CHAPTER 9 ABNORMALITIES OF THE POSTERIOR SEGMENT

THE OPTIC DISC

This lies 3mm nasal to and 0.8mm above the foveola. Features described on clinical examination are:

1. Colour
2. Contour (ie. distinctness of margins)
3. Cupping

Nerve fibres from the macula run directly to the disc - those from more temporal parts of retina arch above and below to enter the disc at its upper and lower poles. The central retinal vessels emerge just nasal to the centre of the disc. Hence the nasal 2/3-3/4 of the disc margin appear slightly blurred and there is a depression at and temporal to the centre of the disc - the physiological cup. As the nerve fibres leave the globe they pass through dehiscences in the thin layer of scleral fibres extending across the disc - the lamina cribrosa. Posterior to the optic disc, nerve fibres are myelinated; anterior to disc they are usually unmyelinated. Occasionally white, flame-shaped patches of myelinated fibres may be seen adjacent to the disc - these are congenital and may cause enlargement of the blind spot. All retinal layers except the nerve fibre layer end abruptly at the disc margin - if certain layers stop short 'crescents' are produced which may completely surround the disc.

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- A scleral crescent usually occurs on the temporal side of the disc and is formed when the choroid and pigment epithelium stop short of the disc margin and allow white sclera to show through the overlying transparent retina.

- Choroidal crescents also occur more frequently on the temporal side and result when the pigment epithelium stops short of the disc margin and allows the underlying choroid to be directly observed.

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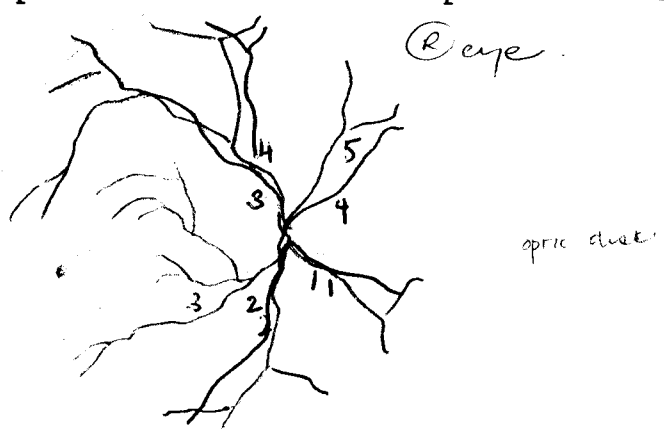
- Pigment 'crescents' are often not crescent-shaped and although most often on the temporal side, may be anywhere on the disc margin. They result from accumulation of more than the usual amount of pigment in the pigment epithelium where it stops at the disc margin.



The most common pathological processes involving the optic nerve are:

1. Glaucomatous cupping and atrophy
2. Papilloedema
3. Optic neuritis
4. Ischaemic optic neuropathy
5. Optic atrophy

1. Glaucomatous cupping and atrophy

The optic disc is unique in that it is subjected to a high tissue pressure (the intraocular pressure) in common with the retina.However its blood supply is derived chiefly from small branches of the short posterior ciliary arteries which have a substantially lower pressure than the central retinal artery. The blood supply of the disc is therefore, much more easily compromised by small increases in intraocular pressure than is the blood supply of the retina. The clinical observation that rapid progression of glaucomatous field defects often follows reduction of blood pressure in hypertensive patients who have concomitant open angle glaucoma is a supportive argument.

SLIDE 85 A & B (STEREO)

From a clinical stand-point scrutiny of the optic disc and cup is of great importance in the diagnosis and management of patients with glaucoma and suspected glaucoma. Discs with small cups and a broad rim of pink disc tissue surround the cup appear to withstand mild elevation of intraocular pressure better than discs with broad cups extending nearly to the disc margin. Eyes with large cups and poor rims of surrounding pale disc tissue are particularly suspect and required vigorous treatment. Careful documentation of the appearance of the disc and cup is essential in the management of glaucoma patients. Recording the cup-disc ratio is a rapid and convenient measure of cupping. In normal eyes, the cupping of the discs is usually symmetrical (cup-disc ratio is equal in both right and left eyes). Asymmetrical cupping is most suspicious of glaucoma as is haemorrhage on the disc margin.

2. Papilloedema

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Papilloedema is a passive swelling of the optic disc secondary to increased intracranial pressure. It is believed that increases in intracranial pressure are transmitted along the subarachnoid space of the optic nerve. This rise in pressure impedes the outflow of the central retinal vein and probably small veins within the optic nerve head causing increased redness and fullness

of the disc. Loss of the physiologic cup, blurring of the disc margins and venous engorgement follow if the intracranial pressure remains elevated. Loss of spontaneous venous pulsation may occur i.e. presence of spontaneous venous pulsation is very much against papilloedema.

The visual symptoms of papilloedema are few, but late in the condition the patient may notice transient blurring of vision. Capillary dilatation, haemorrhages and exudates at the disc, and oedema and wrinkling of the surrounding retina are found. Elevation of the disc may be pronounced (up to 6 or more dioptres as measured with the direct ophthalmoscope). Enlargement of the blind spot can often be plotted on visual field examination.

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Any lesion which increases intracranial pressure can cause papilloedema, i.e. brain tumour, subdural haematoma, pseudo-tumour cerebri or advanced severe hypertension.

Long-standing papilloedema may result in optic atrophy with loss of vision. The disc becomes pale and chronically swollen, i.e. secondary optic atrophy.

Pseudopapilloedema or pseudoneuritis.

Quite commonly there may be elevation and blurring of the disc margins simulating the appearance of papilloedema or papillitis in hypermetropic eyes. Occasionally, small, spherical pale bodies, called 'drusen' (but unrelated to drusen of Bruch's membrane) may be present between the lamina cribrosa and the disc surface, causing elevation of the nerve head and confusion with early papilloedema. The pathogenesis of these laminated basophilic concretions is unknown. Unless haemorrhages or exudates are present on or adjacent to the disc, it may be impossible by ophthalmoscopic examination alone to differentiate physiological blurring from papilloedema or papillitis. Examination of members of the family may reveal similar changes. Arcuate field defects may occur, due to pressure on nerve fibre bundles at the edge of the optic disc.

