 3rd November 1906 walking well, and stating that he felt fit for work.

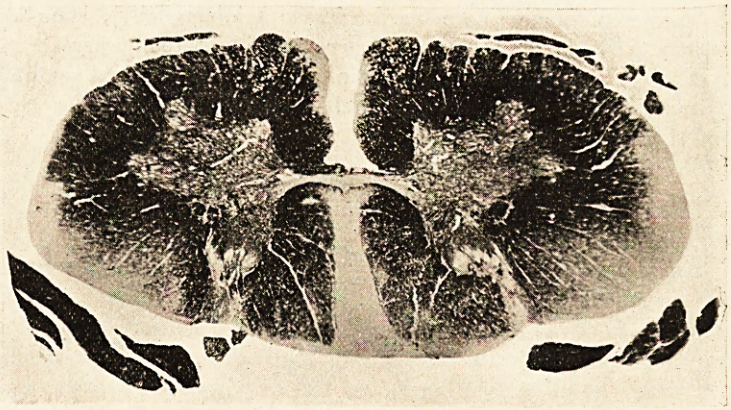

FIG. 1.—Section through the cervical enlargement of the spinal cord in the case of subacute combined degeneration described in the text. (Stained by Weigert-Pal.)

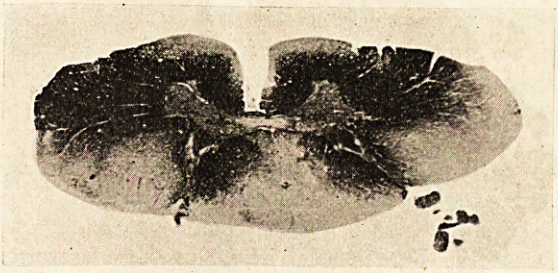

FIG. 2.—Section through the mid-dorsal region of the spinal cord in the case of subacute combined degeneration described in the text. (Stained by Weigert-Pal.)

On 20th February 1907 he was readmitted to the Infirmary. The ataxic-spastic paraplegia was very marked, and he could only walk with support. The urinary difficulties had returned—he had to "force" in order to get the water away. He complained of an aching pain in the left side of the back, of numbness, prickling, and coldness in the legs, and of a sensation as if he were walking on rubber.

He was again treated with arsenic and again improved. On 8th May 1907 he was discharged, able to walk well with the help of one stick, and saying that he was fit for work.

For three months after his discharge he continued well, and was able to follow his occupation. Then the weakness in the legs and difficulty in walking again recurred, and he began to suffer from pain in the back.

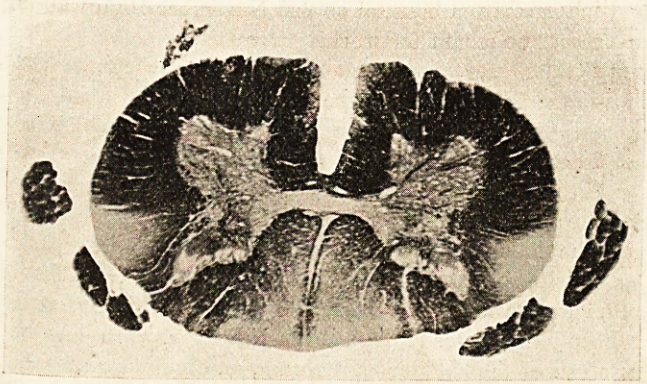

FIG. 3.—Section through the lower dorsal region of the spinal cord in the case of subacute combined degeneration described in the text. (Stained by Weigert-Pal.)

FIG. 4.—Section through the lumbar enlargement of the spinal cord in the case of subacute combined degeneration described in the text. (Stained by Weigert-Pal.)

The periods of marked improvement and relapses which occurred seemed to corroborate the diagnosis of disseminated sclerosis.

