THESIS FOR DEGREE OF M.D.

CEREBRO-SPINAL DISEASE AND ITS RELATION TO THE OPTIC NERVE

A Critical Review

by

N.S. ALCOCK

In this review the optic nerve is interpretated as that part of the optic pathway which lies between the chiasm and the retina. The review is limited to a consideration of the conditions of this part of the visual tract.

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THE DEMYELINATING CONDITIONS.

Of the conditions in which a lesion of the optic nerve is associated with disease of the cerebro-spinal system the commonest is DISSEMINATED SCLEROSIS. This is now the commonest neurological condition seen in this country (Walshe, 1938) and yet at the same time it is one that is least understood. Numbers of theories in recent years have been advanced but none have more than a few adherents and the general feeling is that we are practically no nearer the solution than when the condition was first recognised. The only real step forward that seems to be established is the realisation that disseminated sclerosis does not stand quite alone but that there are a number of conditions, all much rarer than disseminated sclerosis itself, which are more or less allied. These conditions are characterised on the pathological side by the finding that they all show demyelination of the central nervous system and on the clinical side by the occurrence of lesions of the optic nerves, and it is mainly on these two points that the similarities or distinctions are drawn.

These allied conditions are Devic's disease, Schilder's disease, and a group of cases which are usually put together under the name Acute disseminated encephalomyelitis. This last group can be divided into cases which arise spontaneously and those which arise after acute infectious fevers, chiefly

measles, smallpox, vaccination, and chickenpox. Whether this is a true distinction or not is a point which is not yet determined. The pathology is very similar (Turnbull, 1928) and they resemble each other much more nearly than they resemble any of the other three conditions. The question of the distinction of any of the conditions is still an unsettled one and there are those such as Symonds (discussion on Beck's paper) who hold that they should, in our present ignorance of their etiology, be regarded as variants of the one condition and others, such as Greenfield (1938) who maintain that the differences, particularly the pathological appearances, are sufficiently definite to justify a separation of the four conditions leaving sub judice the question as to whether there is a sufficient basis for distinguishing between the various forms of acute disseminated encephalomyelitis.

In distinguishing the conditions emphasis is usually put on the manner in which the optic nerve is affected. The position is perhaps clearest in the case of Disseminated Sclerosis. Adie (1930) stressed the importance of ocular symptoms in this condition, and maintained that retrobulbar neuritis is a presenting symptom in over 33% of cases; others have tended to put this rather lower, e.g. Lillie, who says that in 15% it is the first symptom but that this percentage rises to 35 - 40% if the 2nd or 3rd symptoms are included.

For a long time the etiology of the apparently isolated occurrence of retrobulbar neuritis was disputed but the

the tendency is now to consider that a larger and larger percentage are due to disseminated sclerosis. Berliner (1935) for instance says "I wish particularly to emphasise that in cases of unilateral acute optic neuritis one must always consider the possibility of disseminated sclerosis, even when no other signs of damage to the nervous system are demostrable", and Paton who in 1930 said "I am afraid I am not prepared to follow some of my colleagues in ascribing 99% of all cases of acute retrobulbar to disseminated sclerosis", in 1937 quotes Walter Lillie "I believe that the significance of sinusitis as a common cause of retrobulbar or optic neuritis has been stressed toostrongly by the medical profession", and again quotes "another eminent observer has stated that in his belief 99% of cases of retrobulbar neuritis are due to disseminated sclerosis" and on this occasion does not explicitly express his disbelief - possibly however the different audience may have made him change his wording.

The clinical picture is also most definite in disseminated sclerosis and the features are too well known to need much description. Berliner (1935) has emphasised the speed with which vision is lost - "In most instances complete loss of vision occurs within a few hours". The accompaniment of pain, either on pressure or on moving the eye is also typical. Berliner also emphasises the frequency of changes in the appearance of the nerve head, in particular the venous

engorgement and swelling of the disc. Paton (1936) also believes that a slight degree of oedema is much commoner than is suspected, in fact so common that in 1914 he considered it worth while to give four main points to aid in the differentiation of swelling from papilloedema and swelling from retrobulbar optic neuritis namely:-

1. The loss of sight precedes the ophthalmoscopic change.
2. The ophthalmoscopic changes are of very brief duration.
3. The discs may show no trace of change after the swelling has subsided.
4. The recovery of vision is usually synchronous with the subsidence of the swelling.

With regard to (3) he goes on to say that although the disc may show little change when the swelling subsides, later on the whiteness may be extreme, and quotes a case where the discs were absolutely opaque white, yet vision was 6/5 in each eye and the visual fields were full, although, he adds, this is unusual and small patches of relative scotomata are the rule.

The pallor of the optic disc in disseminated sclerosis is so well known and is so generally accepted that with many the terms are practically synonymous and the diagnosis of disseminated sclerosis means that the disc is therefore pale, a fact which I am convinced gives many students a quite untrue criterion for the judgement of the normal colour of a disc, and the normal range of colour may be thus underestimated.

The fact that pallor of the disc is so universal and

accepted after lesions of the nerve that possibly the occurrence of this does not raise questions in one's mind. It is however an interesting phenomenon. The main bulk of the fibres in the optic nerve arise from cells which lie in the retina, yet a lesion gives rise not only to distal degeneration but also to degeneration of the proximal part of the nerve and of the nerve cell itself. The optic nerve is, of course, not a peripheral nerve but a tract of the brain: one might therefore have expected it to behave in a similar way to say the pyramids or posterior columns. In these however (Greenfield 1938) even distal degeneration is rare in disseminated sclerosis. Why the optic nerve should be so particularly sensitive is a problem as yet unsolved. It has been suggested that vascular causes may play some part, but the observation that pallor follows equally from a lesion in any part of the optic nerve, that a juxta-chiasmal site is the same as one near the vascular supply, does not confirm this suggestion.

The disease which in some ways most resembles disseminated sclerosis is the condition known variously as DEVIC'S DISEASE, neuromyelitis optica or neuropticomyelite. It was first suggested by Clifford Albutt who, in 1870, discussed the ophthalmoscopic changes in cases of acute myelitis and reported a case in which eye disorders supervened. He states "This remarkable case was of very long duration and was followed by partial recovery; in it the sympathetic disorder of the eyes came on many weeks (12 - 13 at least) after the subsidence of the acuter symptoms".

The differences from disseminated sclerosis may at first sight seem marked. Typically it appears in childhood; both eyes are simultaneously affected; the lesion in the spinal cord is a single large patch which involves the whole width of the spinal cord, and it has by no means the same tendency to relapse. In practice however the disease shows many variations from this typical picture. Beck's case for example relapsed a number of times, the optic condition three times and the myelitis twice, so that Symonds in the discussion on this case found difficulty in distinguishing it from disseminated sclerosis. In Balser's (1936) 4 cases, two were adults aged 42 and 50 and in all of them there were relapses. He stresses however the fact that unlike disseminated sclerosis both eyes are commonly affected, that pain is a more frequent symptom in Devic's disease and that involvement of other parts of the nervous system beyond the spinal cord and optic nerves practically never occurs. The onset of the myelitis may be either before or after the involvement of the optic nerves and various figures have been suggested. Beck for instance says that in 25% the eye-changes come on first, whereas Goulden puts the figure at 80%. I have been unable to find any record of cases pathologically proven in which the diagnosis has been made where the optic nerves have alone been affected but the occurrence of cases where the myelitis has followed the optic nerve changes at a considerable interval suggests that such cases probably occur. I have however seen one case in a young

boy whose spinal cord showed a typical condition but who had no ocular symptoms; so far as I know this case has not been reported. It is possible that some cases of bilateral optic atrophy for which no cause is found may belong to this group.

Those who consider the two conditions as separate have laid stress on the pathology; whereas in disseminated sclerosis the demyelinated areas are usually "punched out" in appearance with complete destruction of the myelin sheaths within the involved areas, in Devic's disease the areas are infiltrating at their borders and there are always small bundles of intact myelin sheaths within these borders. The areas tend to be continuous in Devic's disease whereas in disseminated sclerosis they tend to be patchy and asymmetrical.

SCHILDER'S DISEASE.

In a certain number of cases of Schilder's disease or encephalitis periaxialis diffusa, the optic nerves are affected in a very similar way to the condition in disseminated sclerosis and Devic's disease - in fact Berliner ~~who~~ says that in 35 cases which he has been able to find in the literature 90% of the cases with complete amaurosis, bilateral optic nerve atrophy was noticed before death. An analysis of Collier and Greenfield's cases reported in 1924 and those of Grainger Stewart, Greenfield and Blandy in 1927 together with those they report from the literature hardly confirms this high percentage,

although two of the three cases in 1927 had primary affections of the optic nerves as well as the cortical lesion. In their first case the discs were seen during life to be paper white and in their third case histological examination showed that the nerves were paler than normal and that very few of the myelin sheaths were intact. They refer also to an interesting case of Stauffenberg in which both processes appeared to be at work, a female of 21 who had a prodromal affection of the left optic nerve causing papillitis and two months later diminution of vision of the right optic nerve with a normal fundus.

Their third case was instructive also in that the condition was recognised during life as being a "true optic neuritis with papillitis", not a papilloedema. Their illustrations of this case also show demyelination of the optic nerves, a macroscopic picture not altogether unlike what may be seen in disseminated sclerosis.