3. Optic neuritis

This is a demyelination or degenerative process in the optic nerve that may involve the optic disc (papillitis) or the portion of the optic nerve behind the globe(retrobulbar neuritis). Retrobulbar neuritis causes no fundus abnormalities in the acute stage. The single most important symptom of optic neuritis and one that serves best to differentiate it from papilloedema is acute loss of central visual acuity. A large dense central scotoma is found on visual field testing. A dull aching retrobulbar pain intensified by movement of the

eyes is present. After several days or weeks spontaneous improvement occurs and vision returns to near normal levels. The most commonly recognised cause of optic neuritis is multiple sclerosis. Uncommon causes include local extension of inflammatory disease from the sinuses or meninges, drug toxicity (Ethambutol and Methanol) and systemic viral infections such as mumps, measles and rubella. Neuromyelitis optica (Devic's Disease) is a rare demyelinating condition consisting of bilateral optic neuritis and transverse myelitis.

The appearance of the disc in papillitis may be identical to that in papilloedema, but the high elevation sometimes seen in papilloedema does not occur in papillitis.

SLIDE 107A

SLIDE 107B

4. Ischaemic optic neuropathy

Unlike the retina, which is supplied by the central retinal artery, the optic nerve head receives its blood supply from the short ciliary circulation. Blockage of these vessels results in infarction of part or the whole of the optic nerve head, with resulting visual loss. The retinal circulation remains functional unless the central retinal artery is compressed by the disc swelling, leading to a secondary central retinal artery occlusion and retinal infarction. The diagnostic features of anterior ischaemic optic neuopathy are sudden total or partial visual loss afecting one eye, with a swollen optic disc but normal retina. The partial visual loss is usually in the form of an altitudinal field defect.

It is important to distinguish between the two types of ischaemic optic neuropathy - degenerative and inflammatory, as treatment with high-dose steroids is sight-saving in the inflammatory type but is of no value in the degenerative type.

The inflammatory type is usually due to temporal arteritis, a chronic granulomatous inflammatory process involving medium sized arteries of elderly adults. Tenderness over the temporal arteries, pain in the shoulders or in the jaw (on chewing),and generalised malaise or fever precede ocular symptoms.When the ophthalmic artery becomes involved, there is rapid loss of vision. The optic disc becomes pale and blurred and small splinter-like haemorrhages occur around its borders. The temporal arteries may be large, tortuous and pulseless.The sedimentation rate is usually markedly elevated (often 100mm/hr+) but exceptions occur; in these instances, a raised C-reactive protein is a useful indicator of active inflammation. One eye is usually initially involved, followed by involvement of the second eye 1 to 21 days later. Pathological features are

necrosis of the arterial media with surrounding multi-nucleated giant cells and occlusion of the vessel lumen. Biopsy of the artery showing the characteristic pathological picture is diagnostic, but a negative biopsy does not preclude the condition, as the inflammatory changes may be patchy.

Unfortunately, visual loss is permanent. Treatment consists of immediate systemic steroids if the diagnosis is suspected. Steroids will not improve the already involved eye, but will often prevent involvement of the second eye. Time should not be wasted waiting for a temporal artery biopsy, for if the second eye becomes involved, blindness usually results. The steroid therapy should be titrated to the patient's ESR. Treatment may need to be continued for many months and it is important to recognise and treat such side-effects as steroid-induced diabetes and hypertension.

The degenerative type is associated with generalised atherosclerosis and hypertension, and no treatment has yet been shown to be of any value.

5. Optic atrophy

Optic atrophy and pallor of the disc may be the end result of glaucoma, papilloedema, optic neuritis or other less common lesions of the optic nerve, chiasm or tract. Normally the colour of the disc may vary within wide limits; the nasal aspect is more pink and the temporal aspect paler. Normally seven or more vessels of small calibre cross the temporal half of the disc margin. Less than this suggests optic atrophy (Kestenbaum's counting test). Optic atrophy may be primary, which means only that neither papilloedema nor papillitis has preceded the atrophy and therefore the disc margins are sharp.

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SLIDE 106

Optic atrophy may be congenital.

Secondary optic atrophy signifies that the disc margins are blurred, denoting previous inflammation or oedema of the disc. This may be as a result of previous:

1) anterior ischaemic optic neuropathy (either arteritic or non-arteritic)

2) demyelination

3) Vitamin B_{12} deficiency

4) toxicity due to drugs e.g. ethambutol

5) infection e.g. syphilis

6) diabetes mellitus

7) optic nerve compression

DIFFERENTIAL DIAGNOSIS OF BLURRED AND ELEVATED DISCS

	PAPILLOEDEMA	PAPILLITIS	PSEUDOPAPILLOEDEMA
VISION	normal until late when optic atrophy occurs	SUDDEN EARLY LOSS OF CENTRAL VISION (CENTRAL SCOTOMA) ALTITUDINAL DEFECTS WITH ISCHAEMIC DISEASE	usually normal occasional arcuate scotoma
PAIN	none	PAIN ON MOVEMENT OF THE EYE IN DEMYELINATION	none
INVOLVEMENT	usually BILATERAL	usually UNILATERAL (M.S.) ISCHAEMIC OFTEN BILATERAL BUT ASYMMETRICAL	BILATERAL
SPONTANEOUS VENOUS PULSE	ABSENT	present or absent	present
HAEMORRHAGES AND EXUDATES	OFTEN	occasionally with ischaemic disease	rare
ASSOCIATED SIGNS AND SYMPTOMS	HEADACHE, NAUSEA, VOMITING & OTHER NEUROLOGICAL SIGNS AND SYMPTOMS OF RAISED INTRACRANIAL PRESSURE	SIGNS OF MULTIPLE SCLEROSIS TEMPORAL ARTERITIS ARTERIOSCLEROSIS	none
COURSE	PROGRESSIVE	usually improves	stationary
FAMILY HISTORY	nil	nil	occasionally present

VASCULAR DISEASES OF THE RETINA AND CHOROID

Introduction

In 1851 Helmholtz, a German scientist, introduced the ophthalmoscope and for the first time physicians were able to directly scrutinise nervous tissue and examine a variety of arteries, arterioles, veins and venules in vivo under magnification.

