THE BOWMAN LECTURE

PAPILLOEDEMA: 'THE PENDULUM OF PROGRESS'

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London

I. HISTORICAL BACKGROUND

One year after the Battle of Waterloo, William Bowman was born into a world entering a period of dramatic change. The new age of science would see transport and communication revolutionised and the purpose of human existence shaken by Darwin's thoughts on natural selection. Surgery would benefit from the techniques of antisepsis and the first anaesthetic would be administered. In ophthalmology the description of glaucoma and the invention of the ophthalmoscope would enable the specialty to survive in its own right, with the inception of its own society.

Bowman's introduction to medicine probably resulted from an initial injury inflicted to his hand whilst experimenting with gunpowder as a boy.[1] He consulted the Birmingham Surgeon Joseph Hodgson and was so impressed by his care that he vowed to follow suit and become a doctor. Hodgson was Surgeon to the General Hospital in Birmingham,[2] but having trained in London under Travers and Lawrence, he went on to found the Birmingham Eye Hospital in 1824, which he staffed single-handedly for four years. Bowman joined Hodgson as an apprentice at the age of 16, and would probably have received his early introduction to ophthalmology at this time. Hodgson, who ultimately became President of the Royal College of Surgeons, saw his protégé dedicate his days to meticulous study, with papers on paraplegia, and influenza and diseases of the trachea and larynx.[3] An illustration by Bowman at the age of 21, of erisypelas of the trachea, shows the maturity of his work and the artistry inherited from his talented parents. He also measured the cardiac orifices for a physician and received in appreciation a gift in the form of a compound microscope. This may have been one of the crucial events in his life, for though the compound microscope was developed in the previous century, the chromatic aberration was only overcome in 1830 by Lord Lister's father, just before the gift was made to Bowman.

Thus in 1837 Queen Victoria ascended the throne, and William Bowman aged 21 entered the portals of King's College in London's Strand fully equipped to contribute to the explosion in knowledge that was about to erupt. Todd, the new Professor of Physiology at King's, was using his phenomenal enthusiasm to compile two massive books on the anatomy and physiology of the whole body.

Bowman described the voluntary and involuntary muscles[4] and their actions without formal methods of fixing or staining specimens, and no microtome. He was left deciding whether to slice or tease the fresh material, after moistening with water or syrup or salts. He added phosphoric, tartaric and citric acids to his specimens. He was the first person to use the term sarcolemma and his descriptions have survived the test of time.

He is most famous for his work on the kidney[5] and the description of Bowman's capsule, the epithelial covering of the glomerulus, which he studied in man, horse and the boa constrictor after injection of the arteries. So in addition to the variety of the tissues and the complexity of the microscopy, I am amazed at the variety of species studied, the examination, the measurement and the superb illustrations, all drawn by the investigator. Here is an incomplete list of the extent of the comparative anatomy Bowman studied: *Muscle:* eel, newt, haddock, shave, frog, boa, teal, pig, rabbit, crab, hare, lizard, horse, kitten, tipula. *Kidney:* horse, rabbit, parrot, guinea pig, boa, badger, dog, lion, cat, squirrel, tortoise, frog, eel.

It is not surprising that, after qualifying at the age of 24, Bowman was elected a Fellow of the Royal

