Chapter 15

# Neuro-ophthalmology

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- Optic N.: mostly by p. ischemic att. / nerve head by ophthalmic art } ⊗ central retinal artery

- VF & ON: ON = centrocecal, central, arcuate, altitd
  chiasm = bitemp hemi, junct, binasal hemi
  OT = incongru homo hemi
  T Lobe = super quad
  Parietal upper "
  Occipt lobe =

- more congruous VF defect, the more post the lesion
- seen in tunnel vision, further you move back, larger the field they see
- B/L disc edema (mass until proven otherwise) update

  Malig HTN
  Mass
  Increased ICP (hydroceph)
  Meningitis
  Meds
  Pseudotumor (raised ICP)
  Malbreathing (Sleep Apnea)

# OPTIC NEUROPATHIES

## Evaluation of optic nerve disease

### CLINICAL FEATURES OF OPTIC NERVE DYSFUNCTION

The optic nerve head is the exit site for all retinal nerve fibres. The papillomacular bundle contains the small calibre nerve fibres which subserve the cone system of the fovea. Optic nerve lesions have a predilection for suppressing the function of this important anatomical structure and cause the following clinical signs:

1. **Reduced visual acuity** for distance and near.
2. **Afferent pupillary defect** (*see later*).
3. **Dyschromatopsia** (impairment of colour vision), which mainly affects red and green. A simple way of detecting a uniocular colour vision defect is to ask the patient to compare the colour of a red object such as the top of a Mydriacyl bottle. More accurate assessement requires the use of Ishihara pseudo-isochromatic plates (Figure 15.1).
4. **Diminished light brightness sensitivity**, which may be present even if visual acuity is normal, as after a previous attack of optic neuritis. This is best demonstrated as follows:
   (a) Shine the light from an indirect ophthalmoscope first into the normal eye and then into the eye with the suspected optic nerve lesion.
   (b) Ask the patient with which eye the light appears brighter.
   (c) The patient will report that the light appears less bright in the affected eye.
   (d) Another method is to shine lights simultaneouly into both eyes and ask which is brighter.
5. **Diminished contrast sensitivity**, which is tested by asking the patient to distinguish gratings over a range of spatial frequencies. This is very sensitive to subtle visual loss; although not specific to optic nerve disease.
6. **Visual field defects**, which can be of various types depending on the underlying lesion, such as central scotomata (Figure 15.2**a**), centrocaecal scotomata (Figure 15.2**b**), altitudinal (Figure 15.2**c**) and nerve fibre bundle defects (Figure 15.2**d**).

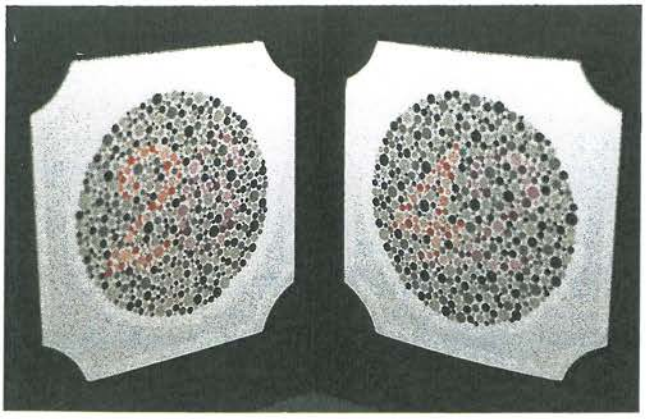


**Figure 15.1** Ishihara pseudo-isochromatic plates

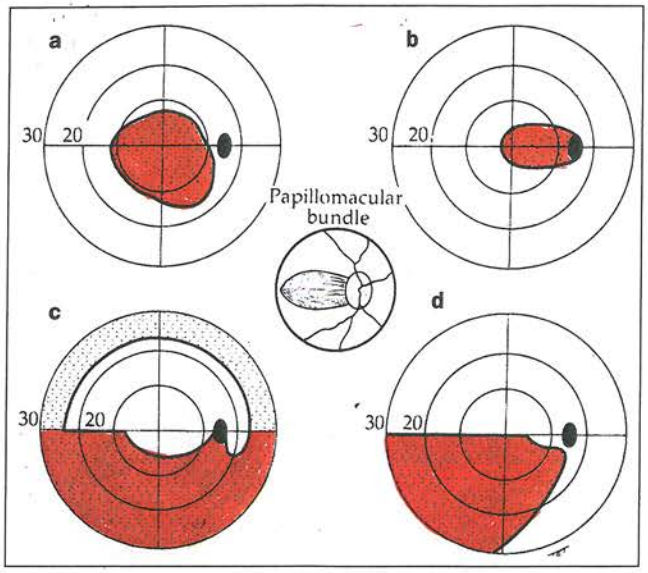



**Figure 15.2** Visual field defects in optic neuropathies

### OPTIC DISC CHANGES

It should be emphasized that there is no direct correlation between the appearance of the optic disc and visual function. The four main appearances in acquired optic nerve disorders are:

1. **Normal disc** (Figure 15.3), which is classically associated with retrobulbar neuritis, although the disc

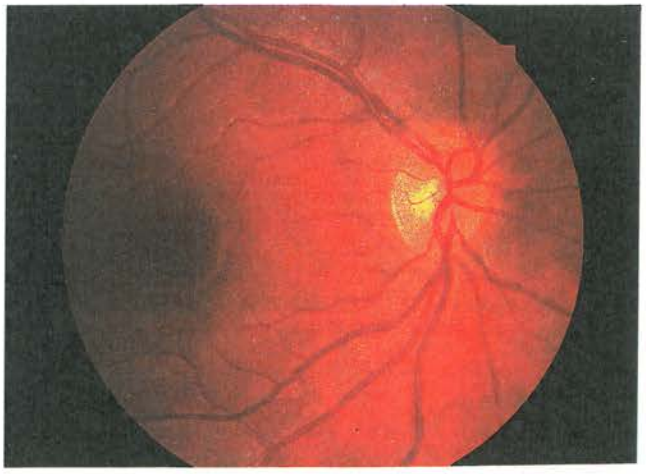


**Figure 15.3** Normal optic disc

may initially appear normal in Leber optic neuropathy and compressive lesions.

2. **Disc swelling**, which is a feature of papilloedema (Figure 15.4), anterior ischaemic optic neuropathy (Figure 15.5), papillitis and the acute stage of Leber optic neuropathy. It may also occur with compressive lesions before the development of optic atrophy.
3. **Optociliary shunts** (Figure 15.6), which are typically associated with optic nerve sheath meningioma and occasionally optic nerve glioma (*see* Chapter 14).
4. **Optic atrophy** (*see next*).

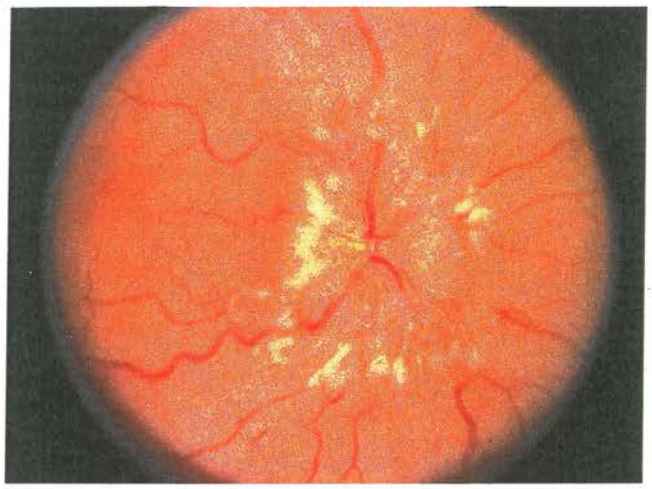


**Figure 15.4** Papilloedema

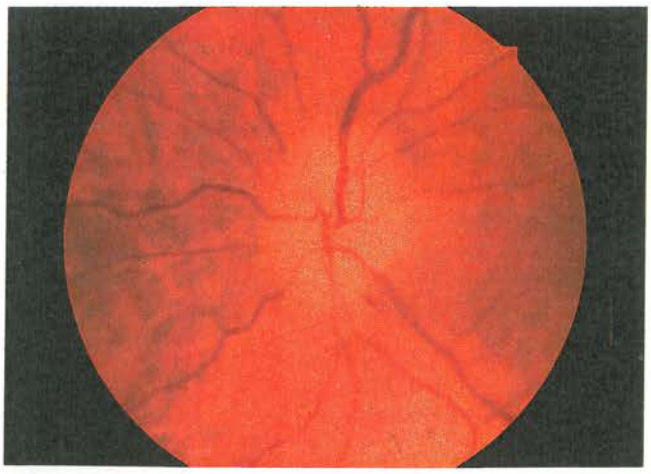


**Figure 15.5** Anterior ischaemic optic neuropathy

## OPTIC ATROPHY

Optic atrophy is an important sign of advanced optic nerve disease. It may be either primary or secondary.

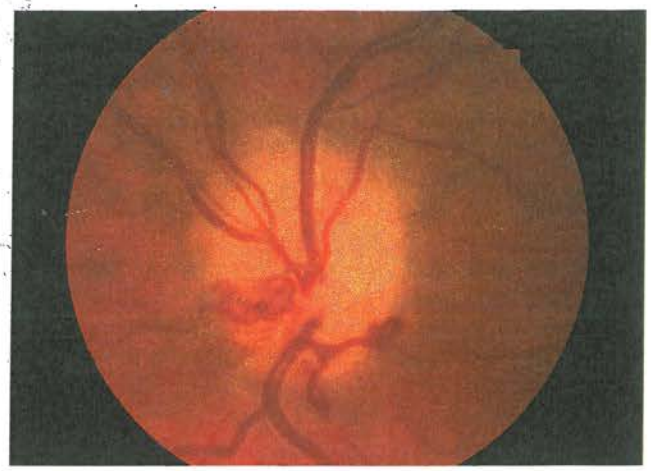


**Figure 15.6** Optociliary shunt vessels

1. **Primary optic atrophy** is caused by lesions affecting the visual pathways from the retrolaminar portion of the optic nerve to the lateral geniculate body. Lesions affecting the optic nerve will result in unilateral optic atrophy, whereas those involving the chiasm and optic tract will cause bilateral optic atrophy.
   (a) ***Causes***
   - Following retrobulbar neuritis.
   - Compressive lesions such as tumours and aneurysms.
   - Hereditary optic neuropathies.
   - Toxic and nutritional optic neuropathies.

   (b) ***Disc appearance*** (Figure 15.7)
   - White, flat disc with clearly delineated margins.
   - Reduction in number of small blood vessels on the disc.
   - Attenuation of peripapillary blood vessels and thinning of the retinal nerve fibre layer.

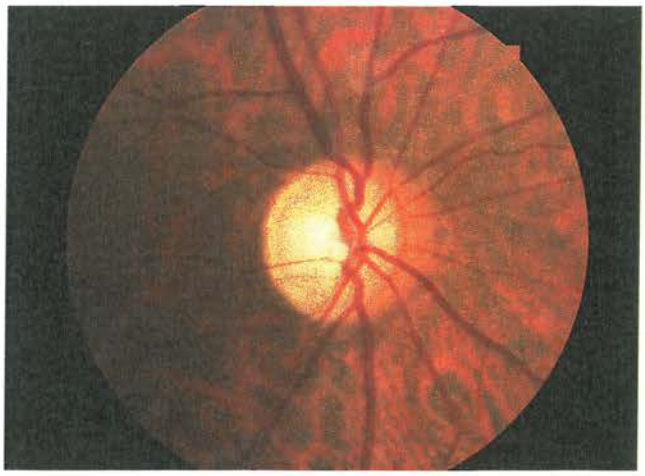


**Figure 15.7** Primary optic atrophy

The atrophy may be diffuse or sectoral depending on the cause and level of the lesion. For example, optic atrophy caused by chiasmal lesions may involve the nasal and temporal portions but spare the superior and inferior.

2. **Secondary optic atrophy** is preceded by swelling of the optic nerve head.
   (a) ***Causes*** include papilloedema, anterior ischaemic optic neuropathy and papillitis.
   (b) ***Disc appearance*** is variable according to the cause. The main features are as follows (Figure 15.8):
   - White, slightly raised disc with poorly delineated margins due to gliosis.
   - Reduction in number of small blood vessels on the disc.

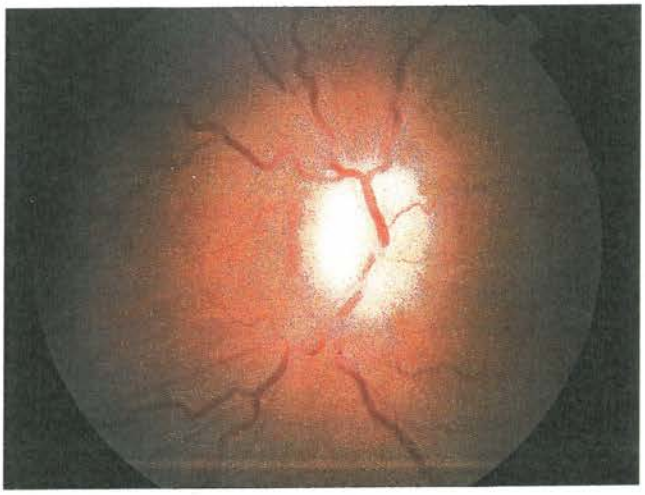


**Figure 15.8** Secondary optic atrophy

## SPECIAL INVESTIGATIONS

1. **Automated perimetry** quantitates the threshold retinal sensitivity to a static target. The most useful strategy in neuro-ophthalmological disease tests the central 30° with points straddling the midline (e.g. Humphrey 30–2).
2. **MRI** is the method of choice for imaging the optic nerves. The orbital parts of the optic nerve are best demonstrated by contrast-enhanced fat-suppression techniques by which the bright signal from orbital fat in T1-weighted images is eliminated. The intracanalicular and intracranial portions of the optic nerves are better visualized on MRI (Figure 15.9) than CT because of the absence of bony artifacts with the former.
3. **Visually evoked potential** (VEP) is an assessment of electrical activity of the visual cortex created by stimulation of the retina. The stimulus is either a flash of light or a reversing checkboard pattern on a screen (Figure 15.10). The two components that are assessed are the amplitude and latency (delay). Several tests are performed and the average is calculated by a computer. In optic nerve disease both parameters are affected, with a decrease in amplitude and an increase in latency.
4. **Fluorescein angiography** may occasionally be helpful in the differentiation of papilloedema, in which there is disc leakage, from optic disc drusen, in which leakage is absent but autofluorescence is present.

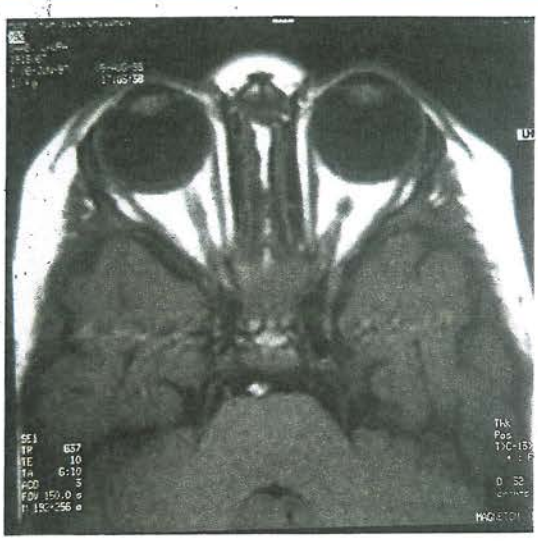


**Figure 15.9** Axial T1-weighted MRI scan showing a left optic nerve glioma involving the chiasm

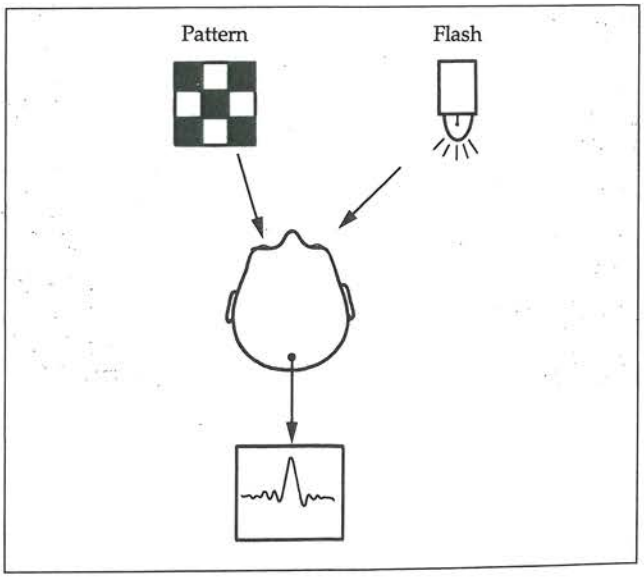



**Figure 15.10** Principles of visually evoked potential

## Classification of optic neuritis

Optic neuritis is an acute or subacute inflammatory or demyelinating process affecting the optic nerve. It can be classified both ophthalmoscopically and aetiologically as follows.

1. **Ophthalmoscopic classification**
   (a) ***Retrobulbar neuritis***, in which the optic disc appearance is initially normal because the pathological process does not involve the optic nerve head. It is the most frequent type in adults and is frequently associated with multiple sclerosis (MS).
   (b) ***Papillitis***, in which the pathological process affects the optic nerve head. It is characterized by variable disc hyperaemia and oedema (Figures 15.11 and 15.12) which may be associated with peripapillary flame-shaped haemorrhages. Cells in the posterior vitreous may also be seen. Papillitis is the most common type of optic neuritis in children, although it can also affect adults.

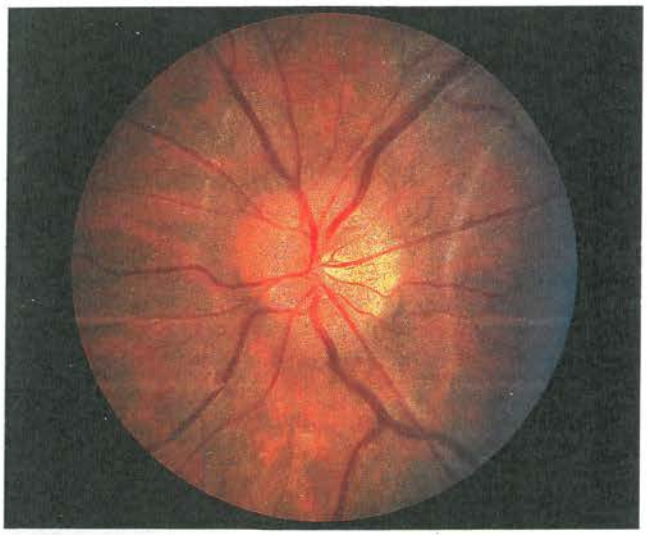


**Figure 15.11** Mild papillitis

   (c) ***Neuroretinitis***, which is characterized by papillitis in association with a macular star figure composed of hard exudates (Figure 15.13). The macular lesion may not be present initially, but it becomes apparent within a few days or weeks and tends to become more prominent when the optic disc swelling is resolving. In some cases there is associated peripapillary retinal oedema and serous elevation of the macula. Neuroretinitis is the least common type of optic neuritis and is most frequently associated with viral infections and cat-scratch fever. Other causes include syphilis and Lyme disease, but it is never a manifestation of MS. In most cases it is a self-limiting disorder which usually resolves within 6–12 months.

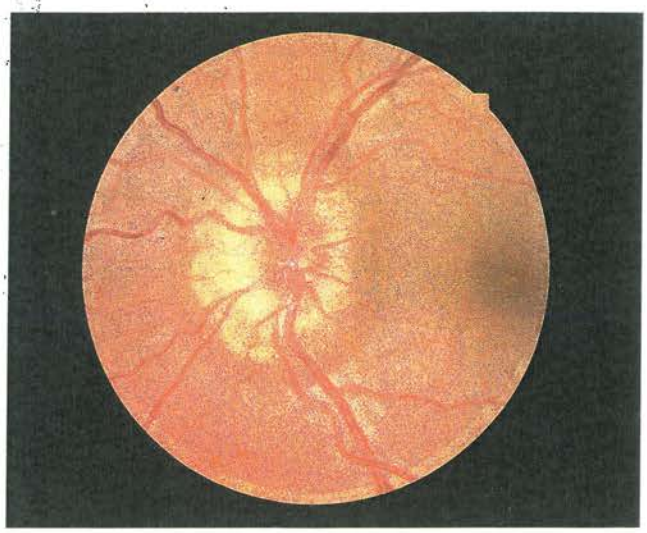


**Figure 15.12** Severe papillitis

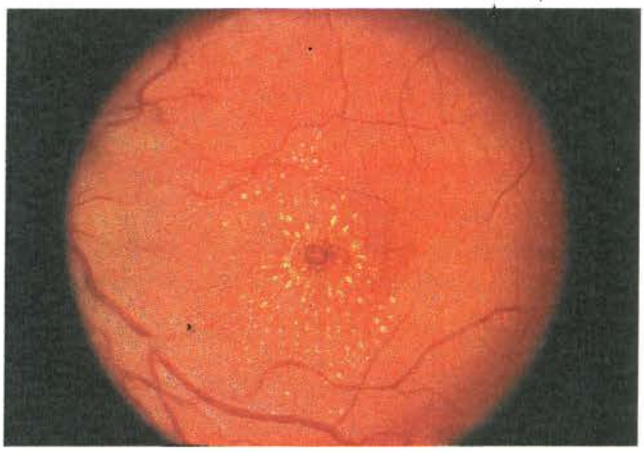


**Figure 15.13** Macular star in neuroretinitis

2. **Aetiological classification**
   (a) ***Demyelinating***, which is by far the most common cause
   (b) ***Parainfectious***, which may follow a viral infection or immunization.
   (c) ***Infectious***, which may be sinus-related, or associated with cat-scratch fever, syphilis, Lyme disease and mumps.

## Optic neuritis and demyelination

### INTRODUCTION

Demyelination is an inflammatory process by which normally myelinated nerve fibres lose their insulating myelin

layer. A demyelinating disease disrupts nervous conduction within the white matter tracts in the brain, brain stem and spinal cord.

1. **Ocular features of demyelination**
   (a) ***Visual pathway lesions***, which most frequently involve the optic nerves and cause optic neuritis. Occasionally demyelination may involve the optic chiasm, and rarely the optic tracts or radiations.
   (b) ***Brain stem lesions***, which may result in internuclear ophthalmoplegia, ocular motor cranial nerve palsies and nystagmus.
2. **Demyelinating diseases** which may cause ocular problems are:
   (a) ***Isolated optic neuritis*** in which the patient does not have clinical evidence of generalized demyelination, although in a high proportion of cases this subsequently develops.
   (b) ***Multiple sclerosis***, which is by far the most common and is discussed in detail below.
   (c) ***Devic disease*** (neuromyelitis optica), which is a very rare disease that may occur at any age. It is characterized by optic neuritis, which is bilateral, and subsequent development of transverse myelitis within days or weeks.
   (d) ***Schilder disease***, which is a very rare, relentlessly progressive, widespread disease with an onset prior to the age of 10 years and death within 1–2 years. Bilateral optic neuritis without subsequent improvement may occur.

## SYSTEMIC FEATURES OF MULTIPLE SCLEROSIS

Multiple sclerosis is a common, idiopathic, remitting neurological disease which typically affects young adults. Women are affected more commonly than men. The disease is characterized by demyelination of the central but not the peripheral nervous system. It is characterized by the following clinical features:

1. **Spinal cord lesions** which give rise to weakness, stiffness and sphincter and sexual function disturbance. Long-lasting lesions may result in muscle spasms. Sensory disturbances have a characteristic 'trouser-like' distribution.
2. **Brain stem lesions**, which may produce diplopia, nystagmus, ataxia, dysarthria and dysphagia.
3. **Hemisphere lesions**, which may produce hemiparesis, hemianopia and dysphasia. Other features include intellectual decline, depression, euphoria and even dementia.
4. **Transient phenomena**, which include Lhermitte sign (electrical sensation on neck flexion), the transient dysarthria–dysequilibrium–diplopia syndrome and tonic spasms. The development of trigeminal neuralgia in a young patient should arouse suspicion of possible demyelination. Another feature is Uhthoff phenomenon, which is characterized by a sudden, temporary worsening of visual or other symptoms brought on by physical exercise or increase in body temperature.

## SPECIAL INVESTIGATIONS

The following tests are helpful in establishing the diagnosis of MS.

1. **Lumbar puncture**, which may show leucocytosis, IgG level >15% of total protein and oligoclonal bands on CSF protein electrophoresis.
2. **VEP** in patients with acute optic neuritis shows decreased amplitude with a more profound increase in latency. However, following an attack the amplitude recovers but the increase in latency remains. For this reason VEP may be useful in patients with suspected MS even in the absence of a definitive prior attack of optic neuritis.
3. **MRI**, which shows the typical periventricular and corpus callosum plaques. The plaques typically have an ovoid shape with their long axes perpendicular to the ventricular margins (Figures 15.14 and 15.15). Acute demyelinating lesions may be highlighted with gadolinium on T1-weighted scans.

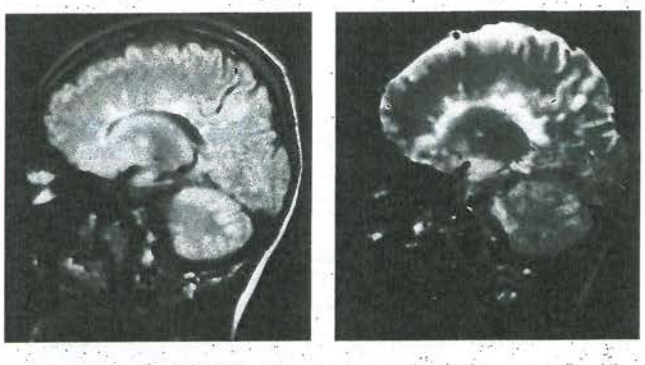


**Figure 15.14** Sagittal MRI scan showing periventricular plaques of demyelination. **Left**: T1-weighted; **right**: T2-weighted

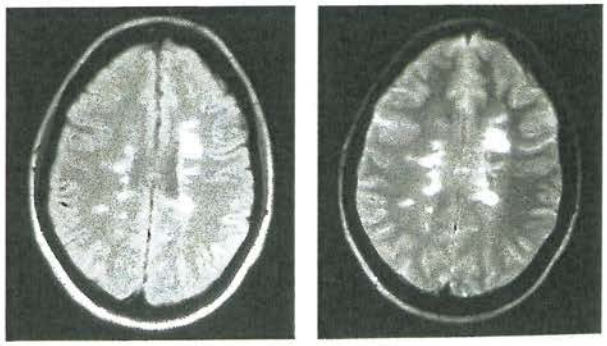


**Figure 15.15** Axial MRI scan showing periventricular plaques of demyelination. **Left**: T1-weighted; **right**: T2-weighted

### OPTIC NEURITIS

1. **Association with multiple sclerosis**
   Although some patients with optic neuritis have no clinically demonstrable associated systemic disease, the following close association exists between optic neuritis and MS.
   (a) Approximately 70% of women and 35% of men with optic neuritis may ultimately develop other neurological dysfunction, and be classified as having MS.
   (b) Evidence of optic neuritis may be found in 70% of established MS cases.
   (c) Up to 70% of patients with clinically isolated optic neuritis have abnormal MRI similar to that seen in MS.
   (d) In a patient with optic neuritis the subsequent risk of MS is increased with winter onset, HLA-DR2 positivity and Uhthoff phenomenon.
2. **Presentation**
   (a) A sudden onset of monocular visual loss is the norm. Rarely both eyes are involved simultaneously.
   (b) Discomfort in or around the eye is very common and is frequently exacerbated by ocular movements. The discomfort may precede or occur simultaneously with visual loss and usually lasts for only a few days.
   (c) Frontal headache and tenderness of the globe are present in some patients.
3. **Signs**
   (a) The disc is normal in two-thirds of cases (retrobulbar neuritis) and the remainder show papillitis. Temporal disc pallor may be seen in the fellow eye, indicative of a previous attack.
   (b) There is also diminished visual acuity, which may be very mild to very severe.
   (c) Impairment of colour vision and contrast sensitivity is almost universal and frequently worse than would be expected for that level of visual acuity.
   (d) Other features of optic nerve dysfunction are present, as previously described.
4. **Visual field defect**, which is typically a central scotoma although other defects may be seen.
5. **Clinical course**
   (a) Visual acuity impairment becomes maximal after 1–2 weeks and is usually between 6/18 and 6/60, although, rarely, it may fall to no light perception.
   (b) Recovery takes 4–6 weeks, although it may be slower in some patients.
6. **Prognosis** is excellent in approximately 75% of patients with recovery of visual acuity to 6/9 or better; 85% recover to 6/12 or better, even if visual acuity was reduced to no light perception during the attack. However, despite return of visual acuity other parameters of visual function, such as colour vision, contrast sensitivity and light brightness appreciation often remain abnormal. A mild afferent pupillary defect may persist and optic atrophy may ensue, particularly in patients with recurrent attacks.
7. **Treatment**
   (a) When the presenting visual loss is mild, treatment is probably unnecessary.
   (b) When visual acuity within the first week of symptom onset is worse than 6/12, treatment may speed up recovery.
   (c) The therapeutic regimen consists of intravenous methylprednisolone sodium succinate (1 g daily) for 3 days followed by oral prednisone (1 mg/kg/daily) for 11 days.
   (d) Treatment does not appear to have any long-term benefit on final visual acuity.

   N.B. Oral steroids alone are contraindicated.

## Other causes of optic neuritis

### PARAINFECTIOUS OPTIC NEURITIS

Optic neuritis may be associated with various viral infections such as measles, mumps, chickenpox, whooping cough and glandular fever. It may also occur following immunization. Children are affected much more frequently than adults.

1. **Presentation** is usually 1–3 weeks following a viral infection with an acute severe visual loss which may involve both eyes. This may be associated with other neurological deficits such as headache, seizures or ataxia (meningoencephalitis).
2. **Signs**. The optic discs most frequently show bilateral papillitis although occasionally there may be a neuroretinitis or the discs may be normal.
3. **Treatment** in the vast majority of patients is unnecessary because the prognosis for spontaneous visual recovery is very good. However, when visual loss is severe and bilateral or when it involves an only seeing eye, intravenous steroids should be considered.

### INFECTIOUS OPTIC NEURITIS

1. **Sinus-related** optic neuritis is characterized by recurrent attacks of unilateral visual loss associated with severe headache and acute ethmoidal sinusitis.
2. **Cat-scratch fever** (benign lymphoreticulosis) is a self-limiting systemic infection characterized by regional lymphadenopathy preceded by a cat scratch. The causative organism is *Bartonella henselae*, a small gram-negative rod. Neuroretinitis (Figure 15.16), which may be unilateral or bilateral, may occur in some patients. The organism is susceptible to a variety of antibiotics including rifampicin, ciprofloxacin and Septrin. The visual prognosis is excellent, with recovery of vision within 1–4 weeks after starting therapy.

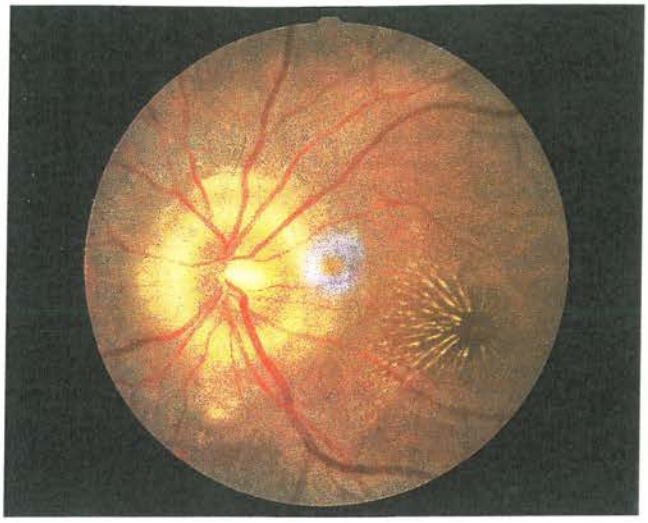


**Figure 15.16** Neuroretinitis

3. **Syphilis** may cause acute papillitis or neuroretinitis during the primary or secondary stages. Involvement may be unilateral or bilateral and is frequently associated with a mild vitritis. Some patients may have associated HIV infection which may also cause optic nerve involvement.
4. **Lyme disease** (borreliosis) is a spirochaetal infection transmitted by a tick bite which may cause a neuroretinitis. In some cases it causes acute retrobulbar neuritis which may be associated with other neurological manifestations which may mimic MS. Treatment of neurological involvement is with intravenous ceftriaxone 2 g daily for 14 days.
5. **Cryptococcal** meningitis in patients with AIDS may be associated with optic nerve involvement and acute visual loss, which may be bilateral.

## Non-arteritic anterior ischaemic optic neuropathy

Anterior ischaemic optic neuropathy (AION) is a segmental or generalized infarction within the prelaminar or laminar portion of the optic nerve, caused by occlusion of the short posterior ciliary arteries. It may be associated with giant cell arteritis (GCA) and is then referred to as arteritic AION. Non-arteritic (idiopathic) AION typically occurs as an isolated event in patients between the ages of 45 and 65 years, who either are otherwise healthy or have hypertension as the only sign of systemic vascular disease. In contrast to patients with retinal artery occlusion, those with non-arteritic AION are not at increased risk of early death from systemic vascular disease.

1. **Presentation** is with monocular, sudden and painless visual loss which is not associated with premonitory transient visual symptoms.

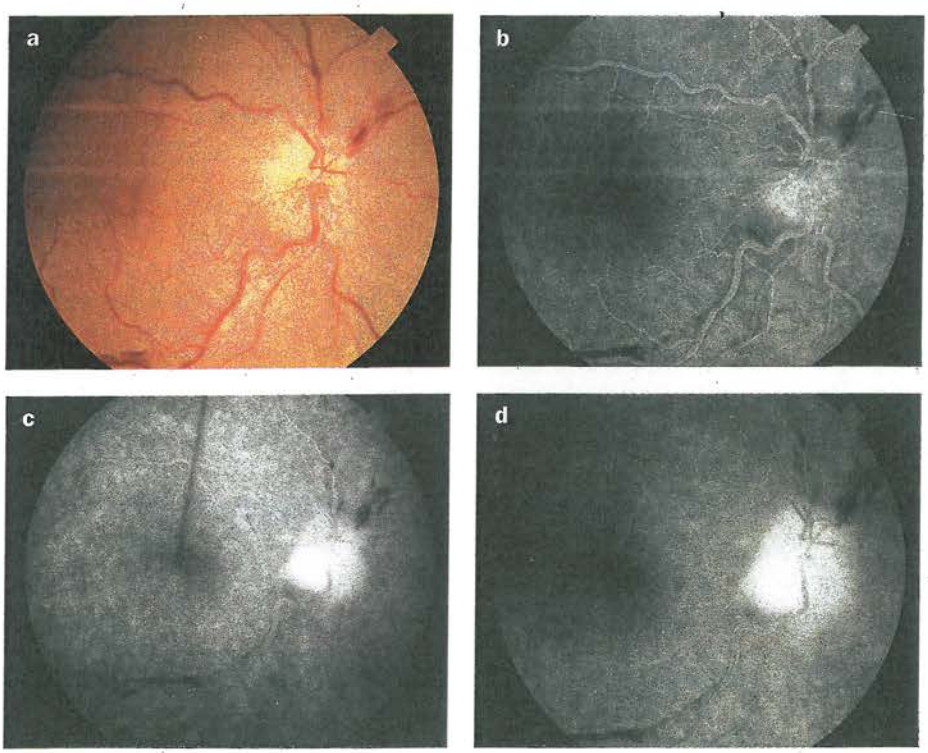



**Figure 15.17** Acute non-arteritic anterior ischaemic optic neuropathy (*see text*)

2. **Signs** in chronological order:
   (a) The acute stage shows a pale disc with diffuse or sectoral oedema which may be surrounded by a few splinter-shaped haemorrhages (Figure 15.17**a**). Fluorescein angiography initially shows localized disc hyperfluorescence (Figure 15.17**b**) which becomes more intense (Figure 15.17**c**) and then eventually involves the entire disc (Figure 15.17**d**). The fellow eye commonly has a small or absent optic cup.
   (b) The disc oedema gradually resolves and the involved portion of the disc becomes pale (Figure 15.18**a**). Fluorescein angiography shows unequal choroidal filling during the arterial phase (Figure 15.18**b**). The late stages show increasing disc hyperfluorescence (Figure 15.18**c** and **d**).
3. **Visual acuity**, in about one-third of patients, is normal or only slightly reduced. The remainder have moderate-to-severe impairment.
4. **Visual field defect** is typically altitudinal, most commonly involving the inferior field.
5. **Colour vision** is diminished in proportion to the level of visual acuity. This is in contrast to optic neuritis in which colour vision is usually severely impaired irrespective of the level of visual acuity.
6. **Management**
   (a) ***Special investigations*** include: serological studies, fasting lipid profile, blood glucose and factors affecting viscosity (fibrinogen and packed cell volume). It is also very important to exclude occult GCA and other autoimmune diseases.
   (b) ***Treatment*** is of any underlying disease and smokers should be advised to stop. Long-term low-dose aspirin should be prescribed to prevent involvement in the fellow eye.
7. **Prognosis** is much better than in arteritic AION. In most patients there is no further loss of vision although, in a small percentage, visual loss continues for 6 weeks and spontaneous subsequent recovery is rare. One-third of patients develop AION in the opposite eye within several months or years. In this situation, optic atrophy in one eye and disc oedema in the other gives rise to the so-called 'pseudo-Foster–Kennedy syndrome.

