of a capillary angioma arising from the palpebral conjunctiva of the upper eyelid. Here the convoluted thin-walled vessels were embedded in great masses of lymphocytes.

Maxted⁵ describes a pedunculated angioma of the conjunctiva of the upper eyelid, which perhaps shows some resemblance to my case.

Summarizing we can say that a tumour similar to the fungus-like haemangioma of the conjunctiva bulbi in my case, has not been previously described. The fact that symptoms of intensive growth synchronised with myxomatous degeneration is noteworthy.

After eight months no recurrence has followed.

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THE PROGNOSIS OF RETROBULBAR NEURITIS*

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VARIOUS theories as to the aetiological factors concerned in the production of retrobulbar neuritis have been postulated from time to time. In the days prior to the Wassermann reaction, a large number of cases were considered to be syphilitic in origin, and further evidence for this aetiology was given by a good response to mercury therapy. We now know that most cases of retrobulbar neuritis clear up rapidly without treatment. English authors have regarded disseminated sclerosis as the commonest cause of retrobulbar neuritis: Buzzard (1930) quotes Gowers as saying that gout is the next most frequent cause after disseminated sclerosis.

Marcus Gunn (1904) listed the following as possible causes in a series of 380 cases (tobacco amblyopia being excluded):—Periostitis 40, exposure to cold 27, dental sepsis 17, nasal sepsis 42, gumma 16, disseminated sclerosis 51, influenza 27, gout 22, varied (ptomaine poisoning, malaria, and constipation) 63, obscure 58, and the proportion of men to women was in the ratio of 31:27.

Marchesani (1936) in Bumke-Foerster's *Handbuch der Neurologie* lists the following figures: tumour (anterior fossa) 6, toxic 15, lactation 2, nasal sepsis 9, lues 24, disseminated sclerosis 113,

* Received for publication, May 26, 1948.

encephalitis 7, meningitis 3, subacute combined degeneration 1, haematomyelia 1, vascular 4, tower skull 2, trauma 4, melaena 1, Mikulicz' syndrome 1, tenonitis 1, obscure 89.

Various factors have been definitely shown to produce retrobulbar neuritis other than those already mentioned. Amongst these must be included that of Cone (1938) and phenylalanine hair dyes described by Keschner and Rosen (1941).

Disease of the nasal passage and sinuses has been regarded as a potent cause of retrobulbar neuritis and operations on the sinuses were frequently advised. However, Traquair (1930) thought that all cases of idiopathic retrobulbar neuritis were probably due to disseminated sclerosis and that operation on the sinuses should not be performed. Chambers (1947), too, states that a series of cases of retrobulbar neuritis which he and Foster Moore examined showed no difference in prognosis whether the sinuses were operated on or not. Most neurologists now consider that disseminated sclerosis is the commonest cause of retrobulbar neuritis.

The incidence of a previous blindness in one or both eyes in patients with multiple sclerosis has varied according to the author concerned: Behr (1924) gives 75 per cent., Adie (1930) 30 per cent., Benedict (1942) 15 per cent. and Lillie (1934) 15 per cent. The percentage of cases of retrobulbar neuritis showing evidence of disseminated lesions at the time of blindness was 34 per cent. in a series of 34 cases recorded by Adie (1932).

Few cases have been followed up over a long period to ascertain how many later developed neurological lesions elsewhere. Bruns-Stolting (1900), Fleischer (1908), Langenbeck (1914), Marburg (1920) all state that varying percentages of patients with retrobulbar neuritis "later" developed abnormal neurological signs indicative of disseminated sclerosis; Fleischer (1908) gives 21 out of 30; Marburg (1920) 14 out of 24; Langenbeck (1914) 33 1/3 per cent.; Behr (1924) states that 70 per cent. "later" developed abnormal neurological signs compatible with disseminated sclerosis; Weill (1923) states that of 23 cases examined, 11 already had disseminated sclerosis and that a further five had developed it "some" years later; Friedinger (1925) followed up 25 cases from five to twenty years, 16 of these being followed for 11 years and two had by that time developed disseminated sclerosis—one other case was found in the other nine cases followed up for 20 years. Lactation optic neuritis described by Langenbeck (1914) and Schöppe (1919) was regarded as probably disseminated sclerosis by the former author, for a third of his cases were later found to develop this disease. Hensen (1924) states that a persisting scotoma is later associated with abnormal neurological signs.