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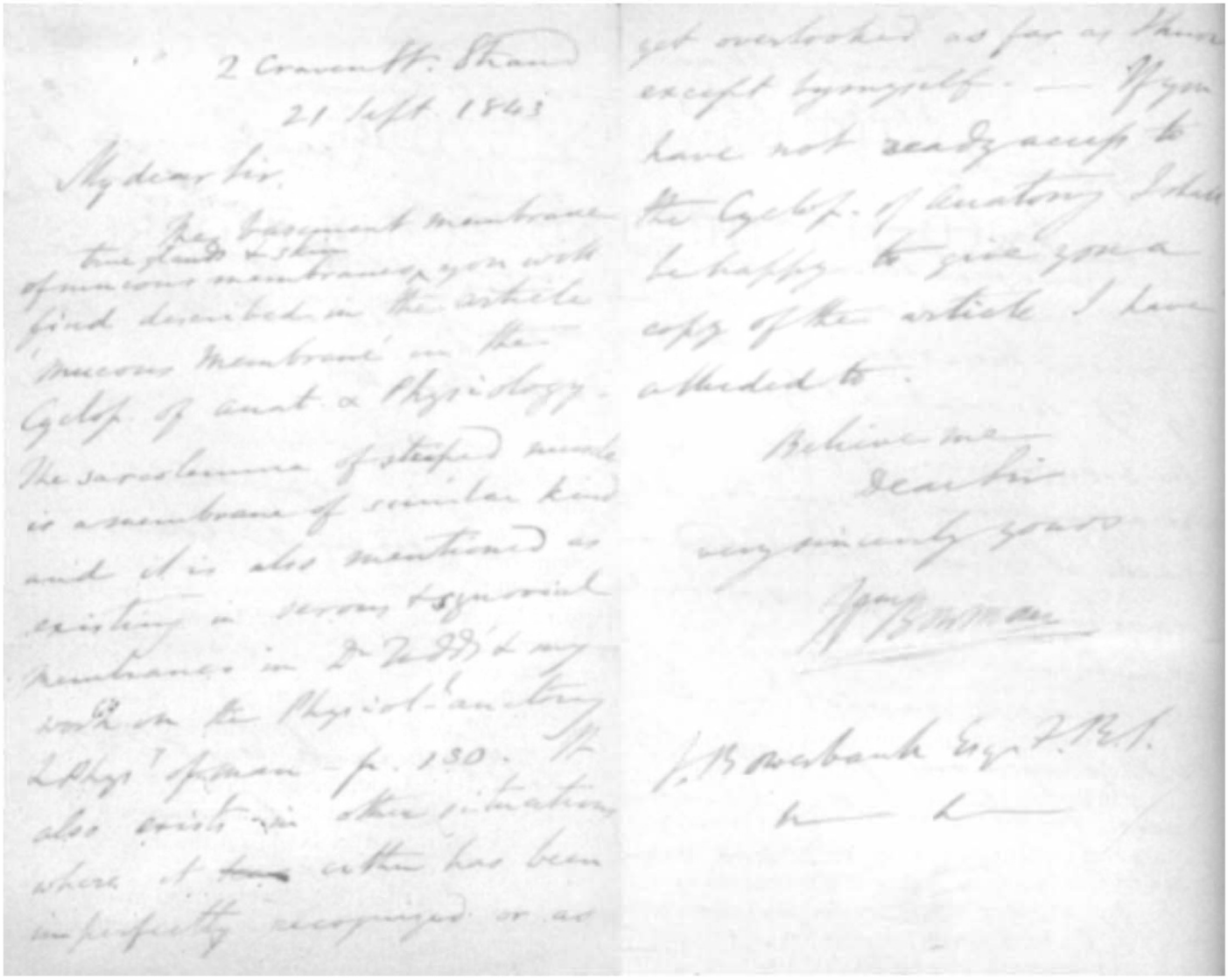


Fig. 1. *Letter by Sir William Bowman in 1843 to J. Bowerbank, FRS, discussing the basement membrane of mucous membranes.*

Society at 25 for his work on muscles and given the Royal Medal of the Royal Society for his work on the kidney at the age of 26. Whilst a Resident at High Holborn I was fortunate to purchase a Bowman letter, one of the few remaining, for the princely sum of £4 (Fig. 1). It refers to the basement membrane, a term initiated by Bowman in relation here to the mucous membranes, and alludes to the *Cyclopedia* and the *Anatomy and Physiological Anatomy of Man*, the two massive tomes compiled by Todd. The letter is written to Bowerbank, also a Fellow of the Royal Society, an amateur palaeontologist and, like Bowman, graced with a banking father. Bowman's father was also interested in botany and geology and a Fellow of the Linnean Society, and his mother a gifted painter of flowers. The hand-writing of this letter is identical to that published by James,[6] with an identical signature; but is in contrast to the hand-writing ascribed to Bowman by others.[7,8]

