THE EYE AS A MIRROR OF SYSTEMIC DISEASE

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Irrespective of speciality, examination of the eyes should be part of the routine physical examination. Quite apart from purely ocular disease, this will yield valuable information regarding systemic diseases, not least because the eye is the only part of the body where vascular and neurological tissue can be viewed directly.

EXAMINATION

Whilst full ophthalmological examination is time-consuming, a rapid examination can pick up many significant abnormalities. The bulbar and tarsal conjunctival surfaces should be inspected for signs of inflammation, haemorrhage, anaemia and jaundice.

Using a small hat-pin, visual fields can be assessed surprisingly accurately by confrontation, a relative field loss being detected if the head of a red pin loses colour at any point. Using this technique, even an enlarged blind spot can be found, but field defects will need to be confirmed with formal perimetry.

Examination of the pupils will reveal asymmetry or irregularity; generally speaking, the older the patient the smaller are the pupils. Light reflexes, both direct and consensual, should be tested as well as pupil constriction with convergence.

It is usually possible to examine the optic discs through an undilated pupil, but if a full fundus examination is necessary the pupils may be dilated with a short-acting mydriatic such as cyclopentolate. This is contraindicated in patients with glaucoma and those whose consciousness is fluctuating or who need neurological observation following a head injury or surgery. The optic discs are examined first and then the retinal arteries and veins are followed out to the four quadrants of the retina. Particular attention should be paid to the area of the macula 1½ disc diameters on the temporal side of the optic disc, since even minor abnormalities in this region produce a profound decrease in visual acuity.

The face should be studied to exclude asymmetry of the eyes; for example one eyeball may be depressed if there is a tumour involving the orbit or a vascular anomaly in the cavernous sinus. Ptosis or inability to close the eyelids may be the result of a weakness of the orbicularis oculi muscles, resulting from a VIth (facial) nerve palsy. Lid retraction with white sclera visible between the iris and eyelids is evidence of thyroid disorder.

The best test of function is to measure the visual acuity, using a reading test type for near vision, and a Snellen chart for distance vision, via a pin-hole to eliminate refractive errors if necessary. If these charts are not available, reasonable assessments can be made with various sizes of newspaper print. If the vision in one eye is greatly reduced compared with the other, enquiry may reveal that the affected eye has been "lazy" (amblyopic) since childhood.

External ocular movements should be tested next, but even if normal it is important to ask the patient whether he sees double as diplopia can occur without clinical evidence of impairment of ocular movements. The presence of nystagmus should also be noted with regard to the direction of the slow and fast phases.

Neurological abnormalities

Cranial nerve lesions

A IIIrd nerve palsy is not uncommon and can be recognized easily by ptosis; with the lid raised the affected eye will be fixed in abduction with a dilated unreactive pupil. A pupil-sparing IIIrd nerve palsy indicates vascular disease (hypertension or diabetes) rather than compression (aneurysm or tumour). A subdural haematoma is more likely to affect the Vth cranial nerve (producing paralysis of abduction), even though it does not have as long an intracranial course as the IVth. It is the nerve most frequently affected by increased intracranial pressure, meningitis or intracerebral haemorrhage. The commonest single cause of an isolated IVth cranial nerve palsy is a head injury, which need not necessarily be severe. In the unconscious patient, a fixed dilated pupil is one of the earliest signs of tentorial herniation.

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Frequently abnormalities of more than one oculomotor nerve are found. A compressive lesion within the cavernous sinus, such as a pituitary tumour, metastatic carcinoma or aneurysm of the internal carotid artery, may affect all three cranial nerves as well as resulting in other symptoms, such as proptosis, pain behind the eye and, in the case of a carotid cavernous fistula, a loud buzzing noise audible on auscultation as a bruit. The finding of a IIIrd, IVth or VIth nerve palsy provokes a search for a surgically remediable cause but, in many cases, especially in the older age group, the cause is an occlusive lesion of the blood vessels serving these nerves and indicative of generalized disease. The commonest is diabetes mellitus, which usually affects the IIIrd nerve but does not often involve the pupil. Pain may occur in diabetic ocular palsies, as with an aneurysm, but it is usually short lived.

