Acute optic neuritis: prognosis for development of multiple sclerosis

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The clinical picture of acute optic neuritis—a rapid failure of vision with a scotomatous visual field defect in one or both eyes and paraorbital pain—may present in a variety of conditions such as retinal vascular lesions, raised intracranial pressure, toxic metabolic and deficiency diseases, or trauma (Woods and Rowland, 1931; Benedict, 1933; Carroll, 1952; Walsh, 1957; Hierons and Lyle, 1959; Kennedy and Carroll, 1960; McAlpine, Lumsden, and Acheson, 1965; *British Medical Journal*, 1965; Björkenheim, 1966). In the majority of these the primary diagnosis can be made by appropriate examination and investigations. There remains a group which may be termed idiopathic or cryptogenic optic neuritis, since the condition does not appear to be a symptom of other primary disease. Of these about one-third have sufficient evidence from the history or current findings of more than one neurological lesion to justify the diagnosis of multiple sclerosis (Adie, 1930 and 1932; Marshall, 1950; Carroll, 1952). However, the other two-thirds, the majority of the idiopathic group, present a problem in aetiology and prognosis. It is with reference to this group in particular that the question has arisen of multiple sclerosis as the final cause of optic neuritis, only to be revealed by subsequent events. Thus McAlpine *et al.* (1965) state that multiple sclerosis is the only common cause of acute optic neuritis. Estimates of the proportion of cases of acute optic neuritis later developing multiple sclerosis vary from 11.5% (Kurland, Auth, Beebe, Kurtze, Lessell, Nagler, and Nafzger, 1963) to 85% (Lynn, 1959, adapted by McAlpine, 1964). Many published reports are irrelevant to this problem, since they fail to distinguish between patients with and without signs and symptoms suggestive of multiple sclerosis at the time of the initial attack. McAlpine (1964) commented that published data on the frequency of later development of multiple sclerosis are scarce.

The present paper contributes evidence on this point from a follow-up study of cases seen in the Neurology Service at Oxford between 1946 and 1966. They do not comprise all the cases in the Oxford area, but are considered to represent an unselected

group since they were referred both from general practitioners to medical and surgical neurology departments and *via* the Oxford Eye Hospital. In addition to the proportion developing multiple sclerosis, the frequency of neurological relapses, the degree of later disability, both visual and general, and factors influencing the ultimate prognosis have been studied.

MATERIALS AND METHODS

The records of a series of 123 patients originally diagnosed as having optic neuritis were analysed in an earlier paper on the clinical features and time course of the acute attack (Bradley and Whitty, 1967). In that series 50 of the original cases were rejected, 12 of these on the grounds that the visual fields were not charted in the initial episode, or that the fields, though charted, did not conform to the particular form of scotomatous defect we required for our clinical definition of optic neuritis. However, when the other clinical features of these 12 and the subsequent changes in visual acuity were examined they were found to behave in an exactly similar manner to the 73 homogeneous cases. We have therefore included them in our present analysis, making a total of 85 cases. Seventy-six of these were successfully traced (Table I): nine were lost to follow-up. Sixty-three of the former were examined personally and three, not seen personally, were house-bound but were under out-patient supervision in the Department, with an established diagnosis of multiple sclerosis. Information on the remaining 10 came from family doctors. Three of these had died of

TABLE I
DATA ON THE FOLLOW-UP OF PATIENTS

	Total	Re-examined or developed undoubted M.S.	Traced		Lost to F.U.
			Not examined	Died of other causes	
Unilateral optic neuritis	64	48	7	2	7
Bilateral at same time	5	3	—	1	1
Bilateral, less than 3-month interval	9	9	—	—	—
Bilateral, more than 3-month interval	7	6	—	—	1
Totals	85	66	7	3	9

other causes (coronary thrombosis, carcinoma of pancreas, riding accident). Information on the remaining seven was considered unreliable, since 33% of 43 patients personally examined who brought letters from their doctors were found to have neurological signs unknown to the doctors. All these 10 were therefore rejected from further study.