Of the 26 cases mentioned in their two papers, 8 are specifically said to have had normal discs and in 8 others the condition of the discs is not mentioned and may therefore be presumed to be normal. In a condition which is characterised by demyelination of the occipital lobes and therefore cortical blindness, this is what should be expected and raises doubts about the 90% figure given by Berliner. In 5 others of their cases the discs are said to have shown either early papilloedema or slight congestion. This may have been the congestion

and swelling which accompanies retrobulbar affections of the optic nerves, but it is also amenable to another explanation; the appearances may have been due to an early papilloedema such as would accompany a rise in the intracranial pressure. That in a number of cases the pressure is increased is corroborated by the finding of enlargement of the head in young infants so that a diagnosis of hydrocephalus has been made (Berliner).

A further difficulty is introduced in this condition by the familial tendency of the disease. Symonds (1928) has reported one such family of which two members had primary optic atrophy and the case which Collier and Greenfield described in 1925 has since proved to be a familial case (Greenfield 1933). In this later paper Greenfield has described two cases which "in some ways form a connecting link between these (cases of Schilder's disease) and the diffuse sclerosis associated with micro- and macro-cephaly". One of these two cases was quite blind but had normal discs. In this same paper Greenfield also stresses the likeness of some types of Schilder's disease to disseminated sclerosis and agrees with others such as Neubuerger and Jakob who have classified Schilder's disease into various groups.

In relating these cases to disseminated sclerosis one is therefore faced with the difficulty of deciding whether one is really dealing with as definite a condition as some writers on the subject would suggest. In some of the cases undoubtedly the resemblance is near but the definite relationship between the conditions will only be decided when the etiological cause or causes of the various

conditions is more established and to regard them all as merely variants of D.S. in various stages of acuteness as Brain(1930) is inclined to do, is, I think, profitless in the present state of our knowledge.

The same question of etiology comes up even more when one goes on to discuss the encephalomyelitic conditions. A number of these cases, pathologically very similar to the spontaneous cases, occur after the infectious fevers. The cases which occur after Measles are perhaps the most definite. Ford (1928) in an exhaustive review records 12 cases of his own and collects 116 cases from the literature.

Before one can ~~go on to~~ review these cases, it is necessary to have some criteria as to the meaning of the terms used. Unfortunately this is a matter of considerable difficulty. In his paper on the classification of optic atrophy Paton (1930) remarks "I believe we may soon hope to see the term "optic neuritis" used in its proper connotation". This time has not yet arrived and the term is still used by many as synonymous with papilloedema.

In trying to analyse Ford's cases from the point of view of the optic nerves I have therefore tried to distinguish the true optic neuritis from the cases of simple papilloedema. If one accepts Paton's criteria mentioned above, an eye which shows obvious changes in the nerve head should have a considerable defect in vision. On the other hand a mild degree of papilloedema such as is sometimes described here would probably be accompanied by no visial disturbance. That this is an alternative diagnosis and that intracranial pressure is raised in these cases is born out by Ford's comment on

the c.s.f. findings. He says "The pressure is increased in most cases and may rise to 400 mm."

Ford divides the cases into 5 groups, in three of these: the first group, those with a complete absence of physical signs and prompt a complete recovery; the fourth group, those which present cerebellar syndromes and the fifth group, those with paraplegia and cord signs: there is no involvement of the optic nerves. The eye changes are confined to the groups which show multiple focal cerebral symptoms and to one case in the group of hemiplegias and aphasias. In this later group one case had optic discs which were "hazy" but no further information is given. In his summary of the group with multiple focal symptoms, he says that they show "very frequently congestion or even moderate oedema of the optic nerve heads", but makes no mention of any visual defect. He himself reports 8 cases, in 4 of which he mentions hyperaemia or congestion of the veins but in none does he suggest any visual defect. From the literature he refers to two cases in which there was visual disturbance. In Calmiel's case there was blindness but the autopsy showed atrophy of the hemisphere and one cannot therefore assume that this was due to optic nerve involvement. The other case, one reported by Neal and Applebaum, there was "loss of vision" but most unfortunately no autopsy, and one cannot exclude the possibility of an occipital lesion for this also. In discussing the other nervous complications Ford adds "optic neuritis may follow all the acute infections and measles is no exception to this rule... These lesions almost always clear up and leave no visual defects",

which leads one to think that he has some evidence to suggest that there may be an involvement of the optic nerves, but unfortunately he makes no attempt to discriminate between papilloedema and true optic neuritis.

Greenfield (1929) in reviewing measles encephalitis says "Papilloedema is fairly common and temporary amaurosis has been observed in a number of cases, sometimes followed by loss of colour vision as the sight returns". This suggests a distinction between increased intracranial pressure and involvement of the optic nerves. The 4 cases he reports, however, had no optic nerve involvement.

Ferraro and Scheffer (1931) review the literature but make no mention of the optic nerves; they report 6 cases, 5 of which had presumably normal eyes as no reference is made to them. One had slight blurring of the margins of the discs of both eyes, but they add that the c.s.f. was under markedly increased pressure, probably sufficient cause for the blurring of the discs.

Wohlwill reports 2 cases (quoted by McAlpine 1931) but again no mention is made of the optic nerves.

Berliner (1935) reports a most interesting case in a child of 6 who had bilateral swelling of the discs up to one dioptre and impairment of vision in both eyes down to light perception only. The fields also showed definite central scotomas - a very typical story of a retrobulbar condition - although his neurological colleague reports "one can be fairly sure of its localisation in the corpora quadrigemina".

Thus, although authorities are agreed that involvement of the optic nerves, apart from papilloedema, does occur, I think its occurrence has been over-emphasised, possibly from confusion with papilloedema. The evidence brought forward here suggests that it is perhaps about the rarest of the well-defined symptoms seen in this condition.

In the nervous complications of VARICELLA the same rarity of involvement of the optic nerves is noted. Miller and Davidson (1914) review the literature thoroughly and can find only one case recorded, that by Chavernac (1908). This case was a girl of eleven who developed varicella February 1905, and during convalescence complained of dimness of vision which gradually got worse, and by June she could only count fingers at a metre. In November 1905 the disc was still slightly swollen with blurred edges and several punctate haemorrhages, and the fields showed a central scotoma. She made a considerable recovery and in March 1906 her discs were pale. Although this is a long drawn out case, distinctly longer than the usual type of retrobulbar neuritis, the central scotoma and severe visual loss with only mild swelling of the disc leave little doubt that it must have been a retrobulbar neuritis. Krabbe in 1925 could still find no other case but this; however, Paton in 1918 reported a case in a boy of 14 who noticed that his left eye was blind on the third day of a severe attack of chicken-pox. In April 1918 the visual acuity was 6/60, the disc pale with blurred edges,and the visual fields showed an irregular central scotoma and some peripheral limitation. Wilson and Ford (1927)

again review the literature from which they report 10 cases and add 3 of their own. The only mention they make of the optic nerve is to say that in one of their own cases there was slight hyperaemia of the disc. They make no mention of the cerebro-spinal fluid pressure, however, and there was no visual loss, so there is no evidence to suggest that this was a retrobulbar neuritis. Berliner (1935) reports one case in which blurred vision and swelling of the discs was noted. This child, however, had a squint and bilateral sixth nerve palsy, which I think were quite sufficient to account for the blurred vision and one cannot exclude a hydrocephalic condition, causing all these signs. Most unfortunately no post-mortem was obtained and the child was unco-operative.

Whether or not this last case is admitted to have optic nerve involvement, it is obvious that in common with measles optic nerve involvement in varicella must be extremely rare. Paton's case is, however, so typical that there can be little question that this boy had a true retrobulbar lesion.

The same remarks hold good with regard to the nervous complications following VARIOLA and vaccination. Turnbull and McIntosh (1926) in an exhaustive and critical paper refer to 34 cases of nervous complications following variola, but although they go carefully into the case history they make no mention of the optic nerves ever being involved. Wilson and Ford (1927) also review the literature carefully and again refrain completely from any mention of the optic nerves being the site of a lesion.

With regard to POST VACCINAL ENCEPHALITIS Turnbull and

McIntosh record in detail the clinical history and pathological appearance of 7 cases. Wilson and Ford record 4 cases and Perdrau 3 cases, but in none of these papers is there any mention of involvement of the optic nerves. Turnbull in reviewing the pathology again in 1928 quotes Schurmann, who found perivascular zones of demyelination in the optic nerves and tract in post-vaccinal encephalitis, but although he goes into considerable detail does not mention the optic nerves in his own cases. Thus again, any involvement of the optic nerves must be of considerable rarity.

Finally there is a type of encephalomyelitis which apparently occurs spontaneously. Involvement of the cranial nerves is rare in these cases also, although perhaps not so rare as in the types that follow the acute infections. Here, however, one is on more debatable ground as many of these cases are very hard to tell from the more acute cases of disseminated sclerosis. Martin in 1928 records 4 cases and his 4th case in a child of 8 developed dimness of sight and later had partial atrophy of both discs. This certainly suggests a retrobulbar affection of both eyes and the age rules out the possibility of disseminated sclerosis. Brain, Hunter and Turnbull (1929) record 6 cases, but there was no incidence of papilloedema, atrophy or demyelinisation of the optic nerves. Redlich (1927) records 12 cases but makes a point of saying that retrobulbar neuritis did not occur in a single case. McAlpine (1931) in a general review records 4 cases, one of which had visual disturbance which suggests a retrobulbar affection. He

adds, however, that this case is now "indistinguishable" from disseminated sclerosis except that the patient had not lost his abdominal reflexes; a point which is hardly of sufficient diagnostic importance to distinguish between the two conditions. He also quotes Flatau as having had cases in which affection of the optic nerve occurred but reference to Flatau's original paper (1929) throws considerable doubt on these as in a collection of 17 cases he has included a number which, from the clinical history, certainly do not suggest encephalomyelitis, and as most of them recovered there was no pathological verification. He includes, for instance, case XI, a man of 20 whose story is typical of subarachnoid haemorrhage with sudden intense headache and a third nerve palsy; case XII, a man of 32 who had a story which suggested left cerebral thrombosis, and case III, a patient of 13 who had myelitis and visual failure, which reads like a typical case of Devic's disease. Other cases also sound doubtful, as case VIII who probably had a posterior inferior cereballar thrombosis. I feel, therefore, that his cases should be omitted from any analysis of this condition.