The other main cause of arteriopathic ocular palsy is hypertension and sometimes a hyperlipidaemia is also found. Treatment consists of controlling the arterial pressure and any lipid abnormality. Before the age of 40 yr, multiple sclerosis should be considered as a possible cause of ocular palsy. Another cause of isolated cranial nerve palsy in younger patients is sarcoidosis, the facial nerve being the commonest affected. Other systemic disorders affecting isolated ocular motor nerves are less common, for example connective tissue disorders, such as polyarteritis nodosa or systemic lupus erythematosis, ascending polynévrites (Guillain-Barré syndrome) and meningo-vascular syphilis; examination for treponemal serology in the blood and c.s.f. should not be forgotten.

**Diseases of the ocular muscles and neuromuscular transmission**

The commonest cause of an impairment of ocular movement involving the external ocular muscles directly is thyroid eye disease. Frequently, only elevation of the eye is affected but there are often other signs, such as proptosis, lid retraction and lid lag.

A space-occupying lesion within the orbit will affect ocular movement and result in proptosis and pain, in which case CT scanning of the orbits is a fruitful investigation. It may be necessary to biopsy a discrete mass, either directly or via the ethmoidal route, since orbital secondaries from various sites such as bronchus, breast or kidney are well recognized.

Sometimes, a mass may appear to be a diffuse increase in intra-orbital soft tissue or may arise from the external ocular muscles themselves; this condition is known as orbital pseudo-tumour and the diagnosis is confirmed by biopsy, which will usually reveal granuloma formation. Orbital pseudo-tumours are frequently painful and respond to treatment with steroids and azathioprine; if left untreated, visual loss as a result of compression of the optic nerves may result.

Proptosis can also occur if the orbit is invaded from the frontal sinus by tumour or mucocoele and suggestive symptoms include nasal or blood-stained post-nasal discharge, or frank epistaxis. Wegener's granuloma affecting the naso-pharynx or sinuses may also invade the orbit directly.

A genetically determined disorder affecting the external ocular muscles is progressive external ophthalmoplegia; this is an ocular muscular dystrophy presenting usually in the second or third decades with bilateral ptosis followed by symmetrical loss of ocular movements. In a few cases other muscle groups may be affected; the diagnosis is confirmed by electromyography and muscle biopsy.

**Myasthenia gravis.** The external ocular, orbicularis oculi and levator palpebrae muscles are amongst the most frequently affected in myasthenia. Some cases remain confined to these muscles when the disease generally has a benign course. The characteristic feature in the history is the fluctuation in symptoms such as diplopia or ptosis during the day so that they are worse in the evening or after exercise. On examination fatiguability of the affected muscles is elicited. The most widely used diagnostic test is the edrophonium (Tensilon) test. It is sometimes difficult to assess the result in mild cases when a therapeutic trial of anticolinesterases such as neostigmine or pyridostigmine may be justified. In cases with a more peripheral distribution, single fibre electromyography can assist in diagnosis. Ninety per cent of patients with myasthenia have increased antibody to acetyl choline muscle receptors, but this test is not yet widely available. Ocular myasthenia can usually be treated with anticolinesterase drugs alone, although the results are not always satisfactory, and other measures such as ptosis splints or muscle resection may be needed. (Widespread myasthenia may be treated with steroids, thymectomy or plasmapheresis. Symptoms of dyspnoea and dysphagia must be taken seriously and assisted ventilation considered if lung function is markedly reduced.)
**The pupil**

The value of pupillary reactions in assessing neurological states following head injury (particularly in connection with a subdural or intra-cerebral haemorrhage) is well known, as are the contraindications to instilling mydriatic drops in such cases. The well-known Argyll Robertson pupil is classically small and irregular, not responding to light, but responding to accommodation. Although usually associated with neuro-syphilis, it can occur with diabetes mellitus and multiple sclerosis.