Lenoir (1917), on the other hand, states that practically no cases developed signs indicative of a disseminated lesion. The literature on the subject is therefore conflicting, few cases having been followed for any length of time; this article is therefore concerned with the ultimate prognosis of retrobulbar neuritis followed up for over ten years.

Investigation

The out-patients record of the Bristol Eye Hospital from 1933 to 1937 were searched for patients diagnosed as suffering from retrobulbar neuritis. Included in this unselected series are cases due to all causes except syphilis, and to them are added patients attending the in-patient department as far back as 1902. Cases were diagnosed on suddenness of onset of visual failure, papillitis in some cases and usually recovery of vision through a central scotoma. Only forty-six patients so diagnosed were found; eleven of these could not be traced due to changes in address and bombing in the war years, but four deaths which were traced are included in the remaining thirty-five of the series.

Age of onset

The age of onset varied from 14 to 63 years; in the untraced series the average age was 30 years and in the traced 27 years; the ratio of female to male was six to five in the untraced and nineteen to sixteen in the traced. There appeared to be no significant difference in the age of onset as regards sex in either series.

Deaths

Four deaths were found in the series studied; one patient was killed in an accident and two died of natural causes; in none of these could death be connected with a demyelinating process. It is of particular interest that one patient who had a bilateral retrobulbar neuritis and had a negative blood Wassermann, but in whom no cerebrospinal fluid examination was made, died of general paralysis of the insane in a mental institution eight years later; it therefore appears that examination of the cerebro-spinal fluid should be carried out in cases of retrobulbar neuritis.

Relation to pregnancy

Out of ten women examined who had had children, only two related their onset of symptoms of eye trouble to pregnancy, but one woman had later developed an acute disseminated lesion following a further pregnancy (Case 14).

Occupation

No special incidence of any occupation was found; one patient out of the traced series had worked as a pottery glazer and he was the only one who was definitely exposed to lead.

The left eye was affected in twenty-three cases, and the right in thirteen; ten patients had bilateral involvement. Six of the latter were examined; two were found to be blind in both eyes (Cases 4 and 29), two had made a complete recovery in one eye and two had made a complete recovery in both eyes. Of the other twenty-four traced cases only one was found to be blind in the affected eye. Indeed, most patients made a complete recovery in visual acuity of the previously affected eye; the ultimate prognosis of visual acuity appears therefore to be quite favourable.

Incidence of nervous disease in relatives

In one case only was there a familial incidence of a nervous disease (Case No. 13). This patient's sister had died three years previously to the patient's onset of retrobulbar neuritis; her hospital record notes showed that she was admitted for investigation of blindness and a "Parkinsonlike" tremor associated with bilateral extensor responses at the age of seventeen, and that she died six months later at home, no post-mortem being performed.

Fundus

Examination of the fundus showed varying degrees of optic atrophy in the eye previously affected by optic neuritis.

Abnormal neurological findings at the onset of ocular neuritis

Available records showed that four out of the thirty-six traced cases had abnormal findings when examined by a neurologist at the time of onset of retrobulbar neuritis; these four cases (Nos. 24, 28, 8 and 11) will now be described briefly.

CASE 24.—Fourteen years previously, when aged sixty-three years, the patient had developed an acute pain in the left eye with vision reduced to $\frac{1}{2}/60$ and a central scotoma present on examination of the fields. At that time he had a left extensor response, but no other abnormal neurological signs; examination of the cerebrospinal fluid showed normal protein, Lange curve and cells with a negative Wassermann. On examination at follow-up, the patient's acuity was now 6/6, the left optic disc was pale and the left plantar response was still extensor; there were no other abnormal neurological findings nor had the patient had any abnormal subjective feelings in the interim period.