Examination of the ocular fundus allows the physician the luxury of seeing directly how a particular disease process is affecting neural and vascular tissues. The direct ophthalmoscope (the commonly used hand held instrument) gives a uniocular view at great magnification (X15). The indirect ophthalmoscope on the other hand allows a binocular view. The magnification is much less (X3) therefore the view of the fundus is much wider.

Histological studies show that the ophthalmic and central retinal arteries have well developed muscular coats and internal elastic laminae.

The muscular coats of the branch retinal arteries rapidly attenuate after branching and the internal elastic lamina disappears. These vessels are now designated arterioles. The retinal capillaries have three layers. An endothelial lining supported by a basement membrane and an external layer of cells called pericytes. The endothelial cells are firmly joined together by zonulae occludentes. These tight junctions represent, in effect, fusion of the outer cell membranes of contiguous cells. The endothelial cells together with their tight junctions form a selective barrier to the constituents of the blood, akin to the cerebral capillaries. It is called the inner 'blood retinal barrier'. It is defects and deficiencies within this layer of cells that lead to many of the retinopathies that we shall describe in this section.

SLIDE 102

Fundus photography. The introduction of the Zeiss fundus camera has revolutionised the documentation of the ocular fundus. Small blood vessels of diameter 50 microns can be accurately resolved and photographed.

SLIDE 109

Fluorescein angiography. This technique introduced in 1959 consists of photographing a fluorescent dye (sodium fluorescein) as it passes through the retinal vessels. Under optimum circumstances even the smallest capillaries (5-10μ in diameter) can be photographed. This technique may be used to identify retinal vascular structural defects not seen on fundoscopy, as well as to diagnose changes in retinal haemodynamics, ie. defects in circulation time, vascular obstructions, etc.

ARTERIOSCLEROSIS

In general three types of arteriosclerosis may be seen in the retinal vessels:

1. Involutionary arteriosclerosis

2. Atherosclerosis

3. Arteriolosclerosis

A. Pathology

1. Involutionary (medial) arteriosclerosis is characterised by fibrosis and hyaline degeneration of the media. It is closely related to ageing and in the retina is usually mild and rarely occurs before the age of 50 years. It seldom becomes severe enough to produce marked narrowing of the vessel lumen or any functional impairment.

2. Atherosclerosis is characterised by formation in large arteries of subendothelial plaques of fat-laden cells. The plaque may encroach on the arterial lumen, ulcerate and act as a focus for thrombus formation. Because of their small size, the retinal arterioles, which have little or no internal elastic lamina, are not common sites for atherosclerosis. The ophthalmic artery and the central retinal artery, however, may be involved.

3. Arteriolosclerosis, as the name indicates, involves arterioles. Pathologically, hypertrophy of the muscularis mucosa is an early change, giving way later to marked hyaline thickening of the vessel wall, frequently accompanied by endothelial proliferation, leading to marked narrowing of the lumen. There is a close relationship with hypertension.

B. Ophthalmic appearances

As would be expected in view of their histological similarities, the ophthalmoscopical pictures produced by these processes overlap to a considerable degree. They may conveniently be considered under four headings:

SLIDE 92, 102

1. Changes in the transparency of the vessel wall and in the light reflex

Normally the retinal arteries and arterioles are transparent and only the red blood column is seen on ophthalmoscopy. The arteriosclerotic process impairs less brilliantly red and the light reflex becomes broader and takes on an orange or copper shade. When this change is pronounced, the vessels

are described as 'copper wire' arteries or arterioles. With further loss of transparency the blood column may appear 'sheathed' by white lines on either side of it or the wall may become completely opaque, leading to the designation of 'silver wire' arteries or arterioles.

SLIDE 110

2. AV crossing phenomena

Normally when retinal veins cross under arteries only the portion of the venous blood column under the arteriolar blood column is obscured. As thickening of the arteriolar wall occurs the venous column immediately adjacent to the arterial column becomes obscured. The sclerotic process frequently involves the vein at the AV crossing, leading to additional obscuration of the venous blood column. This gives the appearance of the vein being compressed by the artery and is referred to as 'AV nipping.'

3. Changes in the calibre of the vessels

SLIDE 112

Severe generalised arterial and arteriolar narrowing is often seen secondary to profound retinal degeneration such as retinitis pigmentosa, but in an otherwise normal fundus it is usually indicative of hypertension. In hypertension the smallest ophthalmoscopically visible branches are particularly involved. Milder degrees of generalised narrowing are a part of involutionary sclerosis.

Focal narrowing is most commonly seen in hypertension.

4. Changes in the course of the vessels

The retinal vessels normally show gently undulating curves without deflection at the AV crossings. With involutionary sclerosis, the arterioles become straighter and the veins may be deflected slightly at the AV crossings. The normally acute angle between artery and vein at a crossing becomes more obtuse, often nearing a right angle. With severe arteriolar sclerosis the small vessels become more tortuous, particularly those near the macular area. This leads to the typical appearance of 'corkscrew' arterioles. The venules in the macular area may also assume a corkscrew configuration, probably as a result of slowing of blood flow associated with partial venous occlusion.

CENTRAL RETINAL ARTERY OCCLUSION

SLIDE 113

Features of central retinal artery occlusion are:

1. sudden painless loss of vision.
2. afferent pupillary defect on the affected side.
3. cherry-red spot at the macula.
4. an embolus may be present in central retinal artery.

The presenting symptom of central retinal artery occlusion is sudden, painless, total or nearly total loss of vision in one eye, usually in a patient in the sixth or later decade. The fundus shows marked narrowing of the retinal arterioles, although blood is still apparent in them. The retina has a grey-white appearance resulting from cloudy swelling of the ganglion cells. Because there are no ganglion cells at the centre of the fovea, no opacity occurs here. The normal red colour of the choroidal circulation becomes very prominent in relation to the surround white retina and is called a 'cherry red spot'. The retina regains normal transparency within several weeks, as some degree of recirculation becomes established. In general this is not before extensive receptor death has occurred.