## Arteritic anterior ischaemic optic neuropathy

### CLINICAL FEATURES OF GIANT CELL ARTERITIS

Giant cell arteritis is a medical emergency because prevention of blindness depends on prompt recognition and treatment. The disease has a predilection for large and medium-sized arteries, particularly the superficial temporal, ophthalmic, posterior ciliary and the proximal part of the vertebral. The severity and extent of involvement are asso-

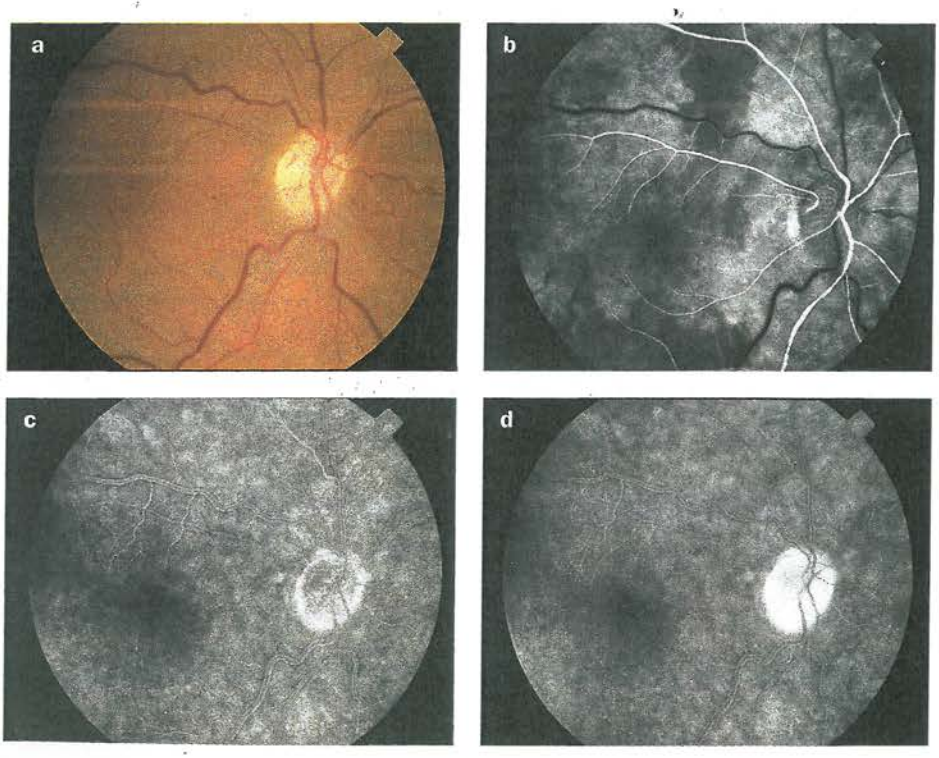



**Figure 15.18** Optic atrophy following non-arteritic anterior ischaemic optic neuropathy (*see text*)

ciated with the quantity of elastic tissue in the media and adventitia of the artery. For this reason, the intracranial arteries, which possess little elastic tissue, are usually spared.

1. **Presentation** is typically during the seventh and eighth decades of life with the following symptoms:
   (a) ***Scalp tenderness***, which is first noticed when combing the hair, is a frequent presenting complaint.
   (b) ***Headache***, which is rarely severe, may be either localized to the frontal, occipital or temporal regions, or more generalized.
   (c) ***Jaw claudication*** as a result of ischaemia of the masseter muscles, which causes pain on speaking and chewing, is virtually pathognomonic.
   (d) ***Polymyalgia rheumatica*** is characterized by pain and stiffness in the proximal muscle groups which is worse in the morning and after exertion. Polymyalgia may occur months or years before the cranial symptoms and it may not be a prominent feature when headaches occur.
   (e) ***Non-specific symptoms*** such as neck pain, weight loss, anorexia, fever, night sweats, malaise and depression are common.
2. **Other features of arteritis**
   (a) ***Superficial temporal arteritis***, which is characterized by tender, inflamed and nodular arteries (Figure 15.19). Initially, pulsation is present although the thickened arteries cannot be flattened against the skull. Later, arterial pulsation ceases and, in very severe cases, gangrene of the scalp may occasionally develop. The best location to feel for pulsation is directly in front of the upper pole of the pinna of the ear. Lack of pulsation is very suggestive of arteritis because it is most unusual for the superficial temporal arteries to be non-pulsatile in normal elderly individuals. Occasionally, the scalp vessels may appear clinically normal and yet show the typical changes of giant cell arteritis when examined histologically.
   (b) ***Arteritis of other arteries***, which may lead to dissecting aneurysms, aortic incompetence, myocardial infarction, brain stem stroke and renal failure.
   (c) ***Occult arteritis*** occurs in some patients in whom systemic features are minimal or absent and the first manifestation is unilateral blindness.

## SPECIAL INVESTIGATIONS

1. **Erythrocyte sedimentation rate** (ESR) is often very high, with levels >60 mm/h. In interpreting the ESR it should be emphasized that levels of 40 mm/h may be normal in the elderly and cases of biopsy proven GCA have been reported in patients with ESR levels <30 mm/h. Approximately 20% of patients with GCA have a normal ESR.
2. **C-reactive protein** is invariably raised in GCA and may be helpful when the ESR is equivocal.
3. **Temporal artery biopsy** should be performed for histological confirmation of the diagnosis (Figures 15.20 and 15.21). Prior treatment with steroids for more than 7 days may be associated with loss of the histological features of active arteritis. In the presence of ocular involvement it is advisable to take a biopsy from the ipsilateral side. At least 2.5 cm of the artery should be taken, and serial sections must be examined as there could be variations in the extent of involvement along the length of the artery. Unfortunately, temporal artery biopsy may fail to confirm the diagnosis in a substantial number of patients. A common difficulty in securing an adequate specimen is inaccurate localization of the artery because of loss of pulsa-

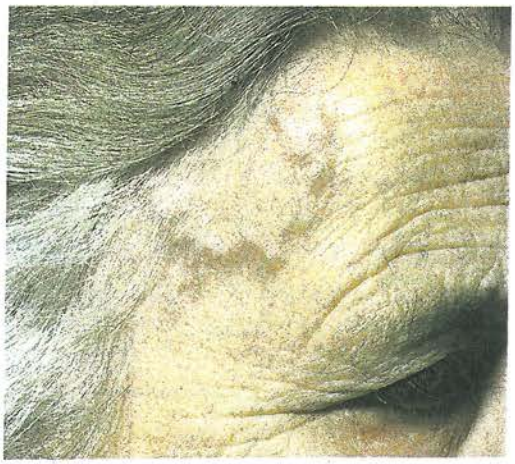


**Figure 15.19** Dilated and nodular superficial temporal artery in a patient with giant cell arteritis

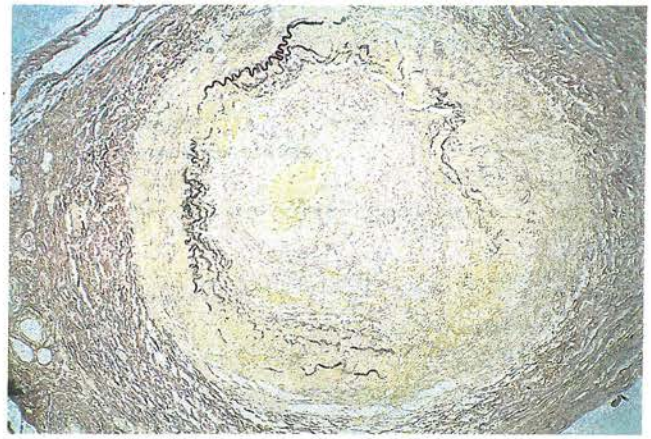


**Figure 15.20** Histology of giant cell arteritis showing granulomatous cell infiltration, disruption of the internal elastic lamina, proliferation of the intima and complete occlusion of the lumen

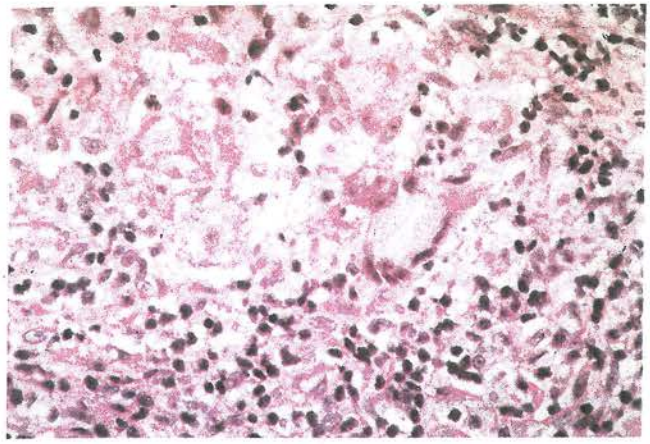


**Figure 15.21** Histology of giant cell arteritis with increased magnification showing giant cell-granulomatous inflammation

tion. The ideal location for the incision is the scalp of the temple because this avoids damage to a major branch of the auriculotemporal nerve.

### ARTERITIC ANTERIOR ISCHAEMIC OPTIC NEUROPATHY

Anterior ischaemic optic neuropathy affects about 25% of untreated patients with GCA.

1. **Presentation** is typically with uniocular, sudden and profound loss of vision which may be accompanied by periocular pain and preceded by transient visual obscurations and flashing lights. AION usually occurs within the first few weeks of the onset of GCA and is extremely rare after 9 months have elapsed – hence the need to start steroid treatment as soon as possible. Although simultaneous bilateral involvement is rare, about 65% of untreated patients become blind in both eyes within a few weeks.
2. **Signs** in chronological order:
   (a) The disc is pale and swollen with small splinter-shaped haemorrhages on its margin (Figure 15.22).
   (b) Within 1–2 months, the swelling gradually resolves and the entire optic disc becomes atrophic.
   (c) Visual acuity is profoundly impaired, as are all other modalities of optic nerve function.
3. **Treatment**
   (a) ***Aim of treatment*** is to prevent blindness of the fellow eye, although, in a few unfortunate patients with initially unilateral visual loss, the second eye also becomes blind in spite of prompt steroid administration.
   (b) ***Therapeutic regimen***
   - Initial treatment is with intravenous methylprednisolone 1 g/day for 3 days together with oral prednisone 80 mg daily.

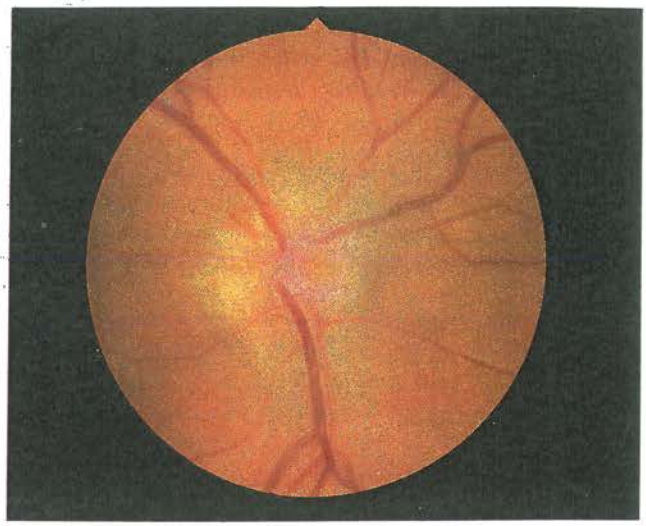


**Figure 15.22** Arteritic anterior ischaemic optic neuropathy

   - After 3 days the oral dose is reduced to 60 mg for 3 days and then 40 mg for 4 days.
   - The daily dose is then reduced by 5 mg weekly until 10 mg is reached.
   - Maintenance daily therapy is 10 mg.

   (c) ***Duration of treatment*** is governed by the patient's symptoms and the level of the ESR or C-reactive protein. Symptoms may, however, recur without a corresponding rise in ESR or C-reactive protein and vice versa. Most patients need treatment for 1–2 years whereas others require indefinite maintenance therapy. It should be emphasized that the injudicious use of steroids may cause greater harm than the disease itself.
4. **Prognosis** is very poor because visual loss is usually permanent, although very rarely the prompt administration of systemic steroids may be associated with partial recovery.

## Leber hereditary optic neuropathy

Leber hereditary optic neuropathy (LHON) is a rare disease which is the result of maternal mitochondrial DNA mutations (3460, 14484, 11778 and 15257). The majority of patients are males in their twenties with the 11778 mutation. In atypical cases the condition may affect females and present at any age between 10 and 60 years. The diagnosis of LHON should therefore be considered in all patients with bilateral optic neuritis, irrespective of age.

1. **Presentation** is typically with a unilateral, acute, severe, painless visual loss. The fellow eye becomes similarly affected within days or several weeks but not longer than two months after the first.

2. **Signs** in chronological order:
   (a) The acute stage shows subtle signs which may be easily overlooked. In some patients the optic disc may be entirely normal.
   (b) In typical cases there is disc hyperaemia, dilated capillaries on the disc surface which may extend onto adjacent retina (telangiectatic microangiopathy), vascular tortuosity and swelling of the peripapillary nerve fibre layer (Figure 15.23). Telangiectatic microangiopathy may be present in asymptomatic female relatives.
   (c) Subsequently, the telangiectatic vessels regress and severe optic atrophy ensues.
   (d) Surprisingly, the pupillary reactions to light often remain fairly brisk.
3. **Fluorescein angiography** shows absence of dye leakage.
4. **Visual field defects** usually consist of centrocaecal scotomas.
5. **Prognosis** is relatively poor, although some visual recovery may occur in a minority of cases even years later. Most patients suffer severe, bilateral and permanent visual loss with a final visual acuity of 6/60 or less. Patients with the 11778 mutation have the worst prognosis and those with the 3460 and 14484 mutations are usually less severely affected.
6. **Treatment** is generally ineffective although many modalities, including steroids, hydroxycobalamin and surgical intervention, have been tried. Patients should, however, be advised to stop smoking and excessive drinking of alcohol to prevent potential stress on mitochondrial energy production.

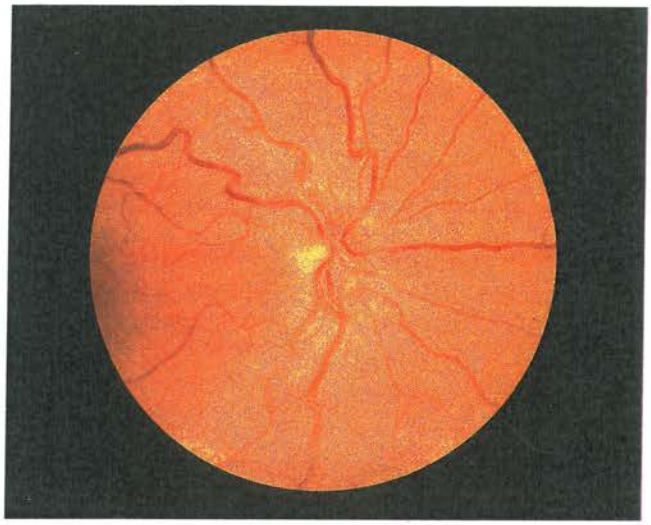


**Figure 15.23** Acute stage of Leber optic neuropathy

## Hereditary optic atrophies

The hereditary optic neuropathies are a very rare heterogenous group of disorders that are primarily manifested by bilateral optic atrophy.

### KJER SYNDROME

1. **Inheritance** is autosomal dominant.
2. **Presentation** is between the ages of 4 and 10 years with insidious visual loss.
3. **Optic discs** show temporal pallor and excavation (Figure 15.24).
4. **Visual prognosis** is variable (6/12–6/60) and there is considerable intra- and inter-familial variation in final visual outcome.
5. **Systemic abnormalities** are absent.

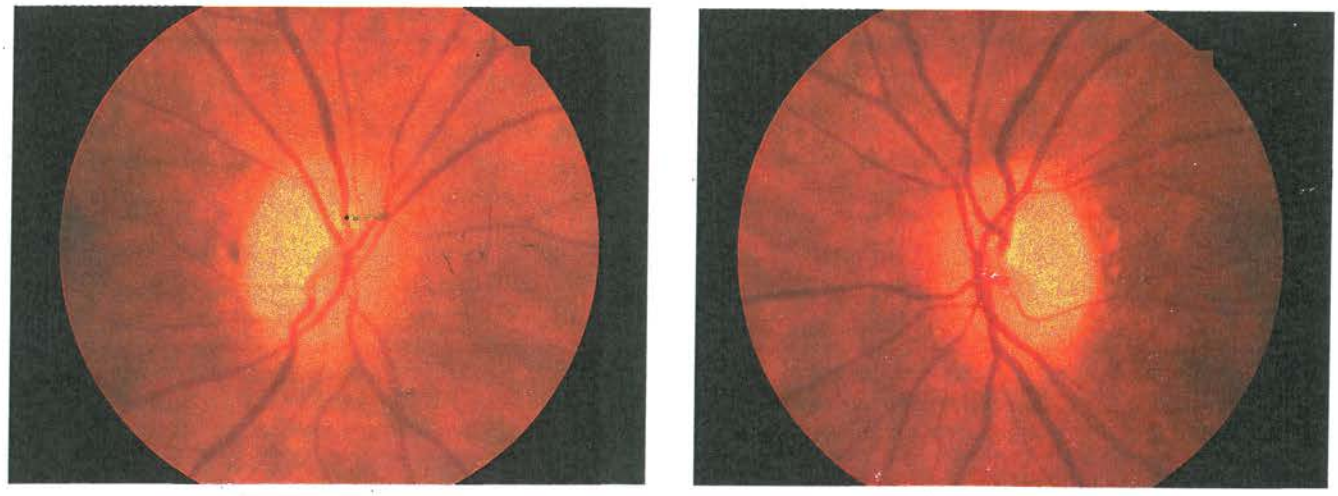


**Figure 15.24** Temporal disc pallor in dominantly inherited optic atrophy

### BEHR SYNDROME

1. **Inheritance** is autosomal recessive.
2. **Presentation** is during the first 10 years of life, with visual loss which stabilizes after a variable period of progression.
3. **Optic discs** show diffuse pallor.
4. **Visual prognosis** is variable with moderate to severe visual loss and nystagmus.
5. **Systemic associations** include spastic gait, ataxia and mental handicap.

### WOLFRAM SYNDROME

Wolfram syndrome is also refered to as DIDMOAD = **D**iabetes **I**nsipidus, **D**iabetes **M**ellitus, **O**ptic **A**trophy and **D**eafness.

1. **Inheritance** is autosomal recessive.
2. **Presentation** is between the ages of 5 and 21 years.
3. **Optic discs** show diffuse pallor.
4. **Visual prognosis** is very poor, with less than 6/60 final visual acuity.
5. **Systemic associations** apart from those described above (DIDMOAD) include anosmia, ataxia, seizures, mental handicap, short stature, endocrine abnormalities and elevated CSF protein.

## Alcohol–tobacco amblyopia

Alcohol–tobacco amblyopia typically affects heavy drinkers and cigar and pipe smokers who are deficient in protein and the B vitamins. Most patients have neglected their diet, obtaining their calories from alcohol instead.

1. **Presentation** is with non-painful, insidious onset, progressive, bilateral, usually symmetrical visual impairment associated with loss of colour vision.
2. **Signs**
   (a) The optic dics at presentation are normal in most cases.
   (b) Some patients show either splinter-shaped haemorrhages on or around the disc, or minimal disc oedema.
3. **Visual field defects** characteristically consist of bilateral, relatively symmetrical, centrocaecal scotomas. The margins of the field defects are difficult to define with a white target but are easier to plot and larger when using a red target.
4. **Treatment** is aimed at replacing the vitamin deficit with weekly injections of 1000 units of hydroxocobalamin for 10 weeks. Multivitamins are also administered and patients should be advised to eat a well-balanced diet and abstain from drinking and smoking.
5. **Prognosis** of early cases with treatment is good, although visual recovery may be slow. In advanced and unresponsive cases there is permanent visual loss as a result of optic atrophy.

## Drug-induced optic neuropathies

The many drugs that may cause optic neuropathy include: (a) ***ethambutol***, (b) ***isoniazid***, (c) ***streptomycin***, (d) ***vigabatrin***, (e) ***amiodarone*** and (f) ***chlorpropamide***. Only ethambutol-induced optic neuropathy will be described because it is the most important. Ethambutol (Myambutol, Mynah) is used in combination with isoniazid or rifampicin in the treatment of tuberculosis. About 1% of patients develop optic neuropathy, which is probably dose-dependent. Eye involvement rarely occurs before the patient has received the drug for at least 2 months (average is 7 months).

1. **Presentation** is usually with symmetrical insidious visual loss associated with impairment of red–green colour perception.
2. **Signs**. The optic discs may be normal or oedematous with splinter-shaped haemorrhages.
3. **Visual field defects** usually consist of central scotomas although bitemporal or peripheral constriction may occur in some cases.
4. **Prognosis** is good once the drug is stopped, although recovery may take up to 12 months. A minority of patients develop permanent visual impairment as a result of optic atrophy.
5. **Screening** should be at 4-weekly intervals if the daily dose exceeds 15 mg/kg. The patient should also be advised to stop taking the drug immediately if symptoms develop.

# PAPILLOEDEMA

## Introduction

Papilloedema is defined as swelling of the optic nerve head secondary to raised intracranial pressure. It is nearly always bilateral, although it may be asymmetrical. All other causes of disc oedema not associated with raised intracranial pressure are referred to as 'disc swelling' and usually produce visual impairment. All patients with papilloedema should be suspected of having an intracranial mass until there is proof to the contrary. However, not all patients with raised intracranial pressure will necessarily develop papilloedema, sometimes as a result of an anatomical quirk. Tumours of the cerebral hemispheres tend to produce papilloedema later than those in the posterior fossa. Patients who have had papilloedema before may develop a substantial increase in intracranial pressure but fail to re-develop papilloedema because of glial scarring of the optic nerve head.

# Raised intracranial pressure

## CAUSES

Cerebrospinal fluid (CSF) is formed by the choroid plexus in the lateral ventricles and the third ventricle (Figure 15.25). It leaves the lateral ventricles to enter the third ventricle through the foramen of Munro. From the third ventricle, it flows through the sylvian aqueduct to the fourth ventricle. From the fourth ventricle, the CSF passes through the foramina of Luschka and Magendie, some flowing around the spinal cord and the rest bathing the cerebral hemispheres. Absorption is into the cerebral venous drainage system through the arachnoid villi. Raised intracranial pressure may therefore be caused by the following mechanisms:

1. **Space-occupying lesions**, including intracranial haemorrhage.
2. **Blockage of the ventricular system** by congenital or acquired lesions.
3. **Obstruction of CSF absorption** via arachnoid villi, damaged by meningitis, subarachnoid haemorrhage or cerebral trauma.
4. **Benign intracranial hypertension** (pseudotumour cerebri).
5. **Diffuse cerebral oedema** from blunt head trauma.
6. **Severe hypertension**.
7. **Hypersecretion of CSF** by choroid plexus tumour, which is very rare.

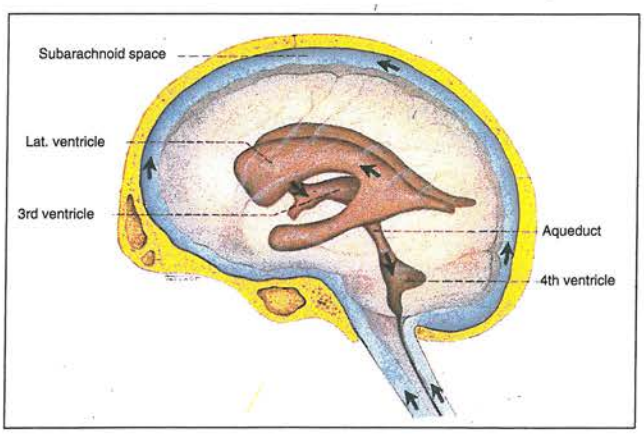



**Figure 15.25** Circulation of cerebrospinal fluid

## HYDROCEPHALUS

Hydrocephalus is dilatation of the ventricles (Figure 15.26). Raised intracranial pressure can cause two types of hydrocephalus.

1. **Communicating hydrocephalus**, in which obstruction to CSF flow is in the basilar cisterns or in the cerebral subarachnoid space. There is therefore flow of CSF from the lateral ventricles to the lumbar subarachnoid space but failure of absorption by the arachnoid villi.
2. **Non-communicating hydrocephalus** is caused by obstruction to CSF flow in the ventricular system or at the exit foramina of the fourth ventricle.

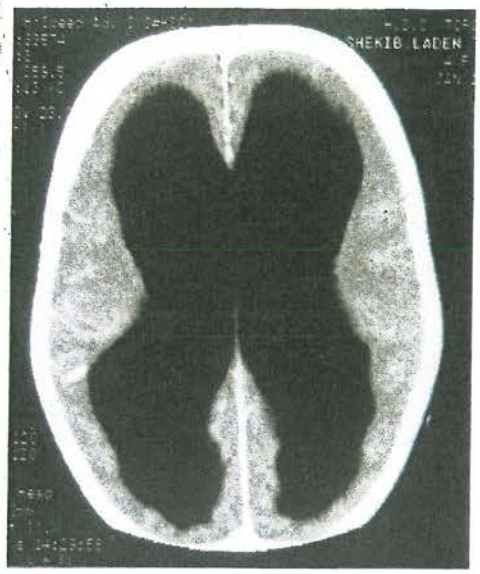



**Figure 15.26** Severe hydrocephalus

## SYSTEMIC FEATURES

1. **Headache**, which is typically most severe in the morning. It tends to get progressively worse and patients usually present to hospital within 6 weeks. The headache may be generalized or localized, and it may intensify with a Valsalva manoeuvre, head movement or bending. Patients with lifelong headaches often report a change in character of the headache. Very rarely, headache may be absent in patients with raised intracranial pressure.
2. **Sudden nausea** and **projectile vomiting**, which may be precipitated by fluctuations in intracranial pressure.
3. **Horizontal diplopia**, which is caused either by involvement of the third nerve or stretching of the sixth nerve over the petrous tip (*see* Figure 15.84).

# Clinical features of papilloedema

Papilloedema can be divided into the following four types.

1. **Early papilloedema** (Figure 15.27) may be difficult to diagnose with certainty. The following are its main features:

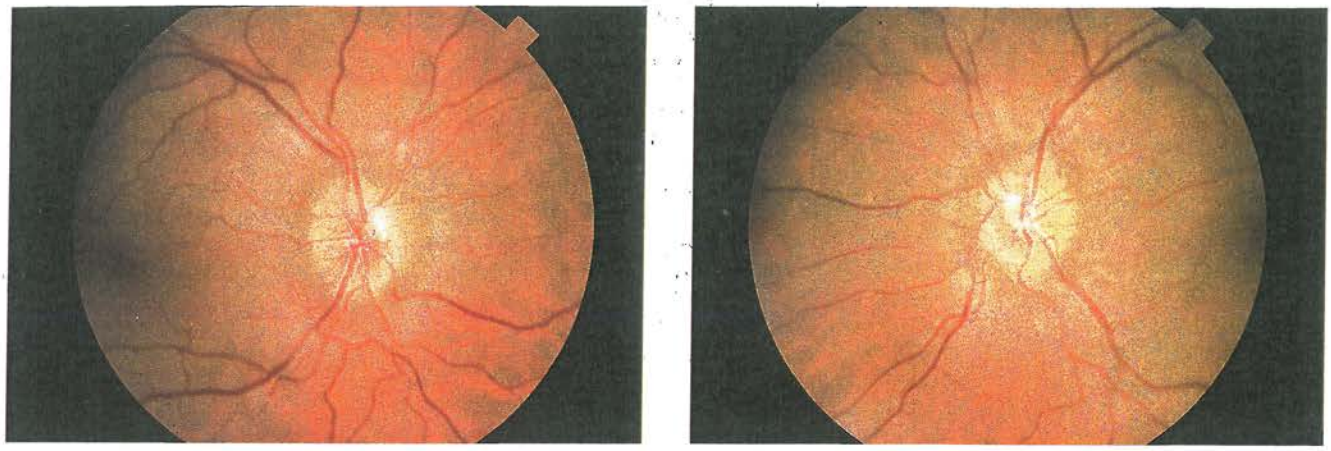


**Figure 15.27** Early papilloedema (*see text*)

(a) Visual symptoms are absent and visual acuity normal.

(b) Optic discs show hyperaemia and mild elevation.

(c) Indistinct disc margins and swelling of the peripapillary retinal nerve fibre layer.

(d) The nasal margins are involved first, followed by the superior, inferior and temporal.

(e) There is loss of previous spontaneous venous pulsation. However, as about 20% of normals do not show spontaneous venous pulsation, its absence does not necessarily mean that the intracranial pressure is raised. If venous pulsation is well preserved the diagnosis of papilloedema is unlikely.

2. **Established papilloedema**

(a) Transient visual obscurations in one or both eyes, lasting a few seconds, often on standing, may be present.

(b) Visual acuity is normal or reduced.

(c) Optic discs show severe hyperaemia, moderate elevation with indistinct margins which may initially be asymmetrical (Figure 15.28).

(d) The small vessels traversing the disc are obscured.

(e) There is venous engorgement, peripapillary flame-shaped haemorrhages (Figure 15.28) and frequently also cotton-wool spots (*see* Figure 15.4). Fluorescein angiography initially shows dilated disc capillaries (Figure 15.29**a**) followed later by increasing hyperfluorescence which extends beyond the disc margin (Figure 15.29**b**).

(f) As the swelling increases, the optic nerve head appears to be enlarged and circumferential retinal folds may develop on its temporal side.

(g) Hard exudates may radiate from the centre of the fovea in the form of an incomplete star with its temporal part missing.

(h) The blind spot is enlarged.

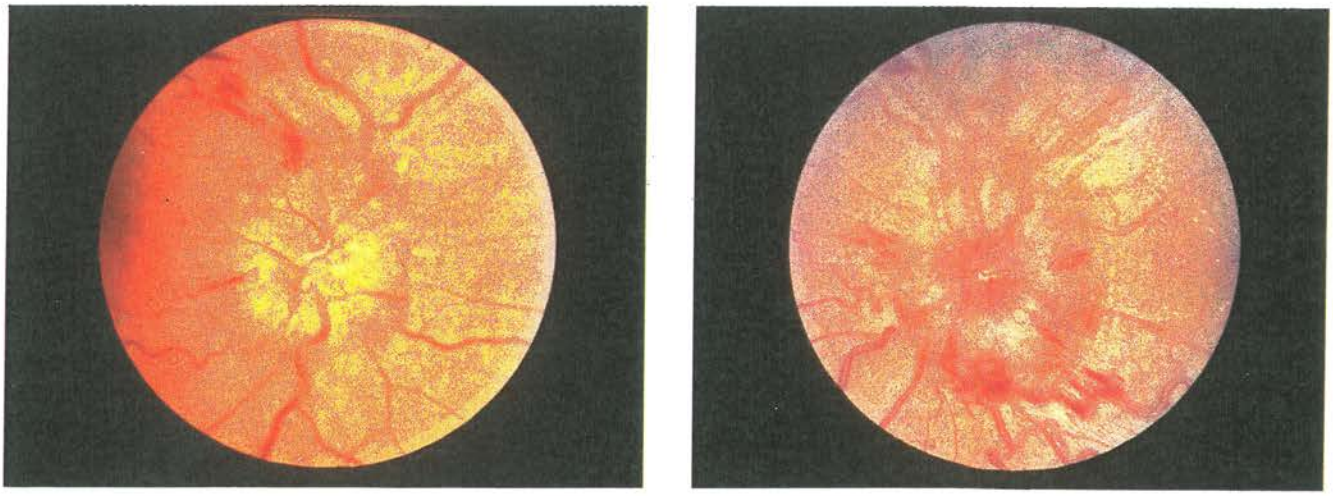


**Figure 15.28** Established papilloedema (*see text*)

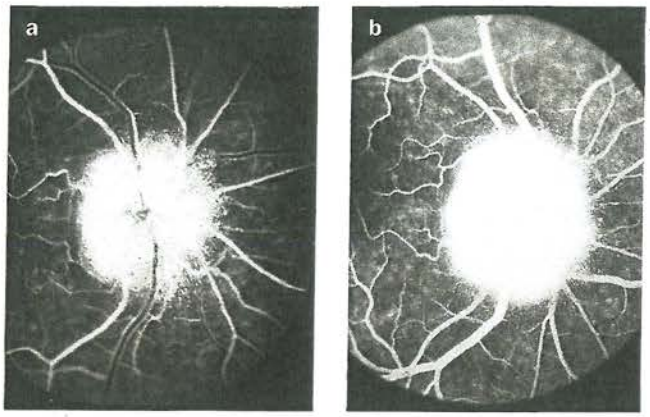



**Figure 15.29** Fluorescein leakage in papilloedema. (**a**) Early stage; (**b**) late stage

3. **Longstanding papilloedema**
   (a) Visual acuity is variable and the visual fields begin to show constriction.
   (b) Optic discs are markedly elevated with a champagne cork-like appearance (Figure 15.30).
   (c) Cotton-wool spots and haemorrhages are absent.
   (d) Optociliary shunts and drusen-like crystalline deposits may be present on the disc surface.
4. **Atrophic papilloedema**
   (a) Visual acuity is severely impaired.
   (b) Optic discs are white, slightly elevated, crossing blood vessels are few and the margins are indistinct (Figure 15.31).

This appearance is also referred to as secondary optic atrophy and is most frequently seen in patients with a history of treated cerebral tumours or benign intracranial hypertension.