CASE 28.—Twelve years previously, when aged fourteen years, the patient's vision had failed suddenly with reduction of acuity to 1/60 in both eyes. X-rays of skull and sinuses were normal; blood and cerebro-spinal fluid Wassermann were all negative, and examination of the central nervous system showed the presence of bilateral extensor responses. When examined at a follow-up the patient felt quite fit and had served throughout the 1939-45 War in the Pioneer Corps. His visual acuity was now limited to perception of finger movements in the right eye, and 6/36 in the left; examination of the fundi showed a bilateral optic atrophy more advanced in the right than in the left. The rest of the central nervous system was normal except for a right extensor response. He, too, had no subjective evidence of any abnormal neurological disorder.

CASE 8.—This patient, an agricultural labourer, developed an acute failure of vision seventeen years ago when aged thirty-two years; at that time he had bilateral blurring of the optic discs with acuity reduced to 4/60 in the left and 6/36 in the right, the cerebro-spinal fluid examination was normal in all respects, except for the Lange curve of 12222100; his plantar responses were extensor. When examined at follow-up, he had a bilateral optic pallor, visual acuity 6/9 right and left, and no abnormal neurological signs except for bilateral extensor responses. He felt well and was actively employed as a farm tractor driver.

CASE 11.—This patient developed a sudden blindness of the right eye twenty years ago when aged eighteen years. At that time she had a papillitis of the right optic nerve and bilateral extensor responses. Since then she had gradually developed further neurological lesions year after year, with intermissions and exacerbations. On follow-up examination she was bed-ridden, with bilateral optic atrophy, nystagmus in all directions, paresis of the left sixth cranial nerve and a gross inco-ordination of arms and legs. She had a severe degree of impairment of joint sensibility, worse in the legs than the arms, and a spastic quadriplegia with bilateral extensor responses completed a depressing picture.

The presence of abnormal neurological findings in a patient with a retrobulbar neuritis does not necessarily indicate a bad prognosis, as the above case records show that some patients lead full and active lives for many years afterwards.

Incidence of further abnormal neurological findings compatible with the diagnosis of a demyelinating disease

Abnormal neurological findings were present in twelve of the thirty patients examined: six of these could be definitely diagnosed as suffering from disseminated sclerosis, and six probably affected

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TABLE I

Years followed up	Number of cases	Number with definite Disseminated (Case series numbers in brackets)	Number with probable Disseminated (Case series numbers in brackets)	Number with no evidence of Disseminated (Case series numbers in brackets)
10	1	0	0	1 (20)
11	2	0	0	2 (12.31†)
12	4	2 (2.3)	1 (28*)	1 (30)
13	7	0	1 (6)	6 (10.15.16.17.18.25)
14	10	3 (5.14.21)	1 (24*)	6 (1.9.12.22.26.27)
17	1	0	1 (8*)	0
19	1	0	0	1 (23)
20	2	1 (11*)	1 (7)	0
45	2	0	1 (4)	1 (29)
47	1	0	0	1 (19)
Total	31	6	6	19

* = Had abnormal neurological findings at onset of retrobulbar neuritis.

† = Refused to be examined.

by this disease. The findings varied greatly, some had numbness of both legs, others transient numbness of leg or arm, and others said they were quite well but on examination abnormal plantar responses were found. One only of the whole series (Case 11) was confined to bed, all the rest were in fact leading useful and productive lives, for the two blind patients were employed at basket making.

Discussion and Summary

The purpose of this paper was to discover how many patients with retrobulbar neuritis eventually developed disseminated sclerosis after a number of years. Only five patients answered a written questionnaire by post, stating that they had nervous diseases, but in fact twelve out of thirty cases actually examined showed evidence of abnormal neurological findings. The incidence of previous organic disease amongst the population is therefore probably much higher than is usually realised, for only three of these twelve patients were under medical supervision and only one of these was bed-ridden. This may indicate that the occurrence of disseminated sclerosis is higher than previous figures have shown.

The prognosis for visual recovery appears to be excellent on the whole, only one out of the twenty-five unilateral cases being blind in the affected eye a considerable number of years after. The prognosis with regard to further demyelination elsewhere in the central nervous system is more difficult to estimate; in fact it is impossible to give a prognosis in these cases, as one patient with a bilateral retrobulbar neuritis was in excellent health forty-seven years later. In addition, it has been shown in this survey that the presence of abnormal neurological findings at the onset of retrobulbar neuritis does not necessarily mean a bad prognosis.

