Neuro-ophthalmology

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Neuro-ophthalmology is the study of the neurological mechanisms concerned with vision and includes disorders of pupils, external ocular movements, fundi and fields. Since the standard reference work on this subject consists of three volumes, each of which contains over 1,000 pages (Walsh and Hoyt, 1969) it would be impossible to provide even a synopsis of the whole subject in the space available here. For this reason emphasis will be given to those aspects that have been of special interest to the author.

PUPILS

The commonest types of pupillary abnormalities include Horner's syndrome, Adie's syndrome and Argyll Robertson pupils.

Although Horner's syndrome has a well-known association with lung cancer this is by no means the commonest cause. An isolated Horner's syndrome is not infrequently seen but the precise aetiological factor may not be ascertained; it is assumed to be vascular in origin and, in some cases, there is a history of migrainous neuralgia (cluster headaches).

Adie's myotonic pupil affects predominantly women, usually of the younger age group. It is of no serious significance but, because of associated tendon areflexia in the lower limbs, may be confused with tabes. Table 1 summarises the chief differences between these syndromes.

EXTERNAL OCULAR MOVEMENTS

Endocrine ophthalmoplegia

One of the commonest causes of ophthalmoplegia referred to a neurologist working with ophthalmologists is endocrine exophthalmos. These are cases that have no overt thyrotoxic signs (since, in that case, they would have been referred to a general physician or endocrinologist). There is often unilateral proptosis with minimal exophthalmos and lidlag. Their endocrine origin can be recognised by the latter sign and special tests which include T3 suppression test (Bowden and Rose, 1969a), the presence of thyroid antibodies, and the TRH test. Treatment is problematical but guanethidine eye drops improve lid retraction (Bowden and Rose, 1969b).

Table 1.

	Adie's syndrome	Argyll Robertson pupils
Sex incidence	Predominantly female	Equal
Age incidence	< 40 years	> 40 years
Laterality	Bilateral	Unilateral
Size of pupils	Large	Small
Reaction to light	Slow	Absent
Reaction to accommodation	Slow	Present

Ptosis

The commonest cause of bilateral ptosis in the elderly is senile ptosis, whereas the commonest cause of unilateral ptosis is myasthenia. Myasthenia may be missed if a prostigmine or Tensilon test is not done (Arnott and Rose, 1972). If the pupil is dilated on the same side as the ptosis the diagnosis of a third nerve palsy is likely; if the pupil is smaller, the diagnosis of a Horner's syndrome is probable.

Isolated Ocular Palsy

Isolated ocular palsy is a syndrome in which the patient presents with an ocular palsy, or palsies unaccompanied, at least at onset, by other neurological signs. These patients complain of diplopia or blurred vision but pain occurs in nearly a third of cases and is the presenting feature in 15 per cent of patients.

In a personal series of 89 cases there was an unexpected predilection for the male sex in roughly the proportion of 5 to 3; 85 per cent occur after the age of forty years. The incidence of either the third or sixth nerve being affected is roughly equal but any combination of third, fourth and sixth cranial nerve palsies can be seen (Rose, 1973a). The aetiology will vary, depending on the cranial nerves affected (*see* Table 2).

Table 2. Aetiology of ocular palsy

	III	IV	VI
Aneurysm	+++	−	+
Vascular	++	+	++
Tumour	+	+	+++
Trauma	+	+++	+

Fourth Nerve Palsy

This is the commonest type of isolated ocular palsy, which is most frequently due to trauma; the head injury may not be severe, the period of unconscious-

ness being less than thirty minutes. Bilateral fourth nerve palsies are associated with severe head injuries and are probably due to a lesion at the anterior medullary velum. The fourth nerve is the only motor nerve arising from the dorsal part of the central nervous system; it is the most slender cranial nerve and, contrary to much teaching, has a longer intracranial course than the sixth.

Third Nerve Palsy

Pupillary dilatation in a third nerve palsy is usually due to a compressive lesion as the pupillo-constrictor fibres are not only smaller but are situated on the periphery of the nerve.

Aneurysm

If a patient with a third nerve palsy complains of pain in the forehead on one side, the putative diagnosis should be an aneurysm until proved otherwise. Although pain may be a feature of an arteriopathic palsy, the pain of an aneurysm is persistent, progressive, and in the distribution of the ophthalmic branch of the fifth nerve, whereas the pain of diabetic ophthalmoplegia occurs in less than 50 per cent of these cases, lasts less than a week, and may be more generalised. Furthermore, only a minority of the latter will have involvement of the pupil. Third nerve palsies due to aneurysm show a sex incidence in favour of the female, the age incidence being in the fifth, sixth, and seventh decades. In these cases the third nerve palsy is usually complete; there is complete ptosis and on lifting up the ptosed lid the pupil is seen to be dilated and fixed, and the eye is deviated laterally due to the unopposed action of the still functioning lateral rectus muscle. There is loss of adduction, elevation, and depression, but intorsion of the eye, due to the integrity of the superior oblique muscle, is still seen.