Causes of retinal artery occlusion:

1.	EMBOLIC	-	atheroma
		-	valvular heart disease
		-	infective emboli
		-	fat embolus
		-	exogenous eg. talc
2.	THROMBOTIC	-	changes in wall
		-	changes in blood
		-	pressure from outside the vessel wall
3.	INFLAMMATORY	-	temporal arteritis (painful)
4.	SPASM	-	ergot
		-	migraine

Frequently the cause of central retinal artery occlusion cannot be determined clinically. In some cases, vasospasm or thrombosis may play a role, but probably of greater importance are emboli from atherosclerotic plaques in the carotid system or diseased heart valves. If the emboli are small enough, branch arterial occlusion may occur. Occasionally a shower of cholesterol crystals will dislodge from atherosclerotic carotid arteries either spontaneously or secondary to manipulation of the carotids. These migrate through the retinal arterioles and can be seen as highly reflective intra-arteriolar bodies. These less frequently cause visual disturbance.

Episodes of transient obscuration of vision frequently herald total loss of vision and should be considered an emergency.

Treatment

If the circulation is not re-established within an hour or two, vision is irreparably lost. Emergency measures include vigorous massage of the eye, pressure on the eye and then sudden release in an attempt to dislodge the plaque. If the patient is fortunate enough to be seen immediately by an ophthalmologist, paracentesis (release of aqueous) by making a small self-closing incision through the cornea, to lower intraocular pressure, may be carried out. IV Diamox may also be given. In the majority of instances even early treatment is not successful.

SLIDE 114

Occlusion of a branch of the central retinal artery may also occur. Loss of vision is then limited to the involved area.

CENTRAL RETINAL VEIN OCCLUSION

Causes of central retinal vein occlusion:

THROMBOTIC:

1. pressure on the vein:
   - atherosclerotic artery
   - raised intraocular pressure
2. vessel wall disease
   - diabetes
   - sarcoidosis
   - Bechet's disease
3. increased blood viscosity
   - polycythaemia
   - leukaemia
   - multiple myeloma

SLIDE 115

Retinal venous occlusion, like arterial occlusion, usually affects older individuals, leading to relatively sudden onset of moderate visual impairment.

Features of central retinal vein occlusion:

1. sudden deterioration in vision (not total)
2. swollen optic disc
3. widespread flame-shaped haemorrhages radiating from the disc
4. cotton-wool spots

Retinal vein occlusion, like retinal artery occlusion, usually occurs in patients with arteriosclerosis. Compression of the central retinal vein by the sclerotic and thickened central retinal artery, as they pass together through the limited space at the lamina cribrosa, causes partial occlusion of the vein. Endothelial proliferation in the vein may also contribute to narrowing of the lumen. Arterial insufficiency nearly always accompanies venous occlusion, leading to slowing of blood flow and thus favouring thrombosis. Ophthalmoscopically, the veins appear engorged and many flame-shaped and blot haemorrhages are seen throughout the fundus, particularly along the veins. Cotton-wool spots, white spots with ill-defined edges in the superficial internal layers of the retina, may also occur. These represent small areas of focal ischaemia secondary to occlusion of small terminal arterioles. Although we generally speak of vein occlusion as though it were complete, this is rarely the case as some circulation is maintained. In young patients an inflammatory component is often present and systemic corticosteroids seem to be of value. Visual impairment in CRV obstruction is less catastrophic than central retinal artery obstruction. In younger patients or those with adequate arterial input, serviceable vision is retained. The small veins often assume the appearance of opaque white threads, but some remain patent in spite of this appearance. Microaneurysms and proliferation of newly formed vessels also frequently occur, producing a picture similar to diabetic retinopathy (see below).

SLIDE 87

New vessels may also proliferate on the surface of the iris and across the trabecular meshwork, partially obstructing aqueous outflow and leading to glaucoma ('neovascular' or 'haemorrhagic' glaucoma).

SLIDE 111

Branch vein occlusion occurs generally at sites where the veins cross under their companion arterioles. Venous flow is presumably impeded at these points by the sharp deviation of the vein as it dips beneath the artery. Remarkable recovery of vision often occurs, due to the ability of the retinal vessels to form collaterals which by-pass the original obstruction.

Impending occlusion of the central retinal vein produces a clinical picture of dilatation of the retinal veins

with occasional scattered flat retinal haemorrhages. Vision is slightly impaired. Treatment with Aspirin or ocular hypotensive agents at this stage seems to be more helpful then in full-blown CRV occlusion, where results are generally disappointing.

HYPERTENSIVE RETINOPATHY

Hypertensive vascular disease is a disease of the arterioles. Thus, examination of the fundus of the eye, where these vessels can be so clearly seen, is an important diagnostic procedure. In the past it was also extremely important in prognosis, but now with the many drugs available for treatment of essential hypertension, the outlook in most cases is good in spite of the initial findings. However, examination of the fundi continues to be a great aid in estimating the degree of arteriosclerosis and thus indirectly the duration of the elevated blood pressure. It helps in deciding on modes of therapy and evaluating their efficacy. The most reliable sign of arteriosclerosis secondary to hypertension is AV nipping.

The basic alteration in hypertensive vascular disease is presumably spasm of the arteriolar musculature with resulting narrowing of the vessel lumen. Initially this is functional in nature and is therefore reversible. Arteriolosclerosis follows in chronic cases and narrowing becomes more severe and permanent. In one-third to one-half of patients with mild or early hypertension the ophthalmoscopical examination may be normal, but as the disease progresses, narrowing of the retinal arterioles frequently becomes visible. Arteriolar narrowing takes two forms, generalised and focal.

SLIDE 112

The latter change is certainly more easily identifiable as it is local and the narrowed segment may be compared with the adjacent segment of more normal calibre.

