CLINICAL STUDIES. XII.—THE PROGNOSIS IN DISSEMINATED SCLEROSIS; DURATION IN TWO HUNDRED CASES OF DISSEMINATED SCLEROSIS.

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.

In the great majority of cases disseminated sclerosis, sooner or later, causes death; consequently the ultimate prognosis is extremely unfavourable.

The duration of the disease varies greatly in different cases. The course is usually slow and chronic—the disease may last for thirty or more years before the fatal termination is reached. In rare cases the disease pursues a rapid course. In a few rare and exceptional cases the disease seems to be permanently arrested, and a cure, or what is, practically speaking, a cure, takes place.

In some cases the symptoms, once they are developed, pursue a progressive course from bad to worse; but in many cases the downward progress is from time to time interrupted by periods of improvement or complete remission of the symptoms. In some cases the symptoms (giddiness, numbness, diplopia, inco-ordination, loss of power, dimness of vision, nystagmus, volitional tremor, speech affection, etc.) entirely disappear, or almost entirely disappear, for a time. These periods of improvement and remission are very deceptive, for they may lead one to give a favourable prognosis, and, if any special plan of treatment is adopted, to attribute the amelioration to that treatment. Unfortunately, experience shows that, in the great majority of cases of this kind, the improvement is merely temporary. Everyone who has had much experience of disseminated sclerosis knows that although the patients often improve, and, in some instances, apparently for a time get quite well, it is only in very rare instances that the improvement is lasting. The great majority of cases sooner or later relapse. In very rare cases the improvement is so marked (the symptoms completely disappearing) and so prolonged as to warrant the belief that a permanent arrest or cure has taken place; and it seems only reasonable to suppose that in a disease like disseminated sclerosis, in which the symptoms may entirely disappear for a time (for several months or years), permanent arrest and a cure would occasionally occur. The wonder is that permanent arrest and cure do not more frequently take place.

In some of the rare cases in which the symptoms completely disappear and an (? permanent) arrest of the disease seems to take place, optic atrophy or the Babinski sign remains; but these conditions are to be regarded as results rather than active manifestations of the disease.

In common with many authorities I have for many years believed and taught that the patches of sclerosis, which are the pathological substratum of disseminated sclerosis, are due to the irritation produced by some form of toxin carried to, and distributed through, the nervous tissues by the blood-vessels. The recurrence from time to time of the symptoms after periods of improvement and remission is very suggestive of repeated intoxications. If disseminated sclerosis is due to a toxin, the toxin, whatever it is, is probably produced within the body. It seems much more difficult to suppose that fresh doses of the toxin are introduced again and again into the body from without during a long period of years.

Now, if the exacerbations and relapses in disseminated sclerosis are due to recurring intoxications, it is not unreasonable to suppose that, in some cases, the development of the toxin from within, or the absorption of the toxin from without, may cease, and that a permanent arrest and cure may occur.

With the object of trying to determine the duration of the disease, and so arriving at one of the data for a satisfactory prognosis, I have carefully analysed the results in 200 of the cases which have come under my observation in hospital and private practice.

Results of Treatment in Two Hundred Cases of Disseminated Sclerosis.

So far as I know, there are no detailed and definite statistics showing the duration and results of treatment in any considerable number of cases of disseminated sclerosis. I have consequently been at great pains to follow up my cases and to ascertain the duration of the disease and the present condition of the patients. In 200 cases, which I have recently analysed, the results up to the present date (October 1916) are as follows:—106 of the 200 cases have died; 64 cases are known to be still alive; and in 30 cases the result is not known. Of the 64 cases which are known to be still alive, 42 are much worse, 12 are *in statu quo*, 7 are greatly improved, and 3 quite well. (See Table I.)

TABLE I.—SHOWING THE RESULTS IN TWO HUNDRED CASES OF DISSEMINATED SCLEROSIS.

Died			106 cases
Still alive—Worse	42 cases	64 „	
In statu quo	12 „		
Greatly improved	7 „		
Quite well	3 „		
Not known			30 „
Total cases			200

The Total Duration of the Disease Since the Commencement up to the Present Date (*October* 1916).—This was definitely ascertained in 170 cases; the average duration of the disease in these 170 (fatal and non-fatal) cases is, up to the present date, 12 years and 1 month. In one case the duration of the disease was 37 years, and in no less than 14 cases the disease has lasted for more than 25 years. (See Table II.)