On 15th October 1907 the patient was admitted to the Infirmary a third time, complaining of severe pain in the lower part of the back and in the legs, numbness and tingling in the feet, and a cold feeling in the knees and elbows. The knee-jerks and Achilles-jerks were still

markedly exaggerated, ankle-clonus, and an extensor response were present on both sides; there was considerable difficulty in making water; the bowels were obstinately constipated.

On 11th November a blood-count showed the red blood corpuscles numbered 4,200,000 per c.mm., the hæmoglobin was 70 per cent., and the colour-index was 0·8. After this date very rapid deterioration in the blood occurred. On 25th November the red blood corpuscles numbered 600,000 per c.mm., the hæmoglobin was 28 per cent., and the colour-index 2·3. During the last stage of the case the microscopical characters of the blood were quite typical of pernicious anæmia; some megaloblasts and normoblasts were present.

After 11th November the legs became completely paralysed, the muscles soft and atrophied; the knee-jerks and Achilles-jerks disappeared; the Babinski sign remained. The legs, lower part of the trunk, and abdomen became anæsthetic; incontinence of the bladder and rectum developed. In short, the spastic condition, with exaggerated knee-jerks, passed into the flaccid stage, with loss of knee-jerks, paralysis of the bladder and rectum, and muscular atrophy.

The patient died on 27th November.

The blood-count at different dates was as follows:—

	Red Corpuscles.	Hæmoglobin percentage.	Colour-Index.
November 11, 1907.	4,200,000	70	0·8
„ 19, „	1,500,000	28	0·9
„ 21, „	1,190,000	25	1·0
„ 23, „	980,000	25	1·3
„ 25, „	600,000	28	2·3

Post-mortem examination showed all the appearances characteristic of pernicious anæmia, free iron reaction in the liver, typical alteration in the bone marrow, etc., and the spinal lesions characteristic of subacute combined degeneration (see Figs. 1, 2, 3, and 4).*

Case IV.—Male, aged 34, single, bank clerk, admitted to Edinburgh Royal Infirmary on 29th October 1910 suffering from pernicious anæmia and spinal symptoms. Duration of the anæmia three years; of the spinal symptoms, seven months. The only apparent cause was loss of blood from piles. For the last six months has suffered from stiffness and weakness in the legs, and some pain in the small of the back, which has been worse during the past three weeks.

The patient was a well-built, muscular man, 5 ft. 8½ ins. in height, 11 st. 3 lbs. in weight. The red blood corpuscles numbered 2,350,000

* Case fully recorded in *British Medical Journal*, 11th June 1910, p. 1396.

per c.mm., the hæmoglobin was 70 per cent., and the colour-index 1·5; the microscopic characters of the blood were typical of pernicious anæmia. The conjunctivæ had a yellow tinge. The gait was spastic and ataxic. The patient complained of a dull aching pain in the small of the back, tightness as if a string were tied round the waist, and a numb feeling in legs and buttocks.

The knee-jerks and Achilles-jerks were exaggerated; there was double ankle-clonus; on the right side an extensor response, no toe movement on the left.

During the next fortnight the weakness in the legs markedly increased, slight nystagmus on looking to the right and left developed, incontinence of the bladder and rectum occurred. The blood condition showed little change.

On 11th November 1910 the red blood corpuscles numbered 2,180,000 per c.mm., the hæmoglobin was 64 per cent., and the colour-index 1·5; the microscopic characters of the blood were typical of pernicious anæmia.

The patient went home on 22nd November 1910. The paralysis rapidly passed into the flaccid condition, with muscular atrophy, loss of all reflexes except the knee-jerks, paralysis of the bladder and rectum, and bedsores. He died on 10th December 1910.

No post-mortem examination.

Treatment.—Arsenic, maximum dose six minims, thrice daily.

Case V.—Male, aged 42, married, admitted to Chalmers Hospital, Edinburgh, on 16th December 1912, suffering from pernicious anæmia and subacute combined sclerosis.