There is another infectious condition, HERPES ZOSTER, which may be included here, although it is doubtful whether this is its correct place. A few cases are recorded of optic atrophy in association with herpes zoster of the 1st division of the 5th nerve. I personally have seen one such case, an elderly lady who was quite blind in the eye on the affected side and whose disc showed typical optic atrophy. Paton has recorded two such cases, one of which

he showed at the Royal Society of Medicine 1923, a patient who had an opaque white disc and a very limited field. The condition is apparently so rare that when he saw his first case he thought it was an unrecorded condition, (Paton (1936) but he has been able to find 6 other reported cases, one by Dr. Clarence Veasey which had a visual field loss, beginning as a central scotoma and spreading out. The disc was pale and Paton comments that this was obviously a retrobulbar affection. The connection of these cases with encephalomyelitis is obscure, although this condition may also complicate herpes. Schiff and Brain (1930) report such a case but the optic nerves were not involved; the invariable association of optic atrophy with herpes of the 1st division on the same side suggests strongly that there must be some more intimate connection between them.

I have analysed these cases of encephalomyelitis at considerable length, as I feel that it has been assumed too readily that retrobulbar affections are common in these conditions. For instance, in discussing post-vaccinal encephalitis and disseminated sclerosis, Perdrau (1928) says "it will be found that the two lesions are identical as regards type and distribution" McAlpine (1931) does not stress the difference in frequency at all and Duke Elder (1940) says, in discussing the encephalomyelitis cases, "despite the widespread and irregular distribution of the areas of demyelination, a constant feature is involvement of two areas, the sub-ependymal zone and the optic nerve, chiasma and tracks. In mild or abortive cases, indeed, the involvement of

the optic nerves may be the chief feature of the disease".

Such statements as these can not, I believe, be substantiated in view of the published cases. It is largely arguing from this hypothesis that the connection between the etiology of these conditions has been suggested, an opinion which has repeatedly been made, e.g. Perdrau, Symonds (1924) and others. The usual argument being that as it appears likely that the encephalomyelitis cases which follow the specific fevers are apparently due to virus etiology then disseminated sclerosis is also due to a virus.

In this connection it is interesting to consider the recent work of Innes and others (1936) (1940) on Swayback. This disease of sheep has a very distinct resemblance to Schilder's disease. A similar condition in a human child has been reported by Winkelman and Moore (1942). The chief point in this condition is Bennett's work showing it can be prevented by the administration of copper to the pregnant ewes. Although this work has yet to be fully confirmed, it is the first real suggestion of an etiology for this group of diseases.

The problem of disseminated sclerosis is, perhaps, the chief neurological problem facing us at present. I believe that accurate classification may be of assistance in elucidating it. I would suggest therefore, that if the vulnerability of the optic nerve is of any significance the diseases can be separated with disseminated sclerosis and DEVIC'S DISEASE on the one hand and the encephalomyelitic cases and SCHILDER'S DISEASE on the other, and that the argument that they have a common etiology is unsound.

PAPILLOEDEMA

The next large group of conditions in which a lesion of the optic nerve is associated with disease of the nervous system are those where an increased intracranial pressure is associated with papilloedema.

After the invention of the ophthalmoscope and the recognition that abnormalities of the nerve head might be present without defect of vision, a feature which Hughling Jackson drew attention to as early as 1865, the next great step was made by Paton and Homes (1911), in this classical paper they reported the histological findings in 50 cases of papilloedema and brought forward extremely strong evidence to show that the production of swelling was due to the rise in the pressure in intracranial fluids being transmitted from the cisterna basalis along the optic nerve sheaths. This rise in pressure occludes or tends to occlude the venous return in the central vein and so increases venous pressure in the whole retinal circulation. This is followed by increased formation of lymph, and as the main lymph channels draining the disc and posterior part of the retina pass back into the nerve sheath, the increased pressure in the sheath blocks also the normal drainage of lymph. Thus the production of the oedema and swelling of the disc is due to these two factors; increased production of lymph from raised venous pressure and blocked drainage of lymph. Their sections refuted entirely the previous suggestions that inflammation had

any part in the production of papilloedema. It followed from this paper therefore that the term optic neuritis was not a suitable one for the condition and their term papilloedema should be adopted instead. Although this is now 33 years ago, it is unfortunately not universal yet.

Even before this paper the factors for the production of papilloedema were being discussed and in a paper in 1908 Paton recorded over 200 cases of cerebral tumour and noted the relationship of their site to the production of papilloedema. He found at that time that in over 80% of cases tumours in the frontal or parietal region gave rise to papilloedema, that in little more than half the cases of subcortical tumour was there papilloedema, but that in every case of cerebellar tumour it was present. Lindsay Rea in his recent book confirms these findings and says that in cerebellar, thalamic, midbrain and tempero-sphenoidal tumours the papilloedema is marked; that in frontal tumours it is severe but is mild in parietal cases. It is perhaps natural that in 1908 before the true mechanism had been demonstrated that a direct correlation should be sought between the site of the tumour and the degree of papilloedema but it is rather surprising to read this in a recent book. Consideration of the mechanism shows that an increased cerebro-spinal pressure is the important factor and primarily the site of the tumour is only important with regard to whether or not it interferes with the circulation of the cerebro-spinal fluid.

For instance a tumour in the 4th ventricle or one blocking the aqueduct will interfere considerably with the circulation of the cerebro-spinal fluid and will produce papilloedema before it is large enough to produce other localising symptoms. On the other hand a tumour in the pons or midbrain will produce other signs of its presence before it gives rise to papilloedema, although, as it is quite inaccessible to removal sooner or later it will almost certainly give pressure signs also.

In the same way a small meningioma which is lying right over the motor area may give rise to focal fits which lead to its recognition and removal while still too small to give rise to any disturbance in the cerebro-spinal fluid dynamics and hence it would be classified as a tumour which did not give rise to papilloedema, whereas one an inch or two further forward or backward might well give rise to pressure before localising signs. Therefore I am convinced that in any analysis of cases with regard to the production of papilloedema the important facts to determine, rather than the actual site, are the questions of, firstly the local signs it produced, secondly as to whether it interferes with the cerebro-spinal fluid circulation and lastly as to how amenable tumours in that particular situation are to removal.

In this same paper (1908) Paton showed for the first time that the belief, that a difference in the amount of the swelling is of value as indicating the side of the brain on which the tumour is likely to be situated, was quite unfounded. His actual figures were that in the 39 cases in which a difference

was found 23 were on the side of the tumour and 16 in the other side. In discussing this question again in 1936 Paton makes two suggestions, one that the presence of firm connective tissue in one eye might restrict the development of papilloedema and illustrates a case in which a dense band of connective tissue has prevented the formation of papilloedema on one side of the disc; and secondly he quotes from a paper by Walter Parker who showed that an in-equality in the intra-ocular tension may cause an inequality in the amount of swelling. This raises an interesting point which so far as I know has not been investigated; that a correlation might be found between the amount of increase in intracranial pressure necessary to cause papilloedema and the intra-ocular tension. It is a familiar experience that in different cases a wide variation may be found between the pressure and the appearance of papilleodema and possibly the height of intra-ocular tension is a factor that has not been sufficently considered. Although rather outside the scope of this paper it is interesting to consider in this connection also the recent observations of Henderson and Smythe (1938) who found that a number of cases of cerebral tumour showed a difference between the cerebro-spinal fluid pressure as measured by lumbar puncture and the pressure as measured by ventricular puncture and they suggested that this difference was due to herniation of the temporal lobe through the tentorium cerebelli with consequent pressure on the aqueduct. This fact must also be taken into consideration in any observations between the cerebro-spinal pressure reading taken in the routine way by the lumbar route and the appearance or amount

of papilloedema.

The nature of the lesion causing the increase of pressure must also be considered in relation to the production of papilloedema. Provided free communication is maintained between the cisterna basalis and the optic nerve sheath, any lesion which causes increase of the cerebro-spinal fluid will act in just the same way as a space filling lesion. Symonds (1937) has shown that thrombosis of the superior sagittal sinus gives rise to delay of absorption of cerebro-spinal fluid with the production of so-called otitic hydro-cephalus and that papilloedema is very frequent in these cases. The importance of the communication over the lateral aspect of the cerebral hemispheres is indicated by this condition and while it would be out of place to discuss at length the mechanism by which space-filling lesions cause a rise in intracranial pressure, it may be pointed out that tumours of the cerbral hemispheres may, by occluding the space between the brain and the dura give rise to obstruction to this pathway, and so cause the same delay in absorption as is found in otitic hydro-cephalus. If this is so then it would follow that a super-ficial tumour would cause papilloedema earlier and more easily than a subcortical one. Reference to Paton's paper in 1908 shows that over 80% of cortical tumours had papilloe-dema while little more than half the subcortical ones had. This suggestion would link up these tumours with the cere-bellar cases and one can correlate the production of papilloe-dema with the ease with which the tumour can interfere with cerebro-spinal fluid circulation.