Generalised narrowing is much more difficult to assess and is much less dependable. It is generally estimated in one of two ways:

1. By comparing the vessels with those of similar order in normal patients in the same age range.

2. By comparing the vessels with something else relatively stable in size in the eye. As the retinal veins are generally not involved in the hypertensive or sclerotic processes, they provide a basis for comparison. Extreme care must be used, to compare vessels of comparable orders of branching, that is, if the segment of arteriole under scrutiny is of the second order (second branch after the central retinal artery), then the venule with which

it is compared must be a second order branch (second branch before the central retinal vein). Using this method, the ratio of arterial or arteriolar width to vein or venular width is determined - the so-called A/V ratio. Varying normal ratios have been proposed but the most common one is a ratio of 2:3 of artery to vein. Narrowing is not generally considered significant unless the ratio has decreased to 1:2 or less.

SLIDE 116

The changes seen ophthalmoscopically are:

1. Silver wiring due to loss of transparency of the arterial or arteriolar wall.

2. AV nipping - obscuration of the venous blood column adjacent to the arterial column.

3. The appearance of retinal haemorrhages. They are usually superficial in the nerve fibre layer and are thus 'flame-shaped', following the orientation of the nerve fibres. They may, however, be deeper and round. Their round configuration occurs because the haemorrhage is confined to a small space by the closely packed vertically orientated fibres of the deeper retina.

4. Commonly associated with hypertensive retinopathy is the 'cotton wool spot', an area of focal ischaemia in the retina (microinfarct). It is now know that these lesions result from sudden occlusion of a retinal arteriole, and generally reflect necrosis of the media due to accelerated or malignant hypertension.

5. Retinal oedema is commonly seen around the optic disc as in papilloedema but may extend for a considerable distance beyond the disc, often involving the posterior pole. Again it indicates a decompensation in the blood retinal barrier.

6. Because of the oedema a fourth change, hard exudates, occurs. These are oedema residues, that is, protein or lipid material from the oedema fluid 'precipitating' in the retina. Exudates in the macular area form a characteristic figure called a 'macular star' because of the distribution of the fibres of the external plexiform layer in this area. Severe hypertension occasionally leads to retinal detachment, the retina being pushed away from the choroid by fluid leaking out of the retinal and choroidal vessels.

Grading of hypertensive retinopathy (Keith Wagner Barker Classification

1. Silver wiring
2. Arteriovenous nipping
3. Grade 2 plus haemorrhages, hard exudates and cotton-wool spots
4. Changes of grade 3 plus disc swelling.

DIABETIC RETINOPATHY

SLIDE 117

Grading of Diabetic retinopathy:

Background Diabetic retinopathy (non proliferative)
Maculopathy - exudative
- oedematous
- ischaemic
Pre-proliferative retinopathy
Proliferative retinopathy
Advanced diabetic retinopathy
NON-PROLIFERATIVE

The pathogenesis of the retinal changes in diabetes is poorly understood as is the basic nature of diabetes mellitus itself. The earliest ophthalmoscopic sign of diabetic retinopathy is the appearance of a few tiny red dots in the retina. Histological studies have shown that most of these are microaneurysms. The capillary walls contain cells known as pericytes. These cells are responsible for maintaining tone in the capillary walls and this is the site of formation of outpouchings of the capillary walls. These are known as microaneurysms. Once the pericytes are lost the endothelial cells lose their tight junctions and leakage of blood and proteins into the retina occurs. These microaneurysms and the small punctate haemorrhages which may also be found cause no symptoms so long as the central fovea is uninvolved. The fundus may remain this way for many years, or alternatively, progression may occur. The microaneurysms are particularly obvious on fluorescein angiography.

SLIDE 118

Many of the microaneurysms develop leaky walls and blood plasma leaks out, causing retinal oedema. Retinal oedema, particularly slight, does not change the retinal transparency and is difficult to recognise with monocular ophthalmoscopy. Deposits of hard-looking yellowish-white material are frequently seen at the periphery of the oedematous areas and it is though that these represent lipid and/or protein which has 'precipitated out' from the oedema fluid (hard exudates).

SLIDE 119

Unfortunately, these changes characteristically occur in the posterior pole near the macula. Oedema of the macula is the commonest cause of impaired visual acuity in patients with the early stages of diabetic retinopathy.

In addition to the microaneurysms, small vascular radicals in the retina become dilated and tortuous. These channels are dilated pre-existing vessels.

It has also recently become clear that cotton-wool spots are common components of diabetic retinopathy. These are areas of focal ischaemia from vascular occlusion.

Another characteristic features of diabetic retinopathy is dilatation and beading of the retinal veins. The mechanism whereby this occurs is obscure, but it is probably related to hypoxia and venous stasis. Fluorescein studies in diabetics uniformly demonstrate gross reduction in the retinal circulation times.

In summary, the characteristic lesions of 'background' or 'non-proliferative' diabetic retinopathy are:

BACKGROUND

1. Punctate red dots representing mostly microaneurysms but also deep haemorrhages

2. Hard exudates which characteristically follow and surround areas of retinal oedema

3. Retinal oedema

PRE-PROLIF.

4. Cotton - wool spots (focal areas of ischaemia-microinfarcts)

5. Dilated intraretinal capillaries

6. Venous dilatation and beading.

SLIDE 120

PROLIFERATIVE DIABETIC RETINOPATHY

Certain patients with diabetic retinopathy go from the relatively benign stage discussed above to a more severe stage in which new vessels proliferate on the surface of the retina and in the vitreous cavity. This is called proliferative diabetic retinopathy. These new vessels arise most frequently on the optic disc or along the course of the major retinal veins. Unfortunately, wherever the vessels grow on the surface of the retina, they become adherent to the vitreous. When the vitreous contracts, it cannot easily separate from the retina and the vitreous pulls on the fragile new vessels causing rupture of their walls and vitreous haemorrhage. The new vessels are attached to the retina and traction is therefore transmitted to the retina, leading to retinal detachment. For reasons that are not fully understood, vitreous contraction occurs at an earlier age in patients with diabetic retinopathy. Unfortunately the majority of eyes with fully developed proliferative retinopathy go on

to marked reduction of vision and often complete blindness.

In summary, the characteristic lesions of 'proliferative' diabetic retinopathy are:

1. retinal ischaemia

2. neovascularisation

3. retinal fibrosis - traction bands and retinal detachment.