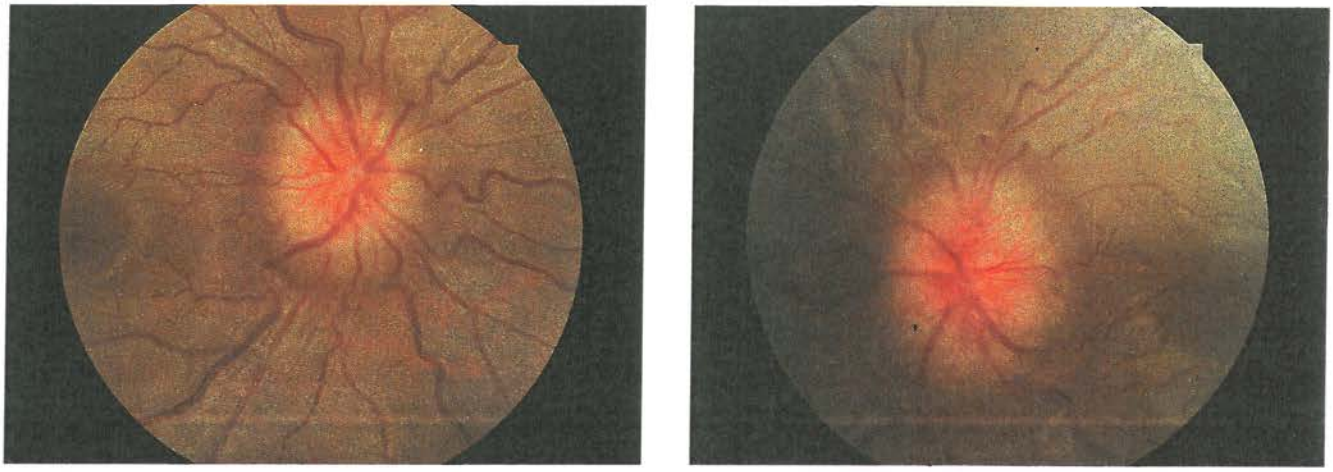


**Figure 15.30** Longstanding papilloedema (*see text*)

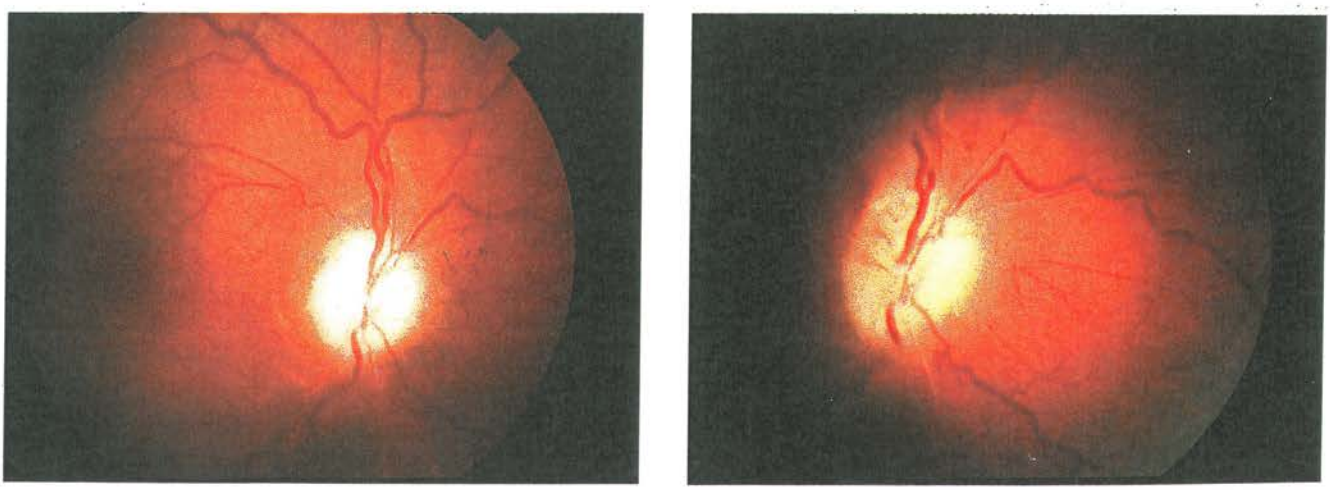


**Figure 15.31** Atrophic papilloedema (*see text*)

### DIFFERENTIAL DIAGNOSIS

1. **Congenital disc anomalies** such as buried drusen and myelinated nerve fibres may be mistaken for early papilloedema *(see below)*.
2. **Bilateral disc swelling** may be caused by the following:
   (a) ***Malignant hypertension.***
   (b) ***Bilateral papillitis.***
   (c) ***Bilateral compressive thyroid ophthalmopathy.***
   (d) ***Bilateral simultaneous anterior ischaemic optic neuropathy.***
   (e) ***Bilateral compromised venous drainage*** in central retinal vein occlusion or carotid–cavernous fistula.

## CONGENITAL OPTIC NERVE ANOMALIES

Congenital optic nerve anomalies are important for the following reasons: (a) they are relatively common, (b) some may be mistaken for papilloedema, (c) some may give rise to visual field defects, (d) some are associated with malformations of the CNS and (e) some may be associated with other ocular abnormalities, both congenital and acquired.

## Without neurological associations

### TILTED DISC

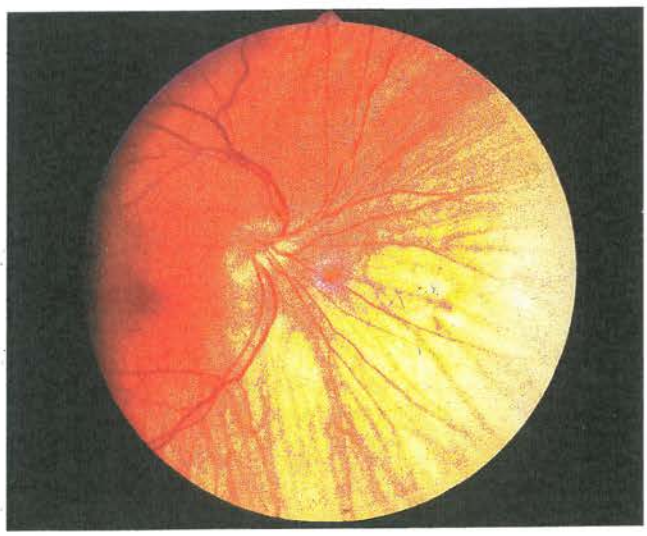
Tilted disc is a fairly common, usually bilateral, condition caused by an oblique insertion of the optic nerve into the globe.

1. **Signs**
   (a) Visual acuity is normal in the absence of complications from myopia.
   (b) The disc is small, oval or D-shaped with the axis most frequently oblique, but it may be horizontal or nearly vertical (Figure 15.32).
   (c) Common associated findings include an inferior crescent, situs inversus of the retinal blood vessels, myopia, hypopigmentation of the inferonasal fundus and moderate oblique astigmatism.
2. **Visual field defects** involving the upper temporal quadrants may be present as a result of the inferonasal fundus changes. If the defects are bilateral they may be mistaken, on cursory examination, for those caused by chiasmal compression. However, it is evident that these defects are not truly hemianopic because they do not obey the vertical midline. In some eyes visual field defects may also involve the other three quadrants.

### OPTIC DISC DRUSEN

Optic disc drusen are composed of hyaline-like calcific material within the substance of the optic nerve head. Clinically, they are present in about 0.3% of the population and are often bilateral and familial. Patients with retinitis pigmentosa and angioid streaks have a higher prevalence of drusen.

1. **Signs**
   (a) Visual acuity is normal in the absence of complications.
   (b) In early childhood drusen may be difficult to detect because they lie deep beneath the surface of the disc tissue. In this setting the appearance may be confused with early papilloedema. However, in contrast to early papilloedema, optic disc drusen show the following features (Figure 15.33).



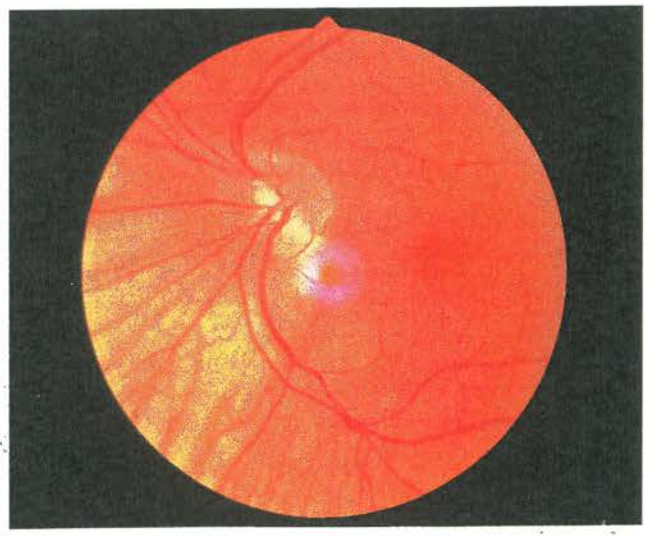


**Figure 15.32** Tilted discs *(see text)*

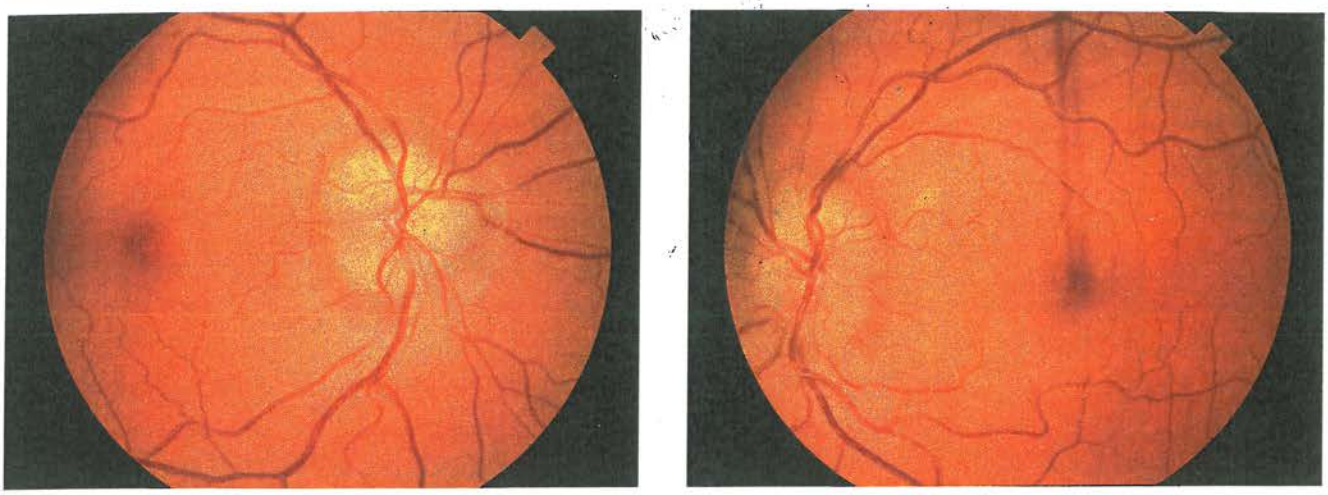


**Figure 15.33** Buried optic disc drusen (see *text*)

- Spontaneous venous pulsation is usually present.
- An absent optic cup.
- The disc itself has a pink or yellow colour and its margin has a 'lumpy' appearance.
- The emerging blood vessels show anomalous premature branching.

(c) During the early 'teens the drusen usually emerge to the surface of the disc and can be recognized as waxy pearl-like irregularities (Figures 15.34).

2. **Special investigations**
   (a) ***Fluorescein angiography*** may occasionally be helpful in differential diagnosis.
   - Drusen show the phenomenon of autofluorescence (Figure 15.35**a**) prior to dye injection, which does not occur in papilloedema.
   - Following dye injection drusen show hyperfluorescence, which is confined to the disc, is well outlined and less intense (Figure 15.35 **b-d**) than in papilloedema.

   (b) ***CT*** may also be helpful in diagnosis by detecting calcification (Figure 15.36).
3. **Complications** are very uncommon and the lesion is usually asymptomatic. A small minority of patients develop visual impairment as a result of peripapillary choroidal neovascularization (Figure 15.37). Occasionally, eyes with drusen develop a progressive but limited loss of visual field which has a nerve fibre bundle pattern.
4. **Systemic association** is Allagille syndrome which is an autosomal dominant condition mapped to chromosome 20p.
   (a) ***Ocular features***, apart from disc drusen, are posterior embryotoxon and pigmentary retinopathy.
   (b) ***Systemic features*** are liver disease, which may present with neonatal jaundice, pulmonary ste-

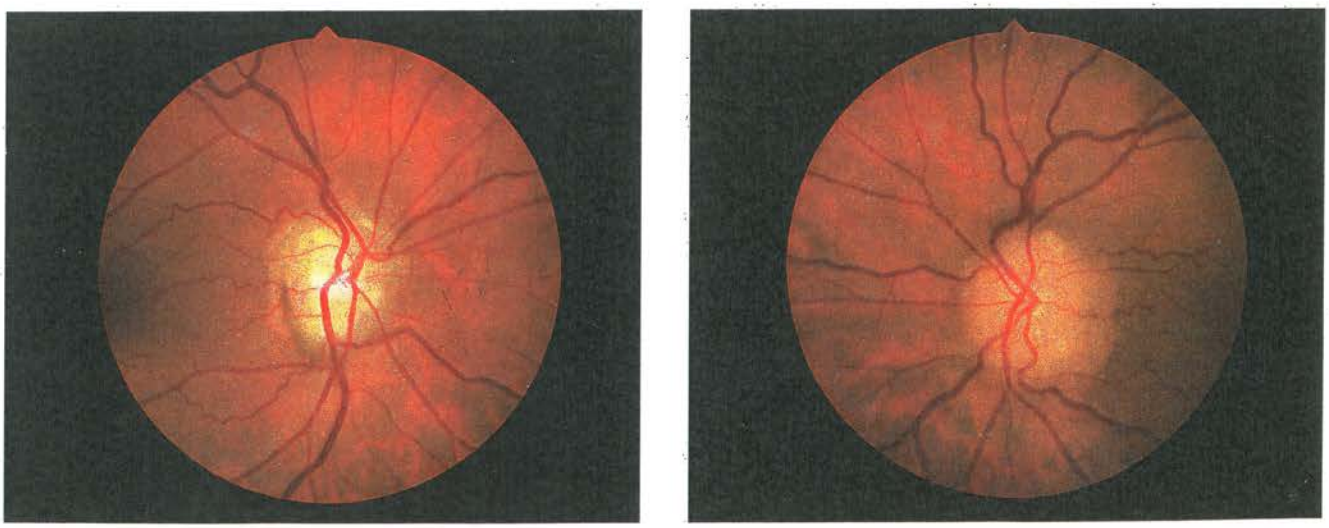


**Figure 15.34** Exposed optic disc drusen (see *text*)

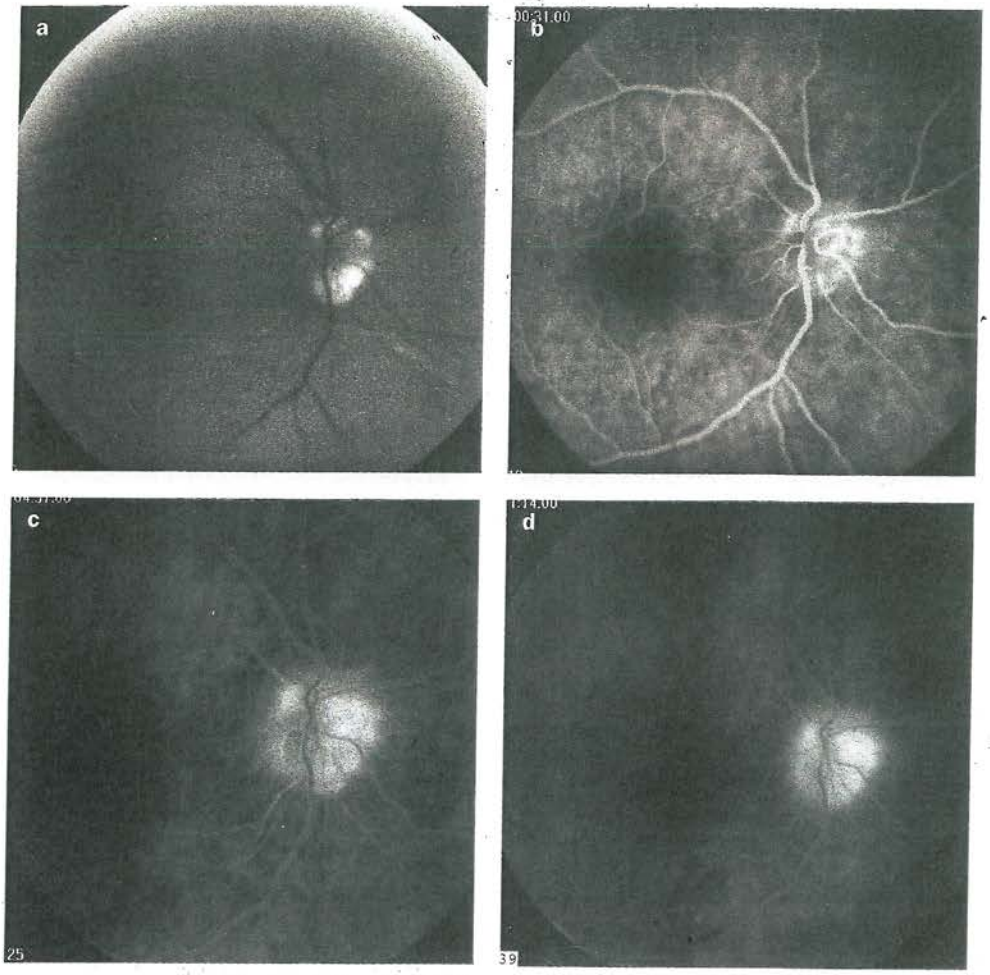



**Figure 15.35** Fluorescein angiogram of optic disc drusen (*see text*)

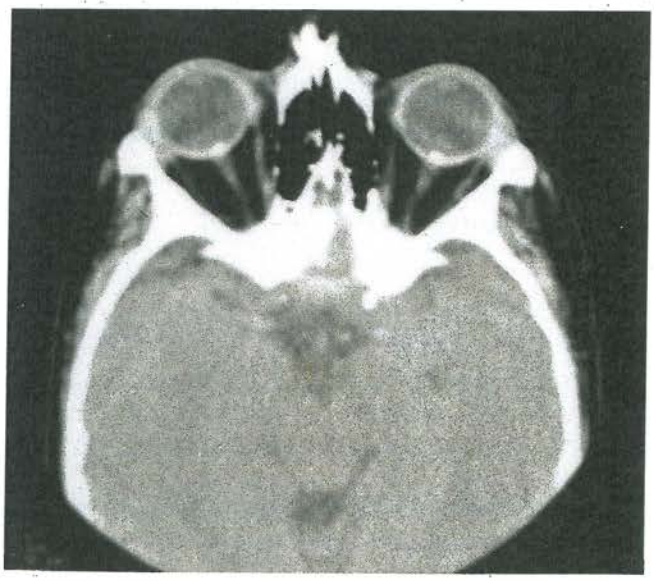


**Figure 15.36** CT scan showing bilateral optic disc drusen

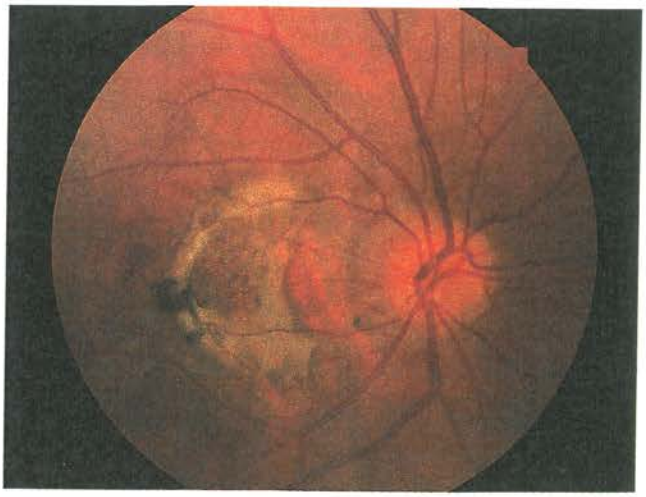


**Figure 15.37** Disciform scarring associated with optic disc drusen

nosis, cardiovascular anomalies, butterfly vertebral arch defects and peculiar facies.

## OPTIC DISC PIT

Optic disc pit is a rare, usually unilateral condition which, in some cases, may cause severe acquired visual problems.

1. **Signs**
   (a) Visual acuity is normal in the absence of complications.
   (b) The disc is larger than in the fellow eye.
   (c) Inside the disc there is a round or oval pit, of variable size (Figures 15.38 and 15.39).
   (d) The pit is most frequently located temporally but may occasionally be central.
2. **Complications**
   (a) About 45% of eyes with non-centrally located pits develop a retinal elevation at the macula (Figure 15.40). Initially, there is schisis-like separation of the inner layers of the retina which communicates with the pit. This is followed by serous detachment of the outer retinal layers.
   (b) The appearance may be mistaken for central serous retinopathy and it is therefore important to examine the optic disc carefully in all patients with suspected central serous retinopathy.
3. **Treatment**
   In most cases the long-term prognosis without treatment is poor as a result of permanent macular damage.
   (a) ***Laser photocoagulation*** of the temporal disc border followed by bed rest may be beneficial in some cases.
   (b) ***Vitrectomy with gas tamponade*** should be considered in unresponsive cases.

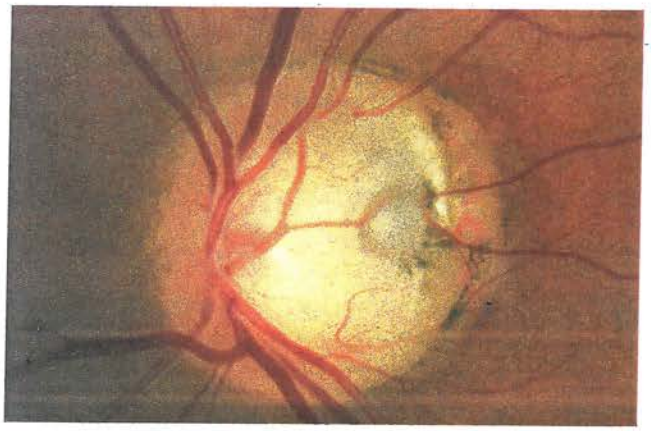


**Figure 15.38** Small optic disc pit

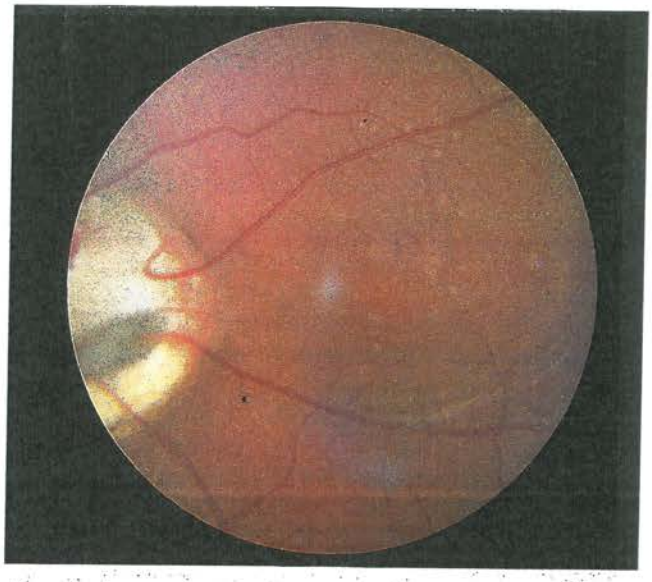


**Figure 15.40** Macular detachment associated with an optic disc pit

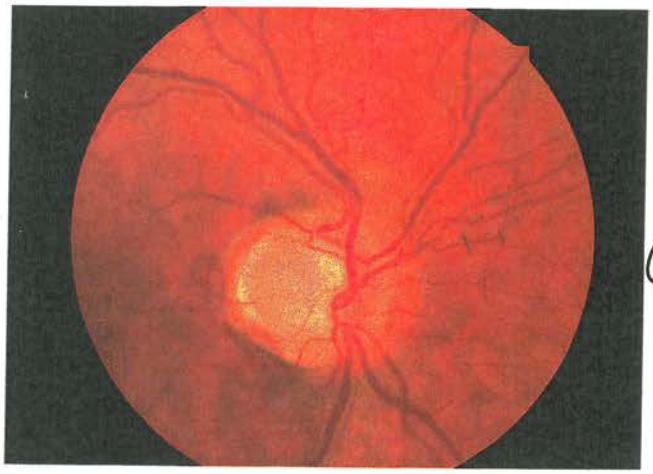


**Figure 15.39** Large optic disc pit

## MYELINATED NERVE FIBRES

Myelinated nerve fibres are relatively common and may follow several patterns:

1. **Isolated** peripheral patches of myelination (Figure 15.41).
2. **Peripapillary** myelination (Figure 15.42), which may be mistaken for papilloedema on cursory examination.
3. **Extensive** myelination starting at the disc and extending towards the periphery (Figure 15.43). The myelinated nerve fibres follow the pattern of normal fibres and extend as irregular feather-like patches, which may or may not obscure the retinal blood vessels. Although myelination usually remains stationary, it

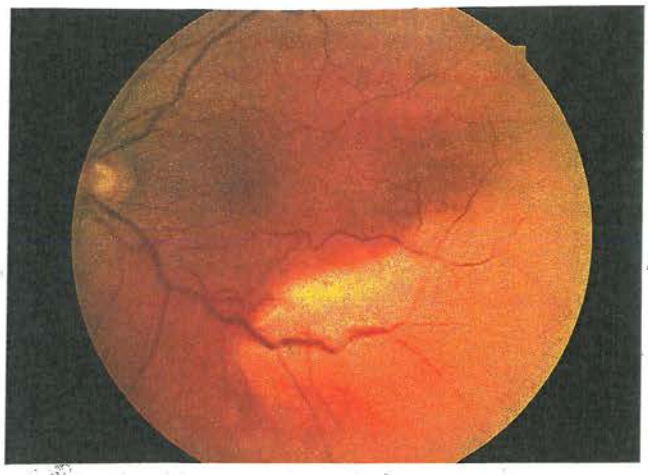


**Figure 15.41** Isolated retinal nerve fibre myelination

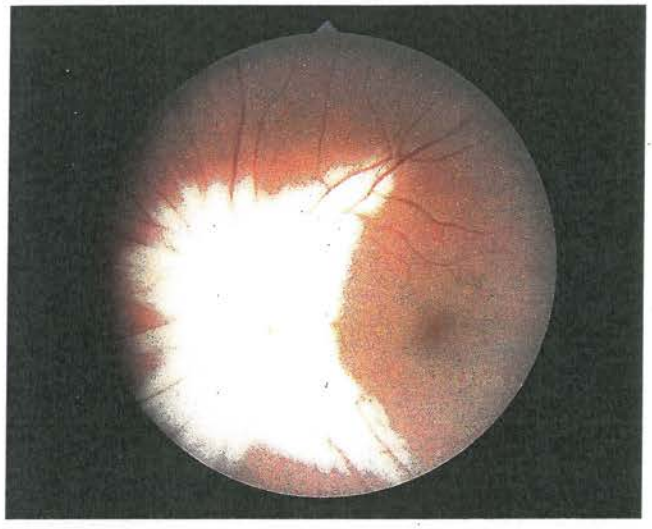


**Figure 15.42** Peripapillary retinal nerve fibre myelination

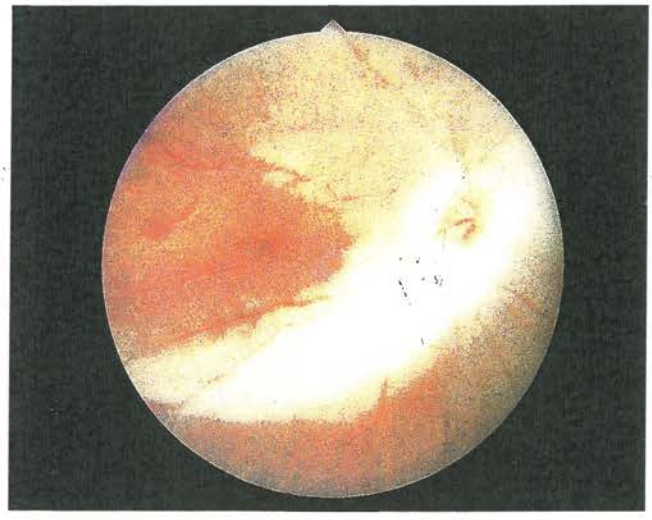


**Figure 15.43** Extensive retinal nerve fibre myelination

may very rarely disappear in patients with optic atrophy following either optic neuritis or ischaemia.

## With neurological associations

### OPTIC DISC COLOBOMA

Optic disc coloboma is a rare condition resulting from incomplete closure of the fetal fissure. Most are sporadic, although autosomal dominant inheritance may occur. Optic disc coloboma occurs unilaterally or bilaterally with equal frequency. In some patients the presence of optic disc colobomas may have profound systemic implications.

1. **Signs**
   - (a) Visual acuity is often decreased.
   - (b) The disc shows a discrete, focal, glistening, white, bowel-shaped excavation, decentred inferiorly so that the inferior neuroretinal rim is thin or absent and normal disc tissue is confined to a small superior wedge (Figure 15.44).
   - (c) The optic disc itself may be enlarged and peripapillary pigmentary changes are minimal or absent.
   - (d) Retinal vasculature is normal.
2. **Visual fields** show a superior defect which, associated with the disc appearance, may occasionally be mistaken for normal-tension glaucoma.
3. **Ocular associations**
   - (a) Chorioretinal coloboma (Figure 15.45), as well as coloboma of the ciliary body and iris (Figure 15.46).
   - (b) Microphthalmos.
   - (c) Serous retinal detachment may develop as a complication.
4. **Systemic associations** are many and only the most important are mentioned.
   - (a) ***Chromosomal anomalies*** – Patau syndrome (trisomy 13), Edward syndrome (trisomy 18) and cat-eye syndrome (trisomy 22).

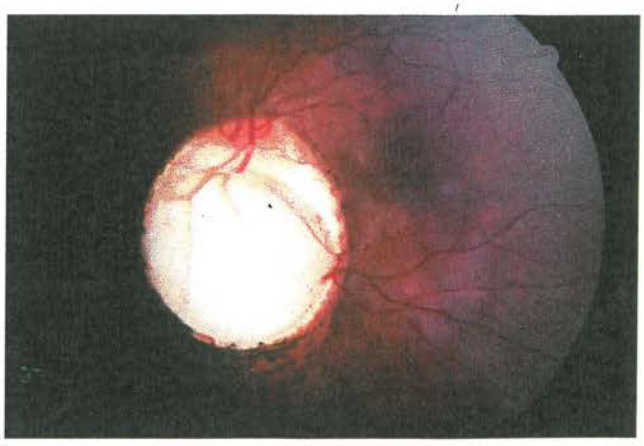


**Figure 15.44** Optic disc coloboma

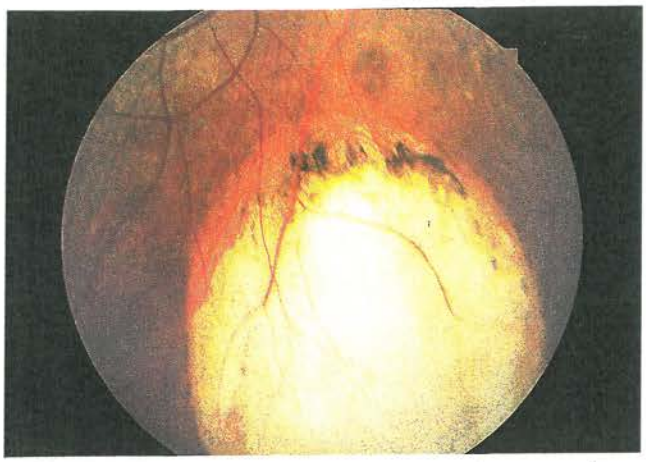


**Figure 15.45** Chorioretinal coloboma

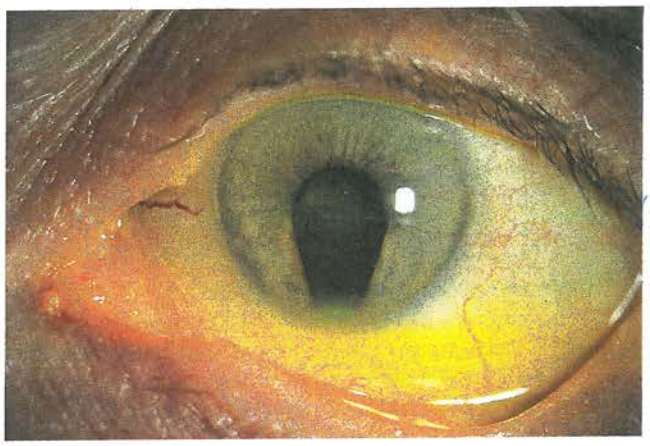


**Figure 15.46** Iris coloboma

(b) ***'CHARGE'*** association – comprises **C**oloboma, **H**eart defects, choanal **A**tresia, **R**etarded growth and development, **G**enital and **E**ar anomalies.

(c) ***Other syndromes*** – Meckel–Gruber, Goltz, Lenz microphthalmos, Walker–Warburg and Goldenhar.

## MORNING GLORY ANOMALY

Morning glory anomaly is a very rare, usually unilateral condition. Rarely bilateral cases may be hereditary. Most cases are isolated and not associated with systemic anomalies.

1. **Signs**
   (a) Visual acuity is usually very poor.
   (b) The disc is enlarged and contains a funnel-shaped excavation (Figure 15.47).
   (c) A central core of whitish glial tissue of persistent hyaloid remnants is present within the base.

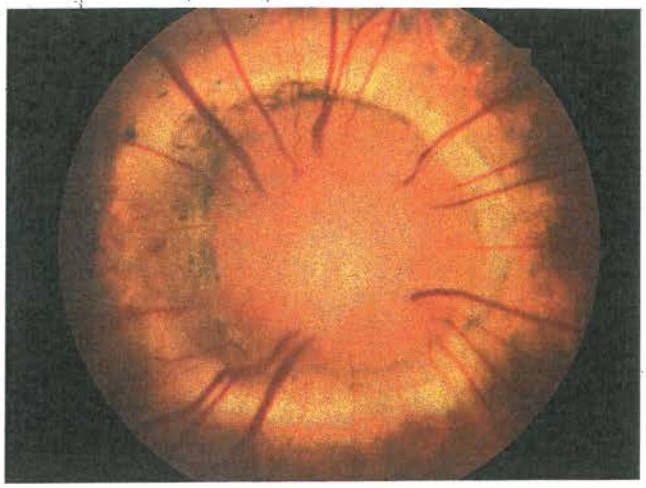


**Figure 15.47** Morning glory anomaly

   (d) The disc is surrounded by an elevated annulus of chorioretinal pigmentary disturbance.
   (e) The blood vessels emerge from the rim of the excavation in a radial pattern like the spokes of a wheel. They are increased in number and it is difficult to distinguish arteries from veins.
   (f) Serous retinal detachment develops in about 30% of cases.
3. **Systemic associations** are uncommon. The most important is trans-sphenoidal basal encephalocele. Patients with this association have a characteristic malformation complex which consists of the following:
   (a) ***Mid-facial anomalies***, which consist of hypertelorism and depressed nasal bridge (Figure 15.48), and cleft palate.
   (b) ***Basal skull defects*** with herniation of pituitary-hypothalamic structures inferiorly into the defect.

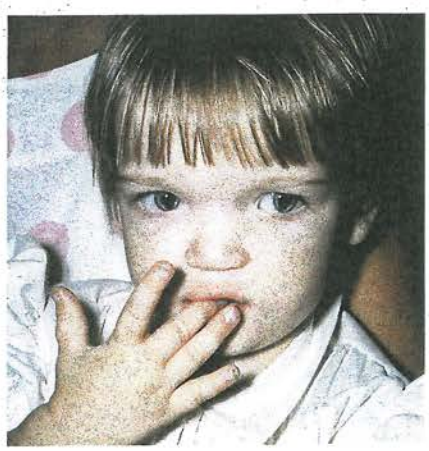


**Figure 15.48** A patient with hypertelorism and depressed nasal bridge

(c) ***Other anomalies*** include absence of the corpus callosum (Figure 15.49) and panhypopituitarism.