There seems little difference between the space-filling lesions themselves and probably the differences between abscess, glioma or secondary carcinoma are explained by the varying amount of oedema that surrounds them.

Paton in discussing the mechanism for papilloedema stressed the importance of a free communication between the sheath of the optic nerve and the cisterna basalis and suggested that the reason why papilloedema is less common in meningitis is because this communication is prevented by the formation of adhesions. In this connection the partiality for both tuberculous and meningococcal meningitis to form adhesions around the base of the brain is well known, as is also the relative infrequency of papilloedema in these two conditions.

There is another factor which should perhaps be considered in this connection and that is the time necessary for papilloedema to form in cases of increased pressure. It is common experience that many cases of cerebral tumour may have other signs of increased pressure, such as headaches and a raised c.s.f. pressure, often for several weeks before papilloedema is apparent. In evaluating these cases, however, the point at which the pressure will cause papilloedema is not known, nor does one know to what extent the pressure fluctuates and how far a fluctuating pressure is more or less efficient in causing papilloedema than a steady one. If the theory is true that in most cases the block in the c.s.f. is the causal factor, then probably the mechanism is in the nature of a vicious circle, once the obstruction is sufficent to raise the pressure, then this pressure will further increase the obstruction and so lead

to further increase in pressure.

That a certain length of time is required for the formation of papilloedema is suggested by the cases of spontaneous subarachnoid haemorrhage where the sudden increase in pressure is often sufficient to raise the tension in the retinal veins to bursting point with the formation of subhyaloid haemorrhages. Papilloedema, however, does not necessarily occur in these cases although the pressure may remain raised for several days. One does not know how long the pressure is above the critical level but it is perhaps a reasonable assumption to say that 24 - 48 hours even at a considerably raised pressure is not enough to cause papilloedema in the ordinary case.

As well as the question of the time factor, the mechanism of the production of papilloedema is not as simple as it seems. Duke Elder (1940) reviewing the theories, dismisses as untenable inflamatory or vasomotor causes, and discusses firstly the suggestion that papilloedema is only a reflection of a general oedematous condition of the brain. Van Heuven (1938) supports this view, quoting Spatz's work, but it is difficult to correlate this theory with either the cases of otitic hydrocephalus in which there is simply an excess of c.s.f. or with the effect of a decompression in relieving papilloedema when the tumour has not been touched, and the amount of surrounding oedema presumably unaltered. Duke Elder next considers the question of venous stasis and in particular the relationship of venous/arterial pressure at the nerve head. The rise in this ratio from the normal 1 : 3 to 1 : 1·5 has been shown to be the critical

threshold for papilloedema to appear. Against this however is the observation that gross venous obstruction may not cause papilloedema. An illustrative example is that of superior vena cava obstruction. In a case personally observed there was marked generalised oedema of the whole of the head and neck but the eye grounds were normal and the c.s.f. pressure was not raised.

Duke Elder concludes that there is a colloid chemical aspect too which he feels must be invoked to explain all the findings.

It is interesting here to consider the not infrequent occurrence of papilloedema in subacute bacterial endocarditis. In several personally examined cases it was associated with a normal c.s.f. pressure, a point also commented on by Hagen (1941) who found papilloedema occurred in 35% of his series of cases. He was able to correlate it to a certain extent with cerebral vascular accidents and the occurrence of petechiac. It is usually dismissed as a toxaemic manifestation, e.g. by Horder, but this fails to explain its absence in other forms of prolonged toxaemia.

In reviewing the various theories, it is evident however that increased intracranial pressure due to or accompanied by an increased c.s.f. pressure is the basis of the great majority of cases. The lack of success in reproducing papilloedema experimentally may well be due to the dynamics of the c.s.f. O'Connell (1943) has shown that our methods of measuring c.s.f.

pressure and in particular of measuring the variations in pressure are inaccurate and that ordinarily the variations are considerably underestimated. It may be therefore that the failure to reproduce a varying pressure is the reason why, for instance, Wolff and Davis (1931) could not produce papilloedema at pressures compatible with life.

Accepting however a simple mechanical theory one must admit that in certain cases other factors are more important, but I believe that their importance in the ordinary case may well be over-emphasised.

A corollary of Paton's theory that it is the generalised increase in pressure which causes papilloedema, is that direct pressure on the optic nerve will cause atrophy and not papilloedema. Paton recognised this as early as 1909 when he published a series of cases in which amaurosis was present on the side of the tumour and states in his conclusions "Tumours directly or indirectly exercising constant pressure on the chiasma, or on the optic nerve, may cause primary pressure atrophy without any preceding oedema of the disc".

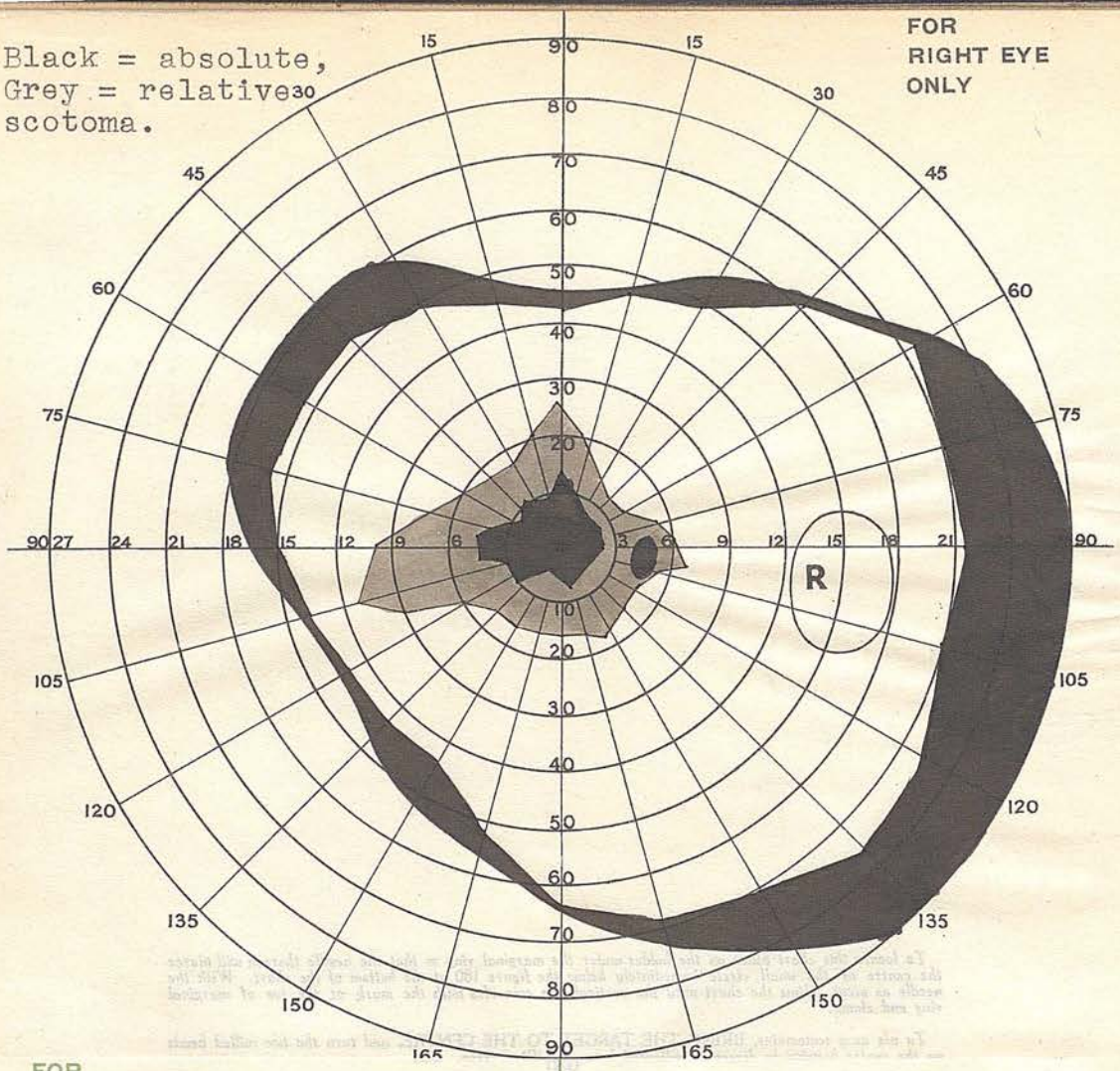
In his paper in 1936 he goes on to say that in the later part of the same year (1909) he had the opportunity of verifying this pathologically and that it formed the subject of Sir William Gower's last public lecture. Paton quotes Gowers as saying "any case which presents this condition (i.e. atrophy in one eye and papiloedema in the other) will probably warrant the same diagnosis..... You may assume that optic neuritis

produced by an ordinary intra-cranial tumour is always produced in both eyes", and quotes the one exception "In this the mononuclear neuritis from cerebral disease having the symptons of a tumour was confined to the right eye but.....the left was artificial!"