TABLE II.—SHOWING THE TOTAL DURATION IN ONE HUNDRED AND SEVENTY CASES OF DISSEMINATED SCLEROSIS IN WHICH THE RESULT WAS KNOWN IN OCTOBER 1916.

½ year	1 case			Brought forward	140	
1 „	2 cases			20 years	5 cases	
2 years	6 „	32 cases		21 „	4 „	
3 „	11 „			22 „	3 „	16 cases
4 „	12 „			23 „	4 „	
5 „	7 „			24 „	...	
6 „	7 „			25 „	2 „	
7 „	9 „	41 „		26 „	3 „	
8 „	10 „			27 „	1 case	7 „
9 „	8 „			28 „	...	
10 „	11 „			29 „	1 „	
11 „	10 „			30 „	3 cases	
12 „	5 „	42 „		31 „	...	
13 „	9 „			32 „	1 case	5 „
14 „	7 „			33 „	...	
15 „	7 „			34 „	1 „	
16 „	4 „			35 „	1 „	
17 „	3 „	25 „		36 „	...	2 „
18 „	8 „			37 „	1 „	
19 „	3 „					
Carry forward	140			Total cases	170	

The Total Duration in 106 *Fatal Cases of Disseminated Sclerosis.*—In the 106 cases in which the disease proved fatal the average duration was 10 years and 8 months; the shortest duration was 7 months, and the longest duration was 37 years.

The exact duration in each of the 106 fatal cases is shown in the following table:—

TABLE III.—SHOWING THE EXACT DURATION IN ONE HUNDRED AND SIX FATAL CASES OF DISSEMINATED SCLEROSIS.

7 months	1 case		Brought forward	78	
1 year	2 cases		15 years	5 cases	
2 years	4 „	23 cases	16 „	2 „	14 cases
3 „	7 „		17 „	1 case	
4 „	9 „		18 „	5 cases	
5 „	6 „		19 „	1 case	
6 „	7 „		20 „	4 cases	
7 „	7 „	31 „	21 „	2 „	8 „
8 „	8 „		23 „	2 „	
9 „	3 „		25 „	1 case	
10 „	8 „		26 „	2 cases	4 „
11 „	5 „		27 „	1 case	
12 „	4 „	24 „	34 „	1 „	1 case
13 „	4 „		37 „	1 „	1 „
14 „	3 „				
Carry forward	78		Total cases	106	

From this table it will be seen that in 23, or 21·6 per cent., of the 106 fatal cases, the disease terminated in less than 5 years; in 54, or 50·9 per cent., of the 106 fatal cases in less than 10 years; in 78, or 73·5 per cent., of the 106 fatal cases in less than 15 years; and in 92, or 86·7 per cent., of the fatal cases in less than 20 years.

The following are brief clinical records of two cases in which a permanent cure seems to have taken place, and of two cases in which the disease lasted respectively for 37 and 34 years:—

CASE I. *Disseminated Sclerosis; Recovery.*—Female, aged 49, seen 23rd June 1902.

Complaints.—Numbness and weakness in left hand and arm.

Previous History.—In 1891 (11 years previously), after influenza and rheumatism, temporary numbness and loss of power in the left hand developed. Several attacks of the same sort have occurred since. In 1892 numbness and loss of power developed in the feet and legs. The patient at this date consulted Sir Christopher Nixon of Dublin, who diagnosed disseminated sclerosis, who on 28th June 1902 wrote me: "My recollection of Mrs. ——'s case is that it was one of multiple cerebro-spinal sclerosis, and I am surprised to hear that she got at any time completely rid of her symptoms. She had, at the time I saw her, spastic gait, intention tremor, slight degree of nystagmus, and some attacks of giddiness. I saw her, I think, twice."

In October 1893 the patient consulted Mr. (now Sir) George Berry on account of loss of vision, first in one eye and then in the other. On 24th June 1902 Mr. George Berry wrote me: "On 30th October 1893 the patient had V = $\frac{20}{100}$ left eye; no ophthalmoscopic changes; no pain on pressing the eye back into orbit. My diagnosis was *retrobulbar neuritis* (peripheral and probably rheumatic)."

State on 23rd June 1902. — Knee-jerks markedly exaggerated, particularly the left; Babinski sign on the left side; some (slight) inco-ordination of the left hand, very slight inco-ordination of the right hand on performing the finger-nose test; no nystagmus, volitional tremor, or speech affection (the articulation had been previously affected); no difficulty in urination; no ankle-clonus; no defects of memory.