Sixty-six patients form the basis of this paper. During the period of follow-up one patient developed rheumatoid arthritis, one pulmonary sarcoidosis, and one had a para-oesophageal mass which was revealed by chest radiograph at the time of the attack of optic neuritis and which remained the same size at the time of follow-up one year later. Inquiries were made about recurrent attacks of optic neuritis, subsequent neurological symptoms, a history of sinusitis, symptoms suggestive of diabetes mellitus, and the family history. Intercurrent illnesses were also noted. Examination included a full neurological examination with measurement of visual acuity on Jaeger and Snellen charts and the plotting of peripheral and central visual fields. The blood pressure was measured in all and a general examination was performed.

A life chart was then constructed for each patient, with details of each neurological episode plotted on a time scale originating from the first attack of optic neuritis. The minimum number of lesions necessary to explain each symptom and sign in each episode was recorded on this life chart. Where a symptom was accompanied by a sign of the same lesion, only this one lesion was recorded, though the occurrence of both symptoms and signs were noted for the diagnosis of multiple sclerosis. The data from all these charts were then analysed as a whole, and in the sub-groups previously described (Bradley and Whitty, 1967). For purposes of this survey of the late sequelae of optic neuritis, the diagnostic criteria used were largely those of McAlpine *et al.* (1965).

DEFINITIONS

Optic neuritis The acute onset of blurred vision in one or both eyes, without demonstrable cause and without pre- or co-existing neurological signs or symptoms other than dizziness.

Definite multiple sclerosis An attack of optic neuritis, later followed by one or more neurological symptoms, relapsing and remitting in character, together with two or more signs (pyramidal and at least one other) of multiple lesions of the central nervous system.

Probable multiple sclerosis An attack of optic neuritis later followed by the development of a sign indicating a separate neurological lesion, without a history of relapsing symptoms.

Devic's disease (neuromyelitis optica) An attack of optic neuritis later followed by rapid transverse myelitis without signs or symptoms of other disseminated lesions.

Mobility grade

Grade 1. Unrestricted—normal employment or domestic life.

Grade 2. Restricted—able to walk unaided up to $\frac{1}{2}$ mile, and able to use public transport.

Grade 3. Markedly restricted—able to move out of doors with difficulty for up to $\frac{1}{4}$ mile, usually with sticks.

Grade 4. Mobile at home—able to move with difficulty about house with help of furniture; unable to climb stairs.

Grade 5. Immobile at home—chair- or wheel-bound.

Grade 6. Bedridden—permanently.

Neurological lesion A patient who developed at any particular time signs and/or symptoms which could have been caused by one lesion of the central nervous system was deemed to have suffered one 'neurological lesion'. If lesions at three sites in the central nervous system were required to explain the signs and symptoms the patient had suffered three 'neurological lesions'.

Neurological episode A patient who at a particular time developed signs and symptoms of one or more neurological lesions which had not been present before was deemed to have suffered a 'neurological episode' at that particular time.

RESULTS

SEX AND SIDE INVOLVED The findings in the 66 cases are essentially the same as in the full series of 73 reported elsewhere (Bradley and Whitty, 1967) and indicate that no bias has been introduced by the loss of 22% of the patients at follow-up. The age structure and distribution of month of onset in the present series were also similar to the full series.

THE FOLLOW-UP PERIOD This ranged from six months to 20 years, the mean being 10.2. Ninety per cent were followed up for four years or more: 33% for 13 or more years.

NEUROLOGICAL LESIONS EXCLUDING OPTIC NEURITIS One hundred and nine recognized lesions developed in the 66 patients—that is, 1.65 lesions per patient. More important, in view of the different periods of follow-up, is the frequency of lesions per patient-year. Over the whole series, 109 lesions developed in a total of 672 patient-years, an average of 0.18 lesions per patient-year. The distribution is shown in

TABLE II
FREQUENCY DISTRIBUTION OF THE NUMBER OF
NEUROLOGICAL LESIONS PER PATIENT-YEAR IN THE
WHOLE SERIES

Neurological lesions per patient-year	Patients	
	No.	%
0	29	44
0.05-0.10	11	17
0.11-0.50	14	21
>0.50	10	15
Devic's disease	2	3
Total	66	100

Table II. Forty-four per cent of patients suffered no recognized subsequent lesion, 38% suffered up to 0.5 lesions per year, and 15% suffered more than 0.5 lesions per year. Three per cent developed a transverse myelitis. There was no significant difference between the sub-groups. The average follow-up period was 9.2 years for those who developed no lesions, which was only slightly less than the period of 10.3 years for those who did develop further neurological lesions.