The eleven patients who were untraced might conceivably have died of disseminated sclerosis, but it is suggested that migration of population during the war years had a great deal to do with the fact that they were untraceable. In fact, three of these were domestic servants and one was an inmate at a Salvation Army Hostel.

Finally, the importance of doing not only blood Wassermann reactions on these patients but full cerebro-spinal fluid examinations to exclude syphilis is stressed in this paper. One patient in whom this was neglected was later found to have developed cerebral syphilis.

Conclusions

1. Forty-six cases of retrobulbar neuritis were taken from hospital records. Eleven were not traced, four were dead and one

refused examination. The thirty cases left were examined from ten to forty-seven years later.

2. Twelve patients were found to have abnormal neurological signs apart from the eyes, but only one was bed-ridden with disseminated sclerosis.

3. The eventual prognosis of visual recovery was good. Of the twenty-four unilateral cases, one was blind; and of the six bilateral cases two were blind in both eyes and two blind in one eye.

4. The importance of examination of cerebro-spinal fluid for evidence of syphilis in cases of retrobulbar neuritis is stressed.

I wish to thank Dr. A. M. G. Campbell for his continued interest and help in the compilation of this work, and the Honorary Staff of the Bristol Eye Hospital for allowing me to see their case notes.

Case histories

A. DEFINITE DIAGNOSIS OF DISSEMINATED SCLEROSIS.

CASE 2. Female. Sudden onset of painful blindness of left eye with papillitis twelve years ago when aged twenty-one. Seven years ago the patient developed transient numbness below the umbilicus, which recovered; since then had further attacks of numbness. On examination there was loss of vibration sense and joint sense in the left arm and right leg. The diagnosis of disseminated sclerosis had been confirmed by Professor Cloake, of Birmingham.

CASE 3. Female. Sudden onset of painful blindness in right eye twelve years ago, when aged twenty-six. Complete recovery of vision in a month followed by a recurrence in the same eye nine years later with an associated numbness up to the middle of the waist. Examination now showed loss of vibration sense in the left leg with bilateral extensor responses.

CASE 5. Female. Sudden onset of loss of vision in the left eye when aged twenty-seven, fourteen years ago. Recurrent ataxic episodes since, transient numbness in face and left arm with peripheral numbness recently. Diagnosed as disseminated sclerosis by Dr. Russell Brain.

CASE 14. Female. Sudden failure of right vision fourteen years ago, when aged twenty-one. The patient had been quite well till nine months prior to examination when, following a pregnancy, she developed subjective numbness from the umbilicus downwards. Physical examination revealed a sensory loss below the level of the eighth thoracic dermatome, and a spastic paraplegia with bilateral extensor responses.

CASE 21. Female. Sudden onset of failure of left vision fourteen years ago, when aged twenty-two. The patient stated she felt quite well, but physical examination showed ataxia and diminished vibration sense in the left leg, with bilateral extensor responses.

B. PROBABLE DIAGNOSIS OF DISSEMINATED SCLEROSIS.

CASE 4. Male. Sudden failure of vision of the right eye forty-five years previously, when aged sixteen. This recovered after a few months, but two years later he developed a visual failure of the left eye; this too recovered. At the age of thirty-three the patient developed blindness in his right eye from which he never recovered, and at forty-two he developed a blindness of the left eye. On examination at the age of sixty-three, the patient was completely blind in both eyes with a bilateral optic atrophy; he had bilateral extensor responses but made

no complaint of any ill-health at all and was actively employed at basket-making.

CASE 6. Male. Sudden onset of painful visual failure in left eye when aged thirty-five, twelve years ago. Complete recovery of visual acuity. Patient stated he felt quite well (a patient in Ham Green Sanatorium for pulmonary tuberculosis), but bilateral extensor responses were found on examination.