Diagnosis.—Disseminated sclerosis, confirmed by the statements of Sir Christopher Nixon and Sir George Berry quoted above.

Subsequent Progress of the Case.—On 24th June 1904 the patient's doctor wrote me: "She is quite well, and has been quite well since you saw her in June 1902; the knee-jerks are still markedly exaggerated; the Babinski sign was not obtained on 23rd June." And again, *on 16th January* 1905: "The patient remains quite well."

On 13th September 1916 the patient wrote me saying that she continued to feel quite well.

CASE II. *Atypical Disseminated Sclerosis; Apparent Recovery.*—Female, aged 26, was seen on 25th July 1899.

History.—The patient, who is a somewhat nervous girl, enjoyed good health until three and a half years ago (*January* 1896); she then gradually lost the sight of the left eye. She consulted Dr. George Mackay, who found optic neuritis present in the left eye, with marked impairment of vision. Under treatment the optic neuritis gradually disappeared and vision was to some extent regained. *In August* 1898 she lost vision in the right eye. On 30th August 1898 optic neuritis was found to be present in the right eye. Under treatment this gradually improved. Her medical man (Dr. Edward Carmichael) has kindly sent me the following report from Dr. George Mackay on the condition of the optic discs and vision: "Miss C. is hypermetropic and astigmatic. In the beginning of January 1896 she began to have pain above the left eyebrow and in the temple.

"*On 15th January* 1896 she first came to me with left optic neuritis, very vivid hyperæmia of the disc substance, but not much tortuosity of veins nor much swelling of the disc. Some tenderness on backward pressure of the *left* globe.

RV with glasses = $\frac{6}{9}$ good field.
LV ,, = hand movements only in the outer part of the field.

She was ordered eye rest, leeches to the temple, and sod. salicyl. Later the temple was blistered, and pot. iod. with hyd. perchlor. given.

"*By* 11*th February* LV had returned to $\frac{6}{36}$.

"*By* 7*th March* exudation gone, disc pale and partially atrophied, but good field for hand movements.

"She returned to work, and did not consult me again until 29th October 1897, when I found vision unchanged. She is naturally high-coloured, and her right disc always looked hyperæmic, but showed no sign of inflammation until 30th August 1898, when, in my absence, Dr. Matthew (my assistant) found the right disc hazy, but RV still $=\frac{6}{9}$ with difficulty.

"*On* 15*th September* I found RV with glasses $=\frac{6}{24}$. No pain nor tenderness. A decided scotoma for colours to the inner side of the point of fixation and across the middle line, and diagnosed a retro-bulbar neuritis. The same kind of treatment was again adopted, but sod. salicyl. pushed more freely, and perspiration encouraged by hot pack.

"*By* 31*st January* 1899 RV returned to $\frac{6}{9}$ partly, and by 7th April continued the same, but trace of scotoma for colours still present. Right disc hyperæmic but not obscured by exudation. LV had improved to $\frac{6}{12}$ partly, and she seemed much better in all respects. Complained that her sight became worse on exertion. I have not seen her since, and much regret to get your report of this new development."

A month ago (*in June* 1899) she was accidentally knocked over in the street. Since then she has complained of numbness and weakness in the legs and unsteadiness and difficulty in walking.

State on 25*th July* 1899.—Optic atrophy present in the left eye; the right disc seemed normal; the knee-jerks were both markedly exaggerated; slight ankle-clonus and a double extensor response were present on both sides; marked Rombergism; inco-ordination and some volitional tremor in the right hand. The general health was good; there was no giddiness, no headache, no vomiting, no nystagmus, no speech affection, no urinary derangement, no objective disturbance of sensation, no loss of the muscular sense. The hands, feet, and face were cold and blue, especially on exposure to cold; menstruation was regular and natural. There were no signs of congenital or acquired syphilis.

Diagnosis.—I diagnosed the case as one of disseminated sclerosis, and my son (Dr. Edwin Bramwell), who saw the patient with me, agreed with this diagnosis.

Arsenic and nitrate of silver were prescribed.

Subsequent Progress of the Case, 10*th June* 1902.—Much better. The only thing she now complains of is blueness and coldness of the face, hands, and feet, and sometimes a numb feeling in the hands and feet.