NEUROLOGICAL EPISODES In Fig. 1 is recorded the proportion of patients at risk developing a neurological episode and a further attack of optic neuritis in either eye at each period after the initial attack of optic neuritis. The episode rate—that is, episodes per patient—was greatest in the first year after the optic neuritis, the frequency decreasing exponentially thereafter. In patients whose progress subsequent to the optic neuritis was observed from six to 20 years it was found that the episode rate during this period was low. Occasional episodes occurred 12 or more years after, but in proportion to the number of patients being observed at that time they were rare when compared with the similar proportion in the first six-year period. The result at 20 years is derived from only five patients and can be discarded. The pattern of recurrence of optic neuritis is similar to that of other neurological episodes. Females continue having neurological episodes for 12 years after optic neuritis, while only one male had a further episode after six years, though the numbers were small in the male group. The length of follow-up was the same for the two sexes.

DIAGNOSIS OF MULTIPLE SCLEROSIS In Fig. 2 we give the number of patients who during the course of follow-up come into the three groups: definite multiple sclerosis (in this we include Devic's disease) 13 (20%); probable multiple sclerosis 21 (31%); and no further neurological disease than optic neuritis 32 (49%). The interval between the initial optic neuritis and the development of signs and symptoms sufficient for the diagnosis of definite multiple sclerosis is plotted, and compared with the group of probable multiple sclerosis and those in whom no diagnosis other than optic neuritis was made. Definite multiple sclerosis had declared itself by four years in all but one case, though patients continued to be observed for up to 20 years in some cases.

The one patient in whom definite multiple sclerosis was diagnosed 18 years after the attack of optic neuritis was a woman of 46 years at the time of attack. At 55 years she had an episode of vertigo and vomiting lasting one week. When seen for this

FIG. 1. The percentage of patients at risk suffering a symptomatic neurological episode or an attack of optic neuritis between each period, findings at follow-up examination excluded. Numbers above columns show total patients at each period.

FIG. 2. The time interval for the development of sufficient symptoms and signs for the diagnosis of 'definite multiple sclerosis' (including Devic's disease), 'probable multiple sclerosis', and the follow-up period of cases with no further neurological disease.

survey she was aged 64 years and had minimal nystagmus and a slight right facial weakness, slight ataxia of both arms, and bilateral extensor plantar responses.

The one neurological sign required for the diagnosis of probable multiple sclerosis was most commonly detected at the time of follow-up. There was no difference between the sexes in the time elapsing before the diagnosis of definite or probable multiple sclerosis. The cumulative proportion of patients at risk suffering definite or probable multiple sclerosis at each period after the initial attack of optic neuritis is shown in Figure 3. The proportion with definite multiple sclerosis and Devic's disease reaches a plateau of 20% in four years after the optic neuritis and shows no significant changes thereafter. The proportion with probable multiple sclerosis rose progressively as more patients came to the follow-up examination.

MOBILITY GRADE FOLLOW-UP Despite the diagnosis of definite multiple sclerosis, including Devic's disease, in 13 cases, and of probable multiple sclerosis in a further 21, the mobility grade at the time of follow-up examination was remarkably high. All the probable multiple sclerosis cases were in Grade 1 (unrestricted). This applied also to seven of the definite multiple sclerosis; of the remainder of this group one was in each of the Grades 2, 4, 5, and 6. Both the cases with Devic's disease however were chair- or bed-bound (Grades 5 and 6). Perusal of the case notes showed that of the total of six

patients who became severely disabled, all had reached that state by four years after the initial attack of optic neuritis.

It will be recalled that of the 85 cases who initially formed the basis of this study (Table I) only three had died, all of unrelated conditions. Thus this favourable prognosis was not due to death of the most affected patients. There is no reason to suppose that patients lost to follow-up were different from those traced, but even if they were all bedridden this would still only increase the proportion in Grade 6 to 13%.

RECURRENT OPTIC NEURITIS Recurrent attacks of optic neuritis occurred in the initially affected eye in 12 patients. Simultaneous bilateral cases and later attacks involving the second eye have been excluded. Thus a recurrent attack occurred in 19%, and of these 74% suffered only one recurrence.