Duration, $3\frac{1}{2}$ years. He had been under the care of various physicians, and had been treated with arsenic by the mouth. The anæmia had been present for some time before the spinal symptoms developed.

On admission, the red blood corpuscles numbered 2,275,000 per c.mm., the hæmoglobin was 80 per cent., and the colour-index 1·46. The legs were rigid, the knee-jerks and Achilles-jerks were exaggerated, ankle-clonus and an extensor response were present on both sides.

The patient complained of numbness in the legs, and localised areas of anæsthesia and analgesia were present. There was occasionally incontinence of urine and fæces.

The patient did not improve under treatment (arsenic by the mouth, two injections of neo-salvarsan, massage, etc.).

On 10th March 1913 the red blood corpuscles numbered 1,530,000 per c.mm., the hæmoglobin was 35 per cent., and the colour-index 1·1. The spastic condition of the lower extremities disappeared, and a flaccid state with loss of reflexes developed.

The patient died on 22nd March 1912. For six days before death the temperature was above the normal; on the day of his death it reached 104·4°.

Post-mortem examination showed the characteristic appearances of pernicious anæmia (free iron reaction in the liver, typical alteration in the bone marrow, etc.) and subacute combined degeneration of the spinal cord.

The Differential Diagnosis of Subacute Combined Paralysis and Disseminated Sclerosis.

It is only in very rare cases, such as the *third case* described above, that there is likely to be any difficulty on this point.

In that case spastic-ataxic paraplegia, with nystagmus, optic atrophy, and derangement of the bladder and rectum, were present in the earlier stages. The disease developed at the age of 31, and was characterised by marked periods of improvement and remission. These facts were strongly suggestive of disseminated sclerosis. It was only when profound anæmia, characteristic of pernicious anæmia, and the flaccid stage of paralysis developed that any doubt arose as to the case being one of disseminated sclerosis. This case teaches that in all cases of suspected disseminated sclerosis in which the patient is in any degree anæmic, careful examination of the blood should be made.

In both subacute combined sclerosis and the spinal form of disseminated sclerosis ataxic-spastic or spastic paraplegia, with exaggeration of the deep reflexes and subjective sensory disturbances, are usually the most prominent spinal symptoms.

The points of difference between the two conditions are as follows:—

Age.—The age-period at which the two diseases develop is very different. Disseminated sclerosis comparatively rarely develops after the age of 35, and subacute combined paralysis very rarely develops before the age of 35.

The age-period at which the disease commenced in 110 cases of disseminated sclerosis and the age-period when the patients came under observation in 140 cases of pernicious anæmia (the age-period at which pernicious anæmia and subacute combined paralysis develop is practically the same) is graphically represented in Figs. 5 and 6.

Sex.—In my experience, disseminated sclerosis is decidedly more frequent in females, while subacute combined paralysis (and

pernicious anæmia) is more common in males. The opinion of other observers, however, differs on this point. My figures are as follows:—In 110 cases of disseminated sclerosis which I

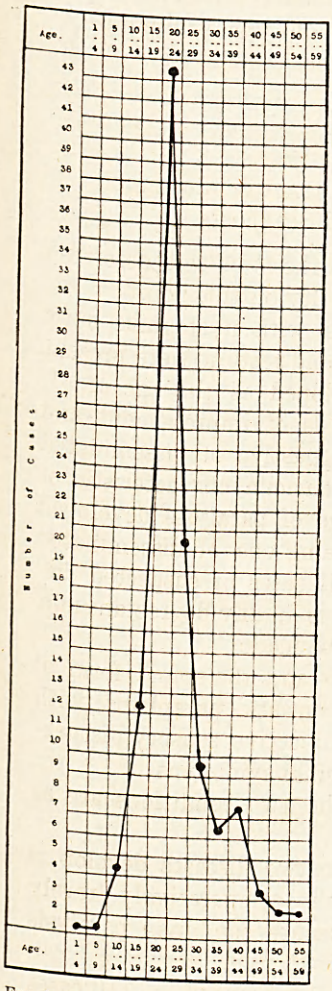

FIG. 5.—Age-period of development in 110 cases of disseminated sclerosis, in periods of five years.