4. Preretinal haemorrhages, vitreous haemorrhages, vitreous fibrosis.

There is considerably controversy regarding the role of accurate control of the diabetes in the prevention of not only retinopathy but nephropathy and other vascular complications. Some recent work on diabetes suggests that well controlled patients develop a less florid retinopathy than those uncontrolled. It is thus probably true that meticulous control of the diabetes, particularly within the first few years after its onset, helps to postpone and possibly prevent vascular complications later in the course of the disease. It is essential that all physicians managing diabetes have a thorough understanding of its complications and are willing to devote considerable time to education of their patients. Patient education is absolutely essential, since it is the patient who must manage his disease from day to day and hour to hour.

Treatment

1. Laser Photocoagulation

SLIDE 123

This technique utilises a strong beam of light (Argon or Krypton Laser) to cauterise ischaemic retina. Recent randomised controlled studies have shown that laser photocoagulation is effective in preserving vision and slowing the rate of usual decline in diabetic patients with preretinal and papillary neovascularisation and early maculopathy.

Advanced retinal neovascularisation and macular oedema respond less favourably to photocoagulation, thus it is imperative to detect disease in its early stages by meticulous screening and careful observation of diabetics.

2. Vitrectomy

Persistent dense vitreous haemorrhage, fibrovascular membranes and traction detachments which threaten macular function may be treated by vitrectomy. This

technique may dramatically improve visual function by irrigating blood from the vitreous cavity by an intraocular infusion and suction system, fitted with a cutting head. Fibrovascular membranes may also be carefully dissected from the retina both improving acuity and preventing traction detachment.

BLOOD DYSCRASIAS

SLIDE 124

Various diseases of the blood have ophthalmoscopic findings, although many of the changes are non-specific in nature. Splinter-shaped haemorrhages, often with white centres, exudates, and retinal oedema may occur. Severe anaemia, whether primary or secondary to leukaemia, seems to be the important factor in producing damage to the vessel walls.

Polycythaemia produces engorgement of the retina veins and may lead to papilloedema.

In the macroglobinaemias, sludging of blood may be seen in the retinal veins. The venous stasis and consequential retinal hypoxia frequently result in neovascularisation and vitreous haemorrhage.

COAT'S DISEASE

Vascular anomalies localised to the retina include a variety of conditions characterised by multiple aneurysmal dilatations of the retinal vessels and arteriovenous shunts. These abnormal vessels may leak causing subretinal exudation, a condition which is called 'Coats Disease'. Treatment by photocoagulation appears to be effective if carried out early.

SICKLE CELL RETINOPATHY

Sickle cell retinopathy is <u>peripheral</u> retinopathy, characterised by small vessel closure, new vessel formation and vitreous haemorrhage. Photocoagulation is an important new tool to obliterate areas of neovascularisation, although its long-term effectiveness is still being evaluated.

INFLAMMATION OF THE CHOROID AND RETINA

A. Terminology

Inflammation of either one of these structures generally involves the other, at least to some degree, and frequently also involves the more anterior part of the uveal tract, ie. the ciliary body and iris.

Uveitis - Inflammation of part or all of the uveal tract.

Anterior uveitis - This is subdivided into iritis (predominantly affecting the iris) and iridocyclitis (affecting the iris and the anterior part of the ciliary body, the pars plicata) - see details on page 40).

Intermediate uveitis - (pars planitis) - predominantly involves the posterior part of the ciliary body (pars plana) and the extreme periphery of the retina.

Posterior uveitis - Inflammation of the choroid. Often the retina is also involved and the condition is then known as: chorioretinitis, if the choroid is primarily involved or retinochoroiditis if the retina is predominantly affected.

Vitritis - This is the infiltration of the vitreous by inflammatory cells.

Panuveitis - Involvement of the entire uveal tract

Endophthalmitis - This is a severe form of intraocular inflammation, often secondary to infection, involving the ocular cavities and their adjacent structures without extension of the inflammatory process beyond the sclera.

B. Pathogenesis

Whereas anterior uveitis is generally thought to represent an antigen-antibody reaction, perhaps related to some autoimmune process, posterior uveitis often represents infection of the tissues with micro-organisms (e.g. toxoplasmosis, tuberculosis, cytomegalovirus,

leprosy, syphilis). Allergy to the organisms, however, also plays an important part in the clinical picture. The inflammatory reaction is granulomatous, with foci of epithelial and giant cells surrounded by lymphocytes and plasma cells. Occasionally with diligent searching the causative organism can be demonstrated histologically, but the opportunity for histopathological examination is rare, as enucleation is only infrequently carried out. The organisms presumably reach the eye via the blood stream from some distant area of chronic infection.

C. Clinical Features

The two main symptoms of posterior segment inflammation are floaters and decreased vision.

In general, three different characteristic clinical pictures are seen:

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1. Acute retino-choroiditis

This condition begins with a fuzzy yellowish-white area in the retina looking somewhat like a cotton wool spot. Massive exudation of inflammatory cells into the vitreous occurs and is the cause of the patient's symptoms, namely, floating specks and blurred vision. At times vitreous opacities are so dense that ophthalmoscopic visualisation of the fundus is impossible. There may be minimal signs of inflammation in the anterior segment, chiefly flare and cells in the aqueous humour on slit-lamp examination, but usually not much ciliary injection. If vitreous opacities are not severe and if the active patch of inflammation does not involve the macula, the patient will usually have no symptoms. After several weeks the inflammation abates, vitreous opacity decreases and the patch of active inflammation loses its diffuse white appearance and becomes converted into a pale scar. Atrophic retinal pigment epithelium and choroid at the site of inflammation allow visualisation of the sclera. The pigment epithelial cells retina their ability to become wandering phagocytes and those that are not destroyed during the acute inflammatory stage proliferate and migrate into the retina at the margins of the lesion. Recurrent lesions frequently occur at the edge of or adjacent to old healed lesions, often after an interval of many years.

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It has been clearly demonstrated that some cases of retinochoroiditis are caused by Toxoplasma gondii, a protozoan parasite which causes both a systemic infection in adults, which is usually asymptomatic,

and an intra-uterine infection which may lead to severe CNS damage in the foetus. Retinochoroiditis is a result of intra-uterine infection.