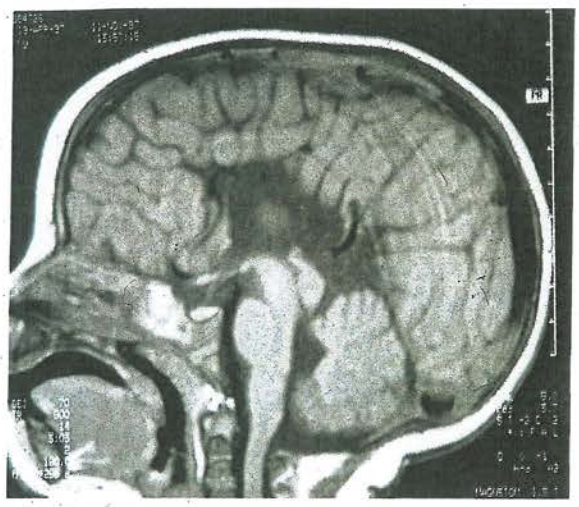


**Figure 15.49** Sagittal MRI scan showing absence of the corpus callosum

## OPTIC NERVE HYPOPLASIA

Optic nerve hypoplasia is a unilateral or bilateral condition characterized by a diminished number of optic nerve fibres. It may occur as an isolated anomaly in an otherwise normal eye, in a grossly malformed eye or in association with a heterogeneous group of disorders most commonly involving the midline structures of the brain. Specific agents used by the mother during gestation which may be associated with optic nerve hypoplasia include alcohol, LSD, quinine, protamine zinc insulin, steroids, diuretics, cold remedies and anticonvulsants. Superior segmental optic disc hypoplasia may be associated with maternal diabetes.

1. **Signs**
   (a) Visual acuity can vary from normal to no light perception.
   (b) The disc is small and grey (Figure 15.50).
   (c) There is a surrounding yellow halo of hypopigmentation caused by concentric chorioretinal atrophy (double-ring sign). The outer ring represents what would have been the normal disc margin.
   (d) In spite of the small size of the disc, the retinal blood vessels are of normal calibre, although they may be tortuous. In some cases only a part of the disc is hypoplastic.
2. **Other ocular features** vary considerably, depending on the severity. They include field defects, defective colour vision, afferent pupillary defect, foveal hypoplasia, aniridia, microphthalmos, strabismus and nystagmus in severe bilateral cases. Mild cases can be easily overlooked and the slight reduction of visual acuity may be mistaken for amblyopia and treated by occlusion.
3. **Systemic associations**
   (a) ***Neurological malformations*** include basal encephaloceles, hypoplasia of the cerebellar vermis, cystic dilatation of the fourth ventricle, posterior fossa cysts and anterior visual pathway space-occupying lesions.
   (b) ***De Morsier syndrome*** (septo-optic dysplasia) consists of the triad of short stature, nystagmus and optic nerve hypoplasia. It is characterized by a spectrum of midline developmental anomalies, including absence of the septum pellucidum, thinning or agenesis of the corpus callosum and dysplasia of the anterior third ventricle. About 60% of patients also have hypopituitarism with low growth hormone levels. If the condition is recognized early, the hormone deficiency can be corrected and normal growth resumed.

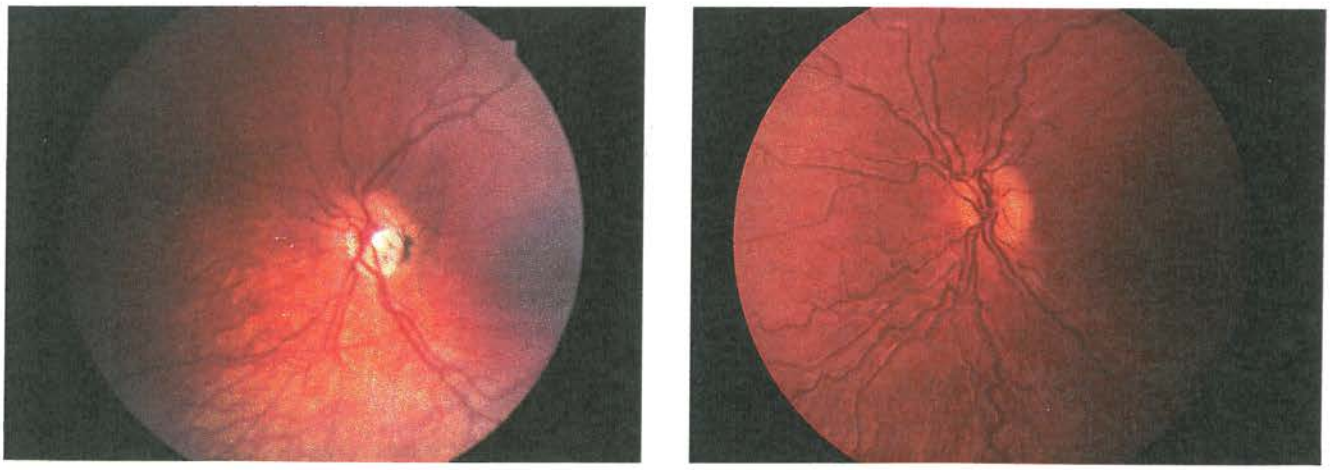


**Figure 15.50** Optic nerve hypoplasia (see *text*)

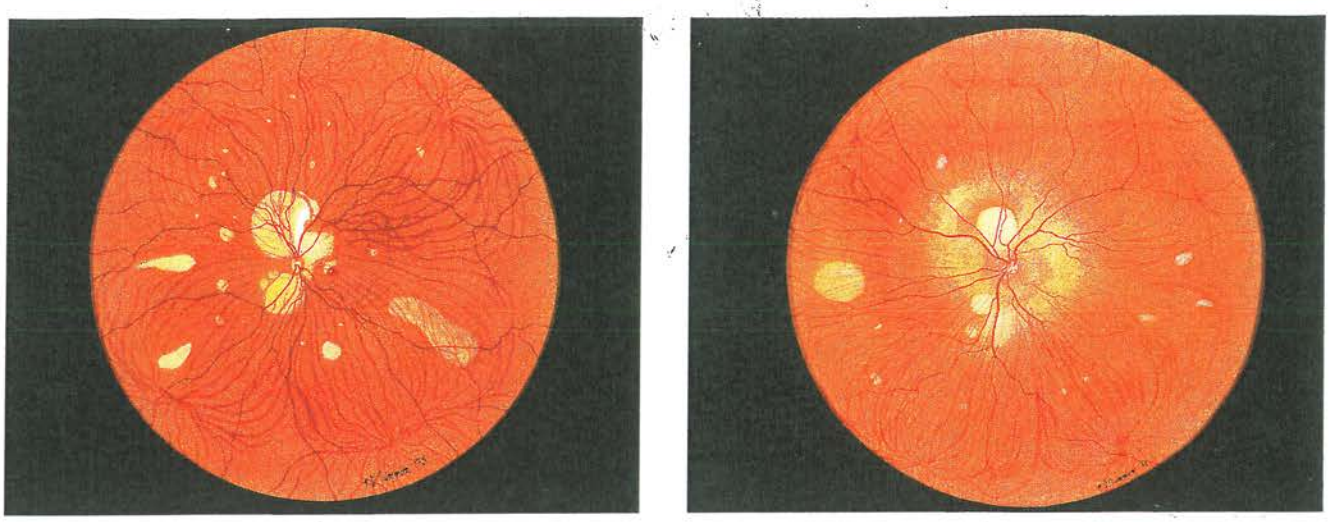


**Figure 15.51** Chorioretinal lacunae in Aicardi syndrome (*see text*)

## AICARDI SYNDROME

Aicardi syndrome is a very rare X-linked dominant disorder which is lethal *in utero* for males.

1. **Signs**
   (a) Multiple depigmented 'chorioretinal lacunae' clustered around the disc are pathognomonic (Figure 15.51).
   (b) Congenital disc anomalies include coloboma, hypoplasia and pigmentation (Figure 15.52).
2. **Other ocular features** include microphthalmos, persistent pupillary membranes and iris colobomas.
3. **Systemic features** include infantile spasms, agenesis of the corpus callosum and developmental delay. Other serious CNS malformations may also be present and death usually occurs within the first few years of life.

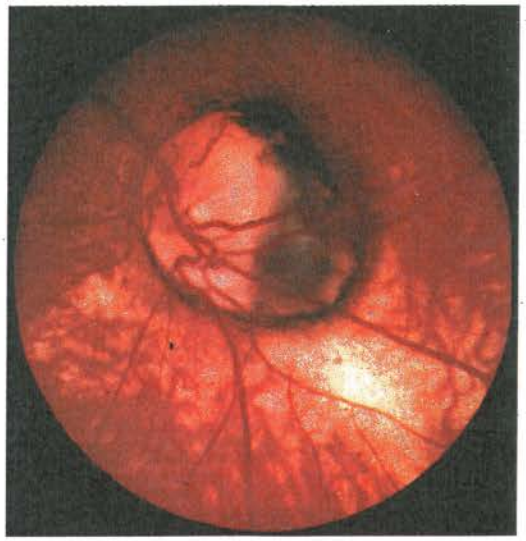


**Figure 15.52** Anomalous disc with pigmentation in Aicardi syndrome

## MISCELLANEOUS ANOMALIES

Miscellaneous rare optic disc anomalies which may occasionally have neurological associations include the following:

1. **Megalopapilla**, in which the horizontal and vertical disc diameters are 2.1 mm or more (Figure 15.53).
2. **Peripapillary staphyloma**, in which a relatively normal disc is seen within a deep peripapillary excavation (Figure 15.54).
3. **Optic disc dysplasia**, which is a descriptive term for a markedly deformed disc (Figures 15.55 and 15.56) that does not conform to any recognizable category described above.

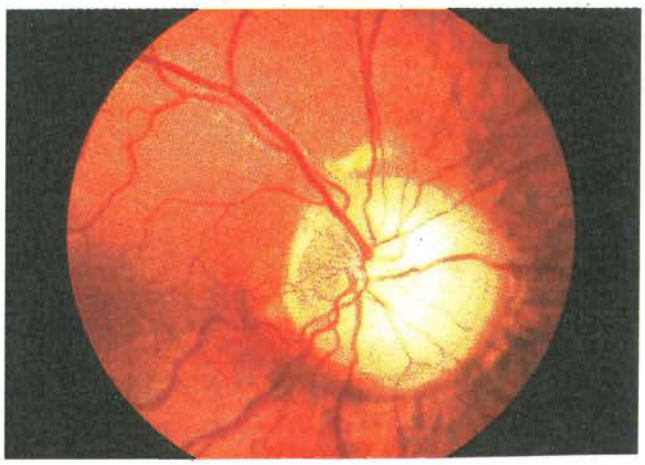


**Figure 15.53** Megalopapilla

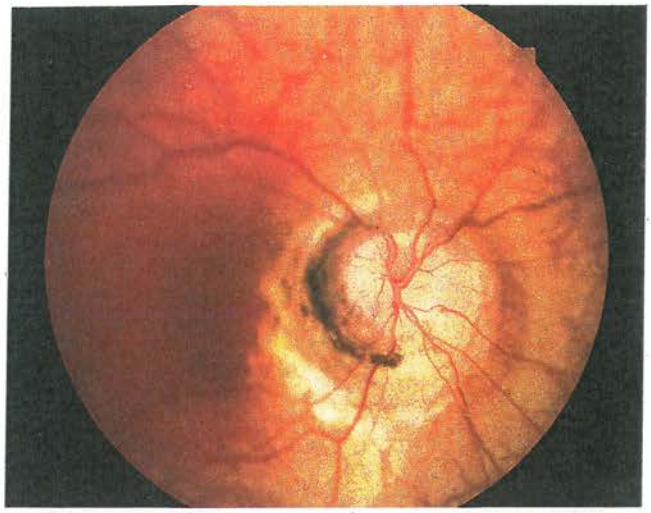


**Figure 15.54** Peripapillary staphyloma

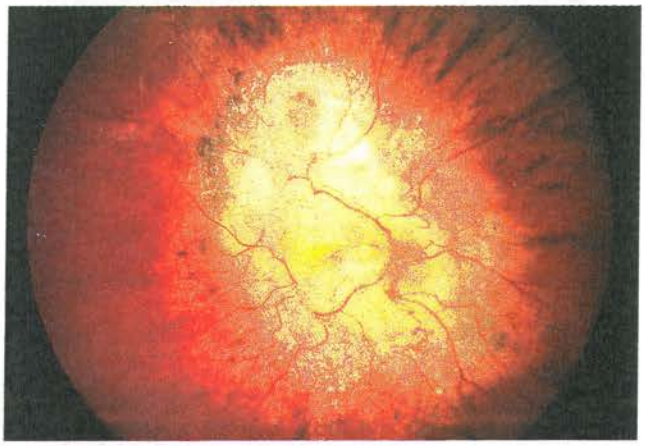


**Figure 15.55** Dysplastic disc

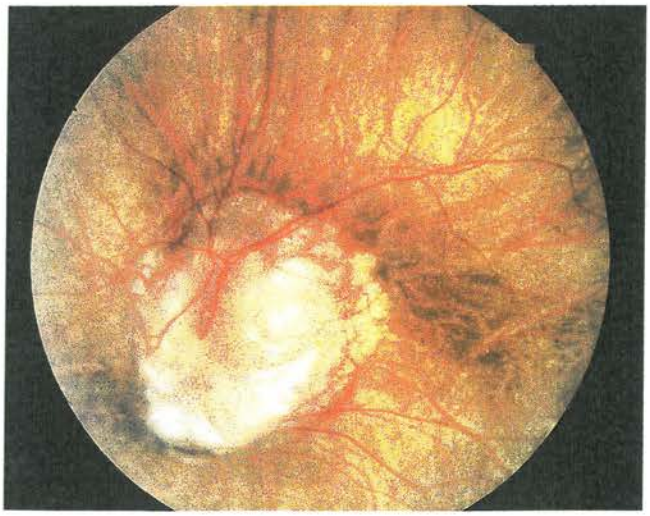


**Figure 15.56** Dysplastic disc

# PUPILLARY REACTIONS

## Applied anatomy

1. **The light reflex** is subserved by four neurones (Figure 15.57):

   (a) ***First***, which connects the retina with the pre-tectal nucleus in the midbrain at the level of the superior colliculus. The reflex is mediated by the retinal photoreceptors. Impulses originating from the nasal retina are conducted by fibres which decussate in the chiasm and pass up the optic tract to terminate in the contralateral pre-tectal nucleus. Impulses originating in the temporal retina are conducted by uncrossed fibres which terminate in the ipsilateral pre-tectal nucleus.

   (b) ***Second***, which connect the pre-tectal nucleus to both Edinger–Westphal nuclei. Thus a unilateral light stimulus evokes a bilateral and symmetrical pupillary constriction. Damage to the internuncial neurones is responsible for light–near dissociation in neurosyphilis and pinealomas.

   (c) ***Third***, which connects the Edinger–Westphal nucleus to the ciliary ganglion. In the orbit, the

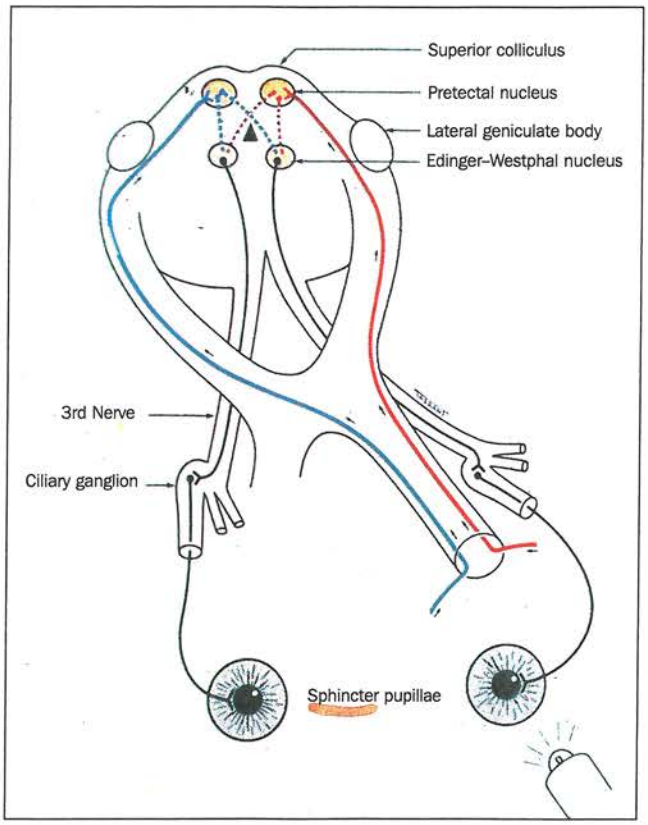



**Figure 15.57** Anatomical pathway of the pupillary light reflex

parasympathetic fibres pass through the inferior division of the third nerve and reach the ciliary ganglion via the nerve to the inferior oblique muscle.

(d) ***Fourth***, which leaves the ciliary ganglion and passes with the short ciliary nerves to innervate the sphincter pupillae. The ciliary ganglion is located within the muscle cone, just behind the globe. It should be noted that, although the ciliary ganglion contains other nerve fibres, only the parasympathetic fibres synapse there.

2. **The near reflex** consists of:
   (a) ***Increased accommodation.***
   (b) ***Convergence of the visual axes.***
   (c) ***Constriction of the pupils.***
3. **Light–near dissociation** refers to a condition in which the light reflex is absent or diminished, although the near response is intact. Vision is not a prerequisite for the near reflex, and there is no clinical condition in which the light reflex is present but the near response absent. Although the final pathways for the near and light reflexes are the same (i.e. third nerve, ciliary ganglion, short ciliary nerves), the centre for the near reflex is ill-defined. There are probably two supranuclear influences: the frontal and occipital lobes. The midbrain centre for the near reflex is probably located in a more ventral location than the pretectal nucleus and this may be why compressive lesions such as pinealomas produce light-near dissociation by preferentially involving the dorsal pupillomotor fibres, sparing the ventral fibres until late.
4. **The sympathetic** supply consists of three neurones (Figure 15.58).
   (a) ***First***, which starts in the posterior hypothalamus and descends, uncrossed, down the brain stem to terminate in the ciliospinal centre of Budge located between C8 and T2.
   (b) ***Second***, which passes from the ciliospinal centre of Budge to the superior cervical ganglion in the neck. During its long course, it is closely related to the apical pleura where it may be damaged by bronchial carcinoma (Pancoast tumour) or during surgery on the neck.
   (c) ***Third***, which ascends along the internal carotid artery to enter the cavernous sinus, where it joins the ophthalmic division of the trigeminal nerve. The sympathetic fibres reach the ciliary body and the dilator pupillae muscle via the nasociliary nerve and the long ciliary nerves.

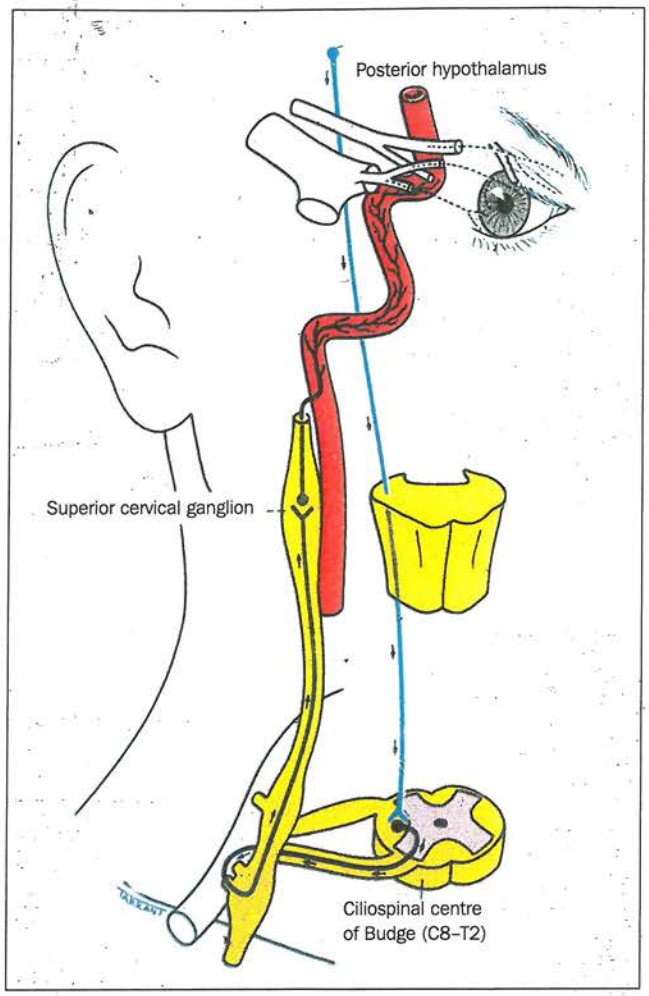



**Figure 15.58** Anatomical pathway of the sympathetic nerve supply

# Abnormal pupillary reactions

## AFFERENT PUPILLARY CONDUCTION DEFECTS

1. **Total afferent pupillary defect** (TAPD, amaurotic pupil) is caused by a complete optic nerve lesion and is characterized by the following:
   (a) The involved eye is completely blind (i.e. no light perception).
   (b) Both pupils are equal in size.
   (c) When the affected eye is stimulated neither pupil reacts but when the normal eye is stimulated both pupils react normally.
   (d) The near reflex is normal in both eyes.
2. **Relative afferent pupillary defect** (RAPD, Marcus Gunn pupil) is caused by an incomplete optic nerve lesion or severe retinal disease, but not by a dense cataract. The clinical features are those of an amaurotic pupil but more subtle. The difference between the pupillary reactions is enhanced by the 'swinging-flashlight test' in which each pupil is stimulated in rapid succession. When the abnormal pupil is stimulated the pupils dilate instead of constricting. This paradoxical reaction of the pupil to light occurs because the dilatation of the pupil, produced by withdrawing the light from the normal eye, outweighs the constriction produced by stimulating the abnormal eye.

## ARGYLL ROBERTSON PUPILS

Argyll Robertson pupils are caused by neurosyphilis and are characterized by:

(a) Involvement is usually bilateral but asymmetrical.
(b) The pupils are small and irregular.
(c) The light reflex is absent or very sluggish but the near reflex is normal (light–near dissociation).
(d) The pupils are very difficult to dilate.

## DIFFERENTIAL DIAGNOSIS OF LIGHT–NEAR DISSOCIATION

(a) ***Unilateral***
- Afferent conduction defect.
- Herpes zoster ophthalmicus.
- Aberrant regeneration of the third nerve.
- Adie pupil.

(b) ***Bilateral***
- Juvenile-onset diabetes.
- Myotonic dystrophy.
- Parinaud dorsal midbrain syndrome.
- Pituitary tumours.
- Familial amyloidosis.
- Encephalitis.
- Chronic alcoholism.
- Neurosyphilis.

## ADIE PUPIL

Adie (tonic) pupil is caused by denervation of the postganglionic supply to the sphincter pupillae and the ciliary muscle which may follow a viral illness. It typically affects young adults.

1. **Signs**
   (a) It is unilateral in 80%.
   (b) The affected pupil is large and regular, although in longstanding cases it may become constricted.
   (c) The light reflex is absent or very slow and is associated with vermiform movements of the iris.
   (d) Constriction to near is strong but very slow and tonic.
   (e) Redilatation is also very slow.
   (f) Accommodation is slow.
2. **Associations** in some patients
   (a) Diminished deep tendon reflexes (Holmes–Adie syndrome).
   (b) Autonomic nerve dysfunction.
3. **Pharmacological testing** can be used to confirm the diagnosis as follows: if 2.5% mecholyl or 0.125% pilocarpine is instilled into both eyes, the normal pupil will not constrict, but the abnormal pupil will because of denervation hypersensitivity. Some pupils in diabetic patients may also show this response and very occasionally both pupils constrict in normal individuals.

## OCULOSYMPATHETIC PALSY (HORNER SYNDROME)

1. **Signs** (Figure 15.59)
   (a) Mild ptosis as a result of weakness of Müller muscle.
   (b) Slight elevation of the inferior eyelid as a result of weakness of the inferior tarsal muscle.
   (c) Miosis resulting from the unopposed action of the sphincter pupillae.
   (d) The pupillary reactions are normal to light and near.
   (e) Reduced ipsilateral sweating, but only if the lesion is below the superior cervical ganglion.
   (f) Heterochromia (irides of different colour) is occasionally present if the lesion is congenital and occasionally acquired and longstanding.
   (g) The pupil is slow to dilate.

**Figure 15.59** Right Horner syndrome

2. **Pharmacological testing** using cocaine may serve to confirm the diagnosis. Hydroxyamphetamine may be used to differentiate a preganglionic from a postganglionic lesion. Adrenaline may also be used to assess denervation hypersensitivity.
   (a) Instil 4% cocaine into both eyes: the normal pupil will dilate but the Horner pupil will not.
   (b) Instil 1% hydroxyamphetamine (Paredrine) into both eyes: in a preganglionic lesion both pupils will dilate whereas in a postganglionic lesion the Horner pupil will not.
   (c) Instil 1:1000 adrenaline into both eyes: in a preganglionic lesion both pupils will not dilate because adrenaline is rapidly destroyed by monoamine oxidase; in a postganglionic lesion, the Horner pupil will dilate and ptosis may be temporarily relieved because adrenaline is not broken down as monoamine oxidase is absent.
3. **Causes**
   (a) ***Central*** (first order neurone) lesions:
   - Brain stem disease (tumours, vascular, demyelination).
   - Syringomyelia (Figure 15.60).
   - Lateral medullary (Wallenburg) syndrome.
   - Spinal cord tumours.

2. **Signs** in chronological order:
   (a) The acute stage shows subtle signs which may be easily overlooked. In some patients the optic disc may be entirely normal.
   (b) In typical cases there is disc hyperaemia, dilated capillaries on the disc surface which may extend onto adjacent retina (telangiectatic microangiopathy), vascular tortuosity and swelling of the peripapillary nerve fibre layer (Figure 15.23). Telangiectatic microangiopathy may be present in asymptomatic female relatives.
   (c) Subsequently, the telangiectatic vessels regress and severe optic atrophy ensues.
   (d) Surprisingly, the pupillary reactions to light often remain fairly brisk.
3. **Fluorescein angiography** shows absence of dye leakage.
4. **Visual field defects** usually consist of centrocaecal scotomas.
5. **Prognosis** is relatively poor, although some visual recovery may occur in a minority of cases even years later. Most patients suffer severe, bilateral and permanent visual loss with a final visual acuity of 6/60 or less. Patients with the 11778 mutation have the worst prognosis and those with the 3460 and 14484 mutations are usually less severely affected.
6. **Treatment** is generally ineffective although many modalities, including steroids, hydroxycobalamin and surgical intervention, have been tried. Patients should, however, be advised to stop smoking and excessive drinking of alcohol to prevent potential stress on mitochondrial energy production.

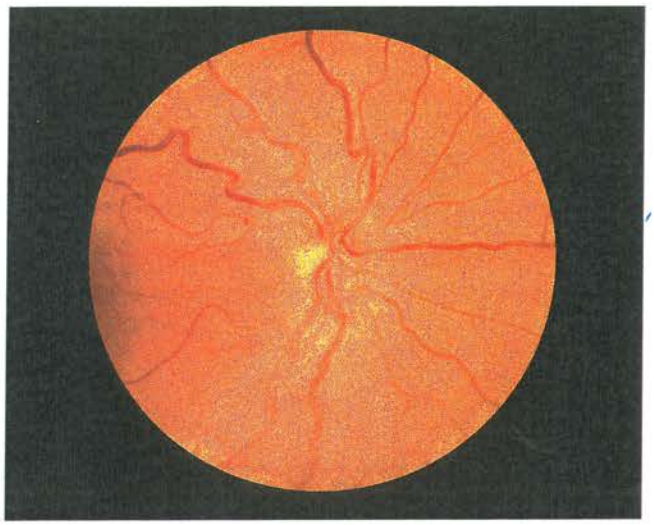


**Figure 15.23** Acute stage of Leber optic neuropathy

## Hereditary optic atrophies

The hereditary optic neuropathies are a very rare heterogenous group of disorders that are primarily manifested by bilateral optic atrophy.

### KJER SYNDROME

1. **Inheritance** is autosomal dominant.
2. **Presentation** is between the ages of 4 and 10 years with insidious visual loss.
3. **Optic discs** show temporal pallor and excavation (Figure 15.24).
4. **Visual prognosis** is variable (6/12–6/60) and there is considerable intra- and inter-familial variation in final visual outcome.
5. **Systemic abnormalities** are absent.

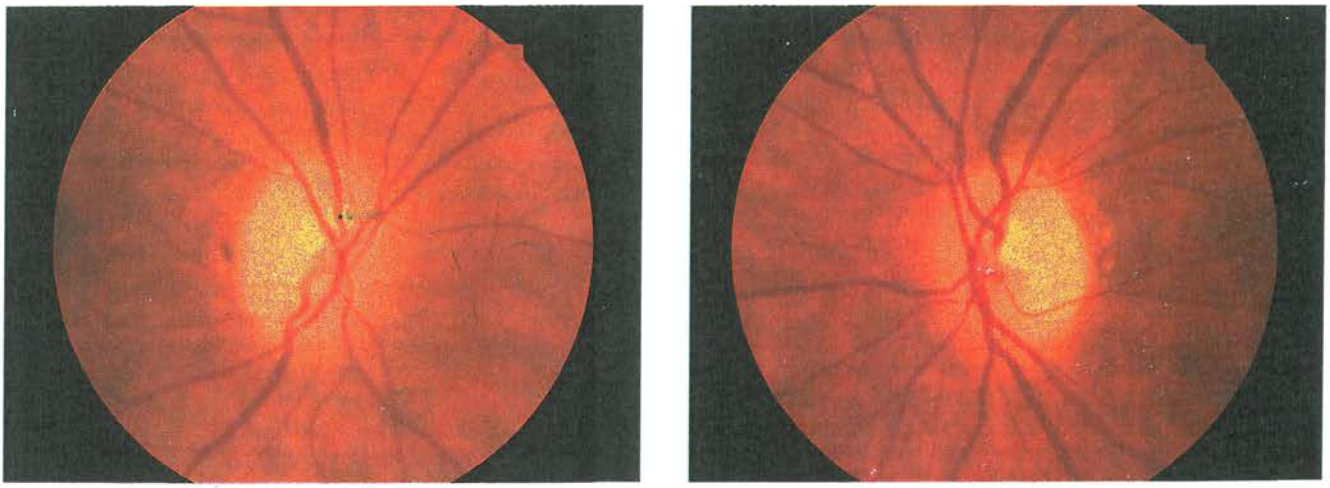


**Figure 15.24** Temporal disc pallor in dominantly inherited optic atrophy

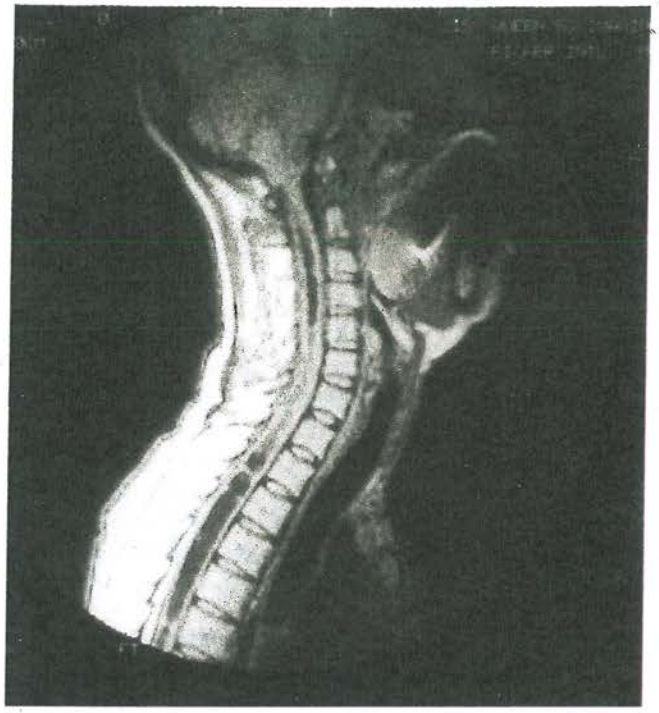


**Figure 15.60** MRI scan showing cavities in the spinal cord in syringomyelia

(b) ***Preganglionic*** (second order neurone)
- Pancoast tumour (Figure 15.61).
- Carotid and aortic aneurysms and dissection.
- Lesions in the neck such as malignant cervical lymph nodes, trauma or following surgery.

(c) ***Postganglionic*** (third order neurone)
- Cluster headaches (migrainous neuralgia).
- Nasopharyngeal tumours.
- Otitis media.
- Cavernous sinus mass.
- Internal carotid artery disease.

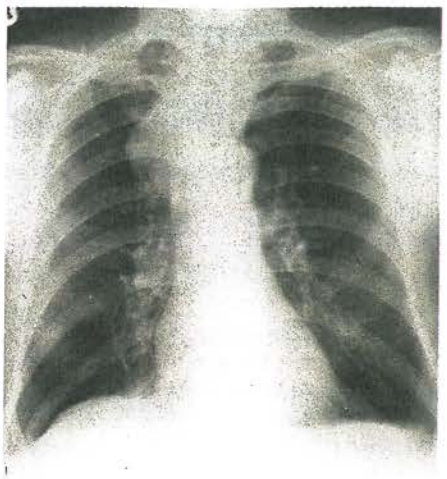


**Figure 15.61** Pancoast tumour at the right apex

(d) ***Miscellaneous***
- Congenital.
- Idiopathic.

# NYSTAGMUS

## Classification

Nystagmus is a repetitive, involuntary to-and-fro oscillation of the eyes. The plane of oscillation may be horizontal, vertical, torsional or non-specific. The three main types are:

1. **Jerk nystagmus**, which is characterized by a slow drift followed by a fast corrective phase. The direction of nystagmus is described in terms of the direction of the fast component as follows: right, left, up, down and rotatory. Jerk nystagmus can be divided into gaze-evoked (i.e. vestibular) and gaze-paretic, which is slow and usually indicates brain stem damage.
2. **Pendular nystagmus**, which is characterized by the following:
   (a) The velocity of nystagmus is equal in both directions.
   (b) Congenital pendular nystagmus is horizontal, conjugate and tends to convert to jerk on lateral gaze.
   (c) Acquired pendular nystagmus has horizontal, vertical and torsional components.
   (d) If the horizontal and vertical components of pendular nystagmus are in phase the perceived direction becomes oblique.
   (e) If the horizontal and vertical components are out of phase the direction becomes elliptic or rotary.
3. **Mixed nystagmus**, which is pendular nystagmus in the primary position and jerk on lateral gaze.

## Causes

### PHYSIOLOGICAL NYSTAGMUS

1. **End-point nystagmus** is a fine jerk nystagmus of moderate frequency found when the eyes are in extreme positions of gaze.
2. **Optokinetic nystagmus** is a jerk nystagmus induced by moving repetitive stimuli across the visual field. The slow phase is a pursuit movement in which the eyes follow the target, and the fast phase is a saccadic movement in the opposite direction as the eyes refixate on the next target. If the optokinetic tape or drum is moved from right to left, the left parieto-occipital region controls the slow (pursuit) phase to the left, and the left frontal lobe controls the rapid (saccadic) phase to the right. The optokinetic nystagmus is useful for detecting malingerers who feign blindness and

for testing visual acuity in the very young. It may also be helpful in determining the probable cause of an isolated homonymous hemianopia (*see below*).

3. **Vestibular nystagmus** is a jerk nystagmus caused by altered input from the vestibular nuclei to the horizontal gaze centres. The slow phase is initiated by the vestibular nuclei and the fast phase by the brain stem and frontomesencephalic pathway. Rotatory nystagmus is usually caused by pathological conditions affecting the vestibular system. Caloric stimulation is as follows:
   (a) When ***cold*** water is poured into the ***right ear*** the patient will develop ***left*** jerk nystagmus (i.e. fast phase to the left).
   (b) When ***warm*** water is poured into the ***right ear*** the patient will develop ***right*** jerk nystagmus (i.e. fast phase to the right).

A useful mnemonic is '***COWS***' (cold–opposite, warm–same) indicating the direction of the nystagmus.

## MOTOR IMBALANCE NYSTAGMUS

Motor imbalance nystagmus is the result of primary defects in the efferent mechanisms.

1. **Congenital** nystagmus presents at birth or soon after and persists throughout life. Inheritance is X-linked recessive or autosomal dominant.
   - Usually jerk, uniplanar horizontal nystagmus.
   - May be dampened by convergence and is not present during sleep.
   - May be associated with abnormal head posture.
2. **Spasmus nutans** is a rare disorder which presents at between 3 and 18 months.
   (a) ***Signs***
   - Unilateral or bilateral, small-amplitude, high-frequency horizontal nystagmus associated with head nodding.
   - It is frequently asymmetrical with increased amplitude in abduction.
   - Vertical and torsional components may be present.