Adie's myotonic pupil is usually unilateral and found in young women, where the patient frequently notices dilatation of one pupil and may complain of blurring of near vision. On casual testing the affected pupil may not appear to react to light at all, but will dilate slowly in response to prolonged darkness and contract again slowly when re-exposed to light; response to accommodation and convergence is also slow. A brisk response to dilute pilocarpine is a useful diagnostic test. In some patients tendon reflexes are absent, although there are not usually other nervous system signs. Treatment other than reassurance is rarely required.

A unilateral constricted pupil with partial ptosis, endophthalmas and anisodromis of the ipsilateral side of the face are characteristic of Horner's syndrome, although the latter two signs are notoriously difficult to detect. This results from a lesion of the sympathetic nerve supply anywhere from the brain stem to the ciliary ganglion which provides stimulatory fibres to part of levator palpabrae superioris and dilator fibres to the pupil; whilst occasionally congenital, the most important possibility to exclude is an apical carcinoma of the bronchus. The commonest cause is cluster headaches—a form of migraine. Other causes of Horner's syndrome are vascular lesions of the pons and medulla, syringomyelia and syringobulbia, cervical spondylisis, disc prolapse and cervical lymph nodes enlarged by infection such as tuberculosis, or by lymphoma or secondary tumour. It occasionally occurs in multiple sclerosis and viral encephalitis.

A dilated unreactive pupil with ptosis and impaired ocular movements is characteristic of a IIIrd nerve palsy; in such cases the pupil has no consensual and no direct reflex, thus indicating that the lesion is in the parasympathetic fibres controlling the pupillary sphincter muscle, rather than in the optic nerve.

Another important sign is the relative afferent pupillary defect. In this sign there is little direct or consensual response to a light shone into the affected eye, but a brisk direct and consensual response when the light is shone into the unaffected eye. When the light is moved to the affected eye again, both pupils dilate. This phenomenon is best elicited by swinging the beam of a bright torch from one eye to the other fairly rapidly. Where there is marked optic atrophy and visual loss in the affected eye this sign does not provide any extra information but, in cases where the sign is positive, if the affected eye has good vision and the optic disc appears normal, it usually indicates a previous episode of optic or retrobulbar neuritis. This finding may assist greatly in the interpretation of neurological symptoms and signs found (Perkin and Rose, 1979).

Many systemic drugs may affect the pupillary responses, particularly if used in excess. Pin-point pupils may result from opiate administration, therapeutically or illegally, and dilated pupils can result from a large range of drugs with anticholinergic effects such as tricyclic antidepressants. This effect must be borne in mind when administering such drugs to patients with closed angle glaucoma in whom an acute attack may be precipitated.

**The optic disc**

The two basic abnormalities which may be seen in the optic disc in systemic disease are disc swelling and disc pallor.

A red swollen disc with blurred margins is frequently referred to as papilloedema, whatever the cause, but preferably this term should be restricted to swelling resulting from increased intracranial pressure produced by cerebral tumour, abscess, haemorrhage, hydrocephalus or other causes. In papilloedema, visual acuity is not affected and the only abnormality on visual field testing is enlargement of the blind spot. If the intracranial pressure is increased for a long period, the patient may notice brief episodes of loss of vision in the affected eye lasting a few seconds and associated with manoeuvres increasing intracranial pressure such as bending or straining. This is a result of intermittent obstruction of the arterial blood supply to the retina by pressure within the optic nerve and is usually termed an obscuration. It is a sign that, if the intracranial pressure is not decreased, permanent ischaemic damage to the disc and retina may ensue, since longstanding papilloedema can result eventually in optic atrophy.

The main causes of increased intracranial pressure are well known, but a syndrome now diagnosed more frequently is benign intracranial hypertension, where symptoms and signs of increased intracranial pressure.
are found without evidence of a space-occupying lesion or ventricular enlargement on cerebral CT scanning. A lumbar puncture (after a CT scan) will demonstrate increased c.s.f. pressure. The condition is most common in obese young women with menstrual irregularity, but there are numerous other causes, including steroid therapy, administration of tetracycline, naladixic acid, endocrine disorders and following head injury and middle ear disease. If left untreated, permanent visual loss may occur by the mechanism described above.