The knee-jerks are still exaggerated; ankle-clonus is still present, especially in the right foot; the plantar reflex shows marked extension in the right foot, no toe movement in the left; slight inco-ordination and some volitional tremor still present in the right hand. Distant vision in the right eye $= \frac{6}{8}$, in the left $\frac{6}{36}$. Near vision with glasses, right $= 0{\cdot}5$, left $= 0{\cdot}5$ (imperfect). The left disc is still very pale.

26th January 1905.—Patient says that she has been quite well since last seen. Face, hands, and feet still blue and cold; knee-jerks still exaggerated; no ankle-clonus; extensor response present in the right, absent in the left foot; left disc still markedly paler than the right. The Rombergism, and the inco-ordination and intention tremor in the right hand, which were noted in 1899 and 1902, are no longer present.

On 11th August 1916 the patient wrote: "My health keeps very well. I may state that I have never been off business except with a slight cold since seeing you."

CASE III. *Typical Disseminated Sclerosis of* 37 *Years' Duration.*—Female, aged 34, was seen on 25th July 1890, and died in February 1913.

History.—The disease commenced, the result, she thinks, of a wetting three weeks before the first symptoms, at the age of 20 (year 1876). The first symptoms were loss of vision in the right eye, and loss of power in the right arm and leg. These symptoms were of temporary duration. During the next ten years she suffered from recurring attacks of powerlessness and loss of feeling in the right side; they usually lasted for two or three days. For the past year (1889) has been much worse; suffered from shaking in the arms, especially the right; some speech difficulty; some loss of vision, particularly in the right eye; some difficulty with water and bowels.

Condition on Examination (*25th July* 1890).—A big, tall, healthy looking woman. Walks in a very ataxic and spastic way (spastic-ataxic paraplegia), the right leg worse than the left; knee-jerks greatly increased; double ankle-clonus (double Babinski noted later); marked volitional tremor, especially in the right arm; articulation typical; some partial optic atrophy; some difficulty both with bladder and rectum (forcing, occasional dribbling, and marked constipation); no nystagmus; menstruation regular.

Subsequent Progress of the Case.—General health continued good. Difficulty in walking and volitional tremor became more marked; the patient suffered from giddiness, speech affection, nystagmus, occasional headache, marked difficulty in making water, marked constipation, knee-jerks greatly exaggerated, double ankle-clonus, double Babinski. Died in February 1913, having been bedridden, and practically helpless, for two years.

CASE IV. *Typical Disseminated Sclerosis of 34 Years' Duration.*—Male, aged 24, was seen on 18th March 1894, suffering from typical disseminated sclerosis.

History.—At the age of 2 had an attack of scarlet fever and bronchitis; volitional tremor developed after this and has continued more or less since. At the age of 18 got very much worse without any apparent cause—the volitional tremor became extremely marked, speech became affected, and there was difficulty with the water.

Condition on Examination.—Walking difficult (spastic and ataxic paraplegia); knee-jerks markedly exaggerated; double ankle-clonus (Babinski detected later); abdominal reflex absent; occasional giddiness; very marked volitional tremor affecting both arms, head, and legs; marked speech affection; expression vacant; more emotional (laughs too easily); occasional pain in the back; occasional difficulty in urination—dribbling and precipitant; bowels very constipated; no nystagmus.

Died in Longmore Hospital, Edinburgh, 6th December 1906. The typical symptoms of disseminated sclerosis had been present since his admission twelve years previously.

DR. PASCAL ROUGON: ZOLA'S STUDY OF A SAVANT.

By J. BARFIELD ADAMS, L.R.C.P., L.R.C.S.,
Member of the Medico-Psychological Association.

THE sequel of a novel is rarely a success. There is the danger of an anticlimax. The puppets, which played the parts of hero and heroine in the first book, often occupy subordinate positions in the second, and in this way disappoint the reader. But the commonest cause of the failure is the inability of the novelist to preserve the identity of his characters while allowing for the effect of the changed times and circumstances under which he presents them to his audience.

If it be difficult to write one sequel, what must it have been for Émile Zola to write nineteen? He had not only to describe with accuracy the mental and physical changes wrought by varying circumstance and by the hand of time upon the actors on his stage, but he had to contend with the alterations in his own mind as years passed by. Zola was twenty-two years writing his Rougon-Macquart series of novels, and who looks at things from the same point of view at the age of fifty-three as he did at thirty-one? But in spite of shifting scenes and different circumstances, whether they rise or fall in the social scale, the master has preserved the identity of his characters. They have,