Carotid arteriography will confirm the presence of an aneurysm which is usually situated at the origin of the posterior communicating artery at the termination of the internal carotid artery. In these cases, carotid ligation, if the patient is under 70 years, is the treatment of choice.

Table 3 shows the frequency of aniscoria and third nerve palsies of nearly a thousand cases of ruptured intracranial aneurysms that were followed up over a period of five years (Sarner and Rose, 1967).

Diabetic Ophthalmoplegia

In this, the sex incidence is equal and the age incidence is similar to that of aneurysm. The average duration of the diabetes is several years or diabetes may

TABLE 3. Ruptured intracranial aneurysms
(Neuro-ophthalmological signs in 962 cases)

	Anterior	Middle	Posterior	Vertebro-basilar	Totals
No. of cases	381	253	292	36	962
Aniscoria	7%	7%	20%	21%	12%
Third nerve palsy	2%	1%	17%	12%	7%
Intra-ocular haemorrhages	13%	15%	9%	21%	13%
Papilloedema	11%	10%	6%	6%	10%
Homonymous hemianopia	5%	16%	10%	3%	10%

be diagnosed at the onset of the ocular palsy (Rose, 1965). The precise pathogenesis is unknown since there have been very few autopsy studies, and these few have suggested occlusion of the vasa vasorum of the ocular motor nerves in their extra-cerebral course. The intra-cavernous portion of the third nerve receives its blood supply from the internal carotid. The anterior part is supplied by recurrent branches from the ophthalmic artery and the posterior part from the circle of Willis via the posterior communicating and posterior cerebral arteries. The nerve becomes septate and enlarged as it proceeds anteriorly in the cavernous sinus. One autopsied case revealed a focal lesion in the intra-cavernous portion of the third nerve which was discrete over a few millimetres, sparing the peripheral fibres.

Sixth Nerve Palsy

Diabetes is also a common cause of a sixth nerve palsy but the next most common cause is neoplasms, half of which are metastatic.

The next commonest cause of a sixth nerve palsy is multiple sclerosis, the average age being in the mid-thirties; in nearly half these cases the palsy is the initial symptom.

Although functional recovery of diplopia is the rule, orthoptic testing reveals residual paresis, and a follow-up of these cases suggests that the mortality from the underlying disease is greater than previously considered (Rose, 1973a). For this reason, an ocular palsy due to a vascular lesion should be regarded as a TIA or 'little stroke' with the same potential for recurrence, morbidity and mortality.

VISUAL FIELD DEFECTS

Optic Neuritis

The commonest of these is a central scotoma and the usual cause is 'optic neuritis'. The essential features of this syndrome are that it is more common in

women than in men, in the proportion of 3:2; 85 per cent of cases occur between the ages of 18 and 55; the patients present with unilateral blurred vision, most often a central scotoma; there is often pain on movement or tenderness of the globe; there are pupillary and colour vision abnormalities, but in over 90 per cent of cases the vision returns to normal or near normal within a few months, to leave—but not invariably—temporal pallor.

Although the literature mentions about 60 different causes for this syndrome, there has never been definite proof of any cause other than demyelination. Not all the cases are disseminated at onset, or will even develop disseminated sclerosis after prolonged follow-up, but the isolated syndrome is identical with that which occurs in the course of disseminated sclerosis and my own view is that demyelination is the only cause of the syndrome (Rose, 1972).

Static Perimetry

Static perimetry is more accurate than kinetic perimetry, e.g. Bjerrum screen, where one part of the retina is compared with another and gives only a generalised picture. With static perimetry, the retinal response at a given point is measured. There are multiple patterns of light stimuli, and the time taken to test a field is less than five minutes; it can be done by a nurse or a technician. Because identical points on the retina are always tested the repeated fields give an accurate indication of any change (Friedmann and Rose, 1970). The Friedmann screener has constant external illumination, which is adjusted for mesopic vision (1 lumen/ft^2). Furthermore, the sizes of the holes vary with retinal sensitivity so that they are larger in the periphery; they have been standardised for normal people over different age ranges. An electronic flashlight is used which does not blacken and since this lasts for only one eight-hundredth of a second, eye movements do not affect the result and, because neutral density filters are used, variations in the intensity of light can be accurate. The machine can also be used for investigating macular threshold and dark adaptation, which can be useful for distinguishing retinal from optic nerve lesions.

Visual field defects may be due to vascular disease affecting either the central retinal or ophthalmic arteries, when the defect will be unilateral (Rose, 1969), or branches of the middle or posterior cerebral arteries, when the defect produced is a homonymous hemianopia. Consideration must be given in some of these cases to angiography and possible surgery (Rose *et al.*, 1971).

Progressive enlargement of a visual field defect suggests a compressive lesion. A central scotoma that spreads and breaks through to the periphery of the visual field suggests optic nerve compression (Rose and Condon, 1967a) whereas a bitemporal hemianopia indicates a chiasmal lesion. It is only in advanced cases that the hemianopia is complete (Richardson and Rose, 1965).