In disc swelling from causes other than increased intracranial pressure, the central vision and therefore visual acuity are affected early and visual field testing will demonstrate a central scotoma in the affected eye. In younger patients, by far the most common cause is optic neuritis, which characteristically presents as blurring of vision in the affected eye with pain on eye movement. This usually recovers after a few weeks, although the visual acuity may be slightly less than before the attack. The optic disc may become pale, but, if normal, the finding of a relative afferent pupillary defect will help elucidate what has occurred. In retrobulbar neuritis the same symptoms occur, but the disc appearance remains normal. If patients with optic neuritis are followed for a sufficient time, the majority will progress to develop lesions of multiple sclerosis (Perkin and Rose, 1979). Sometimes, neurological abnormalities are found at the time of an attack of optic neuritis even when the patient has not noticed other symptoms. Multiple sclerosis is still basically a clinical diagnosis, but supporting evidence may be obtained from visual evoked response testing (which shows a delay in the transmission of nerve impulses from the affected eye to the occipital cortex) and the finding of specific patterns of immunoglobulins (oligoclonal bands) in the c.s.f.

In patients of more than 50 yr, the most common cause of disc swelling is ischaemic papillopathy which results from small vessel vascular disease. This syndrome presents with painless loss of vision occurring over several hours. The field defect is a central scotoma extending irregularly outwards with areas of preserved vision; in some cases only the upper or lower halves of the visual field are lost, whilst in others a crescentic area of the visual field is lost with sparing of central vision.

Optic atrophy frequently follows periods of optic disc swelling, but may occur without disc swelling, when the optic nerve is directly compressed by a tumour, such as a sphenoid ridge meningioma. In such cases a cerebral CT scan is invaluable. Optic atrophy may also follow retinal disease, but this is usually obvious on ophthalmoscopy.

**Visual field defects**

Plotting visual fields can assist greatly in the siting of an intracerebral lesion. Direct pressure on an optic nerve gives a central scotoma, but lesions compressing the crossing fibres of the optic chiasm, for example pituitary tumours, craniopharyngiomas and internal carotid aneurysms, will give rise to classical bitemporal hemianopia. These lesions can be missed on CT scanning so that, if the field defect is definite, it is sometimes necessary to proceed to air encephalography or exploratory craniotomy on the basis of the visual field defect alone.

A lesion of the cerebral cortex posterior to the chiasma, involving the optic tract or radiation, will result in a homonymous hemianopia; if of slow onset, a cerebral tumour should be sought. If there is a history of sudden onset of loss of part of the visual field, this usually indicates a vascular cause; characteristically infarction of the occipital lobe produces an homonymous hemianopia with sparing of the central area as a result of the dual blood supply of the area of cortex relating to the macula and therefore central vision. Postoperative plotting of visual fields following removal of tumours, particularly those arising from the pituitary gland, can often give warning of recurrence even before there is any radiological evidence.

Hysterical blindness can usually be diagnosed on the basis of the patient's behaviour, normal ophthalmological appearances and bizarre field loss. A normal visual evoked response will provide instant confirmation of this diagnosis.

**Inflammatory disorders**

**Uveitis**

The iris, ciliary body and choroid comprise the uveal tract and involvement of one or all of these structures is a feature of a wide range of systemic diseases. Anterior uveitis involving the iris and ciliary body presents as blurred vision with a painful photophobic red eye, whereas posterior uveitis is usually painless. In more than half the cases of uveitis seen, no systemic association can be found— "endogenous" uveitis.

Probably the commonest systemic cause of uveitis in the world is onchocerciasis, but this is normally confined to developing countries. The most common infectious cause of uveitis in the United Kingdom is
congenital toxoplasmosis, which can usually be diagnosed from its distinctive fundal appearance. Toxoplasma dye tests reflect intraocular activity poorly, so ophthalmological observation is the principal method of assessing progress. As this is basically an autoimmune process, steroids are necessary to reduce activity. Pyrimethamine and cotrimoxazole have not been shown to halt intraocular activity in these cases. Tuberculosis may be diagnosed on the basis of choroidal tubercle, and other rare infectious causes of uveitis include syphilis, brucellosis, leptospirosis and toxocara infiltration.