VISUAL ACUITY AT FOLLOW-UP Eighty-six per cent of patients had 6/6 or 6/9 vision in the eye which had suffered the attack of optic neuritis, and in only 6% was it as bad as 6/36. There was a slight tendency for the acuity to be worse where recurrent attacks of optic neuritis had occurred, but this tendency was not statistically significant.

FACTORS IN LONG-TERM PROGNOSIS IN PATIENTS WITH OPTIC NEURITIS The data on the 66 patients in this study were analysed to reveal factors bearing on their long-term prognosis. The neurological lesion rate, the diagnosis of multiple sclerosis, the mobility grade, and the rate of recurrent optic neuritis were sub-divided according to sex, age, side of attack, pain with attack, fundal appearances in attack, sinus radiograph abnormalities, month of attack, visual acuity at its worst, and time for vision to return to normal. The analyses were further sub-divided according to whether the initial attack was unilateral or bilateral and according to the time interval in bilateral attacks. No clear differences were detected between unilateral and bilateral sub-groups, but the numbers were too small in the latter to reveal minor variations.

Sex Males developed slightly less neurological lesions per patient-year than females, though this difference was not statistically significant. The frequency with which definite or probably multiple sclerosis was diagnosed was similar in the two sexes.

Age There was a tendency for all indices to become slightly worse with increasing age at the time of the optic neuritis (Table III), that for the lesion-rate being statistically significant at the 5% level by the method of correlation analysis. The diagnosis of multiple sclerosis was made more

FIG. 3. The cumulative percentage of patients with the diagnosis of 'definite multiple sclerosis' (including Devic's disease), and 'probable multiple sclerosis' at each time interval after optic neuritis.

TABLE III

EFFECT OF AGE AT THE TIME OF THE OPTIC NEURITIS ON THE DEVELOPMENT OF NEUROLOGICAL DISEASE IN WHOLE SERIES

Age (yr)	Diagnosis of M.S.			Lesions per patient-year	Mobility grade	
	'Definite'	'Probable'	Nil		1	2+
	%	%	%		%	%
0-10	100 ¹	—	—	3.33	100	—
11-20	—	60	40	0.60	100	—
21-30	18	18	64	1.56	100	—
31-40	20	26	54	1.61	90	10
41-50	20	35	45	1.75	85	15
51-60	25	75	—	2.08	75	25

¹Only one case.

often, the lesion rate per patient-year increased, and the mobility grade worsened with increasing age.

Side Patients whose initial attack of optic neuritis involved the right eye, though less frequent in numbers, developed more neurological lesions per patient-year (0.23 compared with 0.11), and this difference was statistically significant at the 1% level. A similar though not statistically significant trend was noted for the right eye to indicate a poorer prognosis for the diagnosis of multiple sclerosis, and for the recurrence rate of optic neuritis.

Fundal appearances in initial attack of optic neuritis The presence or absence of papilloedema bore no prognostic significance for later neurological disease.

Sinus radiographic abnormalities Patients in whom radiographs of the paranasal air sinuses showed abnormalities developed fewer neurological lesions per patient-year (0.08) than those with normal sinuses (0.23). The difference was statistically significant at the 1% level. A similar, though not statistically significant trend was noted for the development of multiple sclerosis.

Pain with optic neuritis Patients whose optic neuritis was painful were more likely to develop further neurological lesions (0.19 lesions per patient-year) than those without pain (0.12), this result being statistically significant at the 5% level. A similar but not significant result was found for the diagnosis of multiple sclerosis.

Recurrent optic neuritis As might be expected, patients who developed recurrent attacks of optic neuritis also developed more neurological lesions per patient-year. This was significant at the 0.1% level. A similar though not statistically significant trend was noted for the development of definite multiple sclerosis.

Visual acuity and month of onset These showed no prognostic significance for further lesions.

Atypical scotomata Six cases had scotomata during the attack of optic neuritis which were atypical in being other than central, centrocaecal, or paracentral—most being quadrantic defects and all occurring in the unilateral sub-group. The incidence of the diagnosis of multiple sclerosis and the neurological lesion rate were lower in these, though differences were not statistically significant.

Cerebrospinal fluid at initial attack of optic neuritis The cerebrospinal fluid was examined in only 15 of the cases at the time of the initial attack and was abnormal in only four. The gamma-globulin level was measured in recent cases only and will not be discussed. The frequency of late neurological disease was similar in those with normal and abnormal cerebrospinal fluid.