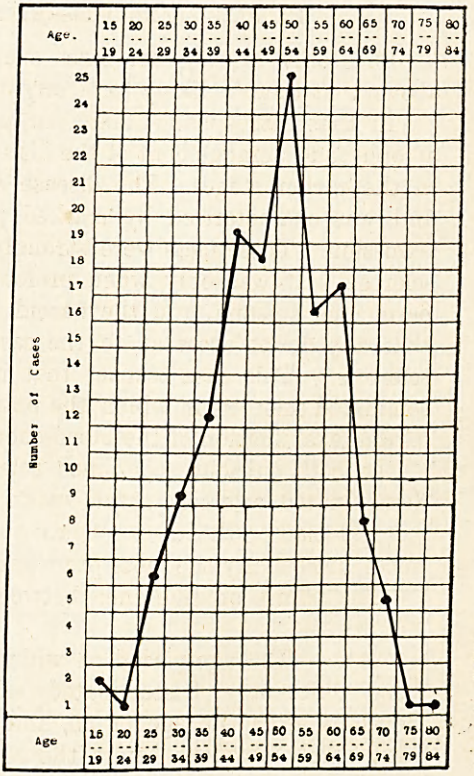

FIG. 6.—Age-period when the patient first came under observation in 140 cases of pernicious anæmia, in periods of five years.

analysed some years ago (*Clinical Studies*, vol. ii. p. 201) 67, or 61 per cent., were females, and 43, or 39 per cent., were males. All of my 5 cases of subacute combined degeneration were males. In my 140 cases of pernicious anæmia 91, or 65 per cent., were males, and 49, or 35 per cent., were females. It is probable,

I think, that if a sufficient number of cases of subacute combined sclerosis were analysed, the male cases would be found to be more frequent than the female cases.

Course and Duration. — Disseminated sclerosis is usually a very chronic disease, and in the majority of cases is marked by periods of improvement and relapse. Subacute combined paralysis rarely lasts more than six years; its duration is usually considerably less than this; periods of remission and improvement very rarely occur except in the earlier stages of a few cases. (Case III. is quite exceptional in this respect.)

Association with Anæmia. — Disseminated sclerosis is not associated with anæmia, except as an accidental occurrence (chlorosis is occasionally accidentally associated with disseminated sclerosis); whereas, in the great majority of cases of subacute combined sclerosis, profound anæmia (usually, I think, pernicious anæmia) is developed at some period or other of the case, frequently in the early stages. The presence of profound anæmia (usually, I think, pernicious anæmia), with characteristic spinal symptoms, is of the greatest diagnostic significance.

Symptoms.—Ataxic-spastic or spastic paraplegia, with exaggeration of the deep reflexes, and the Babinski sign are common features in both diseases; but the passage of an ataxic-spastic or a spastic paraplegia into a flaccid paraplegia, with muscular atrophy and loss of the deep reflexes, does not occur in disseminated sclerosis (except, perhaps, in very rare cases), while it is highly characteristic—in fact one of the most striking features—of subacute combined sclerosis.

Sensory subjective symptoms occur in both conditions, but are usually more marked in subacute combined sclerosis. Objective derangements of sensation are rare in disseminated sclerosis, but common in subacute combined sclerosis; in subacute combined sclerosis the sensory symptoms, both subjective and objective, usually present the stocking-glove distribution in the early stages, and an ascending segmental distribution as the disease advances.

In disseminated sclerosis, pain in the lower part of the back is a frequent symptom, but is usually, in my experience, less prominent and severe than in subacute combined sclerosis.