Bowman was appointed to the staff of the newly opened King's College Hospital in 1840 and was appointed to Moorfields in 1846. His interests now began to concentrate on the eye, where he left his eponymous imprint on the membrane in the cornea, and described the ciliary muscle, previously considered a ring.[9] In 1880 he became the first President of the Ophthalmological Society of the United Kingdom (OSUK), and in recognition of his services Sir William Gowers suggested the founding of the Bowman Lectureship, to provide the best extant information upon some subject, the endeavour being to contribute each year something real towards the advancement of knowledge for the good of man's estate, which had been Bowman's life-long ambition.[10] Gowers gave this Lecture 100 years ago and wrote the first textbook on medical ophthalmology,[11] with early illustrations of papilloedema and ischaemic optic neuropathy. The ophthalmoscope was

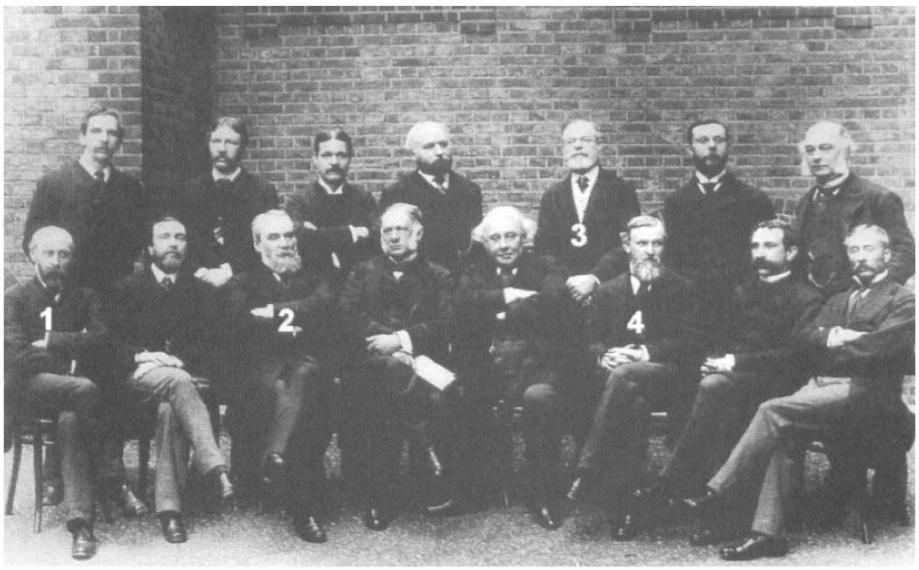


Fig. 2. *Staff at the National Hospital, Queen Square in 1915, showing Marcus Gunn (1), Sir Hughlings Jackson (2), Brudenel Carter (3) and Sir William Gowers (4).*

greeted most enthusiastically by physicians and neurologists for the detection of hypertension and brain tumours, and the early staff of the National Hospital were part of this vanguard (Fig. 2). The great Sir Hughlings Jackson, who was both President of the OSUK and Bowman Lecturer, counted it the luckiest thing in his medical life that he began the scientific study of his profession at an ophthalmic hospital, for 'there', he said, 'one has the opportunity of being well disciplined in exact observation'.[10]

Hughlings Jackson and Gowers persuaded the National Hospital to appoint two ophthalmologists to the staff to use the new instrument. Marcus Gunn was appointed, being both President and Bowman Lecturer of the Society, and Brudenel Carter, who elegantly graced the stage of London ophthalmology and will be mentioned later.