Recurrence of old healed congenital ocular toxoplasmosis is responsible for between 50% and 75% of all cases of posterior uveitis in the USA and the UK. Recurrence usually takes place between the ages of 10 and 35 years (average age 25 years) when the cysts rupture and release hundreds of parasites (Tachyzoites) into normal retinal cells.

Lesions distant from the macula require no treatment, as spontaneous resolution of the disease process occurs. If the patch of active inflammation is adjacent to the macula, attempts are made to eliminate the organism (with Daraprim, Suphadiazine and Clindamycin) and to suppress the inflammation with systemic corticosteroids. Unfortunately, these measures often fail to prevent macular involvement and destruction of central vision.

2. Chorioretinitis

The active lesion appears as a small yellowish spot deep in the choroid. Initially it is partially obscured by the more or less intact pigment epithelium. Pigment migration soon becomes evident at the edges of the lesion. Haemorrhage beneath the pigment epithelium or beneath the retina frequently occurs. The vitreous remains clear, and no symptoms are produced unless the active lesion is in or near the macula. Not infrequently serous fluid from the choroid leaks through Bruch's membrane and the pigment epithelium and accumulates beneath the retina. Should fluid involve the macular area, blurring of vision occurs. In certain parts of the world eg. USA Histoplasma capsulatum is the culprit.

Toxocara, an intestinal parasite of dogs and cats, has occasionally been demonstrated as the cause of chorioretinitis. The clinical picture is an elevated white mass in the posterior fundus with marked vitreous opacities, usually in a child. The lesion may be confused with retinoblastoma.

3. Pars Planitis

This is a less common type of uveitis occurring usually in young adults. The patient complains of floaters or, less commonly, reduction in visual acuity. The anterior chamber is usually clear or shows mild flare and a few cells. White exudates cover the inferior quarter to half of the pars plana and peripheral retina 'snowbanking'. Vitreous opacities, 'snowballs', are extensive, appearing to the patient as specks floating before him. The retinal veins are engorged, and the disc margins are

blurred. Frequently oedema of the macula occurs, leading to impairment of visual acuity. After some months permanent degenerative changes in the macula may ensue. The aetiology of pars planitis is unknown. Treatment is unsatisfactory and high doses of systemic corticosteroids fail to reduce the exudate in the peripheral fundus. These agents are of value, however, in reversing macular oedema and preserving central visual acuity.

Aetiological diagnosis of posterior uveitis

Because fundus lesions are not accessible to culture, it is very difficult to make an aetiological clinical diagnosis with certainty, unless the eye is so disorganised by the inflammation that enucleation is required. Most aetiological diagnoses are based on the clinical appearance of the lesion, skin tests and serological tests, and include:

1. Uveitis secondary to a systemic disease e.g. sarcoidosis, Behcet's Disease, chronic infection (especially TB, Leprosy, Syphilis)

2. Parasitic infestations e.g. Toxoplasmosis, Toxocariasis

3. Viral infections e.g. Cytomegalovirus

4. Fungal infections e.g. Candidiasis, Histoplasmosis

5. Idiopathic specific uveitis e.g. Vogt-Koyanagi-Harada Syndrome

6. Idiopathic non-specific uveitis.

DEGENERATIVE DISEASES OF THE FUNDUS

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A. Drusen are common degenerative lesions. They are small, round, yellow, multiple spots which may be scattered throughout the fundus or concentrated in the macular area. These are commonly mistaken for exudates but are benign and of unknown aetiology. Pathologically, they are hyaline excrescences of Bruch's membrane and probably represent a secretion of the retinal pigment epithelium. Drusen can be inherited in an autosomal dominant pattern.

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B. Angioid streaks are fissures in Bruch's membrane which allow the choriocapillaries to be viewed directly. The fissures assume a reddish appearance mimicking a choroidal vessel, thus their descriptive name. They result from a degeneration in the elastic component of Bruch's membrane and are often associated with the skin disease pseudoxanthoma elasticum.

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C. Retinitis pigmentosa is not an inflammation but a hereditary degeneration chiefly involving the rods of the retina. There is an associated migration of pigment from the pigment epithelium into the retina, attenuation of the retinal vessels and atrophy of the optic nerve. The symptoms are night blindness, reduced peripheral vision ('tunnel' vision) and decreased central vision. This condition is inherited in a dominant, recessive or x-linked fashion, and can appear at any age. Genetic counselling is essential.

ACQUIRED IMMUNE DEFICIENCY SYNDROME

This syndrome is caused by human immunodeficiency virus (HIV) infection. It results in opportunistic infections and tumours, especially Kaposi's sarcoma. Opportunistic infections include:

1. PROTOZOAN INFECTION e.g. Pneumocystitis carinii pneumonia, disseminated toxoplasmosis

2. VIRAL INFECTION e.g.
   disseminated CMV (Cytomegalovirus)
   persistent invasive HSV (herpes simplex)
   herpes zoster
   Epstein-Barr virus
   adenovirus

3. FUNGAL INFECTION e.g. systemic cryptococcosis
   oral and systemic candidiasis

4. BACTERIAL INFECTION e.g. mycobacterium avium - intracellulare

Ocular complications occur in about 75% of AIDS patients.

Kaposi's sarcoma may involve the eyelids and conjunctiva. It appears as a bright red mass, most frequently in the lower fornix. Skin tumours appear as elevated, non-tender purple nodules. Kaposi's sarcoma is sensitive to radiotherapy.

Herpes Zoster ophthalmicus presents with skin lesions in the distribution of the ophthalmic division of the trigeminal nerve. There is usually an accompanying uveitis which may be severe and prolonged.

Posterior uveitis occurs with CMV, candida and toxoplasmosis infections. CMV retinitis occurs in about 30% of homosexual AIDS patients and is the major cause of visual loss. Transient cotton wool spots or scattered haemorrhages in the nerve fibres layer are also seen in AIDS patients. The cause of these is unknown at present.

TUMOURS OF THE FUNDUS

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1. The most common intraocular tumour is the malignant melanoma which arises from pigmented cells in the choroid. It is slow-growing and visual symptoms occur when a serous retinal detachment is produced by fluid exuding from the tumour, or when the tumour involves the posterior pole. Choroidal melanomas are less malignant than melanomas elsewhere in the body, but distant metastases occur. The prognosis is good if the eye is removed before the tumour extends into the orbit, with more than fifty per cent of patients surviving for five years.