In disseminated sclerosis, derangements, usually slight, of the bladder and rectum are common in the early stages of the disease. In subacute combined sclerosis, profound derangements of the bladder and rectum are usually present in the later stages of the

disease, but seem to be less frequent than in disseminated sclerosis during the early stages.

In disseminated sclerosis, nystagmus, volitional tremor, speech affections, and optic atrophy are frequent and characteristic symptoms; they do not occur, or very rarely occur, in subacute combined sclerosis. (Case III., in which there was nystagmus and optic atrophy, is quite exceptional in this respect; in that case the nystagmus was peculiar in character—vertical in its direction; in disseminated sclerosis the nystagmus, in my experience, is horizontal.)

Dr. James Collier, whom I consulted in the year 1910 with regard to the occurrence of optic atrophy and relapses, remissions and periods of improvement in cases of subacute combined degeneration, kindly wrote me as follows:—

"I have just written the article on subacute combined degeneration for Allbutt's *System*, and I have been carefully into all the cases we have had at Queen Square, and also into all the cases that I have found in the literature. I make the following statement upon optic atrophy:—'Optic atrophy has been reported in a good many cases, but it is possible that the pallor of the disc, which is striking in some of the anæmic cases, has been confused with optic atrophy, for I have never myself seen undoubted atrophy of the disc. Dimness of vision is common when anæmia and debility are severe.' In several of our cases at Queen Square the note that optic atrophy was present had been made by the house-physician, but in no case was this opinion upheld by Mr. Marcus Gunn and Mr. Paton, who subsequently saw these patients. We have not as yet found any lesions higher than the encephalon, and, from the anatomical point of view, one would not expect optic atrophy in this disease. Your second question is of great interest, and is one that I should have answered in the negative two years ago. But since then I have followed to autopsy (1) cases in which the onset was an apparently functional paraplegia which improved for a time; (2) cases in which there was a marked temporary improvement; and (3) one case in which the onset was so rapid as to suggest acute myelitis, and in which temporary attacks of paraplegia lasting a week or two had occurred eight months and four months before the onset respectively and had been completely recovered from. This last case was an unusually rapid one, but the pathological condition found by Dr. Holmes was typical. I have always pointed out that the diagnosis of this disease in the early stages from the ataxic paraplegic form of disseminated sclerosis was an important one, but we have not had a case in which this differential diagnosis has been difficult. From our knowledge of the disease and its anatomy it seems to me easy to conceive cases of slow onset in which the clinical picture might be

exactly that of typical disseminated sclerosis, for many cases present no anæmia till late."

With regard to the differential diagnosis of subacute combined degeneration of the spinal cord and disseminated sclerosis, Risien Russell, Batten, and Collier make the following statements:—

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

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

Etiology.—It is interesting to note that in both disseminated sclerosis and subacute combined sclerosis the sclerotic lesions in the spinal cord are supposed by most authorities to be due to some irritant or toxin which is distributed through the nerve centres by the blood. But if this is so, it is obvious that the irritant or toxin is not the same in the two diseases.

The distribution of the lesions in the spinal cord is quite different in the two conditions.

In disseminated sclerosis the lesions are typically "indiscriminate" †—patches of sclerosis scattered here and there haphazard, as it were, over the transverse sections of the cord at any, usually

* *Brain*, 1900, vol. xxiii. p. 58.

† In the first edition of my book on the *Diseases of the Spinal Cord*, published in the year 1882, I suggested the term "*indiscriminate*" as opposed to "*system*" lesions. "*The affections of the cord which are primarily nervous* are either acute or chronic. In some the diseased process is strictly limited to definite physiological tracts. These affections are called *system diseases*. In others the morbid process has no such physiological limitation, but involves at haphazard, as it were, a greater or smaller portion of the transverse section. To these lesions the term *indiscriminate* may be applied. In a third group of

many levels, and in any, usually many, and indeed it may be almost every, segment; in most cases of disseminated sclerosis there is no ascending or descending secondary degeneration; in disseminated sclerosis the grey matter of the spinal cord is often involved; in disseminated sclerosis the brain and the peripheral and cranial nerves are often (usually) involved.