DISCUSSION

The clinical diagnosis of multiple sclerosis is always to some extent tentative; and in cases where it has been confidently presumed for many years it may finally prove to be wrong (Matthews, 1962). At present the necropsy examination is the only certain diagnostic arbiter. Recent work on the gamma-globulin fraction of the cerebrospinal fluid protein (Foster and Horn, 1962; Prineas, Teasdale, Latner, and Miller, 1966) shows that this may help to distinguish established multiple sclerosis from other neurological diseases. It remains to be seen whether the gamma-globulin level at the time of the initial attack of optic neuritis will forecast the development of multiple sclerosis. Gamma-globulin levels were not available in this study and the cell count, total protein, and Lange curves of cerebrospinal fluid were unhelpful.

McAlpine *et al.* (1965) suggested that the diagnosis of multiple sclerosis should be made in patients with an attack of acute optic neuritis followed by one or more neurological relapses and presence of neurological signs of two or more lesions of the central nervous system. However, the numerical approach cannot supersede clinical assessment, lest a patient with a past history of an attack of optic neuritis who suffers bilateral strokes be said to be suffering from multiple sclerosis. The diagnosis of definite multiple sclerosis was made in 13 cases (20%) on McAlpine's criteria and in all the case histories substantiated the diagnosis. However, these criteria have been regarded as too lax, especially for use in therapeutic trials (Schumacher, Beebe, Kibler, Kurland, Kurtzke, McDowell, Nagler, Sibley, Tourtellotte, and Willmon, 1965). The label 'probable multiple sclerosis' is a far less certain one. For this, the requirements of McAlpine *et al.* (1965), if accepted mechanically, could include in this category

patients with cervical myelopathy, a stroke, and many other conditions—and even a careful history might not always exclude them. This diagnosis was applied to 21 (31 %) of the cases in this series, though a sceptical neurologist might have made the diagnosis in fewer.

The total number of neurological lesions deduced from the patient's signs and symptoms offers a quantitative approach which is well suited to the present type of study. A similar attempt to quantify severity and progress of multiple sclerosis was developed by Alexander (Alexander, 1951; Alexander, Berkeley, and Alexander, 1958) and its value cogently argued. We have made no attempt to weight signs in preference to symptoms, though this might improve the method. The present study shows that 44% of those who suffer an attack of optic neuritis will develop no other neurological lesion in the next 10 years, and that over the whole series only 0.18 lesions develop per patient-year.

This relatively benign prognosis is worthy of emphasis. It compares favourably with previous reports of the annual relapse rate (a term based on 'neurological episodes' rather than 'lesions' as defined above) of 0.27 to 1.15 (Müller, 1949; McAlpine and Compston, 1952; Thygesen, 1953; Alexander *et al.*, 1958) in patients with multiple sclerosis.

The present study shows that most symptomatic neurological episodes (Fig. 1) occur in the first six years after the attack of optic neuritis. Similarly, if 'definite multiple sclerosis' were going to develop in a patient during the period of the study, it usually did so in the first four years. The interval between the optic neuritis and the transverse myelitis in the two cases of Devic's disease was six months and four years, respectively. Collis (1965) found that all of his patients who were going to develop multiple sclerosis had shown their first symptom within four years, though he does not record at what time the definite diagnosis was made. Taub and Rucker (1954) found that in more than half of the cases with multiple sclerosis the onset fell within the first five years, and since 'onset' was taken as the time when the patient was seen with the symptoms and not the time of their development (Collis, 1965), the real interval may be shorter.

Despite these findings, there are many cases recorded in the literature with long intervals between an attack of optic neuritis and subsequent symptoms of multiple sclerosis. Adie (1932) recorded a case with an interval of 24 years, and found the average interval 6.8 years. Even longer intervals of 29 years (Lynn, 1959) and 37 years (McAlpine and Compston, 1952) have been recorded. The average interval quoted by other authors ranges from 3.6 years to

eight years (Yaskin, Spaeth, and Vernlund, 1951; Wybar, 1952; Leibowitz, Alter, and Halpern, 1966). However, Otrádovec and Votočková (1962) and Kurland *et al.* (1963) found that the proportion of patients with multiple sclerosis rises with time after the initial optic neuritis, though the latter found the effect small after 10 years.