In 1911 Foster Kennedy elaborated this point considerably and published 5 cases of frontal tumour or abscess which had what he called retrobulbar neuritis, that is a central scotoma with a pale disc, on the side of the lesion and papilloedema on the other side. In 2 of these cases the patient had had papilloedema preceding the development of the atrophy. In his 6th case there was a retrobulbar neuritis on both sides. He reviewed the theories then prevalent about the production of papilloedema and decided definitely that a distention of the optic nerve sheath by the raised pressure of the c.s.f. was the causal factor and went on to point out how a tumour pressing directly on the nerve will prevent papilloedema forming. He stated in this paper "One may say that if there is no doubt that a given patient has a brain tumour and if that patient develops a retrobulbar neuritis, then it is certain that the tumour is situated in the lower part of the frontal lobe on the same side as that on which the retrobulbar neuritis and primary optic atrophy have occurred". In 1916 he published a further illustrative case in which a basal frontal aneurysm pressed first on the right optic nerve producing a central scotoma followed by some pallor of the disc, and then 6 months later involved the left optic nerve in the same way. At the autopsy on this case the aneurysm was found to be pressing

Black = absolute,
Grey = relative
scotoma.

FOR
RIGHT EYE
ONLY



FOR
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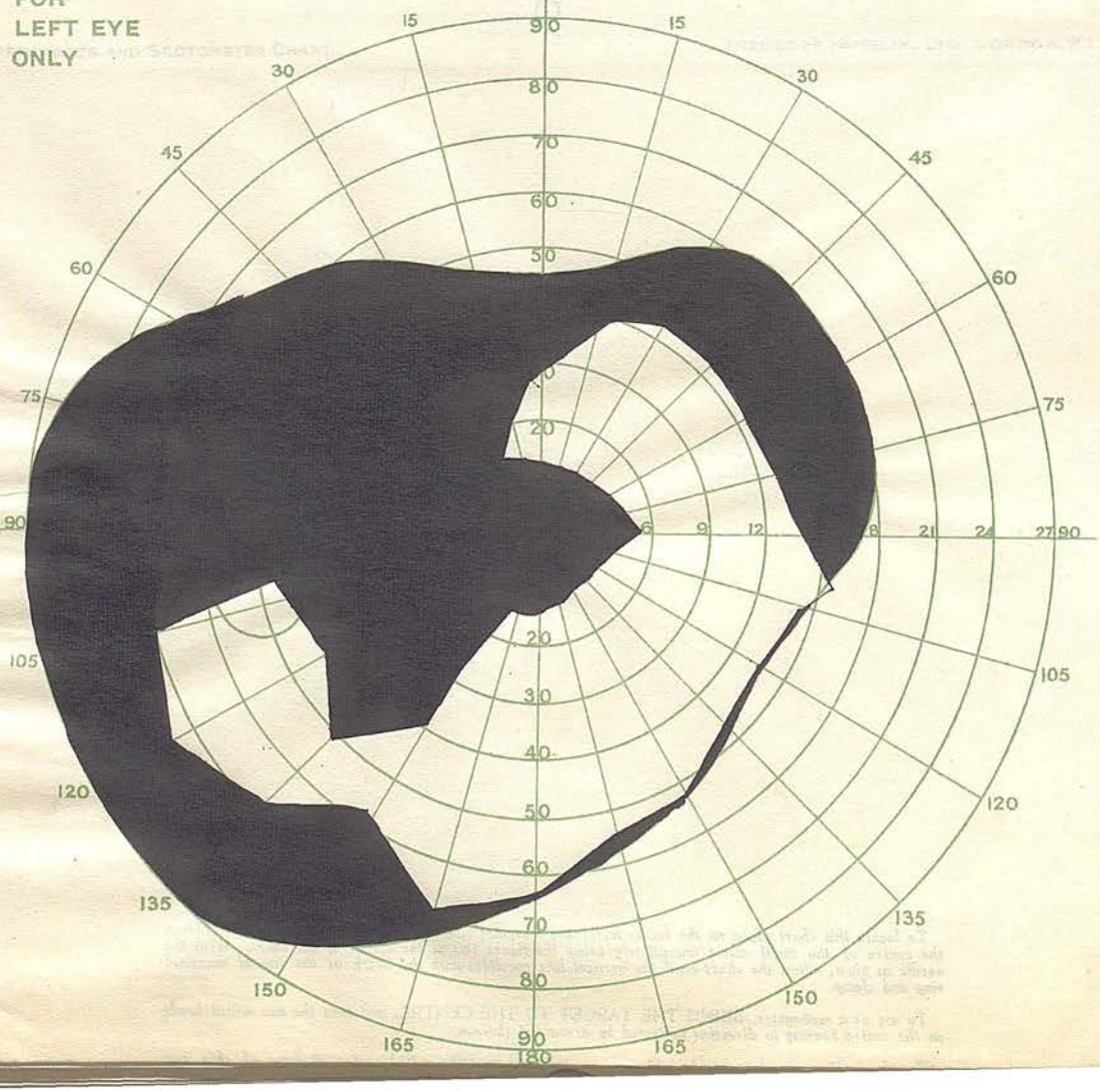


FIELDS OF
CASE ON
PAGE 27.

on both optic nerves, more on the right than the left.

Lillie (1927) in a review of the frontal space filling lesions seen at the Mayo Clinic found 13 basal lesions out of a total of 86 frontal cases. Of these 13, 7 cases had a central or centrocaecal scotoma, 4 of which had a normal or pale disc on the side of the lesion with papilloedema on the other and 3 had bilateral pallor with blurred edges but a considerable difference in colour. Three more of the cases had bilateral lesions with bilateral scotomata, and in the other 3 cases he found a small island of vision only in the temporal or nasal field which he presumed to be due to the progressive enlargement of the scotoma.

I can add a similar case; the patient had had generalised fits for 18 months, for 2 months failure of vision of the left eye, and for 2 weeks of his right eye. When first seen his left disc was pale, and his vision: R.1/36; L. finger counting. Later the right disc became pale also. The post mortem showed an astrocytoma of the basal part of the left frontal lobe which was spreading around his left nerve and pressing on his right. It spread back to, but did not involve, his chiasm. His fields are appended.

Kennedy, although he realised that loss of the sense of smell on the side of the lesion was part of the syndrome, did not unfortunately stress this in his article and so helped to give rise to the belief that it was necessarily a frontal tumour which caused this syndrome.

Since then however it has been pointed out that a similar condition may arise from a tumour in the middle fossa, and

particularly a meningioma growing from the inner end of the sphenoid ridge, although gliomata of this region may also press on the optic nerve and give rise to ipsilateral atrophy with contralateral papilloedema. In Paton's original contribution one of his cases was a temporosphenoidal tumour.

Recently Alpers and Groff (1934) and Gross (1936) have reported a series of meningiomas in this region. In 6 of their nine cases there was a primary atrophy and in one case a papilloedema in the other eye. Presumably others would have developed papilloedema if time was given.

Elsberg and Dyke (1934) have also reported a series of 4 cases of meningiomas arising from the medial part of the sphenoid ridge, which were compressing one nerve only and were recognised and removed while still so small that they caused no further symptoms. They record in the same paper an aneurysm which caused an identical picture. It may be that these cases would have produced the chiasmal picture later and that they should not be included here, but it suggests that the syndrome of optic atrophy in one eye and papilloedema in the other may be produced by tumours other than those lying basally in the frontal lobe.

David and Hartmann (1935) publish notes on 26 cases of meningiomas in this region and again point out that this syndrome is not necessarily due to basal lesions of the frontal lobe and would extend it to meningiomas of the base arising anywhere adjacent to the optic nerve. Six of their cases showed this syndrome. They also go more fully into the question as to

whether the ipsilateral eye showed a central scotoma and found two cases which did and one case which probably did in the early stages. Their other cases were all blind in the ipsilateral eye by the time they saw them. They discuss the frequency of scotomata and consider that they arise more often than is usually realised owing to the fact that so many cases are blind by the time they are recognised. On these grounds they say that the idea of a meningioma of the sphenoid ridge should always be thought of in unilateral, central scotoma especially if this is of slow and gradual onset.

The point that Kennedy made that a central scotoma was typical of these cases, seems to have been rather lost sight of by most of the other commentators on the subject and possibly should be considered more than is usually done.

Henderson, (1938), has also reviewed a large number of anterior basal meningiomas and has divided the 12 cases of olfactory groove tumours he saw into an anterior group of 8 cases which showed papilloedema only, although one case was thought to have had a previous atrophy, and a posterior group of 4 cases, 2 of which showed atrophy in one eye and papilloedema in the other. He comments on this surprisingly low figure, in contrast to what has usually been thought to have been the case in these anterior tumours. He also reports 2 personal cases of tumours on the inner end of the sphenoid ridge both of which had this syndrome. The second of these is interesting in that when it was first seen the contralateral disc was normal whereas 6 months later it had

developed papilloedema - evidence in support of the suggestion above that some of Groff's cases might have done the same if time were given. In addition to these two personal cases he has collected 3 from the records all of which showed this syndrome. Thus in his total of 45 cases, 7 showed ipsilateral atrophy and contralateral papilloedema, of which 2 were frontal and 5 sphenoidal ridge. In all these 7 cases the ipsilateral eye was blind by the time he saw them so that there is no indication of the type of field loss. In one case however there was a clear history that the visual defect had progressed from above downwards as if a dark curtain with a straight lower border were gradually falling. It took six months to reach the centre of the visual field. This certainly does not suggest a central scotoma.