2. Retinoblastoma is a rare, highly malignant congenital tumour of the retina with an incidence of 1 in 125,000 live births. It is inherited in an autosomal-dominant fashion or as a mutation without prior family history. The tumour is present from birth, but is unnoticed until it reaches sufficient size to impair central vision, leading to a squint or a white pupillary reflex (leucocoria) noticeable to the parents.

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Good central vision in both eyes is essential for the development of normal binocular functions and ocular movements. An eye with poor vision frequently squints during infancy. In every case of strabismus the possibility of retinoblastoma must be ruled out by careful ophthalmoscopic examination. If discovered early before extension occurs, enucleation is usually life-saving. In about 25% of cases involvement is bilateral. If the tumour in the less involved eye is small, x-ray and chemotherapy may eradicate the tumour with retention of good vision. Genetic counselling is essential.

3. Metastatic tumours to the choroid occur not uncommonly. The most common primary site is breast carcinoma in women and cancer of the lung in males. The appearance and course is very similar to that of choroidal melanomas. Chemotherapy and oophorectomy are sometimes successful as palliative treatment, producing temporary regression of the tumour.

TRAUMA TO THE EYE

1. Blunt trauma may cause localised oedema of the retina (commotio retinae - Berlin's oedema).

2. Blunt trauma may produce tears in the choroid.

3. A rare form of retinopathy, due to fat emboli to the retina, (Purtscher's retinopathy) is secondary to trauma elsewhere in the body, usually the chest or long bones. Multiple cotton wool spots, haemorrhages and retinal oedema are seen.

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SLIDE 100

4. Retinal tears occasionally result from a direct blow on the eye. The tears occur as a split in the retina at the ora serrata (dialysis) or as round atrophic holes in oedematous and necrotic retina. Retinal detachment may develop.

DISEASES OF THE MACULA

The macula is particularly susceptible to certain conditions which affect it and spare the remainder of the retina. These conditions may be degenerative, inflammatory or toxic, or of unknown aetiology.

1. Macular Degenerations

a) The most common disturbance of the macula is age-related macular degeneration. Patients with the condition are aged usually 60 or more. It is typically bilateral, although one eye may be involved several years before the other. There is gradually failing visual acuity for both distance and near. Mottled pigmentary changes are seen in the macula. The accumulation of cellular debris and waste products between Bruch's membrane and the retinal pigment epithelium is an important aetiological factor.

b) Another form of age-related macular degeneration is disciform degeneration of the macula. It is unilateral initially but many cases become bilateral. It is characterised by serous or haemorrhagic detachment of the sensory retina or the pigment epithelium in the macular area. Eventually fibrosis and scarring occur. Fluid or blood from the choriocapillaris permeates through Bruch's membrane and accumulates beneath the pigment epithelium. New choroidal vessels then invade this space and cause haemorrhage and fibrosis. In some cases the fluid or blood breaks through the pigment epithelium and collects beneath the retina. Laser

photocoagulation may eradicate foci of choroidal neovascularisation provided they are not within 0.4mm of the fovea centralis.

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Younger patients may be affected where there is a predisposing cause such as angioid streaks or presumed histoplasmosis.

2. Inflammatory lesions which may involve the macula have been discussed (toxoplasmosis, toxocariasis, sarcoidosis).

3. Toxic lesions of the macula

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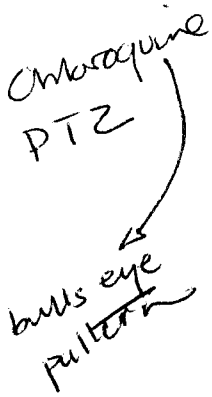
A number of important drugs have toxic effects on the retina, the most notable being chloroquine and certain phenothiazine derivatives (Thioridazine). These drugs have an affinity for the melanin of the retinal pigment epithelium and become concentrated there. Eventually pigment dispersion occurs, especially in the macular area, causing in the case of chloroquine, a typical 'bull's-eye' pattern in the macula, with a central area of increased pigmentation surrounded by a ring of depigmentation, which in turn is encircled by an area of hyperpigmentation. Degenerative changes in the rods and cones occur and central vision is impaired. The changes are related to the total cumulative dose. Before placing a patient on long-term chloroquine therapy, baseline visual functions should be recorded, i.e. visual acuity, central visual fields and colour vision. The appearance of the fundi should be documented.



4. Macular lesions of unknown aetiology

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a) Central serous retinopathy.

There is a shallow elevation of the retina in the macular area caused by clear fluid which has leaked beneath the pigment epithelium from the choroid and percolated into the subretinal space. This condition is usually unilateral, occurs typically in middle-aged patients who are under stress, and frequently undergoes spontaneous remission. The patients complain of distorted vision; however, the visual acuity is rarely worse than 6/18. The leaking source may be identified by fluorescein angiography and 'sealed' by laser photocoagulation if the condition does not heal spontaneously, or recurs.

b) Macular cysts

These occur spontaneously in otherwise apparently healthy eyes. The inner wall of the cyst may rupture to form a partial thickness macular hole. Macular holes may also be the result of trauma. Central vision is lost, but detachment of the retina rarely results from such a hole unless the patient is highly myopic with a posterior staphyloma.

Treatment of Macular Lesions

Previously treatment was not available for these macular conditions. Systemic steroids successfully reduce the inflammatory reaction in certain inflammatory conditions. With the advent of fluorescein angiography, which demonstrates discrete areas of leakage in such conditions as central serous retinopathy and certain macular degenerations, photocoagulation is sometimes helpful. Patients with macular degeneration, despite the loss of central vision, should be reassured that they will never become completely blind, although they may be unable to read or to continue working. Magnifying glasses and telescopic lenses are often helpful.

CONGENITAL ANOMALIES

Coloboma of the choroid and pigment epithelium may occur with or without coloboma of the iris. This congenital anomaly is caused by failure of differentiation of tissues along the fetal ocular fissure.