CASE 7. Female. Sudden onset of failure of vision in the right eye twenty years ago, when aged twenty-three. Patient had developed numbness in the right leg 14 days prior to examination; this was confirmed by sensory testing, and there was found to be a right extensor response.

C. NO EVIDENCE OF DISSEMINATED SCLEROSIS.

CASE 1. Male. Sudden onset of painful blindness of left eye with papillitis fourteen years ago, when aged twenty-five. No abnormal neurological signs now.

CASE 9. Male. Sudden onset of visual failure in the left eye fourteen years ago, when aged twenty-two. No abnormal neurological findings now, and no subjective symptoms.

CASE 10. Male. Sudden onset of right visual failure associated with pain fourteen years ago, when aged twenty-one. No abnormal neurological findings now, and no subjective symptoms.

CASE 12. Male. Sudden onset of left visual failure eleven years ago, when aged thirty-six. Since then there have been no symptoms of neurological disease.

CASE 13. Female. Sudden failure of left vision fourteen years ago, when aged twenty-three. Since then there have been no symptoms of neurological disease.

CASE 15. Female. Sudden failure of left vision thirteen years ago, when aged thirty-four. Since then there have been no symptoms of neurological disease.

CASE 16. Female. Sudden failure of left vision thirteen years ago, when aged fifty-two. Since then there have been no symptoms of neurological disease.

CASE 17. Female. Sudden failure of left vision thirteen years ago, when aged twenty-two. Since then there have been no symptoms of neurological disease.

CASE 18. Male. Sudden failure of right vision thirteen years ago, when aged twenty-one. Since then there have been no symptoms of neurological disease.

CASE 19. Female. Gradual failure in vision in both eyes in a few days without pain associated with a bilateral papillitis forty-seven years ago when aged twenty-one years. Visual acuity in the left eye 6/12, but hand movements only are perceived in the right eye. Since then there have been no symptoms of neurological disease.

CASE 20. Male. Sudden onset of visual failure ten years ago, when aged forty years. Since then there have been no symptoms of neurological disease.

CASE 22. Female. Sudden onset of left visual failure fourteen years ago, when aged thirty-two. Since then there have been no symptoms of neurological disease.

CASE 23. Female. Sudden onset of left visual failure nineteen years ago, when aged twenty-eight. Since then there have been no symptoms of neurological disease.

CASE 25. Female. Sudden onset of bilateral painful failure of vision with papillitis thirteen years ago, when aged twenty-four. Visual acuity now 6/6 right and left. Since then there have been no symptoms of neurological disease.

CASE 26. Female. Sudden onset of left visual failure when aged thirty-eight years, fourteen years ago. Since then there have been no symptoms of neurological disease.

CASE 27. Male. Sudden onset of left visual failure when aged eighteen years, fourteen years ago. Since then there have been no symptoms of neurological disease.

CASE 29. Female. Sudden bilateral failure of vision forty-five years ago, when aged seventeen. Partial recovery for nine months afterwards, and then a relapse into complete and total blindness. Examination showed a bilateral primary optic atrophy but no subjective or objective evidence of disseminated sclerosis.

CASE 30. Male. Sudden onset of right visual failure eleven years ago, when

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aged twenty-nine. Since then there have been no symptoms of neurological disease.

CASE 31. Female. Sudden onset of left visual failure eleven years ago, when aged twenty-six. Patient refused to be examined and said she was quite well.

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TREATMENT OF SEVERE INFECTED CORNEAL ULCERS BY SUBCONJUNCTIVAL INJECTIONS OF PENICILLIN TWICE DAILY WITHOUT HOSPITALIZATION, WITH SHORT REVIEW OF OTHER METHODS*

BY

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OCULISTS, like myself, who work alone in their clinics without medical assistants, look for a method of penicillin administration, which is practical, efficient and economic for the successful treatment of infected corneal ulcers. By the word "practical" I mean that it should not cause much strain either to the doctor or to the patient, or to his attendants at home, and should not interfere with their sleep. By the word "efficient" I mean that it should be able to control the infection instantly so that it spreads no more, and this control must be followed by rapid improvement and progressive healing. By the word "economic" I mean that the method should

* Received for publication, March 9, 1948.