Comparison of the results of this study with others in the literature is difficult, not only because the criteria for the diagnosis of multiple sclerosis are frequently not stated, but also because many authors include all cases of acute optic neuritis, with or without other neurological signs, for follow-up. Here, since we attempted a prognostic study, those already having neurological signs and symptoms suggestive of other neurological lesions, at the time of the attack of optic neuritis, have been excluded. Table IV summarizes some of the previous reports on this problem. Reports in Section 1 may be compared with the present study. Estimates of the frequency of development of multiple sclerosis range from 11.5% in the study of Kurland *et al.* (1963) to 85% from Lynn's (1959) figures adapted by McAlpine (1964). Kurland *et al.* (1963) studied young male servicemen followed for 12 to 15 years and required agreement between a panel of neurologists for acceptance of the diagnosis of multiple sclerosis. McAlpine (1964) selected patients examined by Lynn (1959) after periods of from five to 29 years after the initial optic neuritis. It is difficult to explain such widely different estimates except by postulating a difference of diagnostic criteria. Another difficulty in comparison of such studies rests on the different lengths of follow-up of patients. A life table type of presentation provides information which is more easily compared.

However, for the clinician who has to deal with the individual case the need is to know what the chances are, on the simple data available, of one particular patient subsequently developing multiple sclerosis. Males developed this less frequently in Collis's (1965) series, and a similar result was obtained in the neurological lesion-rate in the present study, though in neither series was the difference statistically significant. Collis (1965) found that all his patients under the age of 20 at the time of the optic neuritis developed multiple sclerosis, while Taub and Rucker (1954) found only 14% (Collis incorrectly stated 6%). Both authors agree that it is unlikely to develop in cases who suffer optic neuritis after the age of 45. Kennedy and Carroll (1960) found 27% of a group of children under 16 years with optic neuritis developed multiple sclerosis, while Hierons and Lyle (1959) found 8% in a group of children under 13 years with bilateral attacks. The present study included only six patients under 20

years at the time of the optic neuritis (Table III): one developed sufficient neurological episodes for the diagnosis of 'Definite Multiple Sclerosis' and three others fell into the group of 'probable multiple sclerosis'. Above this age, there was a tendency for the proportion with 'definite multiple sclerosis' and for the neurological lesion-rate to rise with age; and this continued into the sixth decade. Advanced age seemed to offer no protection.

Kurland *et al.* (1963) tried to correlate a large number of factors in the initial optic neuritis with subsequent development of multiple sclerosis in a group of entrants to the U.S. Armed Forces. However, most of them proved negative. Of the total of 43 factors, only four showed a positive correlation, and, as they note, this number might be expected as a chance finding. Since the four factors were unequal pupils, absence of field defect, poorer than average vision, and higher than average intelligence, chance is perhaps the most likely explanation.

Pain with the initial optic neuritis had no bearing on later multiple sclerosis both in Collis's (1965) series, and in the present study. Similarly the fundal appearances in the attack, visual acuity, month of onset, and cerebrospinal fluid changes were all of no prognostic significance in the present study. Interestingly, Leibowitz *et al.* (1966) found that, in Israel, European Jews are six times more likely to develop multiple sclerosis following optic neuritis than those from Afro-Asia.

In the present study, patients whose initial optic neuritis affected the right eye were more likely to

develop the further neurological lesions of multiple sclerosis. Bradley and Whitty (1967) also found in acute optic neuritis that the right eye was affected less frequently than the left. Both findings remain unexplained. Radiographic evidence of sinusitis at the time of the optic neuritis conveyed a better prognosis for the later development of multiple sclerosis. This might suggest that some attacks of optic neuritis are precipitated by paranasal sinusitis and may form an aetiological category which can be separated from the general group with its proportion of multiple sclerosis. Similarly, patients with scotomata other than the typical central variety tended to develop less multiple sclerosis in later years, and this might suggest that some were due to lesions other than optic neuritis, such as retinal branch artery occlusion. We included these in the present series because all the other clinical features of the immediate attack were similar to the main group, as was the course of the actual optic neuritis. However, the differences shown in this follow-up study lend some support to the argument that the type of field defect should form part of the original diagnosis.