The great father of ophthalmic genetics, Edward Nettleship, was both a President of the OSUK and Bowman Lecturer, and contributed to the subject of this present Bowman Lecture by describing early reports of papilloedema[12] and giving the first description of choroidal folds in papilloedema.[13]

Sir William Bowman would be proud that his Society (the OSUK) has become a Royal College, but probably less enthusiastic about being dislodged from his lofty perch on the representative armorial bearings.

I accept the distinction of being asked to give the 57th Bowman Lecture as a great personal gesture, but also as a tribute to the role of a clinician with an academic interest, and to the role of neuro-ophthalmology in the future of modern ophthalmology. Having read with respect, fascination and humility many of the previous lectures, my thoughts over the past months have veered from Sir Isaac Newton's comment:

> If I have seen a little further,
> It is because I have stood on the shoulders of giants.

to Tennyson's poem:

> The other follies reach us not;
> Nor much their wisdom teaches,
> And most of sterling worth is what,
> Our own experience preaches.

Tennyson was painted by G. F. Watts, who was a friend and patient of Bowman and Bowman owned the painting, which subsequently became known as the Bowman Tennyson.[14,15] One of the significant paintings of Bowman was also painted by G. F. Watts.

II. PAPILLOEDEMA

Guarding the entry and exit of neuronal and vascular elements to and from the eye, the lamina cribrosa comprises two to three hundred pores of varying sizes in a collagen matrix.[16–18] A vascular system consists of an arterial circle of Zinn, producing arterioles of variable pattern that perfuse the lamina cribrosa[19,20] (Fig. 3) with a venous exit in the central retinal vein. One million nerve fibres traverse this area and as the neurones emerge they acquire a myelin sheath. This area is probably the site for the neuronal damage in glaucoma,[21,22] the site of central retinal artery and vein occlusions and of all cases of disc oedema.[23] The optic disc is therefore an area of extreme importance to a wide body of ophthalmologists and merits our meticulous attention.

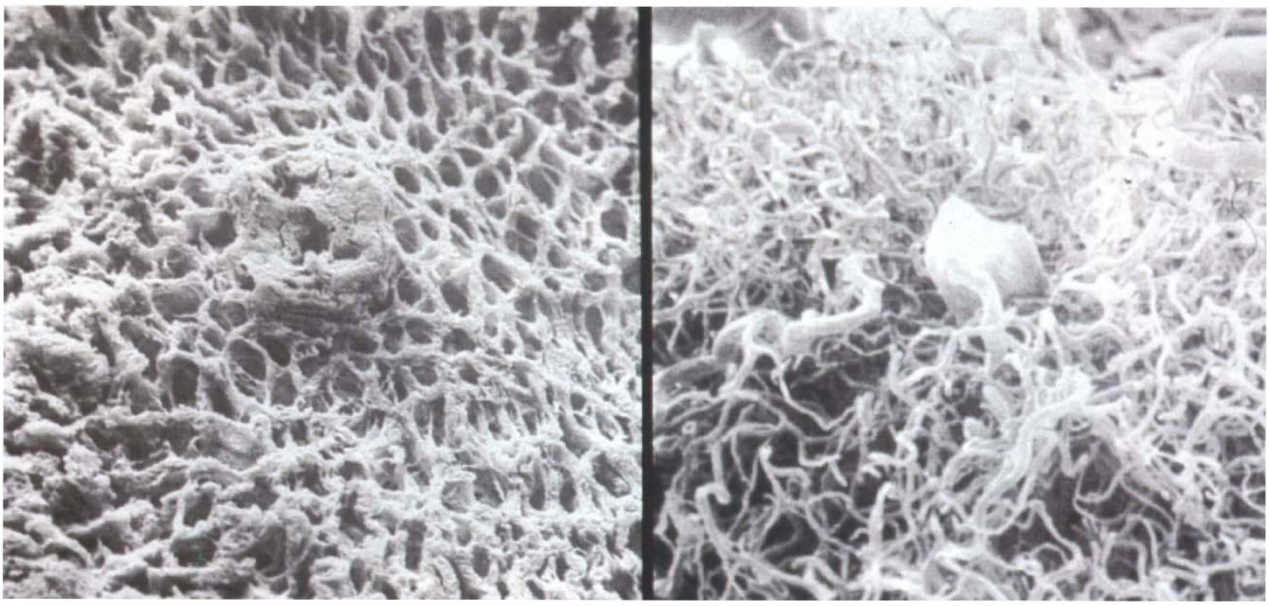


Fig. 3. *The lamina cribrosa and pores (courtesy of Prof. B. Tengroth) and a methacrylate cast of the microcirculation (courtesy of Miss Jane Olver).*