Bitemporal Hemianopia

The commonest chiasmal lesion is a pituitary tumour; signs of hypopituitarism, especially loss of axillary and pubic hair and a smooth waxy discoloration of the facial skin, are often evident to the experienced examiner. A plain lateral X-ray of the skull will show an abnormal sella in over 90 per cent of cases of chromophobe adenoma and the findings include undercutting of the anterior clinoid process with sharpening of its tip, a straightening back and thinning of the dorsum sellae with erosion of the base of the sella turcica often forming a double floor. Ballooning of the sella is often a chance finding and may be without significance.

A craniopharyngioma usually, but by no means invariably, occurs in a younger age group. In these cases, the bitemporal hemianopia may vary in outline on repeated testing, indicating the cystic nature of the tumour. Again, the most useful investigation is a skull X-ray since, in 50 per cent of cases, calcification will be seen in a postero-superior position to the pituitary fossa. Suprasellar meningiomas calcify less commonly and diagnosis will depend on specialised neuro-radiological procedures since the EEG, echo encephalogram and scan are not usually helpful in this situation. Metastases are not an uncommon cause of chiasmal compression and should be considered in all cases where a primary malignancy has been removed, albeit many years previously. Rarer causes are listed in Table 4, and where there is a high index of suspicion and investigations are unrevealing, exploratory craniotomy may be indicated (Rose and Richardson, 1966).

TABLE 4. Chiasmal lesions

1. Chromophobe adenoma
2. Suprasellar meningioma
3. Cranopharyngioma
4. Metastases
5. Glioma
6. Chordoma
7. Aneurysm
8. Dermoid
9. Trauma
10. ? Arachnoiditis

FUNDAL CHANGES

Optic Atrophy

Optic atrophy is not a diagnosis but a physical sign signifying excessive pallor of the optic disc. Physiologically it may be seen in children, the elderly (Rose, 1973b) or myopes; it may be the result of systemic disease, e.g. anaemia, but pathologically it is due to a loss of blood supply to the damaged neurones of

the optic nerve. It may be classified according to its funduscopic appearance (Table 5), anatomically or physiologically, but clinically the most helpful categorisation is aetiologically, as shown in Table 6 (Rose, 1964).

TABLE 5. Optic atrophy

Ophthalmoscopic	
1. Primary	white disc sharp edge
2. Secondary	grey disc blurred edge
3. Consecutive	yellowish disc retinal lesion

TABLE 6. Optic atrophy

Aetiology

1. Genetic
   - (*a*) Dominant
   - (*b*) Leber's
   - (*c*) Behr's
   - (*d*) consecutive
2. Congenital
3. Traumatic
4. Multiple sclerosis
5. Secondary
6. Glaucoma
7. Vascular
8. Compressive

The commonest cause of optic atrophy, if unilateral, is optic neuritis and, if bilateral, glaucoma. The latter gives a deep 'cavernous' appearance to the optic discs.

A careful family history may reveal a genetic basis for the optic atrophy, the commonest type being by dominant inheritance; the next commonest is Leber's optic atrophy where the mode of transmission does not fit in with Mendelian inheritance (Rose and Friedmann, 1964). Eighty per cent of those affected are males; the onset is usually in the second and third decades and is rapid and bilateral but asymmetrical, affecting successive eyes within a few days to a few months. Complete blindness is exceptional and the therapeutic value of hydroxycobalamin is still uncertain as spontaneous improvement can occur. Pathological studies are rare but there is evidence of multi-system involvement, e.g. the heart (Rose *et al.*, 1970). Recessive inheritance of optic atrophy is exceptionally rare but may be associated with other genetic diseases, e.g. juvenile diabetes (Rose *et al.*, 1966).

Disc Oedema

The blurred disc margin often proves a problem since it may be due to hypermetropia and other insignificant variations. A great advance in distinguishing 'pseudo-papilloedema' from true oedema of the disc has been fluorescein angiography (Hill, in preparation) which may then obviate the need for potentially harmful neuro-radiological investigations.

TABLE 7. Disc oedema

Intracranial	*Intra-orbital*
Raised pressure:	Low intra-ocular tension
Space occupying lesion	Ischaemic papillopathy
Hydrocephalus	'Papillitis'
Cerebral oedema	Posterior uveitis
Meningitis	
Venous obstruction	

The causes of disc oedema may be divided into intra-orbital and intracranial (*see* Table 7). Of the intra-orbital causes, posterior uveitis is now the commonest cause because the anterior chamber may be cleared by topical steroid therapy. The awareness of this, e.g. in sarcoidosis, will help in preventing unnecessary neuro-radiological investigations (James *et al.*, 1967). As to intracranial causes, papilloedema is not as commonly noticed in cases of meningitis (Rose and Condon, 1967b) although it may be seen in any type of meningoencephalitis, including herpes zoster (Rose *et al.*, 1964).

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