HLA typing has demonstrated a link between uveitis and certain systemic disorders. The HLA B27 group of diseases, including ankylosing spondylitis, Reiter's syndrome, ulcerative colitis and Crohn's diseases with arthropathy, may all give rise to uveitis. In such cases, however, the arthritic manifestations usually precede the ocular changes. HLA B5 has been found to be associated with Behcet's syndrome, the major features of which are iritis, thrombophlebitis and oro-genital ulceration. Many other systems such as the alimentary tract and the central nervous system are more rarely involved.

The most serious ocular complication of Behcet's syndrome is the progressive obliteration of the retinal vasculature, which can result in complete blindness within a few years. It is important to make the diagnosis as the ocular changes respond poorly to treatment with steroids alone, whereas the addition of immunosuppressive drugs such as azathioprine and chlorambucil may at least retard the visual loss, if not prevent it completely.

In children, the commonest systemic cause of uveitis is Still's disease. Children at risk of developing uveitis can be identified by the fact that 80% of them will be positive for antinuclear factor, whereas only 30% of all patients with Still's disease are positive.

In young adults the commonest systemic cause of anterior and posterior uveitis is sarcoidosis and all such patients should be screened at least with a chest x-ray, Mantoux test (negative in the majority of cases of sarcoidosis) and serum calcium concentration. If any of these are abnormal or there are other suspicious features, more detailed investigations such as a Kveim test, alveolar transfer factor and bronchoscopy may be required. Sarcoidosis may also cause keratoconjunctivitis sicca and conjunctival lesions. Frequently treatment with systemic steroids is necessary to control the ocular manifestations of sarcoidosis as well as involvement of other systems.

Chronic uveitis resulting from sarcoid may have a poor prognosis, in spite of treatment.

Other connective tissue disorders

Other connective tissue diseases may affect the eye although they cause uveitis only rarely. Systemic lupus erythematosus may cause "cystoid bodies" in the retina and a positive DNA binding test is confirmatory.

There is no specific ocular appearance to polyarteritis nodosa, which causes scleritis; renal involvement may lead to the appearance of a hypertensive retinopathy. Rarely, it may cause anterior uveitis and retinal vasculitis, as may the related disease of Wegener's granuloma. Diagnosis of these two conditions usually depends on the histological appearance on biopsy of affected tissue such as kidney, lung or naso-pharynx. Polyarteritis nodosa may also be diagnosed from the characteristic appearances on mesenteric angiography.

By far the most common connective tissue disease is rheumatoid arthritis, the main ocular manifestation of which is kerato conjunctivitis sicca syndrome, in which lachrymal and salivary gland output is diminished, resulting in dry, gritty eyes and difficulty in masticating and swallowing. It is one of the most difficult ocular conditions to treat satisfactorily. Rarely, rheumatoid involvement of the anterior sclera, usually a mild episcleritis, may progress remorselessly to perforation of the eyeball—"scleromalacia perforans".

Giant cell arteritis

This is one of the most important systemic diseases affecting the eyes in the elderly. A history of malaise, severe headaches, scalp tenderness, painful swellings in the temporal areas and pain on chewing are indications for measuring the erythrocyte sedimentation rate (e.s.r.). If this is increased, treatment with large doses of steroids, administered i.m., should be started and temporal artery biopsy carried out within 48 h to confirm the diagnosis. If left untreated, the catastrophe of central retinal artery occlusion and blindness in one or both eyes may ensue rapidly. Even if vision in one eye has already been lost, prompt treatment may save the other eye. It is worth remembering that this disease is not confined to the temporal and ophthalmic arteries; rarely, strokes resulting from the involvement of vertebral, carotid and intracranial arteries may occur and coronary artery occlusion has also been reported.
The syndrome of polymyalgia rheumatica has been shown to overlap with giant cell arteritis, and patients with this condition should be kept under long-term observation with checks of the e.s.r. at regular intervals. The pathogenesis of these two conditions is as yet unknown, but they are confined to patients of more than 50 yr. Rather surprisingly, it has been found that life expectancy is not reduced by giant cell arteritis, even though patients may require treatment with systemic steroids for years.