Thus although the syndrome of ipsilateral atrophy and contralateral papilloedema does undoubtedly arise from lesions other than basal frontal ones, the more posterior cases do not seem to produce central scotomata with the same frequency.

THE OPTIC ATROPHIES

Apart from the demyelinating conditions and the particular tumours which give rise to the syndrome of papilloedema in one eye and optic atrophy in the other, there are a certain number of other diseases of the nervous system which may be associated with optic atrophy.

In his presidential address in 1930 Paton endeavoured to classify this very complicated series of cases. He remarked on the unsatisfactory nature of the present classification into primary and secondary types as it is commonly employed and suggested that these terms should be abolished altogether, and he would prefer an alternative classification into: 1. Atrophy of localised origin, 2. atrophy of diffuse or indeterminate origin, 3. atrophy of unknown origin. He subdivides the first group into those cases of a. retinal, b. papillary and c. retrobulbar type.

1a. THE RETINAL CONDITIONS to be considered are those in which a degeneration of the retinal cells is associated with a similar widespread degeneration of the ganglion cells of the brain. The conditions are grouped together under the name of cerebro-macular degeneration of which several forms have been described according to the age at which the condition develops. The degeneration is of peculiar type and is associated with the formation of lipoids, so that attempts have been made to correlate these

conditions with the other lipoid disturbances such as Niemann-Pick's disease. The clinical manifestations are progressive mental deterioration, visual failure, paralysis and often epilepsy. The disc and retina show atrophy with the production of the "cherry-red spot" at the macula. This latter has been shown (Greenfield, personal communication) to be due more to loss of colour in the retina around the macula than to any actual change of colour in the macula itself.

1b. THE PAPILLARY ATROPHIES include glaucoma, myopia and those consequent on papilloedema. In this latter condition there are two causes at work. The presence of the oedema fluid gives rise to irregular swellings of the nerve fibres. These swellings increase in size and lose their continuity with the nerve fibre becoming more globular as they do so and produce the cytoid bodies which Paton and Holmes illustrate well in their paper, where they show indisputably their origin from the nerve fibres. They discuss here also the immediate cause of this degeneration, and suggest three possibilities: that it is due to stretching and tension of the nerve fibres from their displacement by the oedema; that it is due to imbibition of oedematous fluid; or that it may result from nutritive and circulatory disturbances. The local occurrence at areas of greatest stretching, especially where the nerves are stretched over a blood vessel, makes them conclude that the first possibility is the most important factor, although its occurrence in the neighbourhood of haemorrhages suggests that in some cases other factors may be at work.

At a later stage the degenerated fibres are replaced by a neuroglial proliferation which, as it ages, contracts down and this may lead to the unfortunate result that although the pressure is relieved yet the process may continue and by its contraction kill the remaining nerve fibres. This experience is unfortunately not uncommon and the patient with a progressing visual loss may become blind in spite of decompression. This is the reason why operation should not be delayed because the patient has still got good vision.

1c. It is chiefly however THE RETROBULBAR LESIONS which are of importance in the subject under consideration. These Paton divides into orbital, foraminal and intracranial lesions. In orbital lesions an inflammation may attack the nerve directly and this may be due to any of the forms of meningitis, the demyelinating conditions which have been dealt with, or a tumour either intra or extra neural.

In the foraminal portions the lesions are either traumatic, or due to bony or vascular disease, all of which fall outside the scope of this thesis.

In the intracranial portion, we have to consider the various lesions which may press on or stretch the nerve. Here it is necessary to make a distinction as to which if any of the vascular conditions should be considered, and I have decided to exclude the vascular lesions such as thrombosis of the internal carotid which gives an optic atrophy on one side with a hemiplyia on the other but to include the aneurysms as they may present as space filling lesions.

The tumours which arise in such position as to press directly on one optic nerve have been considered and there remain therefore three groups of conditions to discuss: Tumours of the optic nerve, Aneurysms and Arachnoiditis.

In considering the TUMOURS OF THE OPTIC NERVE, there are three conditions in which these may be associated with lesions elsewhere in the nervous system. Multiple Neurofibromatosis, Tuberose Sclerosis, and von Hippel-Lindau's disease.

This last condition is considered here for the sake of classification but it must be pointed out that the ocular tumours are in the retina rather than in the optic nerve. Treacher Collins (1894) described, in this condition, a capillary naevus of the retina, and demonstrated that tortuosity of the blood vessels of the eye may occur in connection with signs of cerebral tumour. He also emphasised the differentiation of these tumours from the gliomatous growths of the retina. Lindau has shown the association of these tumours with similar tumours elsewhere, particularly in the cerebellum.

In NEUROFIBROMATOSIS one finds multiple neurofibromata and endotheliomata affecting all parts of the nervous system and the skin. In a case which I was fortunate to see at post mortem there was a tumour on every cranial nerve, including both optic nerves, on one of which the tumour was placed far forwards and could be seen ophthalmoscopically during life. There were also multiple tumours elsewhere. It has been shown

also that some of these cases may develop true glioma as well as the neurofibromata.

The recognition of tumours of the retina and optic disc with the condition of tuberose sclerosis is due particularly to van der Hoeve, who in 1932, in the Doyne memorial lecture, reviewed these conditions. He suggests that they should all be classified together as Phakomatoses. He points out that they all show both ocular lesions and lesions of the central nervous system: that the tumours are naevoid growths without true naevus cells and that all three conditions are familial. This view is certainly worthy of consideration although, so far, it has not received general adoption.

The eye changes associated with ARACHNOIDITIS are an interesting group of the lesions which affect the intracranial portion of the optic nerves. In a monograph Bollack, David and Puech have reviewed the literature and collected 63 published cases and have added 66 hitherto unpublished cases from Dr. Clovis Vincent's clinic. They find that 59% showed optic atrophy either complete or partial and only 17% papilloedema or hyperaemia, so that one is justified in including this group among the atrophies. There is, as they point out, no unanimity with regard to the relationship of the ocular lesions to the arachnoiditis, and they review the various possibilities: that they may both be due to some independent cause; that the arachnoiditis is the primary

lesion and that the visual disorders are due to: (1) direct interference; (2) interference with the blood supply either directly or by causing vascular spasm; and (3) finally, that the arachnoiditis may be due to the lesion of the ocular nerve. Their conclusion is that if these three possibilities exist separately then in most cases they are combined. In discussing the etiologic causes they say that some cases are due to infections, either by known organisms, as in those cases caused by infections of the nasal sinuses, or to cerebro-spinal infections, such as syphilis or tuberculosis; others are due to unknown infections such as influenza, and others, again, they attribute to trauma, but there still remains a considerable group of unknown etiology. One of the chief points of interest in these cases, that is the fields associated with them, is discussed later.

The ANEURYSMS which compress the optic nerves have recently been reviewed by Jefferson (1937) who has personally collected 53 cases of intracranial aneurysm. In these cases 12 were associated with lesions of the visual pathways and two of them with lesions of the optic nerve itself. He emphasises that a number of these aneurysms may grow slowly and exactly mimic a benign tumour, and suggests that these conditions are possibly not recognised as often as they should be.
Of those affecting the visual pathways he states that the commonest single pattern present is where an aneurysm

arises from the carotid soon after it has pierced the dura and gives rise to monucular blindness or junction hemianopia. Both of his optic nerve cases were blind, so that one cannot say what their fields were. Jefferson has also collected 25 cases from the literature, and in reviewing these he says that the visual defect varies from dimness of vision, through various scotoma types, to blindness. He adds that very few of the fields were examined by quantitative perimetry and many of them may have had in addition chiasmal pressure.

Kennedy's case and Elsberg and Dyke's case have been referred to above.

VISUAL FIELDS.

If a patient presents with ocular symptoms, the investigation which is usually most helpful in arriving at the correct diagnosis is the visual fields and therefore it has been thought desirable that these should be considered as a whole rather than separately under each disease entity.

As a beginning one may consider the field changes which a simple papilloedema from increased intracranial pressure produces. This may be divided into that caused by the oedema alone, and that due to the ensuing atrophy. The change due to oedema alone is an enlargement of the blind spot. De Schweinitz (referred to by Traquair) has described this occurring before ophthalmological evidence of choked disc is present, but Traquair states that he has found the fields

normal until definite swelling is present and most observers would, I think, agree with this. This enlargement is easy to understand when the histological appearance of papilloedema is considered, and the bulging and distortion of the nerve fibres round the disc is well shown in the illustrations to Paton and Holmes' paper. If the oedema spreads into the macular area then, as might be expected, a slight visual loss at that area develops with the production of a small relative central scotoma, and Traquair emphasises that it does not occur unless there is recognisable macular oedema. This point is of importance in the differentiation of swelling due to papilloedema and the similar appearance that may occur in retrobulbar lesions. Thus if there is a central scotoma without macular change, then the lesion is a retrobulbar one. Paton's criteria for the distinction of these lesions have been referred to above (page 4).