   (b) ***Causes***
   - Idiopathic, which spontaneously resolves by age 3 years.
   - Glioma of anterior visual pathways.
   - Empty sella syndrome.
   - Porencephalic cyst.
3. **Latent nystagmus** is associated with infantile esotropia and dissociated vertical deviation.
   - Horizontal nystagmus, which becomes apparent on covering one eye or reducing the amount of light reaching the eye.
   - Fast phase is in the direction of the uncovered fixating eye.
   - Disappears when both eyes are open.
   - Occasionally, an element of latent nystagmus is superimposed on a manifest nystagmus so that when one eye is covered the amplitude of nystagmus increases (latent-manifest nystagmus).
4. **Ataxic nystagmus** is a horizontal jerk nystagmus which occurs in the abducting eye of a patient with an internuclear ophthalmoplegia (*see below*).
5. **Downbeat nystagmus**
   (a) ***Signs***
   - Vertical nystagmus with fast phase beating downwards.
   - More easily elicited with the patient looking down and laterally.

   (b) ***Causes***
   - Lesions of the craniocervical junction at the foramen magnum such as an Arnold–Chiari malformation (Figure 15.62), cerebellar degeneration, syringobulbia and Paget disease.
   - Drugs such as lithium, phenytoin, carbamazepine and barbiturates.
   - Miscellaneous causes such as Wernicke encephalopathy, demyelination and hydrocephalus.

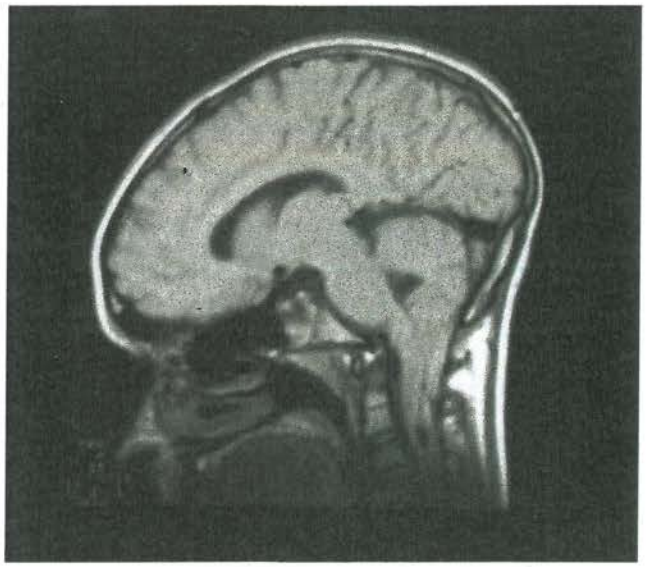


**Figure 15.62** Sagittal T1-weighted MRI scan of Arnold–Chiari malformation

6. **Upbeat nystagmus** has a fast phase beating upwards. Causes include posterior fossa lesions, drugs and Wernicke encephalopathy.
7. **Convergence–retraction nystagmus** is caused by co-contraction of the extraocular muscles, particularly the medial recti.
   (a) ***Signs***
   - Jerk nystagmus, which is induced by attempted upward gaze in which the fast

phase brings the two eyes towards each other in a convergence movement.
- Associated with retraction of the globe into the orbit.

(b) ***Causes*** include lesions of the pre-tectal area such as pinealomas and vascular accidents (*see below*).

8. **See-saw nystagmus of Maddox**
   (a) ***Signs***
   - Pendular nystagmus, in which one eye elevates and intorts while the other depresses and extorts.
   - The eyes then reverse direction.

   (b) ***Causes***
   - Parasellar tumours.
   - Syringobulbia.
   - Brain stem stroke.
9. **Periodic alternating nystagmus**
   (a) ***Signs***
   - Jerk nystagmus with rhythmic changes in amplitude and direction, usually every 2 minutes.
   - As the first half of the cycle finishes, there may be a transitional period during which there may be upbeating, downbeating or square wave jerks before the second phase of the cycle begins.

   (b) ***Causes***
   - Cerebellar disease.
   - Demyelination.
   - Ataxia telangiectasia (Louis–Bar syndrome).
   - Arnold–Chiari malformation.
   - Trauma.
   - Drugs such as phenytoin.

### OCULAR NYSTAGMUS

Ocular (sensory deprivation) nystagmus is caused by defective vision; it is horizontal and pendular. Its severity depends on the extent of visual loss and can often be dampened by convergence. Occasionally, an abnormal head posture may be adopted to decrease the amplitude of the nystagmus. It is caused by severe impairment of central vision in early life (e.g. congenital cataract, macular hypoplasia). In general, all children who lose central vision in both eyes before the age of 2 years develop nystagmus.

### NYSTAGMOID MOVEMENTS

1. **Ocular flutter** and **opsoclonus**
   (a) ***Signs***: Saccadic oscillations with no intersaccadic interval. In ocular flutter they are purely horizontal and in opsoclonus they are multiplanar.

   (b) ***Causes***
   - Viral encephalitis.
   - Metastatic neuroblastoma in children.
   - Paraneoplastic syndrome in adults (bronchogenic carcinoma).
   - Demyelination.
   - Drug-induced (lithium, amitriptyline, phenytoin and imipramine).
   - Myoclonic encephalopathy in infants ('dancing eyes and dancing feet').
   - Idiopathic and transient in healthy neonates.
2. **Ocular bobbing**
   (a) ***Signs***: Rapid, conjugate, downward eye movements with a slow drift up to the primary position.

   (b) ***Causes***
   - Pontine lesions – usually haemorrhage.
   - Cerebellar lesions compressing the pons.
   - Metabolic encephalopathy.

# SUPRANUCLEAR DISORDERS OF EYE MOVEMENT

## Conjugate eye movements

Conjugate eye movements are binocular movements in which the eyes move synchronously and symmetrically in the same direction. The three main types are: (a) ***saccadic***, (b) ***smooth pursuit*** and (c) ***non-optical reflexes***. Control of saccadic and pursuit movements is at both the cerebral and brain stem levels. Gaze palsies caused by supranuclear disturbances are characterized by absence of diplopia and normal vestibulo-ocular reflexes (e.g. oculocephalic movements and caloric stimulation).

### SACCADIC MOVEMENTS

1. **Function** of saccadic movements is to place the object of interest on the fovea rapidly or to move the eyes from one object to another. This can be done voluntarily or it can occur as a reflex triggered by the presence of an object in the peripheral visual field. Voluntary saccades are similar to the gunnery system of rapidly locating a moving target.
2. **Pathway** for horizontal saccades originates in the premotor cortex. From there, fibres pass to the *contralateral* horizontal gaze centre in the pontine paramedian reticular formation (PPRF). The right frontal lobe controls saccades to the left and the left frontal lobe those to the right. Irritative lesions may therefore cause a deviation of the eyes to the opposite side.

### SMOOTH PURSUIT MOVEMENTS

1. **Function** of pursuit movements is to maintain fixation on the target once it has been located by the saccadic system. The stimulus is movement of the image near the fovea. The movements are slow and smooth.
2. **Pathway** originates in the peristriate cortex of the occipital motor area. The fibres then descend and terminate in the *ipsilateral* horizontal gaze centre in the PPRF. The right occipital lobe therefore controls pursuit to the right and the left occipital lobe that to the left.

### NON-OPTICAL REFLEXES

1. **Function** of non-optical (vestibular) reflexes is to maintain eye position with respect to any changes of the head and body as a whole.
2. **Pathway** originates in the labyrinths and proprioceptors in the neck muscles which derive information concerning head and neck movements. Afferent fibres synapse in the vestibular nuclei and pass to the horizontal gaze centre in the PPRF.

## Supranuclear gaze palsies

### HORIZONTAL GAZE PALSIES

Horizontal eye movements are generated from the horizontal gaze centre in the PPRF. From here the output is to the ipsilateral sixth nerve nucleus to abduct the ipsilateral eye. To adduct the contralateral eye, fibres from the PPRF also cross the pons and pass up the medial longitudinal fasciculus (MLF) to the contralateral medial rectus subnucleus in the third nerve complex, which also receives independent descending input from the vergence control centres. Stimulation of the PPRF on one side therefore causes a conjugate movement of the eyes to the same side. Loss of normal horizontal eye movements occurs when these pathways are disrupted as follows:

1. **PPRF** lesions give rise to ipsilateral horizontal gaze palsies, sparing the vestibulo-ocular reflex.
2. **MLF** lesions are responsible for the clinical syndrome of internuclear ophthalmoplegia (INO).
   (a) ***Signs*** of a left internuclear ophthalmoplegia:
   - On right gaze there is defective left adduction (Figure 15.63**a**) and ataxic nystagmus of the right eye.
   - Left gaze is normal (Figure 15.63**b**).
   - Convergence is intact if the lesion is discrete.
   - Vertical nystagmus on attempted upgaze.

   (b) ***Causes***
   - Demyelination, which usually causes bilateral lesions.
   - Vascular disease.
   - Tumours of the brain stem and fourth ventricle.
   - Encephalitis.
   - Hydrocephalus.
   - Progressive supranuclear ophthalmoplegia.
   - Drug-induced.
   - Remote effects of carcinoma.
3. **PPRF** and **MLF** combined lesions on the same side give rise to the 'one-and-a-half syndrome'. A left lesion is characterized by:
   (a) Ipsilateral gaze palsy. Figure 15.64**a** shows the patient attempting to look to the left.
   (b) Ipsilateral internuclear ophthalmoplegia (Figure 15.64**b**).

### VERTICAL GAZE PALSIES

Vertical eye movements are generated from the vertical gaze centre known as the rostral interstitial nucleus of the MLF which lies in the midbrain just dorsal to the red

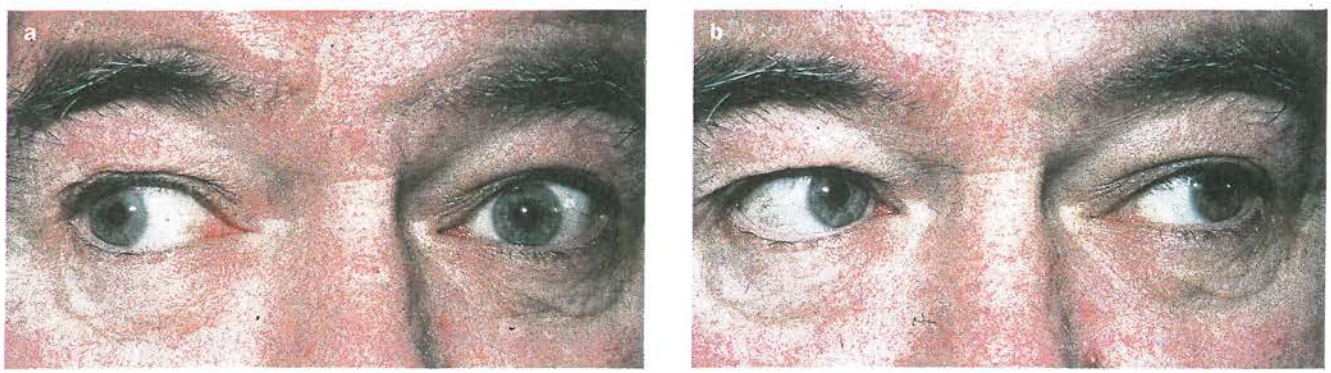



**Figure 15.63** Left internuclear ophthalmoplegia. (**a**) Defective left adduction on right gaze; (**b**) normal left gaze

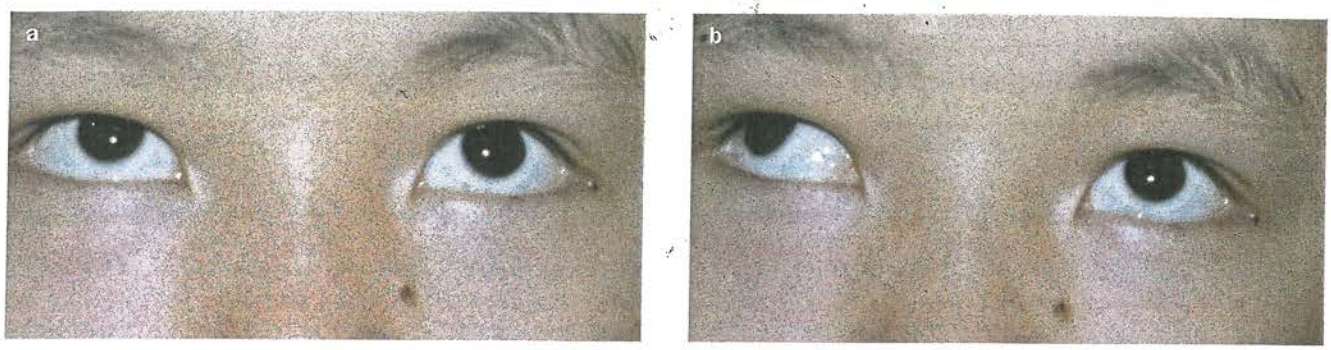



**Figure 15.64** Left 'one-and-a-half syndrome'. (**a**) Defective left gaze; (**b**) defective left adduction and normal right abduction on right gaze

nucleus. From the vertical gaze centre, impulses pass to the subnuclei of the eye muscles controlling vertical gaze in both eyes. Cells mediating upward and downward eye movements are intermingled in the vertical gaze centre, although selective paralysis of upgaze and downgaze may occur in spite of this. The main causes of vertical gaze palsies are:

1. **Parinaud dorsal midbrain syndrome**
   (a) ***Signs***
   - Supranuclear upgaze palsy (Figure 15.65**a**).
   - Large pupils with light–near dissociation.
   - Lid retraction (Collier sign).
   - Paralysis of convergence.
   - Convergence–retraction nystagmus.
   - Other midbrain signs.

   (b) ***Causes***
   - In children: aqueduct stenosis, meningitis and pinealoma (Figure 15.66).
   - In young adults: demyelination, trauma and arteriovenous malformations.
   - In the elderly: midbrain vascular accidents, mass lesions involving the periaqueductal grey matter and posterior fossa aneurysms.
2. **Progressive supranuclear palsy** (Steele–Richardson–Olszewski syndrome) is a severe degenerative disease which presents in old age.
   - Supranuclear gaze palsy, which initially primarily affects downgaze (Figure 15.67**c**).
   - As the disease progresses upgaze is also affected (Figure 15.67**a**).
   - Horizontal movements subsequently become impaired and eventually a global gaze palsy develops.
   - Pseudobulbar palsy.
   - Extrapyramidal rigidity.
   - Gait ataxia.
   - Dementia.

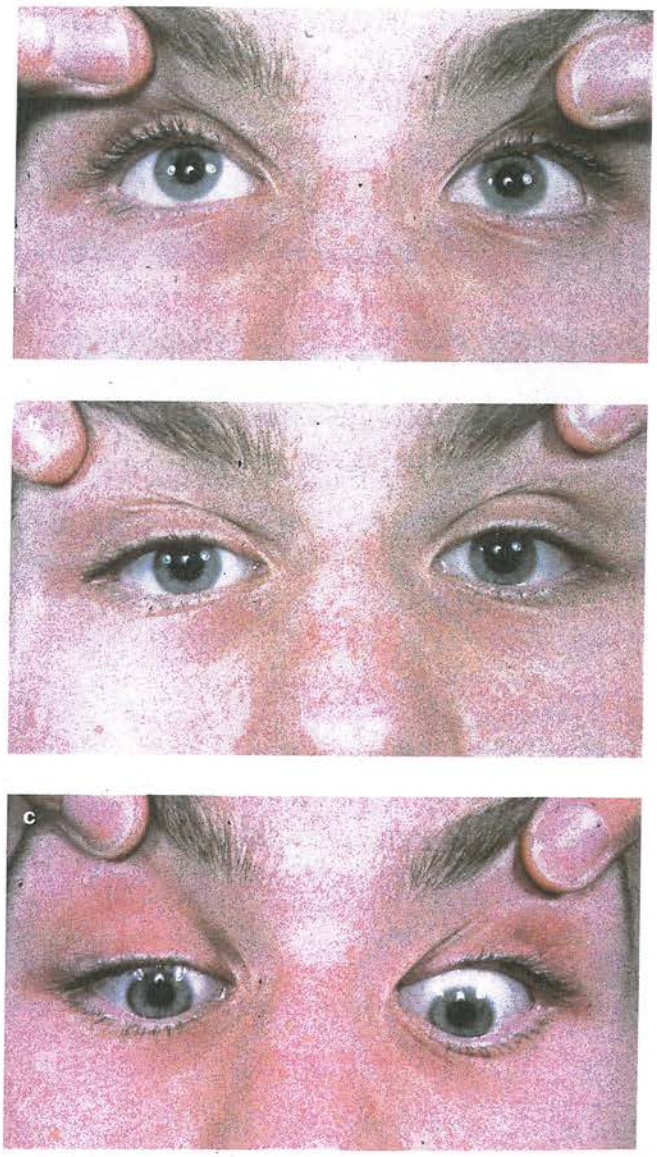
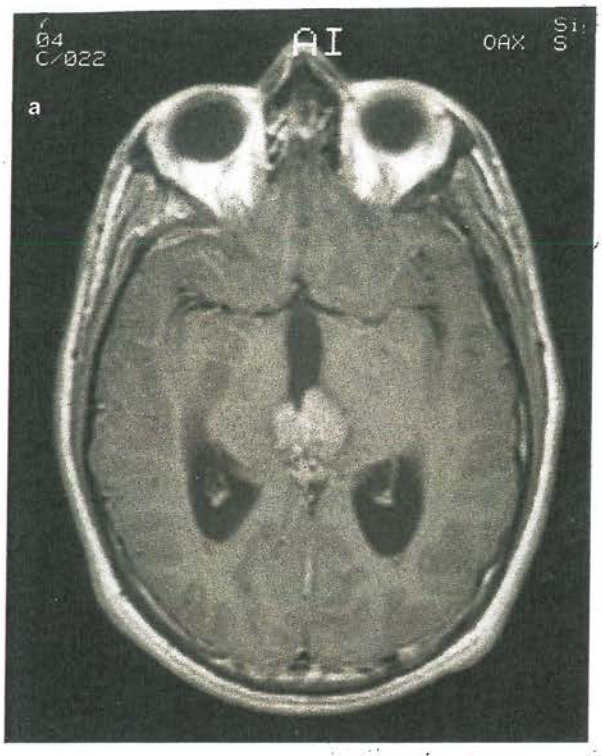



**Figure 15.65** Parinaud dorsal midbrain syndrome. (**a**) Defective upgaze; (**b**) straight eyes in the primary position; (**c**) normal downgaze



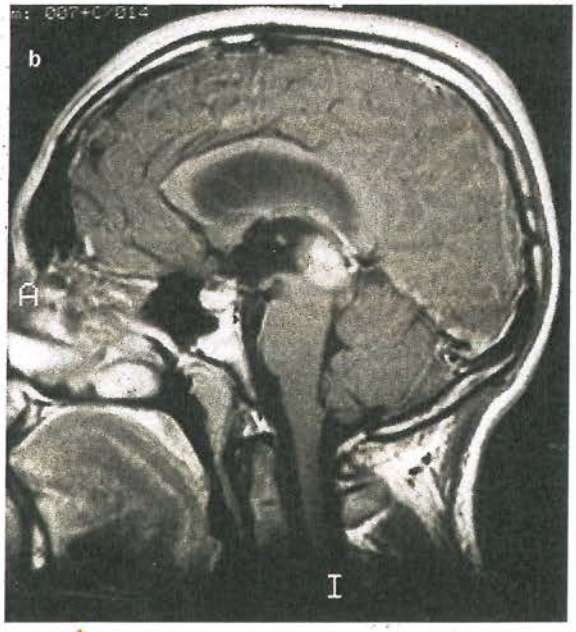




**Figure 15.66** Pineal mass seen on T1-weighted MRI scan. (**a**) Axial view; (**b**) sagittal view – note dilated ventricles



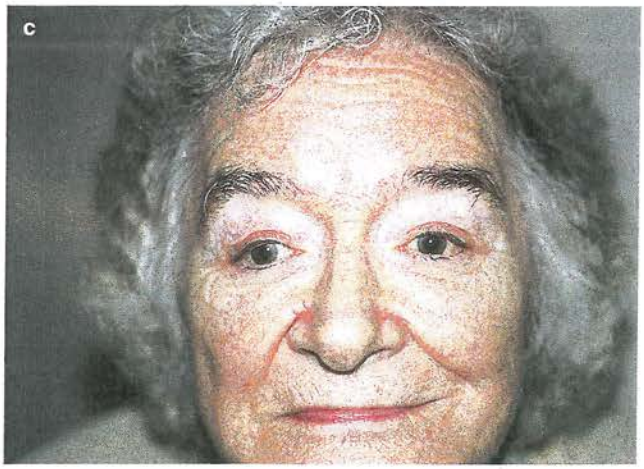



**Figure 15.67** Progressive supranuclear palsy. (**a**) Defective upgaze; (*b*) straight eyes in the primary position; (**c**) defective downgaze

# THIRD NERVE DISEASE

## Applied anatomy

1. **The nuclear complex** of the third (oculomotor) nerve is situated in the midbrain at the level of the superior colliculus, ventral to the sylvian aqueduct (Figure 15.68). It is composed of the following paired and unpaired subnuclei.

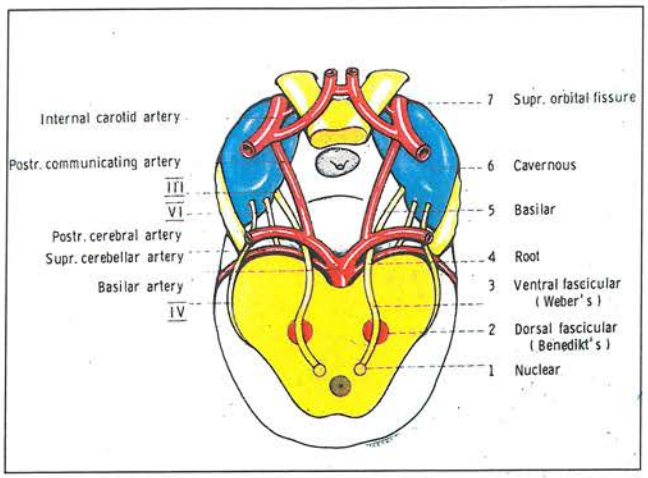



**Figure 15.68** Anatomy of the third nerve from the nucleus to the cavernous sinus

   (a) ***Levator subnucleus*** is an unpaired caudal midline structure which innervates both levator muscles. Lesions confined to this area will therefore give rise to bilateral ptosis.
   (b) ***Superior rectus subnuclei*** are paired and innervate their respective contralateral superior rectus muscles. A unilateral third nerve palsy with sparing of the contralateral superior rectus cannot be the result of an isolated nuclear lesion.
   (c) ***Medial rectus, inferior rectus*** and ***inferior oblique subnuclei*** are paired and innervate their corresponding ipsilateral muscles. Lesions involving purely the third nerve nuclear complex are relatively uncommon. The most frequent causes are vascular disease, primary tumours and metastases. Lesions involving the paired medial rectus subnuclei cause a wall-eyed bilateral internuclear ophthalmoplegia (WEBINO), characterized by exotropia, defective convergence and adduction. Lesions involving the entire nucleus cause an ipsilateral third nerve palsy with ipsilateral sparing and contralateral weakness of elevation.
2. **The fasciculus** consists of efferent fibres which pass from the third nerve nucleus through the red nucleus and the medial aspect of the cerebral peduncle. They then emerge from the midbrain and pass into the interpeduncular space. The causes of nuclear and fascicular lesions are similar:
   (a) ***Benedikt syndrome*** involves the fasciculus as it passes through the red nucleus. It is characterized by an ipsilateral third nerve palsy and a contralateral extrapyramidal signs.
   (b) ***Weber syndrome*** involves the fasciculus as it passes through the cerebral peduncle. It is characterized by an ipsilateral third nerve palsy and a contralateral extrapyramidal signs.
3. **The basilar part** starts as a series of 'rootlets' which leave the midbrain before coalescing to form the main trunk. The nerve then passes between the posterior cerebral artery and the superior cerebellar artery, running lateral to and parallel with the posterior communicating artery (Figure 15.69). As the nerve traverses the base of the skull along its subarachnoid course unaccompanied by any other cranial nerve, isolated third nerve palsies are frequently basilar. The following two are important causes:

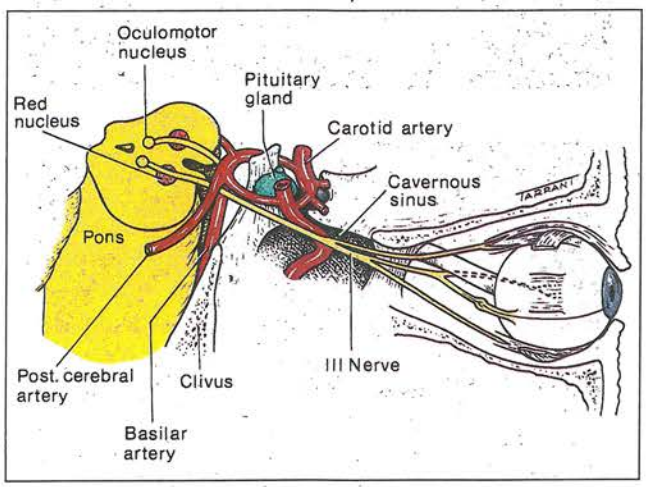



**Figure 15.69** Anatomy of the third nerve

   (a) ***Aneurysm*** at the junction of the posterior communicating artery and the internal carotid artery (Figure 15.70) typically presents with an acute, painful third nerve palsy with involvement of the pupil.
   (b) ***Head trauma***, resulting in extradural or subdural haematoma (Figure 15.71), may cause a tentorial pressure cone with downward herniation of the temporal lobe. This compresses the third nerve as it passes over the tentorial edge (Figure 15.72), initially causes irritative miosis followed by mydriasis and a total third nerve palsy.
4. **The intracavernous part** enters the cavernous sinus by piercing the dura just lateral to the posterior clinoid process. Within the cavernous sinus, the third

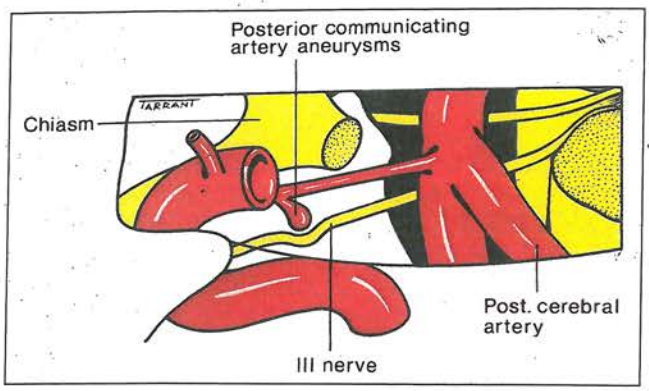



**Figure 15.70** Compression of the third nerve by a posterior communicating aneurysm

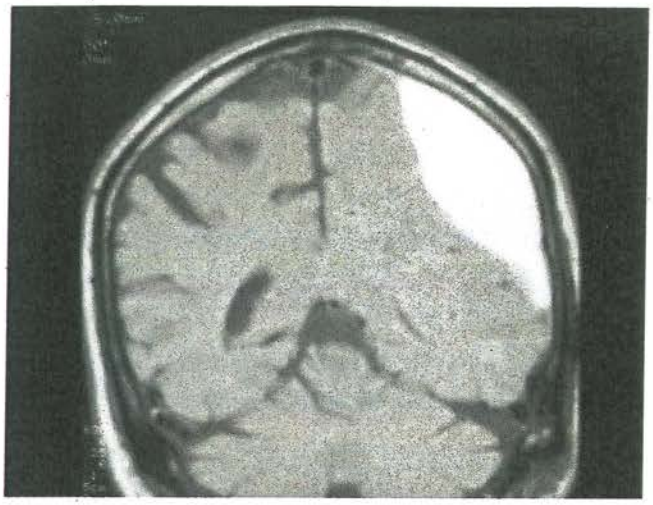


**Figure 15.71** Coronal T1-weighted MRI scan showing a subdural haematoma

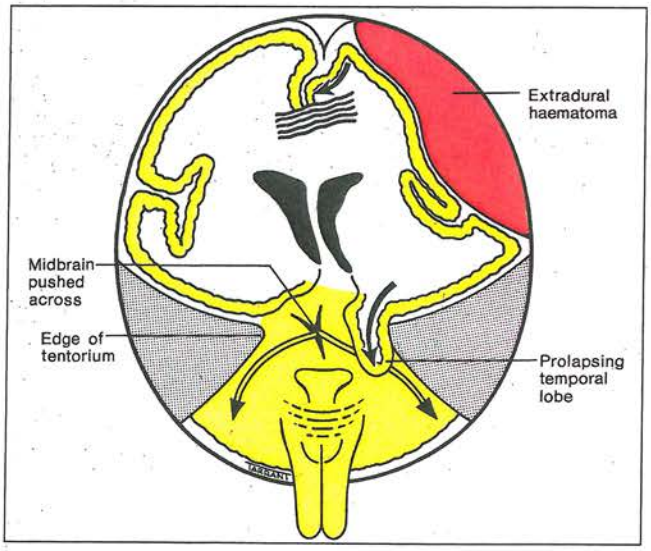



**Figure 15.72** Mechanism of third nerve palsy by an extradural or subdural haematoma

nerve runs in the lateral wall and occupies a superior position above the fourth nerve (Figure 15.73). In the anterior part of the cavernous sinus, the nerve divides into superior and inferior branches which enter the orbit through the superior orbital fissure within the annulus of Zinn. The following are important causes of intracavernous third nerve palsies:

(a) ***Diabetes***, which may cause a vascular palsy.

(b) ***Pituitary apoplexy***, which may cause a third nerve palsy as a result of haemorrhagic infarction of a pituitary adenoma (e.g. after childbirth), with lateral extension into the cavernous sinus.

(c) ***Intracavernous lesions*** such as aneurysms, meningiomas, carotid–cavernous fistulae and granulomatous inflammation (Tolosa–Hunt syndrome) may all cause third nerve palsies. Because of its close proximity to other cranial nerves, intracavernous third nerve palsies are usually associated with involvement of the fourth and sixth nerves and the first division of the trigeminal nerve.

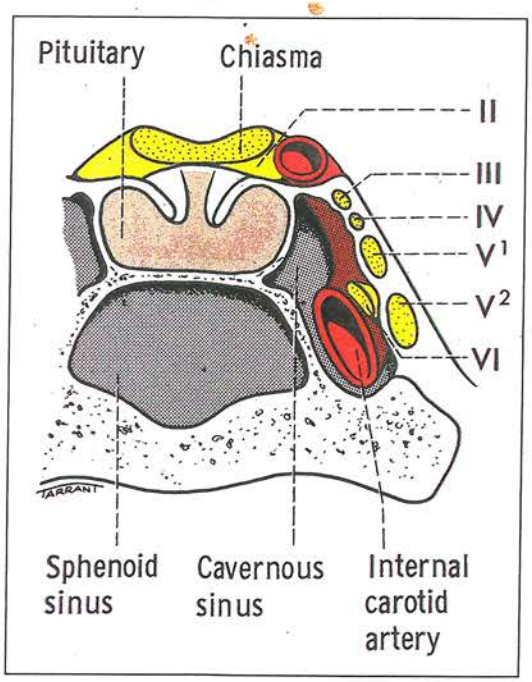



**Figure 15.73** Location of the cranial nerves in the cavernous sinus viewed from behind

5. **The intraorbital part:**

(a) ***Superior division*** innervates the levator and superior rectus muscles.

(b) ***Inferior division*** innervates the medial rectus, the inferior rectus and the inferior oblique muscles. The branch to the inferior oblique also contains the parasympathetic fibres from the Edinger–Westphal subnucleus, which innervate the sphincter pupillae and the ciliary muscle. Lesions of the inferior division are characterized

by limited adduction and depression, and a dilated pupil. The main causes of both superior and inferior division palsies are trauma and vascular disease.

6. **The pupillomotor** parasympathetic fibres between the brain stem and the cavernous sinus are located superficially in the superomedial part of the third nerve. They derive their blood supply from the pial blood vessels, whereas the main trunk of the third nerve is supplied by the vasa nervorum (Figure 15.74). The presence or absence of pupillary involvement is of great importance because it frequently differentiates a so-called 'surgical' from a 'medical' lesion.
   (a) ***Surgical lesions*** such as aneurysms, trauma and uncal herniation characteristically involve the pupil by compressing the pial blood vessels and the superficially located pupillary fibres.
   (b) ***Medical lesions*** caused by hypertension and diabetes usually spare the pupil. This is because the microangiopathy associated with medical lesions involves the vasa nervorum, causing infarction of the main trunk of the nerve, sparing the superficial pupillary fibres.

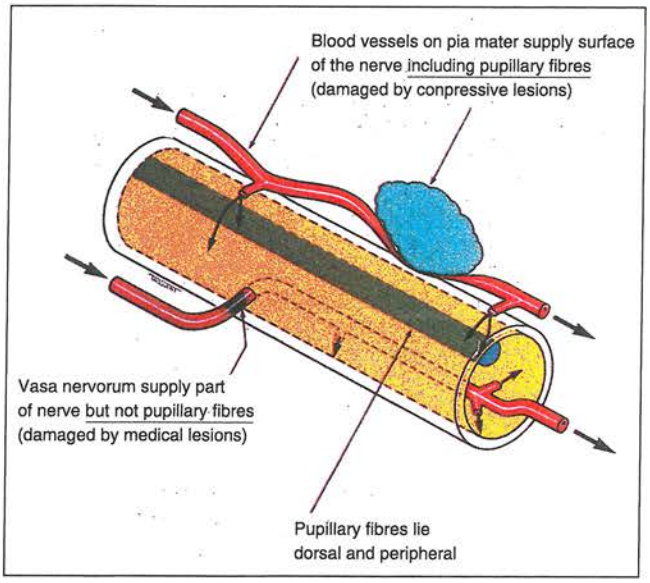



**Figure 15.74** Anatomy of the location of the pupillomotor fibres within the trunk of the third nerve

# Clinical aspects

## CLINICAL FEATURES

A patient with a right third nerve palsy is shown in Figure 15.75.

1. Weakness of the levator causing ptosis (Figure 15.75**a**).
2. Unopposed action of lateral rectus causing the eye to be abducted in the primary position (Figure 15.75**a**).