Viral infections of the eye

The eye is only rarely directly involved in systemic bacterial infections, but is far more commonly infected by viruses. Marked conjunctivitis may be a feature of adenovirus infections and conjunctivitis is frequently part of measles and influenza. More serious are herpes virus infections, especially in the elderly or immunosuppressed patients. *Herpes simplex*, while causing cold sores elsewhere, may result in a keratitic corneal ulcer. This usually responds to local idoxuridine, but disaster may occur if local steroids are administered without slit lamp examination. It is inadvisable to prescribe steroid drops for any eye condition before a specialist opinion has been obtained. *Herpes zoster* may involve the eye in shingles, if this involves the ophthalmic division of the trigeminal nerve. Here again, the mainstay of treatment is local idoxuridine. Many other viruses such as *Papovirus* and *Cytomegalovirus* may involve the eye, but these are not usually serious, except in the case of congenital cytomegalovirus disease.

Vascular disorders

Hypertension and vascular occlusion

Examination of the fundus is essential in the evaluation of the severity and duration of hypertension. The grading of hypertensive retinopathy is well known, but it is probably better to record the actual features of the retinopathy rather than the grade. Hypertension secondary to renal failure shows no specific features. The so-called "macular star" or hard exudates is a reflection of severe prolonged hypertension, rather than a direct result of renal impairment. Obviously, the more severe the retinopathy and thus the hypertension, the more likely the finding of renal failure as a cause, or result, of severe hypertension.

Visual loss is not usually a feature of uncomplicated hypertensive retinopathy, although the patients may notice blurred vision because of macular oedema when papilloedema is present. If there is sudden loss of vision in a patient with hypertension, this is usually produced by occlusion of either the arterial or the venous retinal circulation. These are more common in hypertensive patients, presumably because of more marked sclerotic changes in the vessels. In a central retinal artery occlusion, all retinal arteries are narrowed and attenuated and the retina is pale. In some cases only the short posterior ciliary vessels serving the optic discs are involved, in which case the appearance is that of a swollen disc with a relatively normal looking retina in the early stages. In both these cases the prospect for unimpaired vision is poor.

The appearance of a central retinal vein occlusion is more dramatic with widespread haemorrhages, dilated veins and retinal oedema. However, the prognosis is better, with gradual return of vision to near normal in some cases. In about 15% of cases, a secondary thrombotic glaucoma may ensue. There is no specific treatment for retinal arterial and vein occlusion although, if there is marked macular oedema, laser photocoagulation may be of benefit. Hypertension should of course be treated, but it is important not to reduce the arterial pressure too rapidly as reduced perfusion may result in cerebral or retinal ischaemia, the latter resulting in blindness.

Retinal artery and venous occlusion may also be found in association with hyperlipidaemia and in diseases where blood viscosity is increased, such as myeloma, polycythaemia and leukaemia and retinal vein occlusion is also found in association with diabetes.

Diabetes mellitus

The eye is frequently involved in diabetes. Diabetic neuropathy may involve cranial nerves, but blurring of vision is common when the diabetic state is not well controlled, because of dehydration of the lens. Cataracts occur in people with diabetes more frequently than those who are not diabetic and glaucoma may result from rubeosis when small vessels form in the angle of the anterior chamber. The most serious form of diabetic eye disease, however, affects the retina and vitreous. The characteristic retinal lesions are microaneurysms and blot haemorrhages with hard and soft exudates and the retinal veins are usually dilated and irregular. If this progresses, small new vessels may arise with fibrosis. This can result in retinitis proliferans with severe impairment of vision and may also lead to vitreous haemorrhages, adding to visual loss, although this aspect may recover.
Although not conclusively shown to improve prognosis, it is reasonable to keep patients with diabetic eye disease under particularly good control. Cataracts and glaucoma respond to the usual measures but retinopathy is a far more serious problem. Clofibrate speeds the resolution of exudates, but does not improve vision. Pituitary ablation may retard new vessel formation and venous dilatation, but its ultimate effect in preserving sight is still not definitely known. The most hopeful form of treatment at the moment is laser photocoagulation of new vessels, which may prevent retinitis proliferans and vitreous haemorrhages. Where vitreous haemorrhage has occurred and does not clear, vitrectomy may result in recovery of vision. In spite of these measures, diabetic eye disease remains a significant cause of blindness in the United Kingdom.