As atrophy begins, so a concentric contraction of the field occurs and the field gradually becomes smaller and smaller until usually only a small patch, either central or around the blind spot, is left. In this latter case, the earlier loss of the nasal fields may produce a semblance to binasal hemianopia. (Traquair). The loss does not always proceed quite so regularly as these remarks might suggest and in cases with moderately advanced atrophy the general constriction may take various shapes, but the character can usually be fairly easily recognised. Traquair considers that the

cause for this change is that the interstitial changes in the nerve, while present in the whole cross section of the nerve, are as a rule most severe peripherally and spread inwards, causing a diminution in the blood supply of the fibres. Paton and Holmes, in their paper on papilloedema, give modified support for this theory. They state that the optic disc in the state of atrophy consequent to a papilloedema is characterised by general shrinkage and an increase of neuroglial fibrils. In addition there is generally an increase of the connective tissue that surrounds the vessels. They go on to say, however, that the earliest evidence is an increase in neuroglial nuclei near the apex of the swelling, which is followed by an increase of the neuroglial matrix. At the same time, or later, a similar proliferation can be seen in the lateral portion of the disc. At a somewhat later stage this neuroglial sclerosis spreads over the rest of the disc. Thus one might presume that it is the central fibres which would be first affected. This argument cannot, however, be taken much further, as there is no agreement yet as to the actual arrangement of the fibres in the papilla. A further point may be considered here, the papillo-macular bundle certainly occupies more than its fair share of the circumference of the papilla and the consequent crowding together of the other fibres may predispose them to the damage done by the oedema and subsequent gliosis.

From consideration of this, it might be thought that

external pressure on the optic nerve would also tend to affect the peripheral fibres. Here, however, the position is not so clear. In Kennedy's original paper of six cases of basal frontal space-filling lesions, he found that the field on the side of the lesion showed a central scotoma. In a further case (1916) of frontal aneurysm, he found the same condition, first on one side and then on the other. Sachs (1912) emphasises the central scotoma due to frontal lobe growths pressing directly on the optic nerve - Lillie (1927) in a larger series of 13 cases, found the same condition; 7 of these cases had either a central or a caeco-central scotoma on the side of the lesion, 3 cases with bilateral lesions had bilateral scotomata, and in 3 cases the condition had advanced so far that there was only a small peripheral isle of vision in either the temporal or nasal field.

Kennedy, in discussing the phenomenon, says that the macular fibres are physiologically more delicate and that presumably, therefore, they are proportionately more fragile, and suggests that this is the reason why they are affected first.

This attractive theory is, unfortunately, open to several objections; firstly, if the macular fibres are more delicate, why should they not go first in a more or less uniform sclerosis, such as occurs in atrophy following papilloedema. Again, in considering, above, the causes of

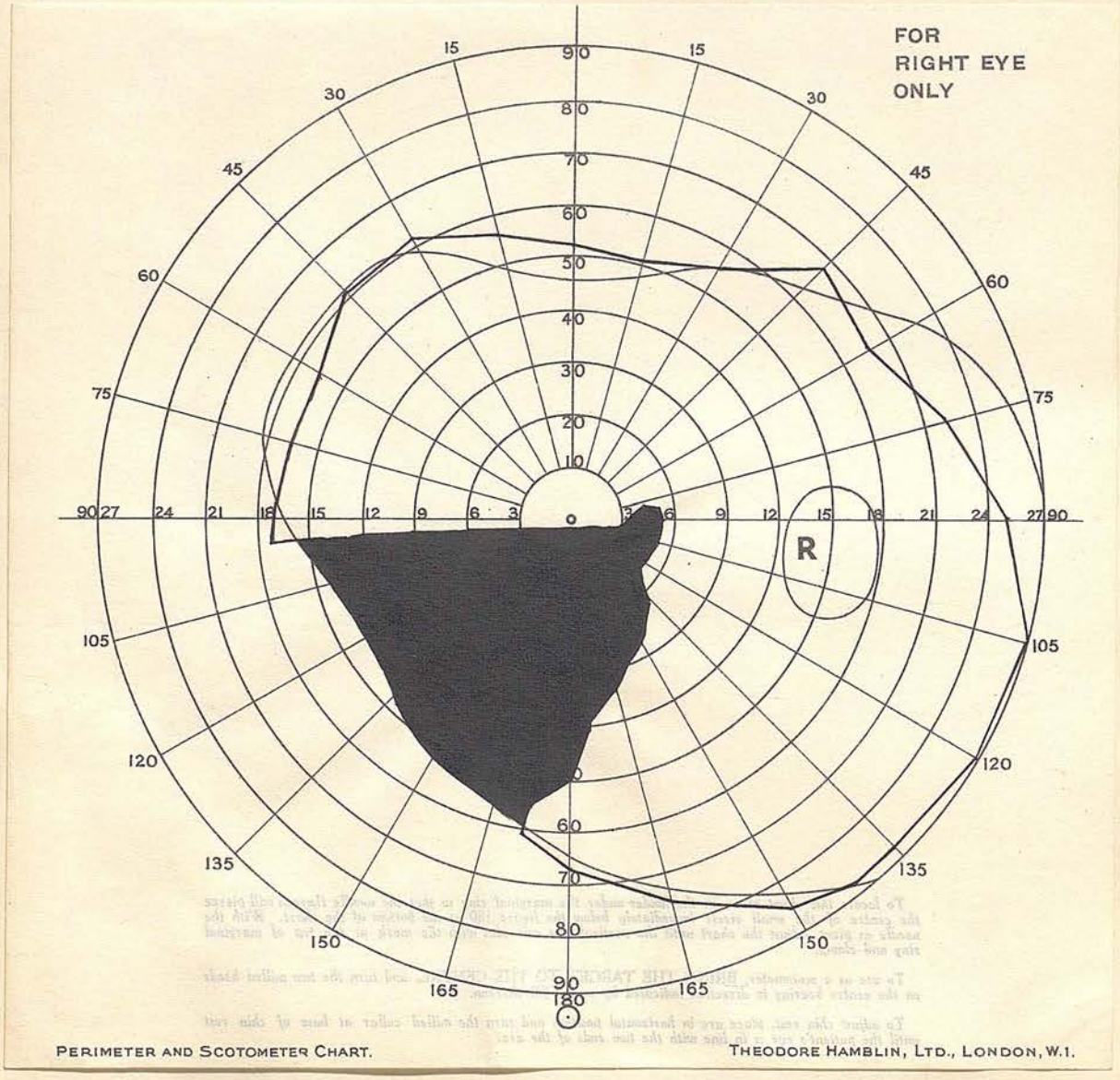
atrophy on one side and papilloedema on the other, it was pointed out that a tumour growing from the sphenoid ridge might give rise to direct pressure on the optic nerve. If, therefore, Kennedy's theory is the true one, these should show central scotoma also. An illustrative case is Groff's 3rd case where the tumour was circling the nerve and compressing it, but the fields showed concentric contraction. In Elsberg and Dyke's 4 cases, the visual loss was:- in Case 1, the upper half of visual field and lower temporal field; in Case 2, mainly in the upper half; in Case 3, only in the upper temporal quadrant; and in case 4, in the lower temporal quadrant. Commenting, they say that in general a sector of retina corresponds to the same sector of nerve and that the lesion is caused either by direct pressure on the nerve or by pressure from the margins of the optic foramen. They add their opinion that a larger experience will probably show that in these tumours a loss of vision from pressure on the optic nerve may occur in any part of the visual field of the affected eye.

Henderson's case of pressure on an optic nerve from a sphenoid ridge tumour also did not show a central scotoma. Gliomas of the optic nerve might be expected to give rise to a general disturbance of the nerve and so lead to a lesion of the most vulnerable tract. However, the fields they produce show a slowly progressing depression and constriction and are not in any way characteristic (Traquair).

Kennedy's theory would have to be modified then to explain these cases. It is interesting that pressure from above seems to cause a central scotoma while pressure from below more often causes other types of field loss. Consideration of the arrangement of the fibres in the optic nerve does not seem to give the clue, although the exact position of these is still an unsettled point. Traquair does not go further than to quote provisionally Henschen's scheme, which shows the papillo-macular bundles as lying in the lateral quadrant when just behind the eye and gradually adopting a more central position as they approach the chiasm. It is possibly, therefore, the fact that frontal tumours press on the nerve more anteriorly, or that they press more from above, that gives rise to the difference in the fields. This, however, is a speculation and must be left for further work to show the answer.

As mentioned above, David and Hartmann suggest that scotomata occur early in sphenoidal ridge cases and may not be recognised, as by the time they are seen, the eye is blind. This does not seem to apply to the cases mentioned above, although, of course, in each of the series a number of patients were blind in one eye when first seen. Even with this theory there are still some points to explain, such as why, in frontal cases, do the patients present when they still have scotomata, whereas in these sphenoidal ridge cases they do not come until blind? Probably the fact that most of Kennedy's and ~~most of~~ Lillie's cases were gliomatous may have some significance.

FIELD OF CASE ON PAGE 44. Object:- white 3/330.



The occurence of central scotomata in the demyelinating conditions might give assistance in the solving of these questions. In Disseminated Sclerosis the commonest finding is a central or centrocaecal scotoma and Paton (1924) considered that he found paracentral scotomata in more than 50% of cases. A simple vascular origin cannot explain these cases as the lesions in Disseminated Sclerosis are entirely haphazard in their distribution and there is no correllation between their site and the vascular supply although the frequency of hyperaemia and vascular changes in the disc, referred to above, might lend support to such a theory. Other types of field loss are by no means unknown in disseminated sclerosis and Traquair has seen both sectional defects and peripheral contraction. Some time ago I was fortunate in seeing one of these unusual field changes in disseminated sclerosis. A woman of 28 complained that a fortnight before she had begun to have pain when she moved her right eye and had developed a wedge shaped cloud in her nasal field, so that she could see above and to the right of it, but not below it. Her fields ~~are~~ *is* appended. Her disc at that time showed blurring of the upper and lower margins but no measurable swelling. She had also lost her abdominal reflexes and one plantar was extensor. The blurring of the disc settled down rapidly.