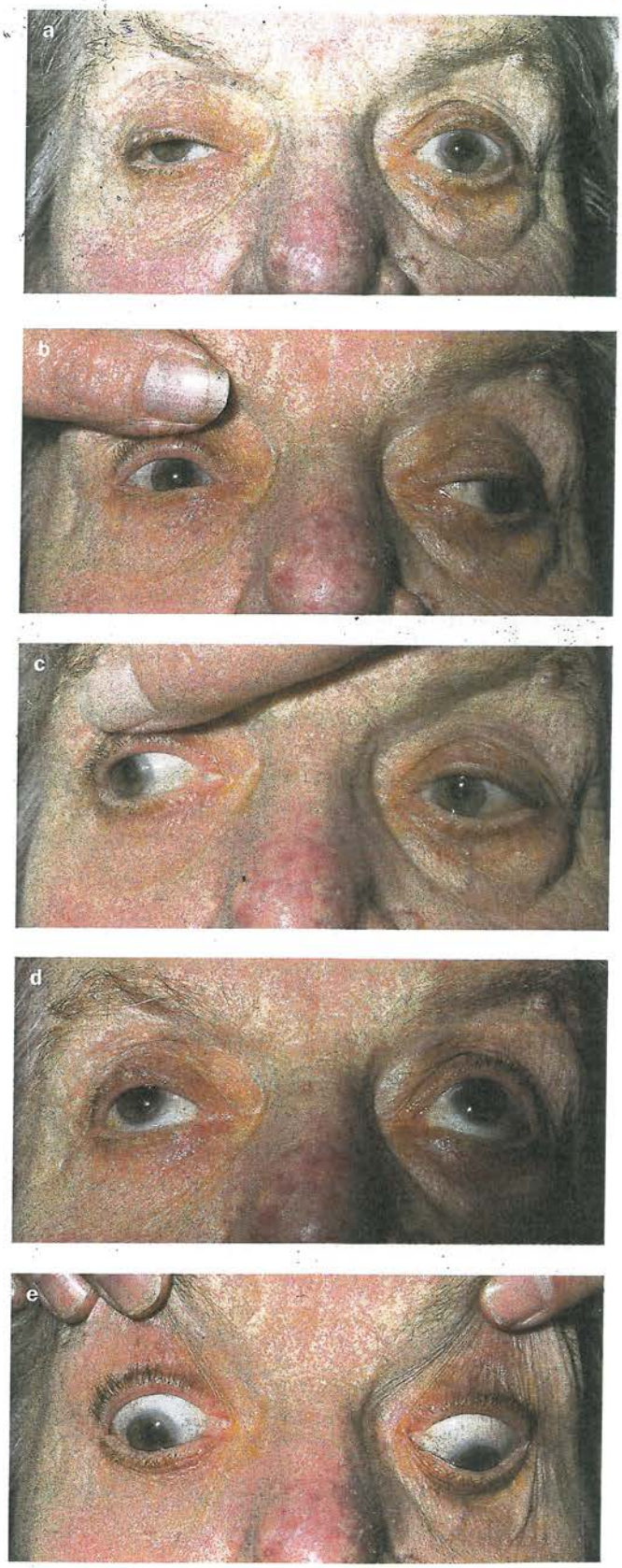



**Figure 15.75** Right third nerve palsy (*see text*)

3. The intact superior oblique muscle causes intorsion of the eye on attempted downgaze.
4. Weakness of medial rectus limiting adduction (Figure 15.75**b**).
5. Normal abduction because the lateral rectus is intact (Figure 15.75c).
6. Weakness of superior rectus and inferior oblique limiting elevation (Figure 15.75**d**).
7. Weakness of inferior rectus limiting depression (Figure 15.75**e**).
8. Parasympathetic palsy causing a dilated pupil associated with defective accommodation (e.g. difficulty in reading small print).

### ABERRANT REGENERATION

Aberrant regeneration (*see* Figure 1.119) may occasionally follow acute traumatic and aneurysmal, but not vascular, third nerve palsies. The bizarre defects in ocular motility, such as elevation of the upper eyelid on attempted adduction or depression, are caused by misdirection of sprouting axons reinnervating the wrong extraocular muscle. The pupil may also be involved in some cases.

### CAUSES OF ISOLATED THIRD NERVE PALSY

In order of frequency the following are the causes of an isolated third nerve palsy:

1. **Idiopathic**: about 25% have no known cause.
2. **Vascular disease**, such as hypertension and diabetes, is the most common cause of a pupil-sparing third nerve palsy. All patients should therefore have blood pressure measurement, urinalysis and plasma glucose estimation. In most cases recovery occurs within 3 months. Diabetic third nerve palsies are often associated with periorbital pain and are occasionally the presenting feature of diabetes. The presence of pain is not helpful in differentiating between an aneurysmal and a diabetic third nerve palsy because both are frequently accompanied by pain.
3. **Trauma** is also a common cause. However, the development of a third nerve palsy following relatively trivial head trauma, not associated with loss of consciousness, should alert the clinician to the possibility of an associated basal intracranial tumour which has caused the nerve trunk to be stretched and tethered.
4. **Aneurysm** at the junction of the posterior communicating artery with the internal carotid is a very important cause of an isolated painful third nerve palsy with involvement of the pupil. Medium-sized aneurysms (4 mm or larger) can be detected by magnetic resonance angiography (MRA), which uses the same general imaging technique as MRI. Although MRA is non-invasive, a significant proportion of smaller aneurysms are missed by this modality. Conventional angiography (Figure 15.76), despite its potential hazards, remains the method of choice for accurate diagnosis of intracerebral aneurysms and planning of operative treatment.
5. **Miscellaneous** uncommon causes include tumours, vasculitis associated with collagen vascular disorders, and syphilis.

As with all ocular motor nerve palsies, surgical treatment should be contemplated only after all spontanous improvement has ceased. This is usually not earlier than 6 months from the date of onset.

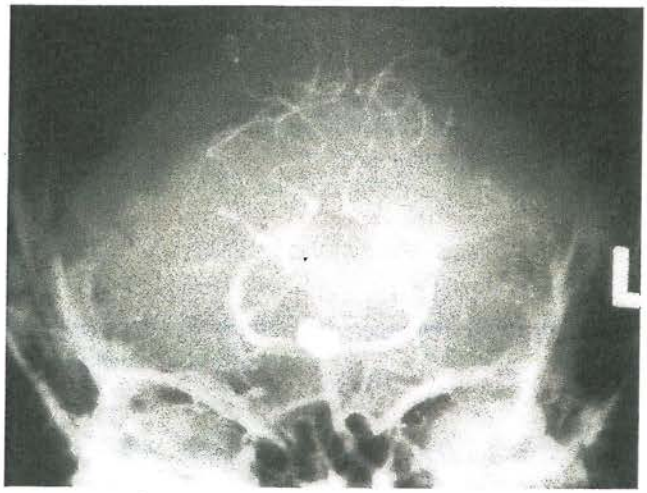



**Figure 15.76** Conventional angiogram showing an aneurysm involving the circle of Willis

# FOURTH NERVE DISEASE

## Applied anatomy

1. **Important features**
   The fourth (trochlear) nerve has the following important features:
   (a) It is the only cranial nerve to emerge from the dorsal aspect of the brain.
   (b) It is a crossed cranial nerve; this means that the fourth nerve nucleus innervates the contralateral superior oblique muscle.
   (c) It is a very long and slender nerve.
2. **The nucleus** of the fourth nerve is located at the level of the inferior colliculus ventral to the sylvian aqueduct (Figure 15.77). It is caudal to, and continuous with, the third nerve nuclear complex.
3. **The fasciculus** consists of axons which curve around the aqueduct and decussate completely in the anterior medullary velum.
4. **The trunk** leaves the brain stem on the dorsal surface, just caudal to the inferior colliculus. It then curves

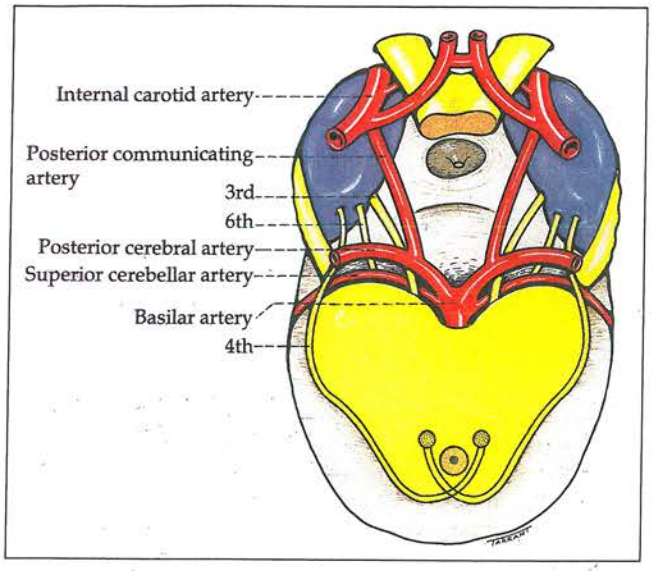



**Figure 15.77** Anatomy of the fourth nerve from the nucleus to the cavernous sinus

forwards around the brain stem, runs beneath the free edge of the tentorium, and (like the third nerve) passes between the posterior cerebral artery and the superior cerebellar artery. It then pierces the dura and enters the cavernous sinus.

5. **The intracavernous part** runs laterally and inferiorly to the third nerve and above the first division of the fifth. In the anterior part of the cavernous sinus it rises and passes through the superior orbital fissure above the annulus of Zinn.
6. **The intraorbital part** innervates the superior oblique muscle.

# Clinical aspects

## CLINICAL FEATURES

The features of nuclear, fascicular and a peripheral fourth nerve palsies are clinically identical. Patients with a right fourth nerve palsy are illustrated.

1. Right superior oblique weakness results in right hyperdeviation (the involved eye is higher) in the primary position when the uninvolved left eye is fixating (Figure 15.78a).
2. A positive Bielschowsky test in which the hyperdeviation increases on ipsilateral head tilt (Figure 15.78b), and decreases on contralateral head tilt (Figure 15.78c).
3. Right underaction on depression in adduction (Figure 15.79a) due to superior oblique weakness and right overaction on left gaze (Figure 15.79b) due to right inferior oblique overaction.
4. Excyclotorsion.
5. Diplopia which is vertical and worse on looking down.
6. To avoid diplopia, the patient may adopt an abnormal head posture with contralateral head tilt, contralateral turn and chin depression.

## CAUSES OF ISOLATED FOURTH NERVE PALSY

1. **Congenital** lesions are frequent, although symptoms may not develop until adult life. Examination of old photographs for the presence of an abnormal head posture may be helpful.

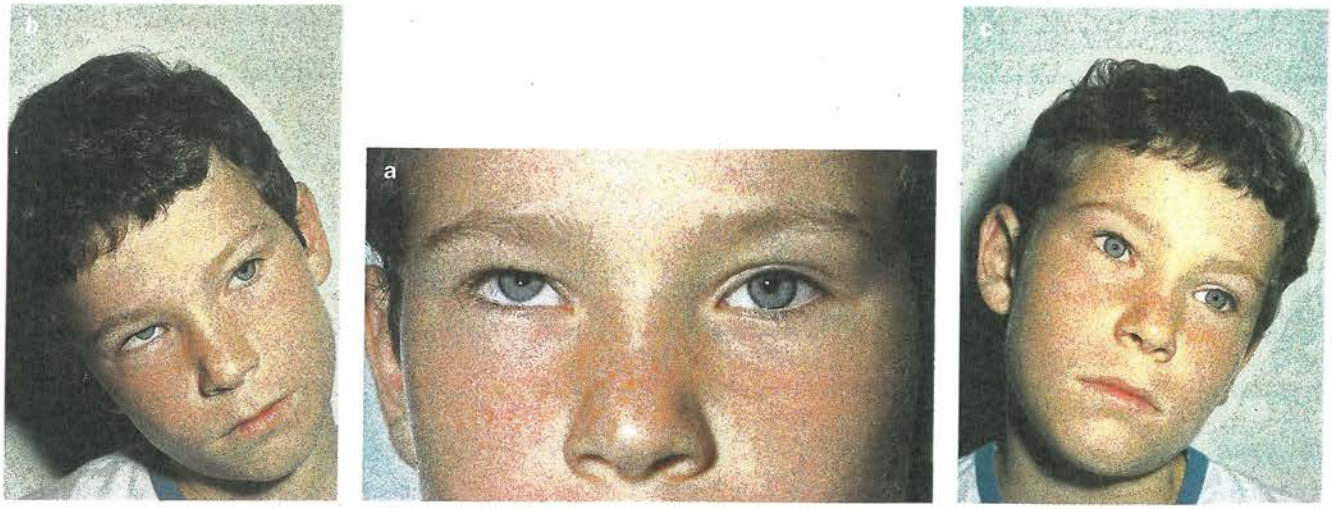



**Figure 15.78** Right fourth nerve palsy. (**a**) Right hypertropia in the primary position; (**b**) increase in right hypertropia on head tilt to the right (positive Bielschowsky test); (**c**) eyes are straight on head tilt to the left

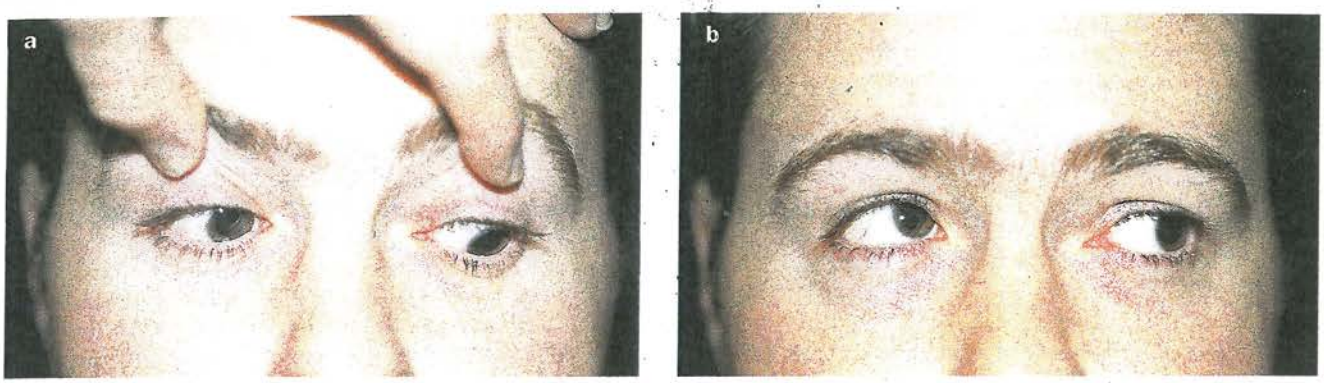



**Figure 15.79** Right fourth nerve palsy. (*a*) Right underaction; (*b*) right overaction

2. **Trauma** frequently causes bilateral fourth nerve palsies. The very long and slender nerves are vulnerable as they decussate in the anterior medullary velum through impact with the tentorial edge.
3. **Vascular** lesions are common but aneurysms and tumours are rare.

# SIXTH NERVE DISEASE

## Applied anatomy

1. **The nucleus** of the sixth (abducens) nerve lies in the midpoint of the pons, ventral to the floor of the fourth ventricle, where it is closely related to the fasciculus of the seventh nerve (Figure 15.80). An isolated sixth nerve palsy is therefore never nuclear in origin. A lesion in and around the sixth nerve nucleus causes the following signs.
   (a) Failure of horizontal gaze towards the side of the lesion resulting from involvement of the horizontal gaze centre in the pontine paramedian reticular formation (PPRF).
   (b) Ipsilateral weakness of abduction as a result of involvement of the nucleus.
   (c) Ipsilateral lower motor neurone facial nerve palsy caused by concomitant involvement of the facial fasciculus which is also common.
2. **The fasciculus** consists of emerging fibres which pass ventrally to leave the brain stem at the pontomedullary junction, just lateral to the pyramidal prominence.
   (a) ***Foville syndrome*** involves the fasciculus as it passes through the PPRF and is characterized by the following ipsilateral signs.
      - Sixth nerve palsy combined with a gaze palsy.
      - Facial weakness caused by damage to the facial nucleus or fasciculus.
      - Facial analgesia from involvement of the sensory portion of the fifth nerve.
      - Central Horner syndrome.
      - Deafness.
   (b) ***Millard–Gubler*** syndrome involves the fasciculus as it passes through the pyramidal tract and is characterized by the following.
      - Ipsilateral sixth nerve palsy.
      - Contralateral hemiplegia.
      - Variable number of signs of a dorsal pontine lesion.
3. **The basilar part** leaves the brain stem at the pontomedullary junction and enters the prepontine basilar cistern. It then passes upwards close to the base of the pons and is crossed by the anterior inferior cerebellar artery (Figure 15.81). It pierces the dura below the posterior clinoids and angles forwards over the tip of the petrous bone, passing through or around the inferior petrosal sinus, through Dorello canal (under the petroclinoid ligament), to enter the cavernous sinus. The following are important causes of damage to the basilar portion of the nerve:
   (a) ***Acoustic neuroma***, which may damage the sixth nerve as it leaves the midbrain at the ponto-

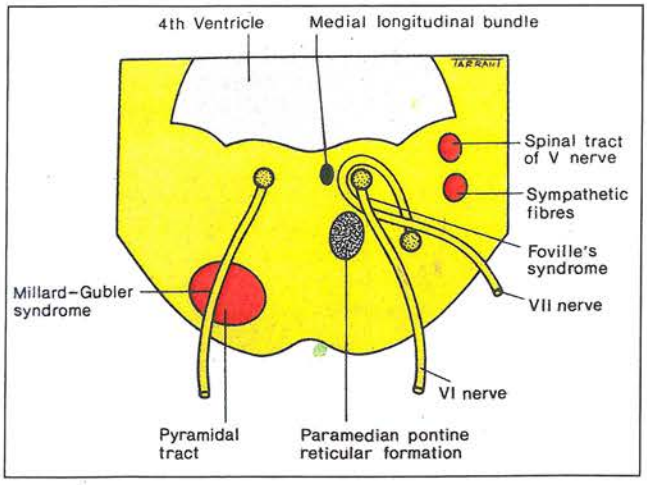



**Figure 15.80** Cross-section of the pons at the level of the sixth nerve nucleus

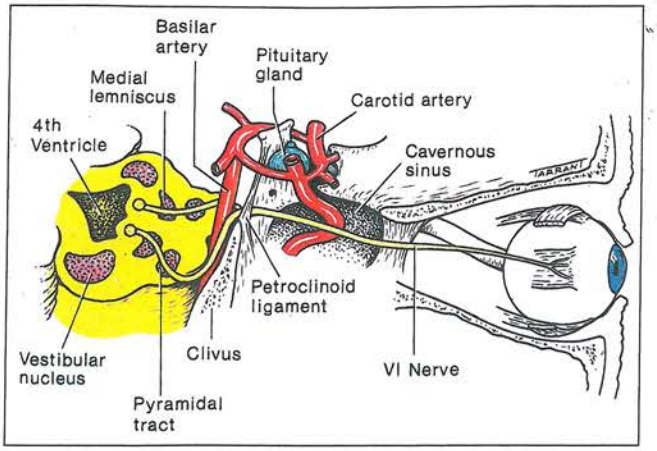



**Figure 15.81** Anatomy of the sixth nerve

medullary junction (Figures 15.82 and 15.83). It should be emphasized that the first symptom of an acoustic neuroma is hearing loss and the first sign diminished corneal sensitivity. It is therefore very important to test hearing and corneal sensation in all patients with sixth nerve palsy.

(b) ***Nasopharyngeal tumours*** may invade the skull and its foramina and damage the nerve during its basilar course.

(c) ***Raised intracranial pressure*** associated with posterior fossa tumours or benign intracranial hypertension (pseudotumour cerebri) may cause a downward displacement of the brain stem. This may stretch the sixth nerve over the petrous tip between its point of emergence from the brain stem and its dural attachment on the clivus (Figure 15.84). In this situation, sixth nerve palsy, which may be bilateral, is a false localizing sign.

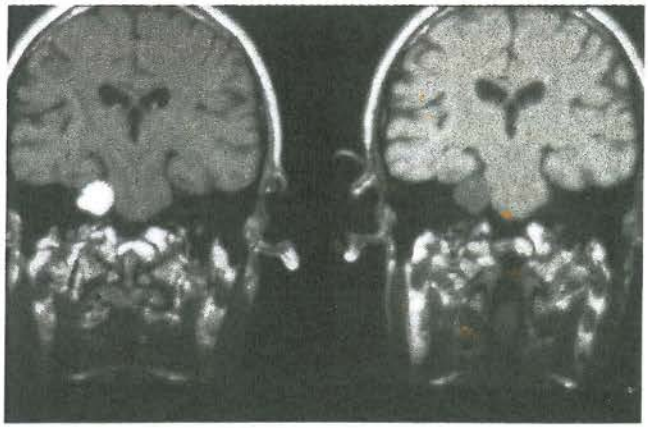


**Figure 15.82** Coronal T1-weighted MRI scan showing a right acoustic neuroma. Before enhancement (**right**) and after enhancement with gadolinium (**left**)

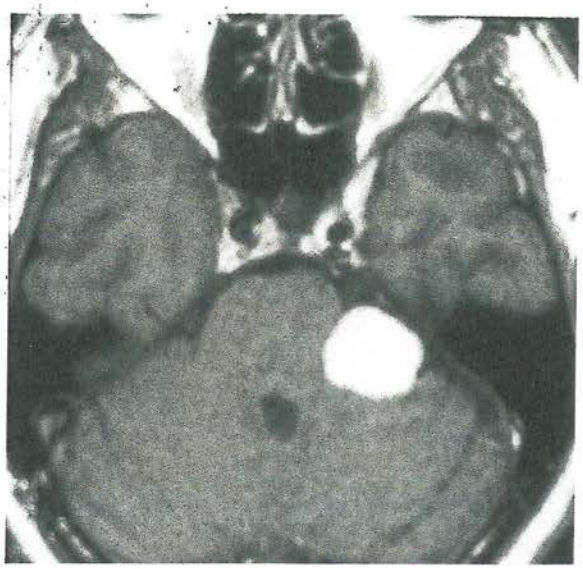


**Figure 15.83** Axial T1-weighted MRI scan with enhancement showing an acoustic neuroma

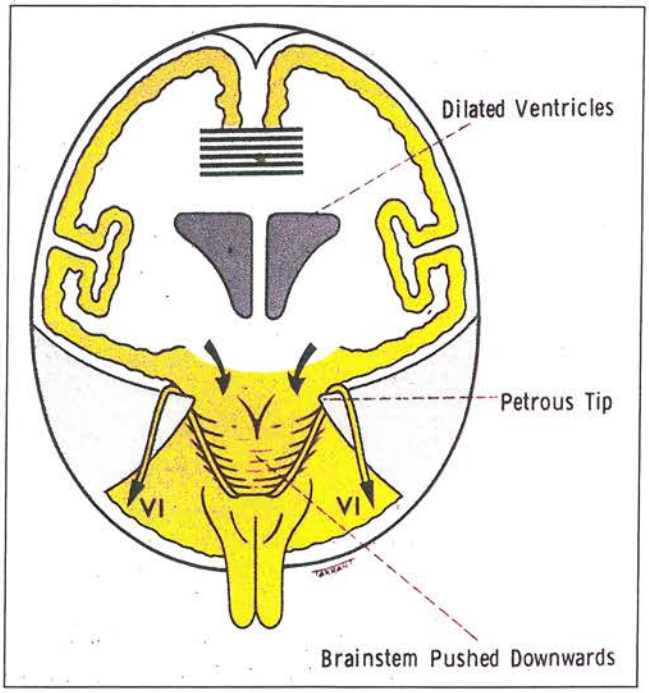



**Figure 15.84** Mechanism of bilateral sixth nerve palsies resulting from raised intracranial pressure

(d) ***Basal skull fracture***, which may cause both unilateral and bilateral palsies.

4. **The intracavernous part** runs forwards below the third and fourth nerves, as well as the first division of the fifth (*see* Figure 15.73). Although the other nerves are protected within the wall of the sinus, the sixth is most medially situated and runs through

the middle of the sinus in close relation to the internal carotid artery. It is therefore more prone to damage than the other nerves. Occasionally, an intracavernous sixth nerve palsy is accompanied by a postganglionic Horner syndrome (Parkinson sign), because in its intracavernous course the sixth nerve is joined by the sympathetic branches from the paracarotid plexus. The causes of intracavernous sixth nerve and third nerve lesions are similar.

5. **The intraorbital part** enters the orbit through the superior orbital fissure within the annulus of Zinn to innervate the lateral rectus muscle.

## Clinical aspects

### CLINICAL FEATURES

The clinical features depend on whether the palsy is of recent onset or longstanding, as follows.

1. **Recent onset** right sixth nerve palsy (Figure 15.85).
   (a) Right esotropia in the primary position due to unopposed action of the right medial rectus (Figure 15.85**a**).
   (b) Marked limitation of right abduction due to weakness of the right lateral rectus (Figure 15.85**b**).
2. **Longstanding** left sixth nerve palsy (Figure 15.86).
   (a) Straight eyes in the primary position due to partial recovery (Figure 15.86**a**).
   (b) Limitation of left abduction due to residual weakness of the lateral rectus (Figure 15.86**b**).
   (c) Horizontal diplopia is worse in the field of action of the paralysed muscle and least away from its field of action.

Compensatory face turn into the field of action of the paralysed muscle to minimize diplopia, so that the eyes are turned away from the field of action of the paralysed muscle. For example, a patient with a left sixth nerve palsy will turn the face to the left.

### CAUSES

Most of the causes of isolated sixth nerve palsies have already been mentioned, but, in contrast to third nerve palsy, aneurysms rarely cause sixth nerve palsies. Vascular causes (especially diabetes and hypertension) are, however, common.

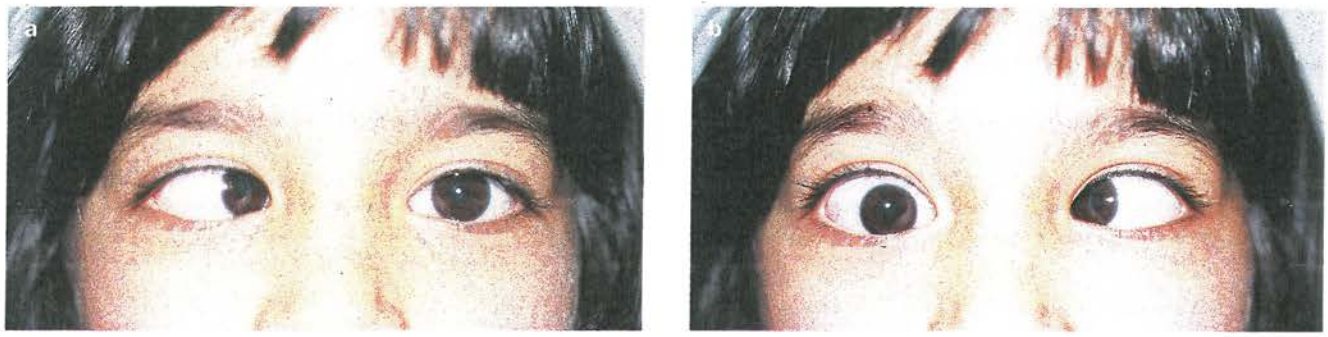



**Figure 15.85** Recent-onset right sixth nerve palsy. (**a**) In primary position with left eye fixating; (**b**) on attempted right gaze

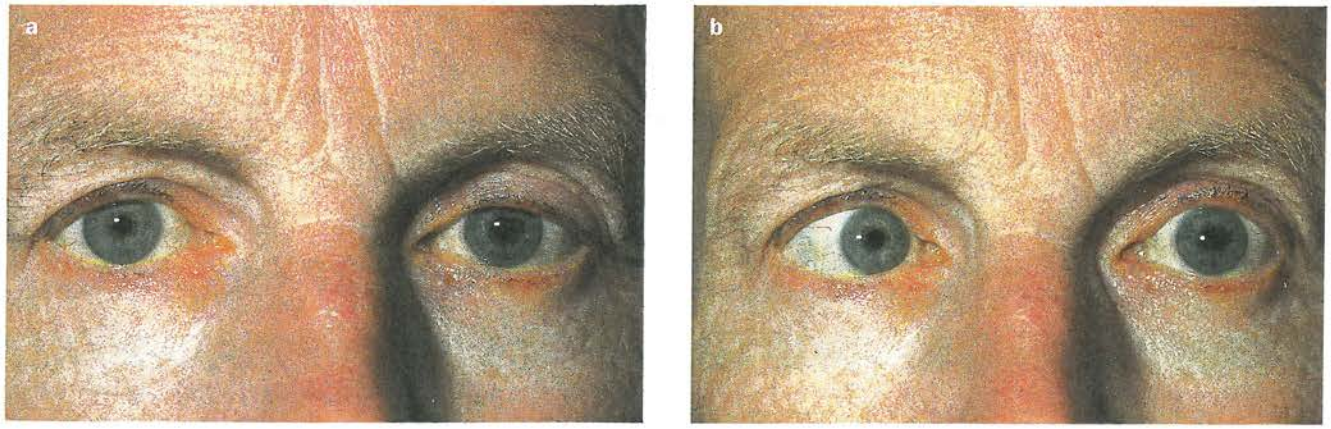



**Figure 15.86** Longstanding left sixth nerve palsy. (**a**) In primary position; (**b**) on attempted left gaze

# DISORDERS OF THE CHIASM

## Classification

Disorders of the chiasm can be divided into the following three main groups.

1. **Tumours** include: pituitary adenoma, craniopharyngioma, meningioma, glioma, chordoma, dysgerminoma, nasopharyngeal tumours and metastases.
2. **Non-neoplastic masses** include: aneurysm, Rathke pouch cyst, fibrous dysplasia, sphenoidal sinus mucocele and arachnoid cyst.
3. **Miscellaneous disorders** include: demyelination, inflammation, trauma, radiation-induced necrosis and vasculitis.

## Applied anatomy

1. **The sella turcica** (Turkish saddle) is a bony cavity in the sphenoid bone in which the pituitary gland lies (Figures 15.87). The roof of the sella is formed by a fold of dura mater which stretches from the anterior to the posterior clinoids (diaphragma sellae). The optic nerves and the chiasm lie above the diaphragma sellae and therefore the presence of a visual field defect in a patient with a pituitary tumour indicates suprasellar extension. Tumours confined to the sella will not cause visual field defects. Posteriorly the chiasm is continuous with the optic tracts and forms the anterior wall of the third ventricle. Figure 15.88 shows a sagittal section of the brain which demonstrates normal anatomical landmarks.
2. **Nerve fibres** passing through the chiasm are arranged as follows:

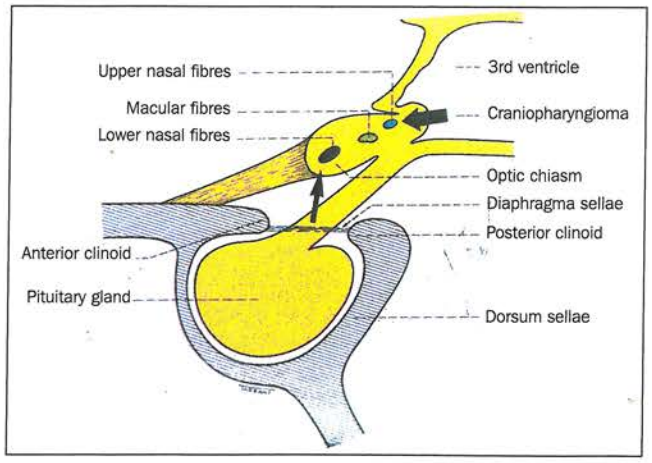



**Figure 15.87** Anatomy of the optic chiasm in relation to the pituitary gland

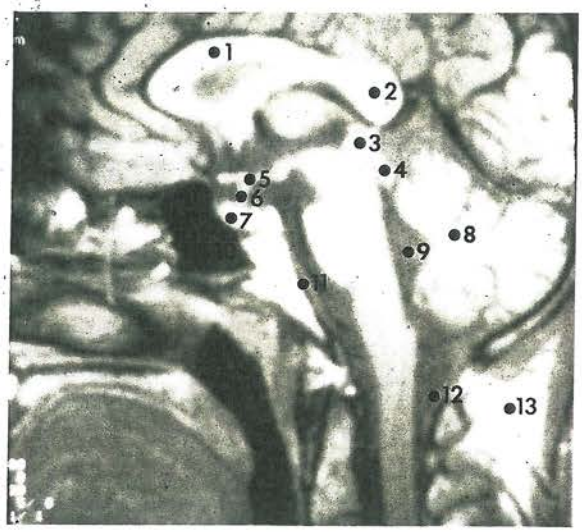



**Figure 15.88** Sagittal MRI scan showing normal anatomy. **1**: body of the corpus callosum; **2**: splenium of the corpus callosum; **3**: superior colliculus; **4**: inferior colliculus; **5**: infundibular recess in the floor of the third ventricle; **6**: infundibulum; **7**: pituitary gland; **8**: cerebellum; **9**: fourth ventricle; **10**: sphenoid sinus; **11**: clivus; **12**: foramen magnum and craniocervical junction; **13**: subcutaneous fat. The pineal gland is not shown clearly; it is situated supero-posterior to the colliculi

   (a) ***Lower nasal fibres*** traverse the chiasm low and anteriorly. They are therefore most vulnerable to damage from expanding pituitary lesions, so the upper temporal quadrants of the visual fields are involved first.
   (b) ***Upper nasal fibres*** traverse the chiasm high and posteriorly and therefore are involved first by lesions coming from above the chiasm (e.g. craniopharyngiomas). If the lower temporal quadrants of the visual field are affected more than the upper, a pituitary adenoma is unlikely.
   (c) ***Macular fibres*** decussate throughout the chiasm.
3. **Anatomical variations** in the location of the chiasm may have important clinical significance (Figure 15.89).
   (a) ***Central chiasm***, which is present in about 80% of normals, lies directly above the sella so that expanding pituitary tumours will involve the chiasm first.
   (b) ***Prefixed chiasm***, which is present in about 10% of normals, is located more anteriorly, over the tuberculum sellae, so that pituitary tumours may involve the optic tracts first.
   (c) ***Postfixed chiasm***, which is present in the remaining 10% of normals, is located more posteriorly, over the dorsum sellae, so that pituitary tumours are apt to damage the optic nerves first.
4. **The cavernous sinuses** lie lateral to the sella (*see* Figure 15.73) so that laterally expanding pituitary tumours affect the cavernous sinus and may damage

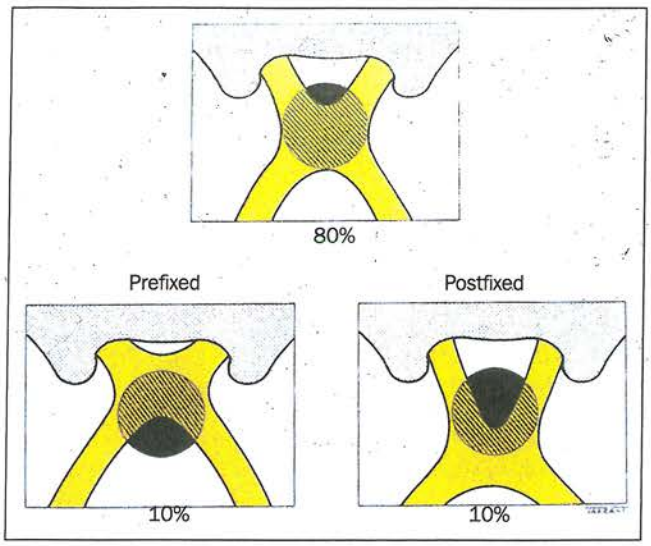



**Figure 15.89** Anatomical variations in position of the normal chiasm

the intracavernous parts of the third, fourth and sixth cranial nerves. Conversely, aneurysms arising from the intracavernous part of the internal carotid artery may erode into the sella and mimic pituitary tumours.

5. **The internal carotid arteries** curve posteriorly and upwards from the cavernous sinus and lie immediately below the optic nerves. They then ascend vertically alongside the lateral aspect of the chiasm. The precommunicating portion of the superior cerebral artery is closely related to the superior surface of the chiasm and optic nerves (Figure 15.90). An aneurysm in this region can therefore compress the optic nerve or the chiasm.

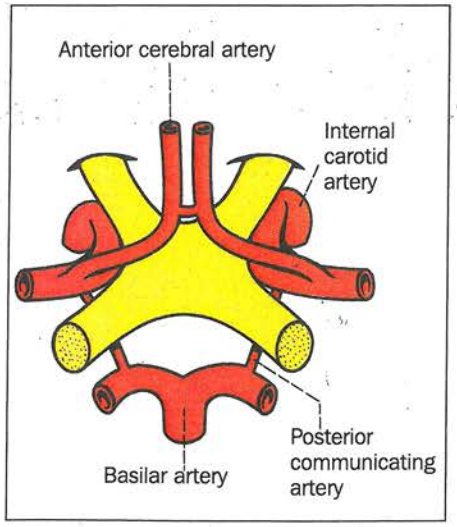



**Figure 15.90** Relationship between the internal carotid arteries and the chiasm

# Applied physiology

The lobules of the anterior part of the pituitary gland are composed of six cell types. Five of these secrete hormones and the sixth (follicular cell) has no secretory function. The main hormones secreted by the anterior pituitary gland are: growth hormone, prolactin, follicle stimulating hormone (FSH), adrenocorticotrophic hormone (ACTH) and thyroid stimulating hormone (TSH).

## HYPERPITUITARISM

Although pituitary adenomas are classified as basophil, acidophil and chromophobe, tumours of mixed-cell types are common and any of the six cell types may proliferate to produce an adenoma (Figure 15.91).