**Transient visual loss**

Complete loss of vision in one or both eyes, lasting for only a short period is known as amaurosis fugax. It results from a temporary reduction of the retinal arterial supply. This may occur with any episode of systemic hypotension, such as during cardiac arrhythmia, iatrogenic postural hypotension or a simple vaso-vagal episode. In such cases bilateral visual loss frequently occurs but, if retinal perfusion is reduced in one eye, such as from increased intraocular pressure, it may be unilateral.

The major cause of transient unilateral visual loss is emboli passing through and occluding the ophthalmic, central retinal and retinal branch arteries. The emboli may be composed of platelet aggregates or cholesterol crystals and arise from two main sources, the heart and the carotid arteries. Occasionally, emboli may actually be seen passing through the retinal circulation. Cholesterol emboli are bright and refractile and may leave an area of sheathing of the artery they have traversed. Platelet emboli are more usually detected by an interruption of a column of blood within an artery. Emboli from the heart may form during episodes of paroxysmal arrhythmia such as supraventricular tachycardia or within an atrium affected by atrial fibrillation. They may arise from abnormal valves, either congenital, such as bicuspid aortic valves or prolapsing mitral valve leaflet, valves damaged by rheumatic fever or bacterial endocarditis, or prosthetic valves. Emboli may originate from mural thrombus in the weeks following a myocardial infarct, or from the thrombus contained within a subsequent left ventricular aneurysm. Patients with mitral valve leaflet prolapse, left ventricular aneurysm and rheumatic heart disease are, of course, also more prone to paroxysmal arrhythmia.

Investigation of patients with amaurosis fugax and a history or physical signs suggesting cardiac abnormalities, including all younger patients with amaurosis fugax, should include, as well as routine radiography and electrocardiography, an echocardiogram and 24-h ECG recordings. In the older age groups emboli more commonly arise from atheromatous plaques in the common and internal carotid arteries. These may be detected as bruits over the arteries, but this is not always the case and carotid arteriography is the investigation of choice.

The significance of amaurosis fugax is not so much the possibility of permanent loss of vision, which is not common, but that such patients are at risk from cerebral embolism and infarction. It is important, therefore, to eliminate the formation of emboli if possible. Cardiac sources will require specific treatment such as drug treatment of arrhythmia and surgery to damaged valves and ventricular aneurysms. Carotid atheromatous plaques are frequently accessible to surgery by endarterectomy. However, sometimes it is not possible to eliminate entirely the risk of embolus formation, and therapy directed primarily at preventing formation is required. In most patients with cardiac emboli and in all in whom there is a history of cerebral embolism, full anticoagulation with warfarin is required. However, platelet embolus formation within the carotid artery has been shown to be inhibited with a small dose of aspirin and trials are in progress to determine whether sulphinpyrazone and dipyridamole are equally as effective.

The visual disturbance of migraine is usually characteristic fortification spectra and shimmering lights warning of the onset of an attack, but occasionally the aura may consist of an homonymous hemianopia lasting a few minutes. Rarely, this aura may occur regularly without being followed by a headache, resulting in diagnostic confusion. The limited duration of these episodes, however, gives a clue as to their aetiology.