The same tendency to show central scotoma is seen in both Devic's disease and in Schilder's disease, and is, so far as one can judge from the rather sparse reports, the usual finding

in the encephalomyelitis group. This tendency for these conditions is still unexplained, it has been pointed out above that it is not explainable on a simple vascular basis, and Kennedy's theory that the papillo-macular bundle is more vulnerable does not seem to explain all these cases.

In arachnoiditis also the tendency is to show central scotomata. In Bollack, David and Puech's collection of cases 31% showed central scotomata and 23% peripheral constriction, and in their own cases 23 of the 66 they report show central scotomata, an even higher percentage of 39%. In their illustrations the arachnoiditis is always above the nerves binding them down and apparently this is the common form for it to take. It may be, therefore, that the mechanism is similar to that of frontal tumours which press on the optic nerves from above.

Whatever the true explanation of the production of the changes in the visual fields, a point of clinical importance seems to be that in cases which show a persistent and advancing scotoma it is profitable to consider lesions which lie above the nerve, whereas if the fields show a peripheral constriction, or a quadrant loss, then a lesion beside or below the nerve is more likely. This, of course, is not meant as an absolute rule, but in these often puzzling cases any point which may be helpful is always welcome.

In contradistinction to these cases there are those of tabetic optic atrophy, where the predominating field is one which shows peripheral constriction. The position

of tabetic optic atrophy is, however, so uncertain that it is probably more profitable to discuss it separately.

TABETIC OPTIC ATROPHY.

The question of where to classify this condition is still left undecided. Of any large series of cases it forms one of the major groups. In Wood and Rowland's group of over 200 cases of all forms of optic neuropathy it represented 16%. Yet, despite the frequency and familiarity of the condition, Paton (1930) says "Various and discordant as are the theories advanced to explain the pathology of the changes in the posterior roots and columns, we find that the theories of optic atrophy are just as diverse." In his paper in 1922 Paton has reviewed and discussed the various theories. He excludes, on Stargardt's evidence, the possibility of a retinal site for the lesion and discusses the various theories as to whether the lesion is interstitial or parenchymatous. His conclusion is that it is a combination of both, with at times the one predominating and at times the other.

He adds that a consideration of the field changes which may be produced give support for this theory and points out that two main types are found. One class shows a slow onset with fairly good central visual acuity maintained over a long period and the segmental losses in the peripheral fields are fairly sharply delimited. In the other, the loss of central visual acuity occurs fairly quickly and vision may be grossly

diminished while the peripheral fields for white are hardly affected.

Almost every type of field change may be found and Stargardt's classification into 7 types covers nearly all possible variants. The commonest is the circumscribed loss of field with good function in the remaining field. This Paton considers to be caused when the interstitial structures are the most affected, whereas the other common type with poor vision and full fields is where the parenchymatous tissue is that predominatingly diseased.

Hemianopic defects and fields which are more or less symmetrical are also illustrated in this paper and give support to the theories which place the lesion behind the eye and in some cases it certainly must be near the chiasm.

The rarest field loss of all has been considered to be the scotomatous loss. So much is this so that to illustrate it, Paton has to reproduce illustrations from Uhthoff's paper, as he had not at that time seen any cases of this type himself. This point however is questioned by Woods (1942) who states that recent perimetry with modern methods has shown that the cases may be divided into 4 groups:

1. Those showing concentric contraction of the peripheral fields - 12%;
2. Sector shaped or nerve bundle defects 34%;
3. Central or centrocaccal scotomata with normal peripheral fields - 14%, and

4. Central or centrocaccal scotomata with defects in the peripheral fields.

Thus 54% of his cases showed scotomatous defects; a surprising contrast to the earlier opinions on the condition.

There are many points about tabetic atrophy which are still unclear. One of the most important is the relative lack of response to treatment. In a discussion in 1926, the general opinion expressed was that the outlook was very poor, in fact, Sir Arnold Lawson regarded it as "practically hopeless". Martin suggested that there were 4 reasons why this was so; first, that the optic nerve was part of the brain and therefore more vulnerable than the peripheral nerves, as its fibres were devoid of the sheath of Schwann; secondly, it may suffer considerable anatomical impairment before any functional defect is recognisable; thirdly, fibres destroyed cannot be replaced, and fourthly, fibres are replaced by glia and contraction of this glia may bring about slow destruction of still more fibres.

Gordon Holmes, speaking at this discussion, was not so depressing about the outlook. He referred to Stargardt and Leri's work, in which they pointed out that it was an interstitial syphilitic process, but that it was associated with a primary degeneration of a certain number of nerve fibres. He had himself confirmed that there was a considerable interstitial change, that is cellular infiltration at, or most

intense, at the optic foramen. He therefore considered the prospect was not so bad as had hitherto been believed. He also said that there was no doubt that a considerable number of patients with optic atrophy preserved vision for years, especially under treatment.

This more hopeful view, however, is not widely held. Lindsay Rea (1938) says that in a patient with a concentric diminution of the visual fields and a partial loss of colour vision, it usually takes about 2 years for complete atrophy to ensue. However, in another place in his book, he qualifies this statement by saying: "the two year rule does not always hold. I am quite certain from experience that by the diligent use of mercurial inunction, combined with the iodides and intravenous bismuth, loss of vision can be delayed for at least a further twelve months".

More recently various other methods have been recommended. Lauber (1938) has suggested general tonic measures to raise the blood pressure combined with operative treatment to lower the interocular tension, although he is enthusiastic others have failed to confirm his results. Moore and his co-workers (1942) have reviewed a large series of cases and make out a reasonable case for pyrotherapy but further confirmation of this is still necessary. The position in general remains in Duke Elders words "an unusually unsatisfactory and melancholy record of failure".

This however can not be regarded as the final word on the subject. The time to treat tabetic atrophy is at the time of the primary infection. The importance of examining the c.s.f. before pronouncing a case cured is only now being recognised and the failure to appreciate this in the past has, I am convinced, been the cause of many unnecessary cases of neurosyphilis. It is instructive to note that only 3 out of 235 patients in Moore's series had received anything approaching adequate treatment for early syphilis.

The modern treatment of syphilis is undoubtedly producing a steady disappearance of syphilitic conditions of the central nervous system and I believe that, despite the distressing increase in primary infections seen at present, tabetic optic atrophy will become a rarity and our failure to treat it will be of academic interest only.

Occasionally, however, one may meet cases of a different character in syphilitic disease; Lindsay Rea, for instance, records a case in which there was an atrophoid disc with complete absence of vision, yet as a result of anti-syphilitic treatment, central vision rose to 6/9 and the extreme limits of the field of vision returned, although, between the two there was a large horseshoe shaped scotoma. He adds that it was not obvious in this case that the atrophy was secondary. The late W.J. Adie had a similar case which, so far as I know, is not published but which he used to

teach on, and in which a very similar picture was present. The vision was down to light perception and the optic discs were apparently quite atrophied, yet, following anti-syphilitic treatment, good vision returned.

On account of the response to treatment, Lindsay Rea classifies these cases as secondary (post neuritic) atrophy, but as mentioned above, it is not always possible to tell this from the appearances, and one wonders if there is anything, apart from the recovery, to guide one as to the true diagnosis and prognosis. Lindsay Rea does not, unfortunately, discuss this interesting point and the late Dr. Adie was quite at a loss to explain the mechanism or to give any clue as to how to recognise another such case.

There remains some of the rarer types of optic atrophy to discuss. A small proportion of cases of pernicious anaemia and subacute combined degeneration of the spinal cord develop optic atrophy. Brain (1933) states, in fact, that 5% of cases have bilateral optic atrophy with some visual impairment, and Lindsay Rea (1938) gives this same figure, although possibly he is quoting from Brain. Most observers, however, do not believe the incidence is as high as this. Cohen (1936) has reported 2 cases in which it was the presenting sympton and in which improvements took place with treatment. Box (1936) added another case and Kampmeier and Jones report 3 cases and review the subject

shortly, giving their opinion that it is definitely rare. Janet Vaughan, in a personal communication, has said that she has not seen a case, although her experience in this condition must be very considerable. Woods and Rowland (1931) in a series of over 200 cases of patients presenting with visual symptons, do not report a single case due to subacute combined degeneration or to pernicious anaemia.

Turner (1940) has reviewed the subject and adds three further cases. He has recorded the visual fields which he considers have characteristic features in that the defects are oblong with the fixation point at one end of the scotoma rather than pericentral.

I feel that these cases have an importance greater than their frequency alone would warrant, firstly because we know the cause and secondly because they respond well to treatment if this is begun in time.

Optic Atrophy has also been reported in association with some of the familial ataxias and Barrett (1927) in a review of FREIDREICH'S ATAXIA with eye symptons, quotes two cases which had optic atrophy and one of his own cases also showed the same. I have personally also seen one such case. In the associated conditions of MARIE'S ATAXIA and SANGER-BROWN'S ATAXIA, optic atrophy is rather more common.

Optic atrophy and papilloedema are also occasionally seen in SYRINGOMYELIA. The papilloedema has been thought to be due to hydrocephalus. Both are rare.

In the familial condition of hypertrophic peripheral neuritis, papilloedema may rarely occur; I have seen it in one proven case but optic atrophy is not recorded.

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