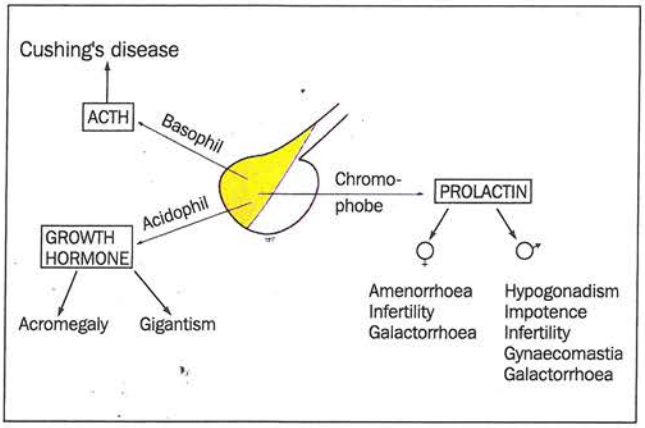



**Figure 15.91** Hormones secreted by the anterior pituitary tumours

1. **Basophil tumours** secrete ACTH and cause Cushing disease which is characterized by:
   (a) Moon face, hirsutism and pigmentation (Figure 15.92).
   (b) Obesity and skin striae (Figure 15.93).
   (c) Other features include plethora, bruising, muscle weakness, ankle oedema, hypertension, diabetes and osteoporosis.
2. **Acidophil tumours** secrete growth hormone, which causes gigantism in children and acromegaly in adults. The main clinical features of acromegaly are:
   (a) Enlargement of the hands and feet which may be associated with osteoarthritis (Figure 15.94).
   (b) Enlargement of the lower jaw, which gives rise to malocclusion (Figure 15.95).
   (c) Facial coarseness (Figure 15.96).
   (d) Enlargement of the tongue (Figure 15.97) and vocal cords.
   (e) Other features include carpal tunnel syndrome, organomegaly, cardiomyopathy, neuropathy, hypertension, diabetes and gonadal dysfunction.

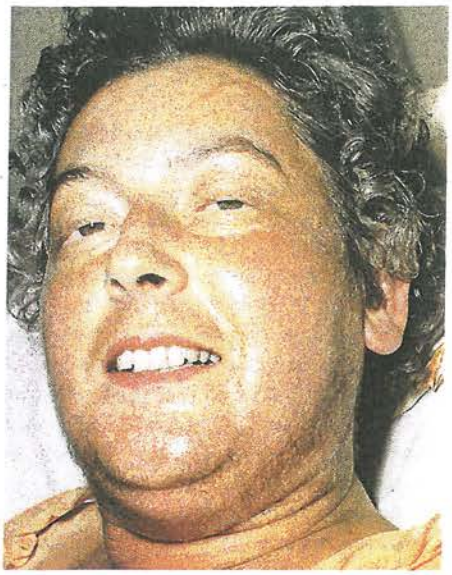


**Figure 15.92** Patient with Cushing disease showing moon face, hirsutism and pigmentation

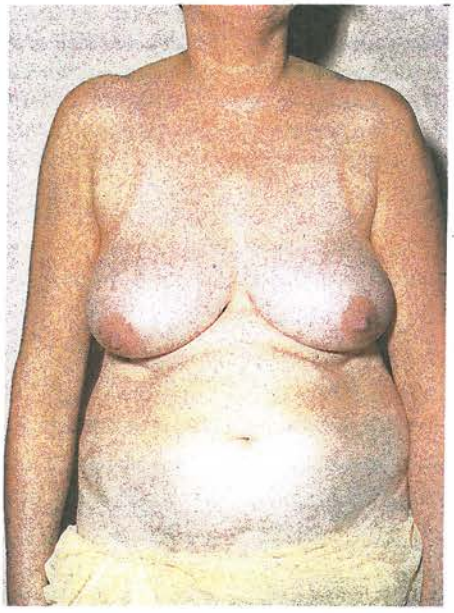


**Figure 15.93** Patient with Cushing disease showing obesity and striae of abdominal skin

3. **Chromophobe adenomas** may secrete prolactin and are referred to as prolactinomas. Excessive levels of prolactin in women lead to the infertility–amenorrhoea–galactorrhoea syndrome, and in men cause hypogonadism, impotence, sterility, decreased libido and occasionally gynaecomastia and even galactorrhoea. Some chromophobe adenomas appear to be non-secreting.
4. **FSH- or TSH-secreting adenomas** are exceedingly rare.

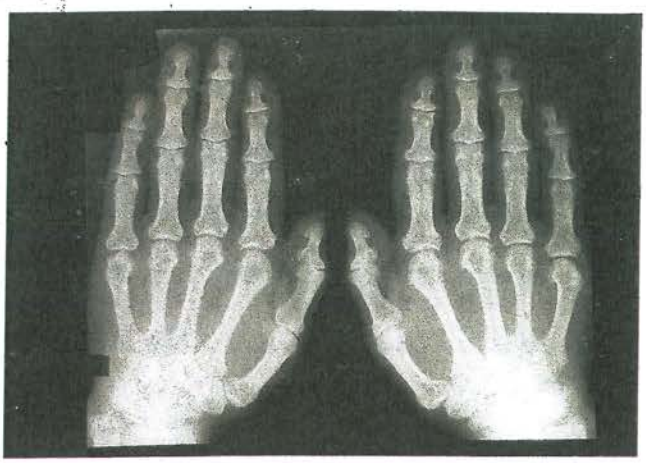


**Figure 15.94** Plain radiograph of the hands of an acromegalic showing lips and hooks of terminal phalanges, enlarged bones with prominent muscle attachments and early osteoarthritis

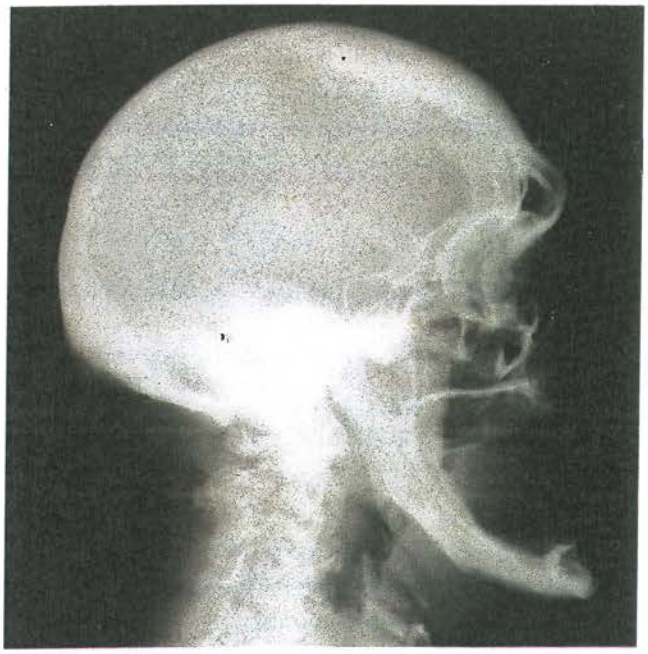


**Figure 15.95** Plain skull radiograph of an acromegalic showing an enlarged mandible with widening of the mandibular angle (prognathism), enlarged frontal sinus, thickening of the skull vault and an expanded pituitary fossa

## HYPOPITUITARISM

The anterior pituitary is itself under the control of the various inhibiting and releasing factors which are synthesized in the hypothalamus and pass to the anterior pituitary through the portal system.

1. **Causes** of hypopituitarism are as follows:
   (a) Direct pressure on the secreting cells in the anterior pituitary by a mass. Secondary deposits are

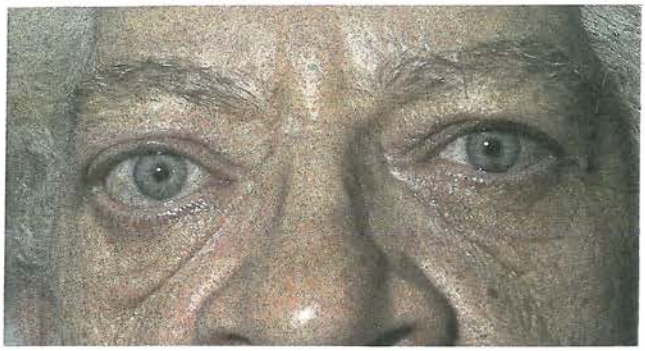


**Figure 15.96** Facial coarseness in acromegaly

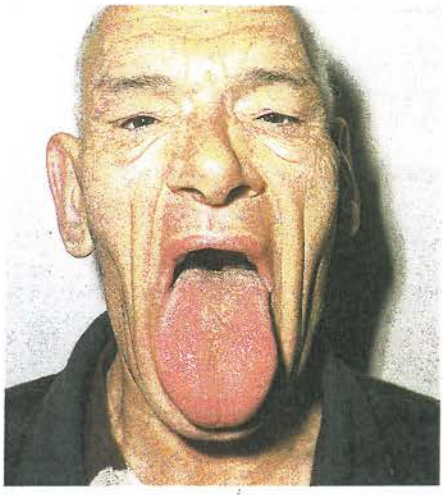


**Figure 15.97** Macroglossia in acromegaly

common in the pituitary but do not normally affect hormonal activity.

(b) Vascular damage to the pituitary (e.g. pituitary apoplexy after childbirth – Sheehan syndrome).

(c) Pituitary surgery and/or radiotherapy.

(d) Interference with the synthesis of inhibiting and releasing factors in the hypothalamus by gliomas or impediment of their transport in the portal system.

2. **Clinical features** of hypopituitarism are dictated by both the pattern of hormone deficiency and the state of growth and development of the patient at the time. Usually gonadotrophin secretion is impaired first, followed by impairment of growth hormone; deficiencies in other hormones occur later.

## Pituitary adenoma

### CLINICAL FEATURES

The chromophobe adenoma is the most common primary intracranial tumour to produce neuro-ophthalmological features. Most are detected by endocrinologists, although non-secreting tumours may first present to ophthalmologists.

1. **Presentation** is typically during early adult life or middle age and only occasionally in the elderly with the following:

(a) ***Headache*** may be the prominent feature as a result of involvement of pain-sensitive fibres in the diaphragma sellae. As the tumour expands upwards and breaks through the diaphragma the headaches may stop. The nature of the headache is non-specific and does not have the usual features associated with raised intracranial pressure. For this reason delays in diagnosis are common in the absence of obvious endocrine disturbances.

(b) ***Visual symptoms*** associated with bitemporal visual field defects usually have a very gradual onset and may not be noticed by the patient until well established. It is therefore essential to examine the visual fields in all patients with non-specific headaches or endocrine disturbance.

2. **Visual field defects** depend on the anatomical relationship between the pituitary and chiasm. If the chiasm is central, both superotemporal fields are initially affected as the tumour grows upwards and splays the anterior chiasmal notch, compressing the crossing inferonasal fibres (Figure 15.98). The defects then progress into the lower temporal fields. As growth of the tumour is often asymmetrical, the degree of visual field loss is usually different on the two sides. Patients may not present until central vision is beginning to be affected from pressure on the fibres serving the macula. The eye with the greater field loss usually also has more marked impairment of visual acuity. It should be emphasized that the absence of a visual field defect does not exclude the presence of a pituitary

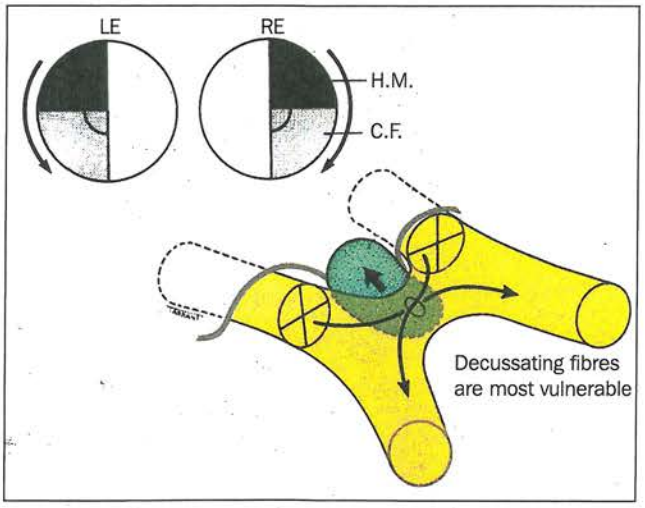



**Figure 15.98** Visual field defects caused by compression of the chiasm from below by a pituitary adenoma

tumour because many remain confined to the pituitary fossa (microadenomas). Acidophil adenomas do not expand beyond the sella as frequently as chromophobe adenomas, and basophil adenomas are usually small and rarely compress the chiasm.

3. **Colour desaturation** across the vertical midline is the earliest sign of a chiasmal field defect. It can be detected very simply by using a small red object, such as a red pin or a red Mydriacyl bottle top. The patient is asked to compare the colour and intensity of the target as it is brought from the nasal to the temporal visual field. Another technique is to present simultaneously identical red targets in precisely symmetrical parts of the temporal and nasal visual fields, and to ask if the colours appear the same. Many patients may miss the temporal number on Ishihara testing.
4. **Optic atrophy** is present in approximately 50% of cases with field defects caused by pituitary lesions. Patients are invariably more aware of difficulties with central vision (e.g. when reading) than with peripheral vision. It is therefore important to perform very careful visual field examinations on both eyes in patients with an unexplained unilateral deterioration of central vision.
5. **Miscellaneous features** include diplopia as a result of lateral expansion into the cavernous sinus and involvement of cranial ocular motor nerves and rarely, see-saw nystagmus of Maddox.

### SPECIAL INVESTIGATIONS

1. **MRI** is very useful in demonstrating the relationship between a mass lesion and the chiasm (Figure 15.99). The coronal plane (Figure 15.99**b**) is optimal for demonstrating sellar contents. Repeated MRI to monitor progress is safe because there is no ionizing radiation risk.
2. **CT** may be useful for demonstrating bony involvement.
3. **Endocrinological evaluation** should be tailored to the individual patient. All patients suspected of having a pituitary adenoma should have assays of (a) serum prolactin, (b) FSH, (c) TSH and (d) growth hormone. An insulin stress test may also be required in selected cases. Patients with large adenomas with visual field defects are at some risk of pituitary apoplexy if the hypoglycaemic response is profound.

### TREATMENT

1. **Surgery** is usually through a trans-sphenoidal approach. Very occasionally patients require both a trans-sphenoidal hypophysectomy and a craniotomy to remove tissue well above the pituitary fossa.
2. **Bromocriptine** may shrink a prolactin-secreting tumour. All patients with significant visual field defects should have an urgent prolactin level assay and, if elevated, treatment with bromocriptine should be started as soon as possible. In some patients visual function improves within hours. In many patients, endocrine function is also improved with cessation of galactorrhoea, improvement of libido and return of menstruation.
3. **Radiotherapy** may be used alone or in combination with the other two modalities in selected cases.

## Craniopharyngioma

Craniopharyngioma is a slow-growing tumour arising from vestigial remnants of Rathke pouch along the pituitary stalk.

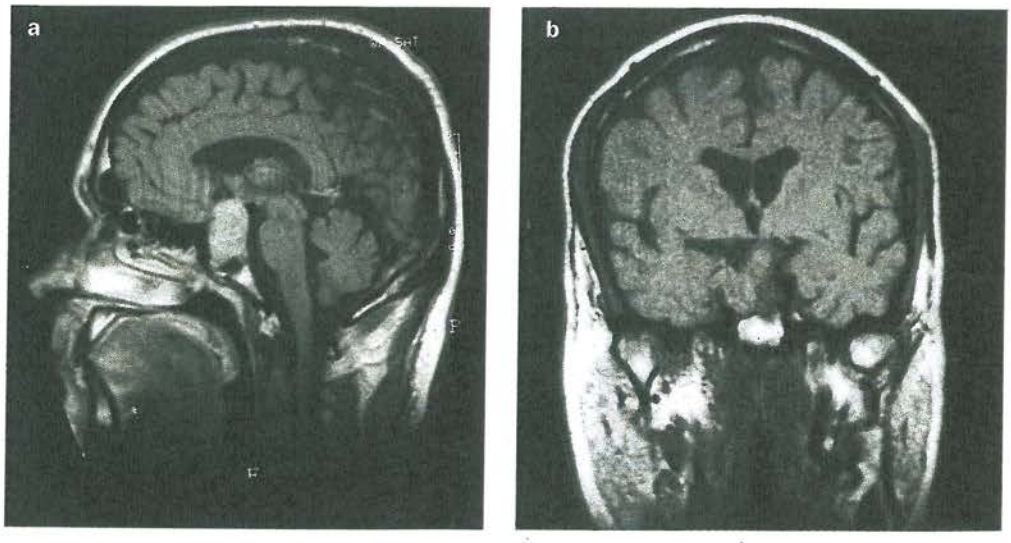



**Figure 15.99** T1-weighted MRI scan showing a pituitary adenoma. (**a**) Sagittal view; (**b**) coronal view

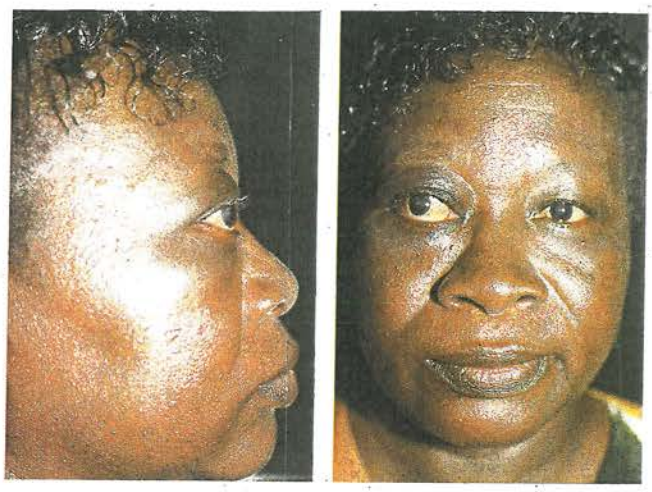


**Figure 15.103** Advanced right sphenoidal ridge meningioma causing proptosis and reactive hyperostosis

classic feature in the latter is a fullness in the temporal fossa as a result of hyperostosis (Figure 15.103).

(c) ***Olfactory groove*** meningioma may cause loss of the sense of smell, as well as optic nerve compression.

2. **Treatment** is surgical but postoperative radiotherapy is frequently used in the event of incomplete excision.

# DISORDERS OF RETROCHIASMAL VISUAL PATHWAYS AND VISUAL CORTEX

## Clinical features of optic tract lesions

1. **Contralateral pyramidal signs**: the optic tracts arise at the posterior aspect of the chiasm, diverge and extend posteriorly around the cerebral peduncles, to terminate in the lateral geniculate bodies. A lesion which damages the optic tract may therefore also involve the ipsilateral cerebral peduncle and give rise to mild contralateral pyramidal signs.
2. **Incongruous homonymous hemianopia**: each optic tract contains crossed fibres which originate in the contralateral nasal hemiretina, and uncrossed fibres which originate in the ipsilateral temporal hemiretina. The nerve fibres originating from corresponding retinal elements are, however, not closely aligned. For this reason, homonymous hemianopias caused by optic tract lesions are characteristically incongruous. Geniculate lesions also produce asymmetrical hemianopic defects.
3. **Wernicke hemianopic pupil**: the optic tracts contain both visual and pupillomotor fibres. The visual fibres terminate in the lateral geniculate body but the pupillary fibres leave the optic tract anterior to the lateral geniculate body, projecting through the brachium of the superior colliculus to terminate in the pre-tectal nucleus. An optic tract lesion may therefore give rise to an afferent pupillary conduction defect. Characteristically, the pupillary light reflex will be normal when the unaffected hemiretina is stimulated, and absent when the involved hemiretina is stimulated. In practice, this Wernicke hemianopic pupillary reaction is difficult to elicit because of scatter of light within the eye – hence the need for a very fine beam of light.
4. **Optic atrophy** may result when the optic tracts are damaged because the fibres in the optic tract are the axons of the retinal ganglion cells. The causes of optic tract disease are similar to those affecting the chiasm. The optic tract is particularly vulnerable when the chiasm is pre-fixed (*see* Figure 15.89).

## Lesions of optic radiations

### APPLIED ANATOMY

The optic radiations extend from the lateral geniculate body to the striate calcarine cortex which is located on the medial aspect of the occipital lobe, above and below the calcarine fissure (Figure 15.104). The optic radiations and visual cortex have a dual blood supply from the middle and posterior cerebral arteries. As the optic radiations pass posteriorly, fibres from corresponding retinal elements lie progressively closer together. For this reason, incomplete hemianopias caused by lesions of the posterior radiations are more congruous than those involving the anterior radiations. However, a complete hemianopia obviously has no localizing value because the extent of congruity cannot be assessed. As the visual fibres synapse in the lateral geniculate body, lesions of the optic radiations do not produce optic atrophy.

### CLINICAL FEATURES

1. **Temporal radiations**
   (a) ***Visual field defects*** consist of contralateral homonymous superior quadrantanopia ('pie in the sky'), because the inferior fibres of the optic radiations, which subserve the upper visual fields, first sweep anteroinferiorly in Meyer loop around the anterior tip of the temporal horn of the lateral ventricle, and into the temporal lobe.
   (b) ***Associated features*** include contralateral hemisensory disturbance and mild hemiparesis, because the inferior fibres pass very close to the sensory and motor fibres of the internal cap-

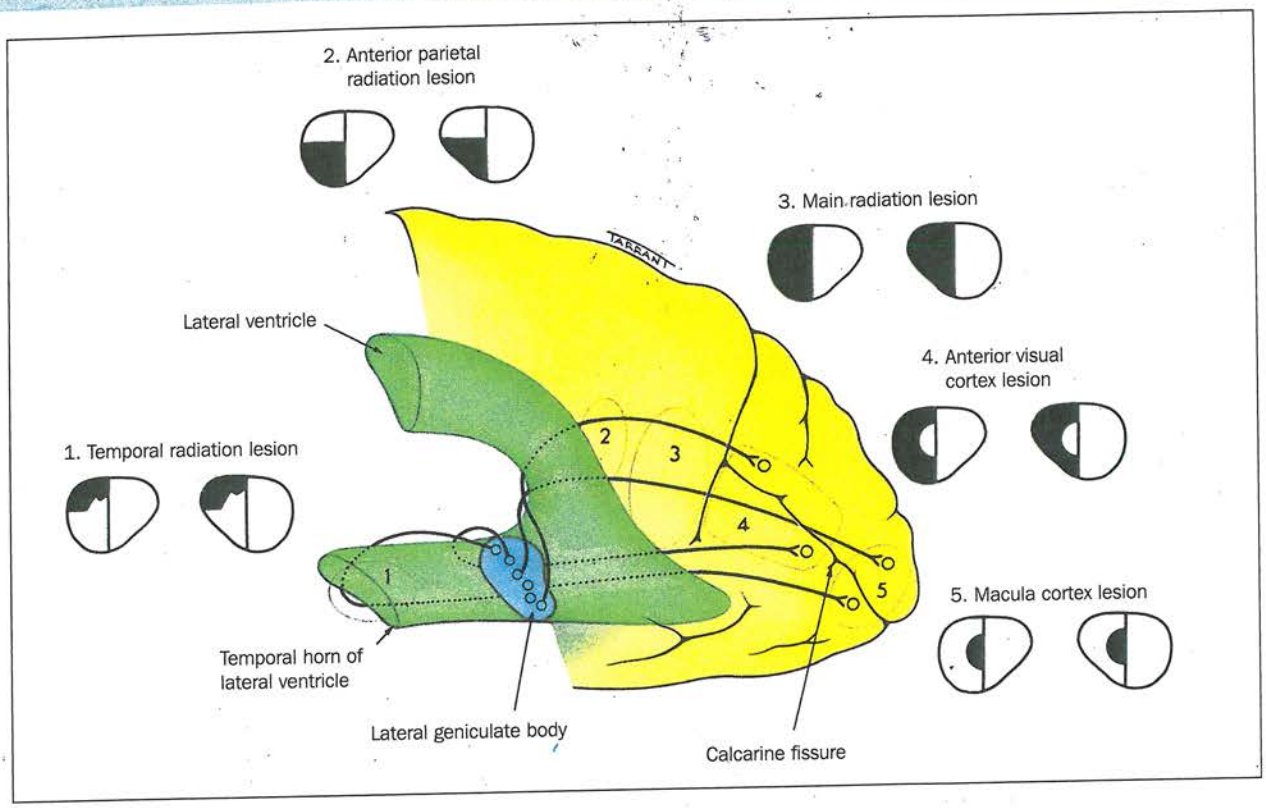



**Figure 15.104** Visual field defects caused by lesions of the optic radiations and visual cortex

sule before passing posteriorly and rejoining the superior fibres. Other features of temporal lobe disease are: paroxysmal olfactory and gustatory hallucinations (uncinate fits), formed visual hallucinations, seizures and receptive dysphasia.

2. **Anterior parietal radiations**
   (a) ***Visual field defects*** consist of contralateral homonymous inferior quadrantanopia ('pie on the floor') because the superior fibres of the radiations, which subserve the inferior visual fields, proceed directly posteriorly through the parietal lobe to the occipital cortex. A lesion involving only the anterior parietal part of the radiations, which is very rare, will therefore cause an inferior quadrantanopia. In general, hemianopias resulting from parietal lobe lesions tend to be relatively congruous and either complete or denser inferiorly.
   (b) ***Associated features*** of parietal lobe disease are: agnosias, visual perception difficulties (particularly with right parietal lesions), right–left confusion and acalculia (particularly with left parietal lesions).
3. **Main radiations**
   Deep in the parietal lobe, the optic radiations lie just external to the trigone and the occipital horn of the lateral ventricle. Lesions in this area usually cause a complete homonymous hemianopia.

## Lesions of the striate calcarine cortex

1. **Visual field defects**
   In the striate calcarine cortex the peripheral visual fields are represented anteriorly. This part of the occipital lobe is supplied by a branch of the posterior cerebral artery. Central macular vision is represented posteriorly just lateral to the tip of the calcarine cortex, which is supplied mainly by a branch of the middle cerebral artery. Occlusion of the posterior cerebral artery will therefore tend to produce a macular sparing congruous homonymous hemianopia. Damage to the tip of the occipital cortex, as might occur from a head injury, tends to give rise to congruous homonymous macular defects, although asymmetrical macular sparing may sometimes occur with vascular lesions of the occipital lobe.
2. **Associated features** of visual cortex disease are: (a) formed visual hallucinations, particularly involving the hemianopic field and (b) denial of blindness (Anton syndrome).
3. **Causes**
   (a) ***Vascular lesions*** in the territory of the posterior cerebral artery are responsible for over 90% of isolated homonymous hemianopias with no other neurological deficits.

(b) ***Other causes***, which are less common, include migraine, trauma and primary or metastatic tumours.

4. **Optokinetic nystagmus** (OKN) may be useful in localizing the lesion causing an isolated homonymous hemianopia that does not conform to any set pattern in patients with no associated neurological deficits. If the optomotor pathways in the posterior hemisphere are damaged, the OKN response will be diminished when targets are rotated towards the side of the lesion (i.e. away from the hemianopia). This is called the positive OKN sign. In most cases, the combination of a homonymous hemianopia and OKN asymmetry suggests a parietal lobe lesion, often a neoplasm. Rarely occipital lobe lesions may also cause OKN asymmetry.

# MIGRAINE

## Clinical features

Migraine is an often familial disorder characterized by recurrent attacks of headache widely variable in intensity, frequency and duration. Attacks are commonly unilateral and are associated with nausea and vomiting. In some cases they are preceded by, or associated with, neurological and mood disturbances. However, all these characteristics are not necessarily present in each attack or in each patient. The main types of migraine are as follows:

1. **Common migraine** is characterized by headache accompanied by autonomic nervous system dysfunction (e.g. pallor and nausea), but with no other neurological features.
   (a) Premonitory features include changes in mood, frequent yawning or other non-specific prodromal symptoms such as poor concentration.
   (b) The headache starts anywhere on the cranium and is pounding or throbbing. It usually spreads to involve one half or the whole head. In some cases the pain is retro-orbital and may be mistaken for eye or sinus disease.
   (c) During the attack, which lasts for hours to a day or more, the patient is frequently photophobic and phonophobic and seeks relief in a quiet dark environment or through sleep.
   (d) Because of the absence of the well-known migrainous visual distortions, severe nausea and vomiting, many patients with common migraine do not recognize that they have it.
2. **Classical migraine** is less common but better recognized.
   (a) The attack is heralded by a visual aura which lasts about 20 minutes. The aura may consist of bright or dark spots, zig-zags, heat haze distortions, jig-saw puzzle effects, scintillating scotomata, tunnel vision, homonymous hemianopia, altitudinal hemianopia and fortification spectra.
   (b) A small bright positive paracentral scotoma develops, lined on one side with luminous zig-zag lines (Figure 15.105**a**).
   (c) After several minutes the fortification spectrum gradually enlarges with the open end pointing centrally. It is often lined on the inner edge by an absent area of vision (negative scotoma) (Figure 15.105**b**).
   (d) As the scotoma expands it may drift or march towards the temporal periphery (Figure 15.105**c**) before breaking up (Figure 15.105**d**).

   These features are said to be pathognomonic of migraine, but rarely they may be caused by degenerative arterial problems in the occipital poles. The headache is similar to that in common migraine but may be absent, trivial or very severe, with considerable variation between attacks even in the same individual.
3. **Focal migraine** is characterized by transient dysphasia, hemisensory symptoms or even focal weakness in addition to other symptoms of migraine.
4. **Migraine sine migraine** is characterized by episodic visual disturbances but no subsequent headache. Elderly patients with a past history of common or classical migraine are typically affected.
5. **Retinal migraine** is characterized by acute but transient unilateral loss of vision which is similar to amaurosis fugax. As it may occasionally occur in middle-aged patients with no past history of migraine

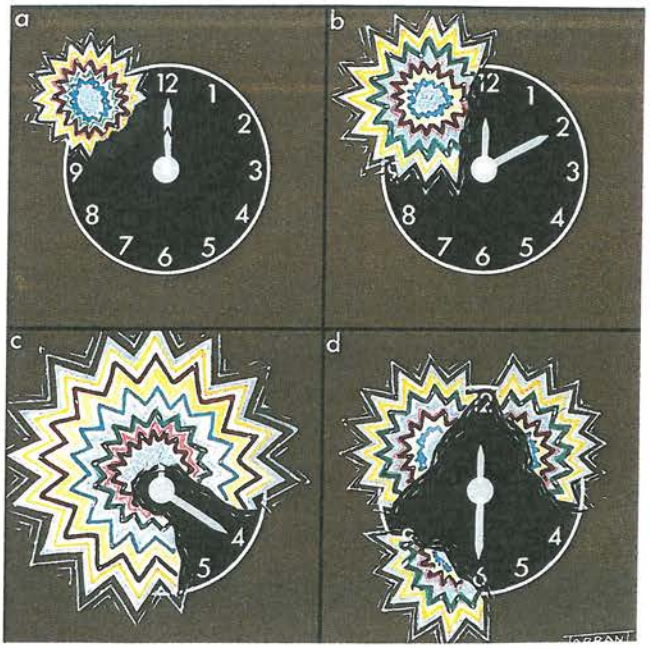



**Figure 15.105** Progression of classic migrainous fortification spectrum and scintillating scotoma

it is prudent to investigate as if they were having attacks of amaurosis fugax.

6. **Ophthalmoplegic migraine** is rare and typically starts before the age of 10 years. It is characterized by a recurrent transient third nerve palsy which begins after the headache.
7. **Familial hemiplegic migraine** is characterized by a failure of full recovery of focal neurological features after the migraine attack is over.
8. **Basilar migraine** occurs in children. It is characterized by a typical migrainous aura associated with numbness and tingling of the lips and extremities which is often bilateral. Ataxia of gait and speech also occur, with occasionally impairment of consciousness.
9. **Cluster headache** is a migraine variant which typically affects men during the fourth and fifth decades of life. It is also characterized by a typical, stereotyped headache accompanied by various autonomic phenomena occurring almost every day for a period of some weeks.
   (a) The headache is unilateral, oculotemporal, excruciating, sharp and deep.
   (b) It begins relatively abruptly, lasts between 10 minutes and 2 hours, and then clears quickly.
   (c) It may occur several times in a 24-hour period often at particular times, not infrequently at around 2 a.m.
   (d) Once the 'cluster' is over, there may be a long headache-free interval of several years.
   (e) Autonomic phenomena associated with the headache include lacrimation, conjunctival injection and rhinorrhoea. Cluster headaches are also a common cause of a transient or permanent postganglionic Horner syndrome.

## Management

1. **General measures** include elimination of conditions and agents that may precipitate an attack of migraine, such as coffee, chocolate, alcohol, cheese, oral contraceptives, stress, lack of sleep and long intervals without food.
2. **Prophylaxis** may be with beta-adrenergic blockers, calcium channel blockers, amitriptyline, clonidine, pizotifen and low-dose aspirin.
3. **Treatment** of an acute attack can be with simple analgesics (aspirin, codeine analogue, paracetamol or a non-steroidal anti-inflammatory agent) and if appropriate an anti-emetic such as metoclopramide. Other drugs, which are usually reserved for patients who do not respond to analgesics include sumatriptan and ergotamine tartrate.

# OCULAR MYOPATHIES AND RELATED DISORDERS

## Myasthenia gravis

### CLINICAL FEATURES

Myasthenia gravis is an uncommon autoimmune disorder, characterized by a destruction of available postsynaptic acetylcholine receptors on the end-plates of neuromuscular junctions of skeletal muscle; it results in weakness and fatiguability of voluntary musculature. The condition affects females more commonly than males by a ratio of 2:1. The main types are: (a) ***ocular***, (b) ***bulbar*** and (c) ***generalized***.

1. **Presentation** is typically during the third and fourth decades with excessive fatiguability of ocular, bulbar and skeletal muscles. Symptoms are typically worse in the evenings, although some patients may be troubled on first waking. Involvement of bulbar muscles interferes with chewing and swallowing. Facial muscle involvement may cause a lack of expression. Tendon reflexes are normal or exaggerated and sensory changes are absent.
2. **Ocular involvement** is present in 90% of cases and is the presenting feature in 60%. It is characterized by the following:
   (a) ***Ptosis***
   - Insidious, bilateral but frequently asymmetrical ptosis, which is worse with fatigue and in upgaze.
   - If one eyelid is elevated manually as the patient looks up, the fellow eyelid will show fine oscillatory movements.
   - Cogan twitch sign is a brief upshoot of the eyelid as the eyes saccade from depression to the primary position.

   (b) ***Diplopia***, which is frequently vertical, although any of the extraocular muscles may be affected. In some cases a pseudo-internuclear ophthalmoplegia is seen.
   (c) ***Nystagmoid movements***, which may be present on extremes of gaze.

### SPECIAL INVESTIGATIONS

1. **An edrophonium** (Camsiton) test should never be performed without an assistant, and a resuscitation trolley should also be close at hand in case of sudden cardiorespiratory arrest. The test is performed as follows:
   (a) Obtain an objective baseline by measuring the amount of ptosis or performing a Hess test in patients with diplopia.
   (b) Inject intravenously atropine 0.3 mg.

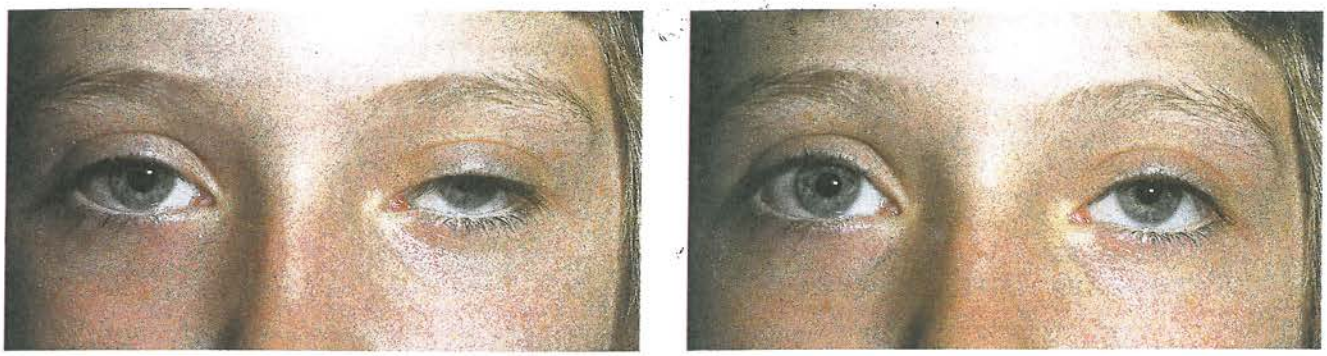


**Figure 15.106** Positive edrophonium test in a patient with myasthenic ptosis. (**a**) Prior to injection; (**b**) 2 minutes after injection

(c) Inject intravenously a test dose of 0.2 ml (2 mg) edrophonium hydrochloride.
(d) Inject the remaining 0.8 ml (8 mg) after 60 seconds, provided there is no hypersensitivity.
(e) Take measurements and compare the results (Figure 15.106), remembering that the effect lasts only 5 minutes.