The relatively benign overall prognosis revealed in the present study is worth emphasis. At an average of 10 years after the attack of optic neuritis 91% of patients were completely unrestricted in their activities. Even in those with 'definite multiple sclerosis', 64% were unrestricted. This is far better than might be expected in multiple sclerosis in general (Müller, 1949; Lazarte, 1950). Bauer and Firnhaber (1965) found only about a third of patients

TABLE IV

Author	Date	Follow-up Period (yr)	Details	Def. M.S. (%)	Prob. M.S. (%)	Devic's Disease (%)	Leber's Disease (%)	Diabetes (%)	Nil (%)
<i>I. Excluding those with neurological signs and symptoms at initial attack of optic neuritis</i>									
Taub and Rucker	1954	10-15	—	32	—	—	—	—	68
Hierons and Lyle	1959	6	Bilateral adults	24	—	—	—	—	76
		4	Bilateral children	8	—	—	—	—	92
Lynn	1959	6/12-29	—	50	—	—	—	—	50
Lynn (adapted by McAlpine)	1964	5-29	—	85	—	—	—	—	15
Kennedy and Carroll	1960	8	Children	27	—	—	—	—	73
Kurland <i>et al.</i>	1963	12-15	Males	11.5	1.5	—	—	—	87
Collis	1965	7-20	—	36	—	—	—	3	61
Present series	1968	6/12-20	—	17	31	3	—	—	49
<i>II. Including those with neurological signs and symptoms at initial attack of optic neuritis</i>									
Marshall	1950	5-20	—	36	—	—	—	—	—
Kinnier Wilson	1954	?	From literature	65	—	—	—	—	35
Hyllested and Moller	1961	2-15	—	13	25	—	13	—	49
<i>III. Only considering neurological signs at initial attack of optic neuritis</i>									
Adie	1930	?	—	34	33	—	—	—	33
Adie	1932	?	—	31	42	—	—	—	27
Marshall	1950	0	—	13.5	17	—	—	—	69.5
Carroll	1952	0	—	32	16	4	—	—	48

with multiple sclerosis in the unrestricted category after 10 years. Our results agree with McAlpine's (1961) findings in 241 patients with multiple sclerosis followed for more than 10 years, that 57% of those whose first symptom was optic neuritis were unrestricted, while only 27% of those who had some other presentation were in that category. He suggests that there is a benign form of multiple sclerosis which is commoner in those presenting with acute optic neuritis. Our study would support such a view.

SUMMARY

Cases of acute optic neuritis, with no other pre- or co-existing neurological signs, seen in the Department of Neurology at Oxford from 1946 to 1966 are reviewed to determine the proportion who subsequently developed multiple sclerosis and the prognostic factors for this. Eighty-five cases complied with stated criteria for the diagnosis of optic neuritis. Sixty-six of these were available for follow-up: 63 were examined personally; three others were attending the Department regularly with undoubted multiple sclerosis. Three of the total had died of other causes. The follow-up period ranged from six months to 20 years with a mean of 10.2 years.

By stated criteria, 13 (20%) were diagnosed as having definite multiple sclerosis, and 21 (31%) as probable multiple sclerosis. Thirty-two (49%) had not developed subsequent neurological disease. Reasons are given for scepticism about the diagnosis of probable multiple sclerosis. The diagnosis of subsequent discrete neurological lesions was made from signs and symptoms in each episode; and 109 such lesions were found in 66 patients, a rate of 0.18 lesions per patient-year.

With regard to prognosis, patients with left-sided attacks, younger patients, those with painless attacks, and those with abnormal sinus radiographs at the time of attack developed neurological lesions statistically less frequently. There was a tendency for females, and those with typical rather than atypical scotomata (as defined), to do worse, though this was not statistically significant. Presence or absence of papilloedema, degree of loss of visual acuity, and month of onset were not significant prognostically. Symptomatic neurological episodes and attacks of recurrent optic neuritis became less frequent as time passed after the initial optic neuritis. As for the degree of disability, 60 (91%) were unrestricted in their activities at the end of the follow-up, two (3%) bedridden, and a further four (5%) housebound. Of the patients with definite multiple sclerosis 64% were unrestricted and 27% house- or bed-bound.

These findings are discussed and compared with previous reports. The relatively favourable prognosis for patients with acute optic neuritis as the onset of multiple sclerosis is emphasized.

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