**Haematological disorders**

Any haematological disorder which increases blood viscosity, such as leukaemia, thrombocythaemia, polycythaemia and dysproteinaemia, may cause retinal artery and vein occlusions and may encourage the formation of emboli resulting in amaurosis fugax. More specific ocular abnormalities occur in pernicious
anaemia, which may result in a swollen optic disc with a central scotoma and decreased visual acuity, and the various forms of sickle cell disease which may cause retinitis proliferans, vitreous haemorrhages and retinal detachments. Prophylactic laser photocoagulation may reduce the risk of these complications.

Endocrine disorders

Pituitary tumours

The majority of intrinsic pituitary tumours are slowly growing chromophobe adenomas. These can cause endocrine disturbances so insidiously that the first symptom noticed by the patient is visual loss resulting from the bitemporal hemianopia of chiasmal compression and they will initially present to the ophthalmologist. When a bitemporal hemianopia presents, a careful history of possible symptoms of hypopituitarism (with direct questions concerning impotence and loss of libido) should be taken. The patient will then require admission for a full radiological and endocrine work-up before surgery or radiotherapy, or both. The same considerations apply to any other tumour causing chiasmal compression, such as hypothalamic secondaries and craniopharyngioma. It should be noted that any patient with a suspected pituitary tumour should have a booster dose of steroids before any general anaesthetic, although the endocrinologists should be informed in case this interferes with their investigations.

Thyroid eye disease

Graves' disease is accompanied typically by the eye signs of upper lid retraction and swelling and unilateral or bilateral exophthalmos. More severe cases may show chemosis, corneal abrasions as a result of inability to close the eyelids, ophthalmoplegia and diplopia (usually on upward gaze). Very severe cases may lead to visual loss as a result of compression of the optic nerve from the increased pressure within the orbits. Such cases are medical emergencies and require immediate treatment with high doses of steroids, with or without azathioprine; if there is no improvement or vision continues to deteriorate, orbital decompression must be performed. Plasmaphoresis has been used in these conditions with success, but is still experimental.

While most cases of thyroid eye disease develop concurrently with clinical and biochemical hypothyroidism, some cases occur in euthyroid patients with normal free thyroxine concentrations. However, more than half such patients will show a flat TSH response to i.v. TRH which is characteristic of hyperthyroidism and many patients will develop overt hyperthyroidism in the future. In some cases, thyroid eye disease occurs after hyperthyroidism has been brought under control and it may be precipitated if the patient is rendered hypothyroid. The mechanism of thyroid eye disease is believed to be mediated by immunoglobulins, but routine tests for thyroid-stimulating immunoglobulins are not yet generally available. However, antithyroid antibodies, which can be measured in most hospitals, are also frequently present in such cases.

Abnormalities of calcium metabolism may be suspected from ocular examination. Hypercalcaemia can cause deposits of calcium at the lateral margins of the cornea, while prolonged hypocalcaemia may cause cataracts and papilloedema as part of the syndrome of bining intracranial hypertension.

DRUGS

Many drugs can affect the eye. Some of these have already been mentioned, but the most commonly used drugs with the most serious ocular side-effects are corticosteroids, chloroquine and ethambutol. Use of local and systemic steroids can cause cataracts as well as increasing intraocular pressure and precipitating glaucoma. As mentioned above, applying local steroids to herpetic keratitis may make the condition worse and result in permanent corneal scarring. Chloroquine is deposited in melanin-containing tissues including the choroid, and when used for prolonged periods can cause a toxic retinopathy with a characteristic Bull's Eye appearance at the macula. Once visual loss has occurred it is usually irreversible and use of this drug for extended periods of treatment, such as in rheumatoid arthritis and systemic lupus erythematosus should be accompanied by regular tests of visual acuity and colour vision. Such checks are also necessary when treating tuberculosis with ethambutol as this drug can cause toxic optic neuropathy. The usual regime of 15 mg kg\(^{-1}\) daily is considered unlikely to cause visual loss, but cases have been recorded at this dose, and although vision frequently improves after the drug has been withdrawn, this is not always the case.

Although this paper has reviewed only some of the more important systemic disorders affecting the eye, it has emphasized particularly that examination of the eye is a revealing and essential part of the general examination of any patient.
SUGGESTED READING