2. **Electromyography** may be very helpful in confirming fatigue with repetitive stimulation. This may be combined with an edrophonium injection to clinch the diagnosis.
3. **Antibodies** to acetylcholine receptors are present in 90% of cases of generalized myasthenia. If antibodies to striated muscle are present the possibility of a thymoma should be considered.
4. **CT** or **MRI** of the anterior mediastinum should be performed to rule out a thymoma (Figure 15.107). Thymic enlargement is seen in 10–20% of patients, usually men.

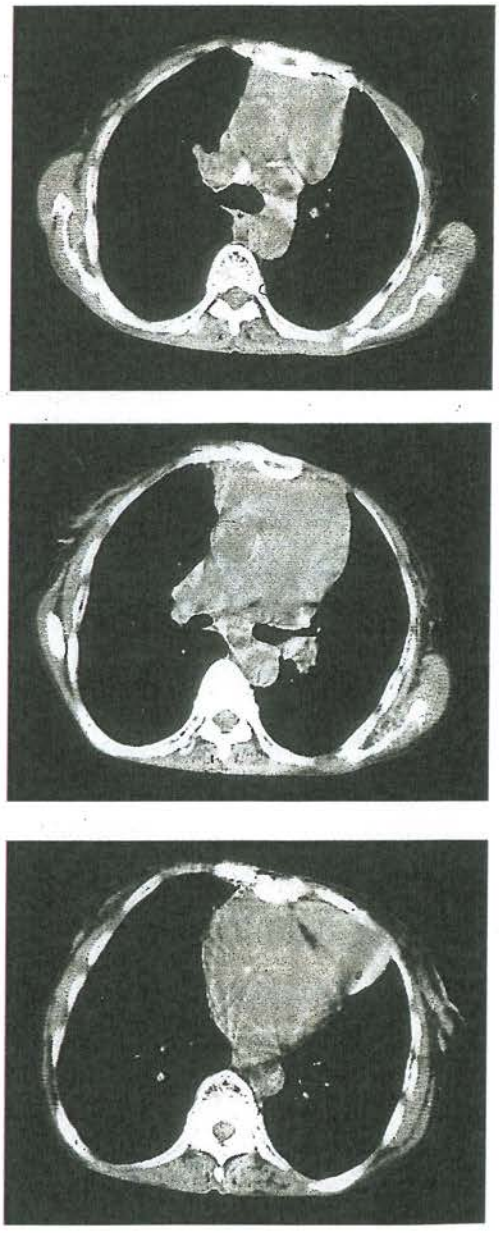


**Figure 15.107** CT scan of the mediastinum showing a thymoma

## TREATMENT

1. **Medical therapy**
   (a) Long-acting anticholinesterase drugs (pyridostigmine, neostigmine) do not alter the disease process, but they allow the acetylcholine released at the neuromuscular junctions to be effective for a longer period of time.
   (b) Systemic steroids are particularly useful in ocular myasthenia and produce remission in 80% of myasthenia gravis patients.
   (c) Azathioprine is also effective in reducing anti-acetylcholine receptor antibody levels, but it may take 6–12 weeks before there is evidence of improvement.
   (d) Other methods include plasmapheresis and intravenous immunoglobulin.
2. **Thymectomy** may be considered in all patients with generalized myasthenia gravis, especially young patients who have circulating receptor antibodies. There is an 80% chance of improvement or remission after thymectomy, although this may not be evident

for up to 2 years. Thymectomy is certainly indicated in patients with thymoma.

3. **Strabismus surgery** may be beneficial in selected patients in whom persistent loss of binocularity has caused chronic disability. Conventionally, diplopia is managed by prisms or occlusion, although these measures may be poorly tolerated and leave unacceptable cosmetic and functional results. Surgery may be considered, provided both the systemic disease and the strabismus have been stable for some time.

## Ocular myopathies

The ocular myopathies are a mixed group of rare disorders, some of which are sporadic, while others show a dominant inheritance pattern. Muscle biopsy in some patients shows mitochondrial cytopathy (inherited through the mother's DNA). The main clinical features are chronic progressive external ophthalmoplegia, initially involving upgaze. Lateral movements may later be affected and the eyes become virtually fixed. Because muscle involvement is symmetrical (Figure 15.108), diplopia does not usually occur, even in advanced cases. There is also a slowly progressive bilateral ptosis (Figure 15.109). Although there may be some overlap, the three main forms of ocular myopathy are:

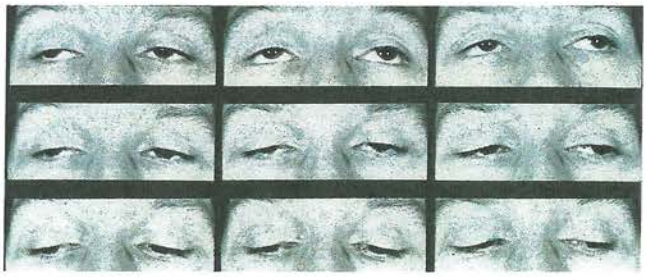


**Figure 15.108** Ptosis and symmetrical restrictions of all ocular movements in ocular myopathy

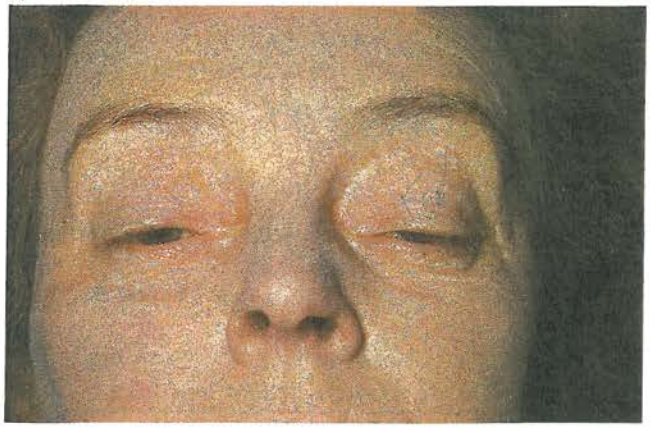


**Figure 15.109** Severe ptosis in advanced ocular myopathy

1. **Primary ocular myopathy**, which is not associated with other features.
2. **Oculopharyngeal dystrophy**, which is characterized by weakness of the pharyngeal muscles and wasting of the temporalis.
3. **Kearns–Sayre syndrome**, which is characterized by:
   (a) Pigmentary retinopathy with coarse granularity (Figure 15.110).
   (b) Heart-block, which may result in sudden death.
   (c) Other features include short stature, muscle weakness, cerebellar ataxia, neurosensory deafness, mental handicap and delayed puberty.

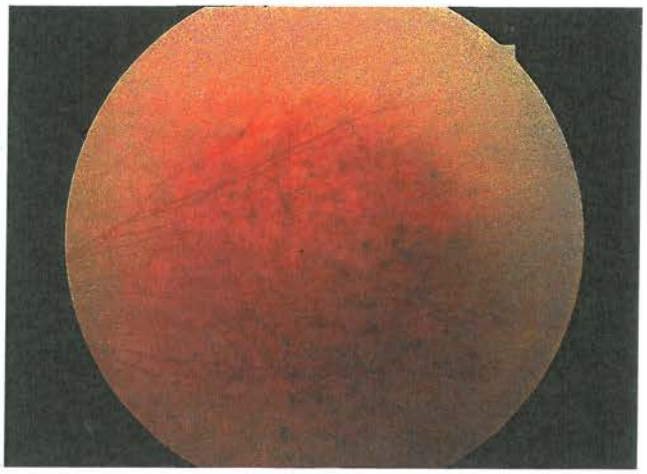


**Figure 15.110** Pigmentary retinopathy in Kearns–Sayre syndrome

## Myotonic dystrophy

### SYSTEMIC FEATURES

Myotonic dystrophy (dystrophia myotonica) is a generalized, dominantly inherited disease which exhibits considerable variation in the severity of involvement, even within the same family. The myotonic dystrophy gene is located on chromosome 19q.

1. **Presentation** is usually during the third decade with myotonic features and ptosis.
2. **Myotonia**
   (a) Peripheral muscle involvement, which makes release of grip difficult.
   (b) A mournful expression caused by bilateral facial wasting (Figure 15.111).
   (c) Slurred speech from involvement of the tongue and pharyngeal muscles.
3. **Muscle wasting** involves the facial muscles, temporalis, masseter, sternomastoid, shoulder girdles, quadriceps and small muscles of the hands. Tendon reflexes may be absent.

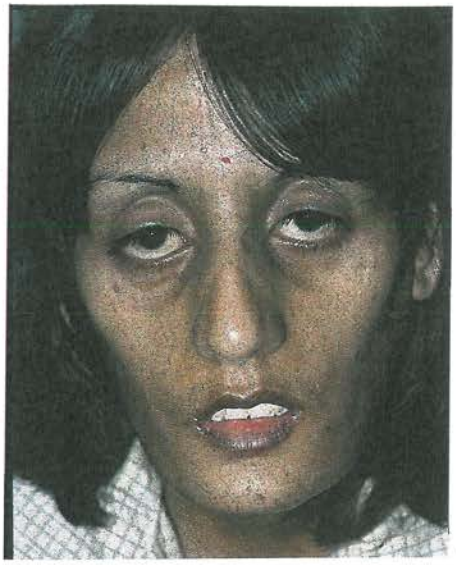


**Figure 15.111** Ptosis and mournful expression in a patient with myotonic dystrophy

4. **Other features**
   (a) Hypogonadism with preservation of secondary sexual characteristics.
   (b) Frontal baldness in males.
   (c) Intellectual deterioration.
   (d) Pulmonary and cardiac complications, which may lead to premature death.

### OCULAR FEATURES

1. **Presenile cataracts** are the most common ocular abnormality. The opacities are usually small, iridescent, polychromatic crystals, although small white opacities and posterior subcapsular stellate plaques may also occur (*see* Figure 5.11)
2. **Ptosis**, which is usually bilateral.
3. **Pigmentary retinopathy** which is usually innocuous involves the macula or periphery.
4. **Light–near dissociation** of pupillary reactions may be seen.
5. **Low intraocular pressure** may be present but is clinically unimportant.
6. **External ophthalmoplegia.**

## Essential blepharospasm

### CLINICAL FEATURES

Essential blepharospasm is an idiopathic disorder with progressive involuntary spasm of the orbicularis muscle and upper facial muscles. In severe cases the blepharospasm is very disabling because it may temporarily make the patient functionally blind (Figure 15.112). The spasm may be precipitated by certain factors such as reading, driving, stress or bright light, and alleviated by others such as talking, walking and relaxation. The condition typically presents in the sixth decade of life and affects women more commonly than men by a 3:1 ratio. Some patients develop ocular irritation as a result of filamentary keratitis.

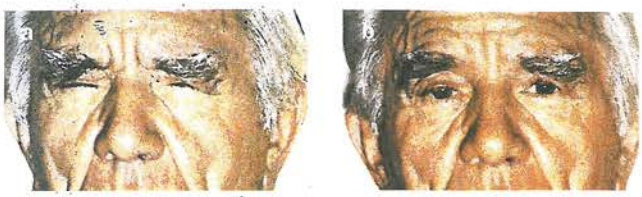


**Figure 15.112** Essential blepharospasm. (**a**) During an attack; (**b**) after an attack

1. **Meige syndrome** is a combination of blepharospasm and involvement of the lower facial and neck muscles.
2. **Breughel syndrome** is associated with severe mandibular and cervical muscle involvement.

### TREATMENT

1. **Medical treatment** with a great variety of drugs has been reported to ameliorate specific types of blepharospasm, but their efficacy is disappointing.
2. **Botulinum toxin** injected along the upper and lower eyelids and eyebrow gives temporary relief in most patients (Figure 15.113). By interference with acetylcholine release from nerve terminals it results in temporary paralysis of the injected muscles. Most patients require a repeat injection after 3–4 months and then more injections of larger doses may be needed. The side-effects of injections include lagophthalmos and ectropion or entropion, depending on the tone of the eyelids before the injection. Accidental migration of the toxin into the levator or extraocular muscles may result in ptosis and diplopia.

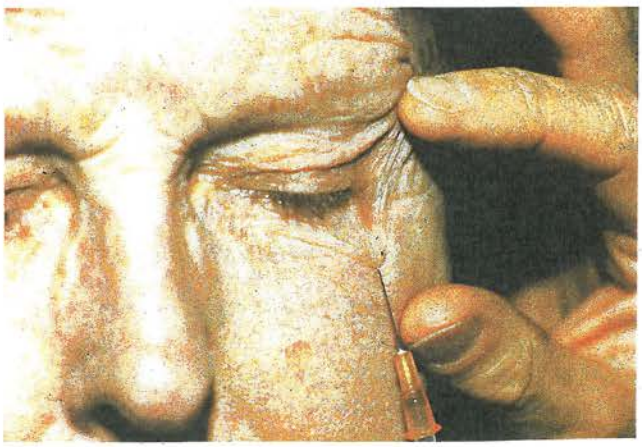


**Figure 15.113** Botulinum toxin injection for essential blepharospasm

3. **Surgical treatment** is usually reserved for patients who cannot tolerate or are unresponsive to botulinum injections. The procedure involves removal of the orbicularis, corrugator and procerus muscles.

# NEUROFIBROMATOSIS

Neurofibromatosis is a hereditary disorder that primarily affects cell growth of neural tissues. Inheritance is autosomal dominant with irregular penetrance and variable expressivity. The mutation rate is high. The two main types are ***type 1 (NF-1)*** and ***type 2 (NF-2)***.

## Neurofibromatosis type 1 (NF-1)

NF-1 (Von Recklinghausen disease) is the most common phakomatosis, affecting 1 in 4000 individuals and it presents in childhood. The gene responsible has been localized to chromosome 17q11.

### SYSTEMIC FEATURES

1. **Neural tumours** may develop in the brain, spinal cord and the cranial, spinal and autonomic nerves.
2. **Skeletal defects**
   (a) Acquired scoliosis.
   (b) Dysplasia of the sphenoid bone.
   (c) Dysplasia or thinning of long bone cortex.
   (d) Facial hemiatrophy (Figure 15.114).

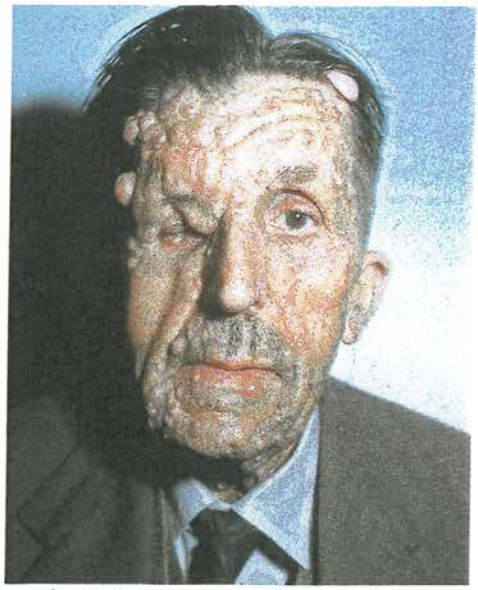


**Figure 15.114** Right facial hemiatrophy and multiple fibroma molluscum in NF-1

   (e) Short stature, which is common.
   (f) Mild macrocephaly (enlarged head), which is uncommon.
3. **Skin lesions**
   (a) ***Café-au-lait spots***, which are flat, light-brown patches which vary in size from a few millimetres to several centimetres (Figures 15.115). They appear during the first year of life and increase in size and number throughout childhood so that teenagers and adults invariably have more than six.

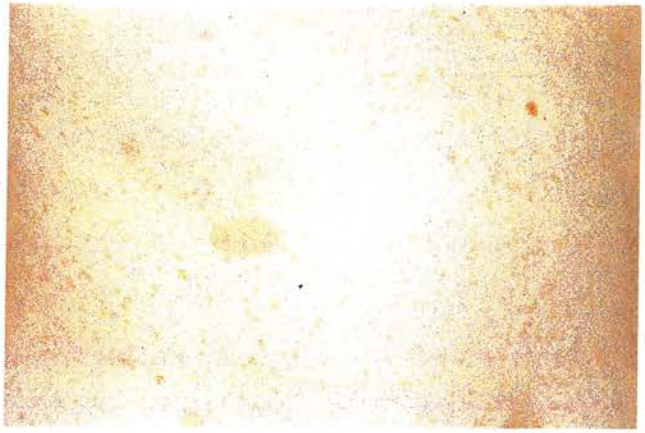


**Figure 15.115** Café-au-lait spots in NF-1

   (b) ***Axillary freckles***, which usually become obvious around the age of 10 years and, when present, are pathognomonic.
   (c) ***Fibroma molluscum***, which consist of pedunculated, flabby, pigmented nodules which are frequently widely distributed over the body (Figures 15.116 and 15.117). They begin to appear at about puberty and increase in number throughout life. The number of lesions varies from a few to several hundred. Histologically,

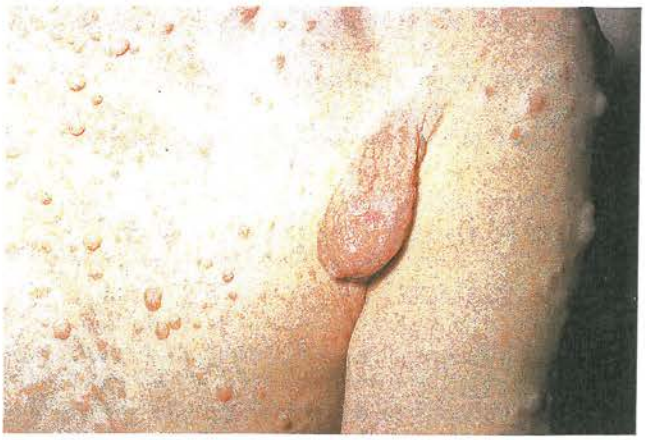


**Figure 15.116** Fibroma molluscum in NF-1

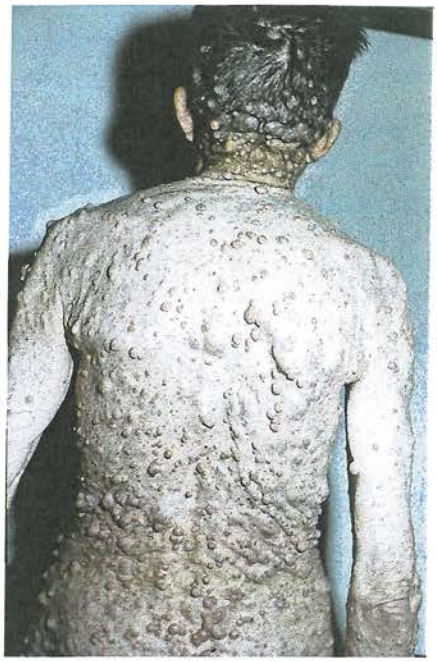


**Figure 15.117** Extensive fibroma molluscum in NF-1

they consist of neurofibromas or schwannomas of cutaneous nerves.

(d) ***Plexiform neurofibromas***, which are less common than fibroma molluscum. They are usually much larger, less well defined and tend to merge with the surrounding tissue. They may be associated with pigmentation and overgrowth of the overlying skin (Figure 15.118) or, if located on a limb, of the underlying bone. Plexiform neurofibromas may be present at birth or appear during childhood. They may occur anywhere on the body and in a very small number of patients may involve the face and cause disfigurement (the Elephant Man – Figure 15.119).

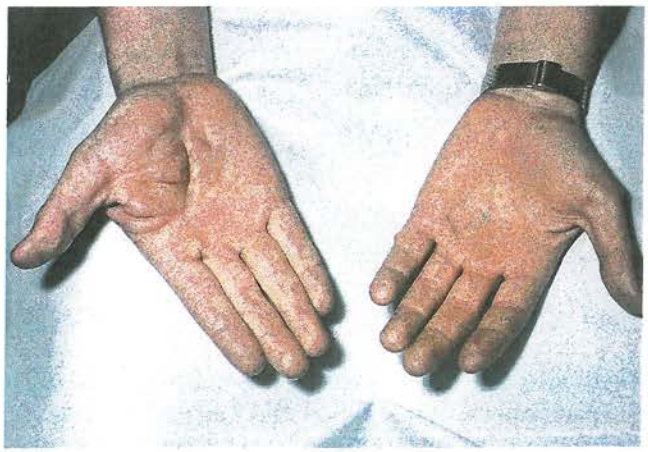


**Figure 15.118** Plexiform neurofibroma of the right palm in NF-1

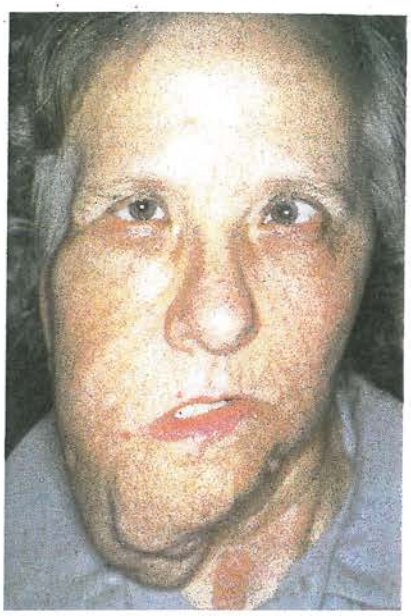


**Figure 15.119** Extensive facial neurofibroma with overgrowth of soft tissues in NF-1

4. **Miscellaneous features**
   (a) ***Malignancies***, which are either embryonal tumours of childhood or neurofibrosarcomas, develop in about 5% of patients. There is also an increased risk of leukaemia and lymphoma.
   (b) ***Hypertension***, which may be secondary to phaeochromocytoma or renal artery stenosis.
   (c) ***Mental hdndicap*** and ***epilepsy***.

## OCULAR FEATURES

1. **Orbital involvement** may be caused by one of the following:
   (a) ***Optic nerve glioma*** develops in about 15% of patients. It may be unilateral or bilateral and tends to extend posteriorly to involve the chiasm (*see* Figure 15.9) and hypothalamus (Figure 15.120).
   (b) ***Other neural tumours***, such as neurilemmoma, plexiform neurofibroma or meningioma.
   (c) ***Spheno-orbital encephalocele***, which is caused by a congenital absence of the greater wing of the sphenoid bone (Figures 15.121 and 15.122). It characteristically causes a pulsating proptosis which is not associated with either a bruit or a thrill.
2. **Eyelid neurofibromas**, which may be either nodular (Figure 15.123) or plexiform, tend to develop early in life. When involving the upper lid, they may frequently give rise to a mechanical ptosis.
3. **Iris lesions**
   (a) ***Lisch nodules*** (Figure 15.124) develop during the second and third decades of life, and are eventually present in 95% of cases.

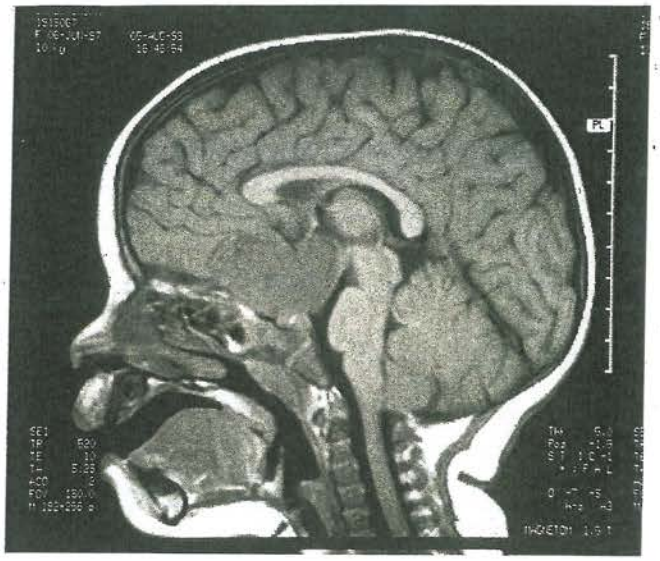


**Figure 15.120** Sagittal T1-weighted MRI scan showing invasion of the hypothalamus by an optic nerve glioma in NF-1

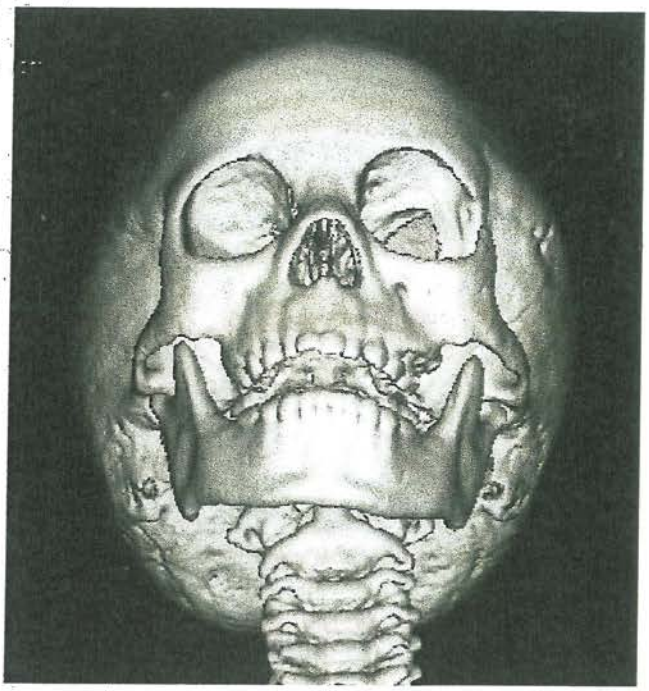


**Figure 15.122** Three-dimensional CT scan showing absence of the left greater wing of the sphenoid bone

(b) ***Congenital ectropion uveae*** (Figure 15.125) is uncommon and may be associated with glaucoma.

4. **Prominent corneal nerves** (Figure 15.126) may occur in some patients.
5. **Glaucoma** is relatively rare and, when present, is usually unilateral and frequently congenital. About 50% of patients with glaucoma have an ipsilateral neurofibroma of the upper eyelid and facial hemiatrophy. The following factors may be responsible for the pressure rise:

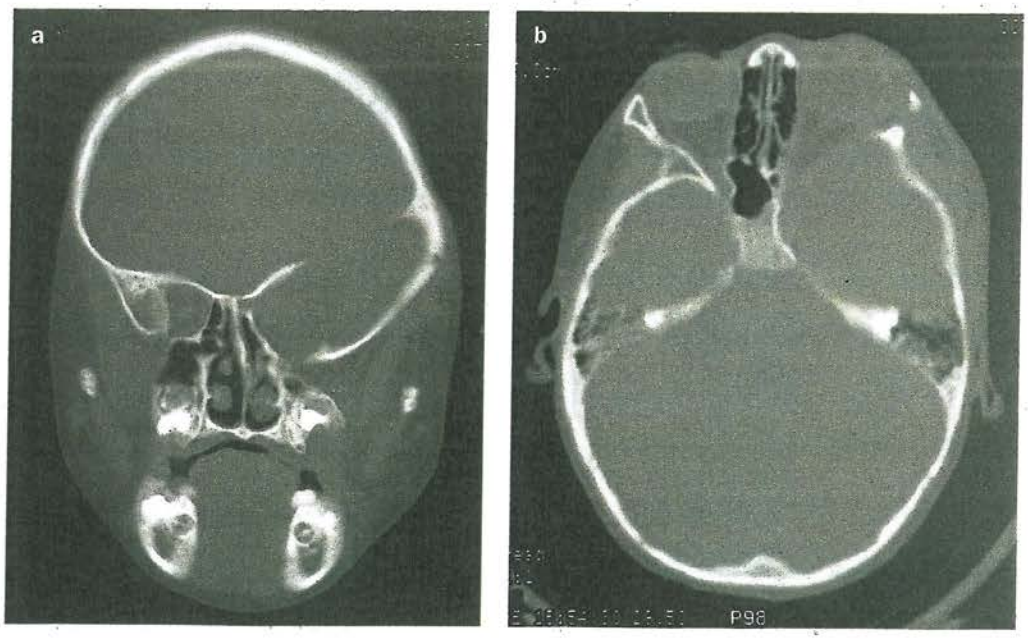



**Figure 15.121** CT scan showing congenital absence of the left greater wing of the sphenoid bone. (**a**) Coronal view; (**b**) axial view

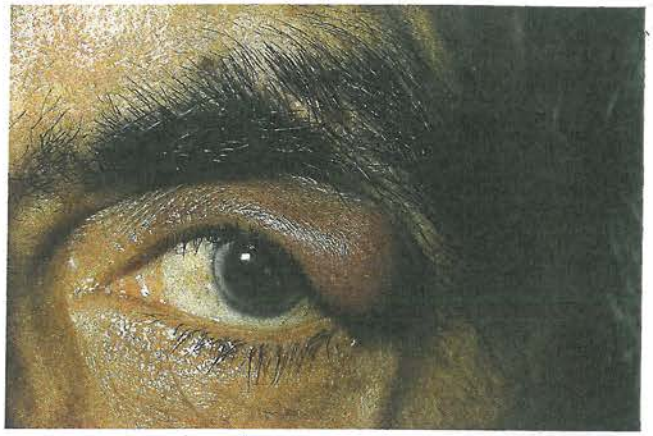


**Figure 15.123** Nodular neurofibroma of the eyelid in NF-1

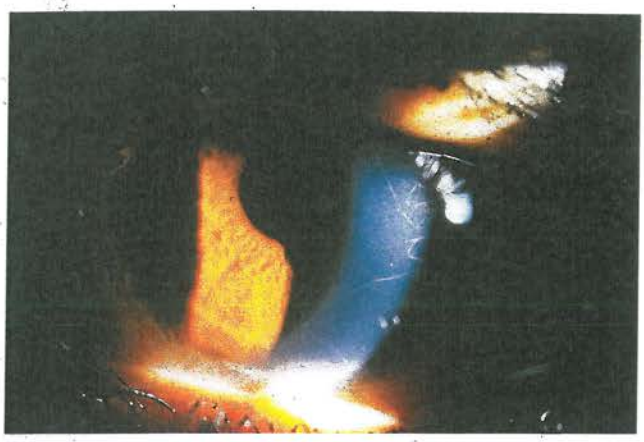


**Figure 15.126** Prominent corneal nerves

**Figure 15.124** Lisch nodules

(a) Obstruction of aqueous outflow by neurofibromatous tissue in the chamber angle.
(b) A developmental angle anomaly which may or may not be associated with ectropion uveae.
(c) Secondary angle closure by forward displacement of the peripheral iris associated with neurofibromatous thickening of the ciliary body.
(d) Secondary synechial angle closure by contraction of a fibrovascular membrane in the angle.

6. **Fundus lesions**
   (a) ***Choroidal naevi***, which may be multifocal and bilateral, are common. Patients with NF-1 and naevi tend to have an increased risk for the subsequent development of choroidal melanoma.
   (b) ***Retinal astrocytomas*** (Figure 15.127), which are identical to those found in tuberous sclerosis, are rare.

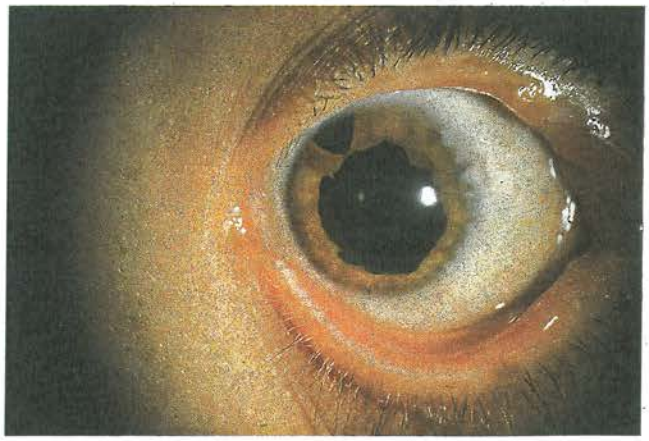


**Figure 15.125** Ectropion uveae

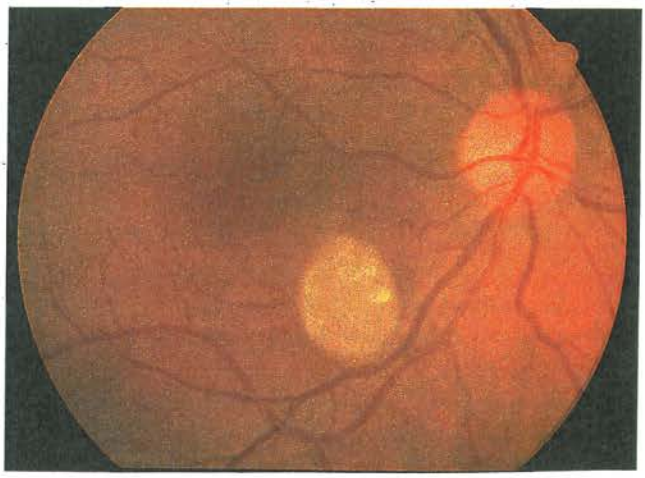


**Figure 15.127** Retinal astrocytoma

## Neurofibromatosis type 2 (NF-2)

NF-2 is much less common than NF-1 and affects 1 in 40 000 individuals. The gene responsible is localized to chromosome 22q12.

1. **Systemic features**
   (a) ***Bilateral acoustic neuromas*** usually present in the 'teens or early twenties with hearing loss or tinnitus. Most acoustic neuromas are schwannomas arising from the vestibular nerve. Studies on early small tumours have suggested that tumour cells may originate in the vestibular ganglion. In young patients tumour growth is invariably fast, whereas in older patients the lesion may be either slow- or fast-growing. With recent advances in microsurgical techniques, the results of surgery have improved significantly. The gamma-knife (stereotactic radiotherapy) provides a therapeutic option.
   (b) ***CNS tumours*** – neurofibromas, meningiomas, gliomas and schwannomas – are seen in some cases.
2. **Ocular features** may assist in presymptomatic diagnosis.
   (a) ***Cataract*** affects about two-thirds of patients. The opacities develop prior to the age of 30 years and may be posterior subcapsular or capsular, cortical or mixed.
   (b) ***Fundus lesions***, consisting of combined hamartomas of the retinal pigment epithelium and retina (Figure 15.128) and epiretinal membranes, are relatively common.
   (c) ***Extraocular motility defects*** are present in about 10% of cases.

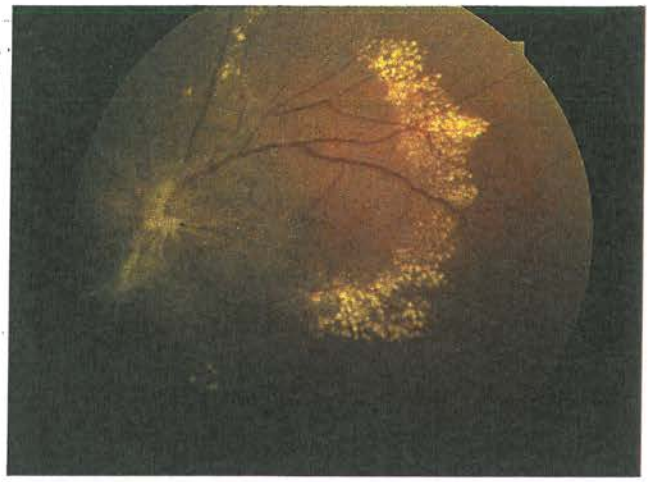


**Figure 15.128** Combined hamartoma of the retinal pigment epithelium and retina