In disseminated sclerosis the toxin seems to have a selective action for the white matter of the nerve tubes as well as for the neuroglial tissue, for, as I figured in the first edition of my book on the *Spinal Cord*, published now thirty-three years ago, compound granule corpuscles and fatty globules are, in some cases, met with in large numbers, not only in the sclerotic patches, but in the lymphatic spaces and around the blood-vessels, while the axis-cylinders are characteristically spared.

Subacute combined degeneration does not appear to be a primary "system" disease of the spinal cord. The lesion seems to commence in the form of isolated patches of degeneration in the posterior, lateral, and anterior columns; the coalescence of these isolated patches, in which the axis-cylinders are destroyed, leads to the production of secondary ascending and descending degeneration, which at certain stages of the disease might lead one to suppose that the lesion was a "system" disease (primary degeneration) of the affected tracts.

It seems probable that in disseminated sclerosis some developmental or congenital defect of the neuroglial or nervous tissue (perhaps similar to or analogous to the gliomatosis in syringomyelia), which renders it more vulnerable or liable to be affected by irritation than the neuroglial or nervous tissue of the normal individual, is an important factor in the production of the disease. The comparatively early age at which disseminated sclerosis is developed, and the fact that it occasionally occurs in young children, seem in favour of this view.

In subacute combined sclerosis the lesion is greatest in extent

cases, as we shall afterwards see, these two forms of lesions are combined" (p. 31).

"*The system lesions* of the spinal cord are either *primary* (*i.e.* arising independently of any previous lesion) or *secondary* (*i.e.* resulting from some previous morbid condition). To the secondary system lesions the term '*secondary degeneration*' is usually applied" (p. 32).

"The great characteristic of an 'indiscriminate' lesion is that it is not, *of necessity*, limited to any particular physiological tract, but may affect any part of the transverse section, though it occasionally, but rarely, happens that an indiscriminate lesion may be limited to a definite physiological tract" (p. 51).

in the mid-dorsal region, and involves more particularly the posterior columns, the crossed pyramidal tracts, the direct cerebellar tracts, and the direct pyramidal tracts; ascending and descending secondary degenerations are conspicuous features; the grey matter of the spinal cord is not involved; and the lesions very rarely indeed occur above the middle of the pons, and not, so far as I know, in the peripheral nerves.

The rapid passage of the ataxic-spastic or spastic stage of the disease, with increase of the deep reflexes, into the flaccid stage, with complete paraplegia, muscular atrophy, and abolition of the deep reflexes, has not, so far as I know, been satisfactorily explained by any post-mortem findings. No pathological changes in the anterior cornua, anterior nerve-roots, or motor peripheral nerves have, so far as I know, been found to explain the condition; perhaps there may be a lesion in the motor nerve-endings. So far as I know there are no observations on this point; it should be investigated.

ON AN OUTBREAK OF SEPTIC PHARYNGITIS.

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DURING the latter part of January and in February an outbreak of septic pharyngitis was prevalent in Edinburgh. A number of cases occurred among the domestic staff of the Royal Infirmary. They were admitted to a special ward, and came under my care, thus affording me an opportunity of studying the condition.

Up to the end of February I had seen 35 cases among the hospital maids alone, and this account is based on these cases.

Symptoms.—All the patients complained of a sore throat, and in most instances this was the only complaint. Headache was frequently admitted on direct inquiry. Earache, backache, and pains in the bones were present in a few instances.

The temperature was usually raised. It never exceeded and seldom reached 103° F. The common figure was 101° F. A few cases were afebrile.

The tongue was densely coated with fur in nearly all the cases.

In all the tonsils were greatly swollen. The uvula was swollen and often deviated to one side, generally the left. All the cases showed a membranous exudation. This seemed to begin as discrete, yellowish, translucent patches over the crypts. In the