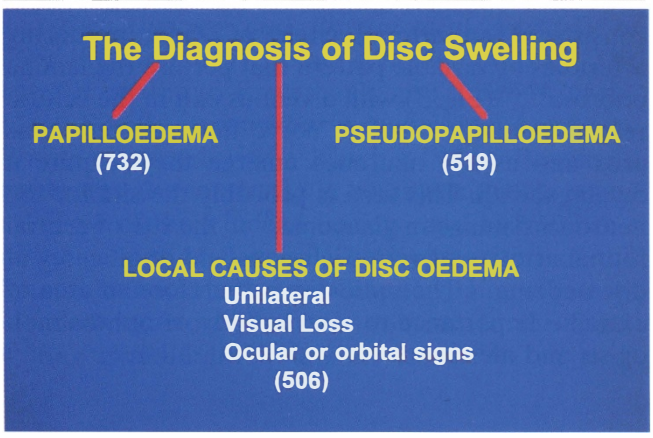
This lecture will consider papilloedema, which I would like to consider in the general context of optic disc swelling, because all ophthalmologists are confronted at some time with the swollen disc.

DIFFERENTIAL DIAGNOSIS

Papilloedema has to be differentiated from pseudo-papilloedema, which is a benign often congenital source of disc swelling mimicking papilloedema,[24] and local causes of disc oedema, which tend to be unilateral, to be associated with visual loss and to have other orbital or ocular signs, due to varied pathology in the laminar and retro-laminar region. A fundus camera installed at the National Hospital in Queen Square, London in 1963, has enabled us to record 732 cases of papilloedema, 519 cases of pseudo-papilloedema and 560 cases of local causes (Table I).

Disc swelling on presentation should be considered in terms of: (1) papilloedema, (2) pseudo-papilloedema, (3) local causes of disc oedema (Table I) and appropriate investigations instigated. It is convenient in medicine to have a single diagnosis, but when these conditions overlap diagnosis is more exacting.

Table I. The diagnosis of disc swelling



Pseudo-papilloedema

Of our 519 cases of pseudo-papilloedema, the great majority were due to small anomalous discs, but drusen was responsible in 124 cases. Pseudo-papilloedema may reflect differing morphological appearances (Fig. 4), with small hypermetropic discs with no physiological pit and congenitally tortuous vessels, myopic discs that are asymmetrical, with prominent nasal tissue often leaking fluorescein. Patients presenting with headaches, vomiting and swollen discs are a problem to neurologists and ophthalmologists.

A 14-year-old girl presenting with headaches, swollen discs and a haemorrhage was admitted to the National Hospital. Her cerebrospinal fluid (CSF) pressure was normal and 1 month later the haemorrhage had cleared, leaving a swollen disc (Fig. 5). Two years later the first signs of drusen appeared, with some extension over the ensuing year. Thus buried drusen may become exposed and may bleed, either superficially or under the retina, and may be indistinguishable[25] from early papilloedema. Buried drusen do not, however, show dilated capillaries in the earlier phases of fluorescein angiography, though they show irregular late leakage.[26] Exposed drusen appear as large refractile white globules on the surface of the disc, shown best with retro-illumination. The discs are always small,[27] never have physiological cups and have the central emergence of vessels, which are often anomalous. Drusen occur in the pre-laminar region, represent altered axonal function[28] and show calcification; thus Tso[29] sug-

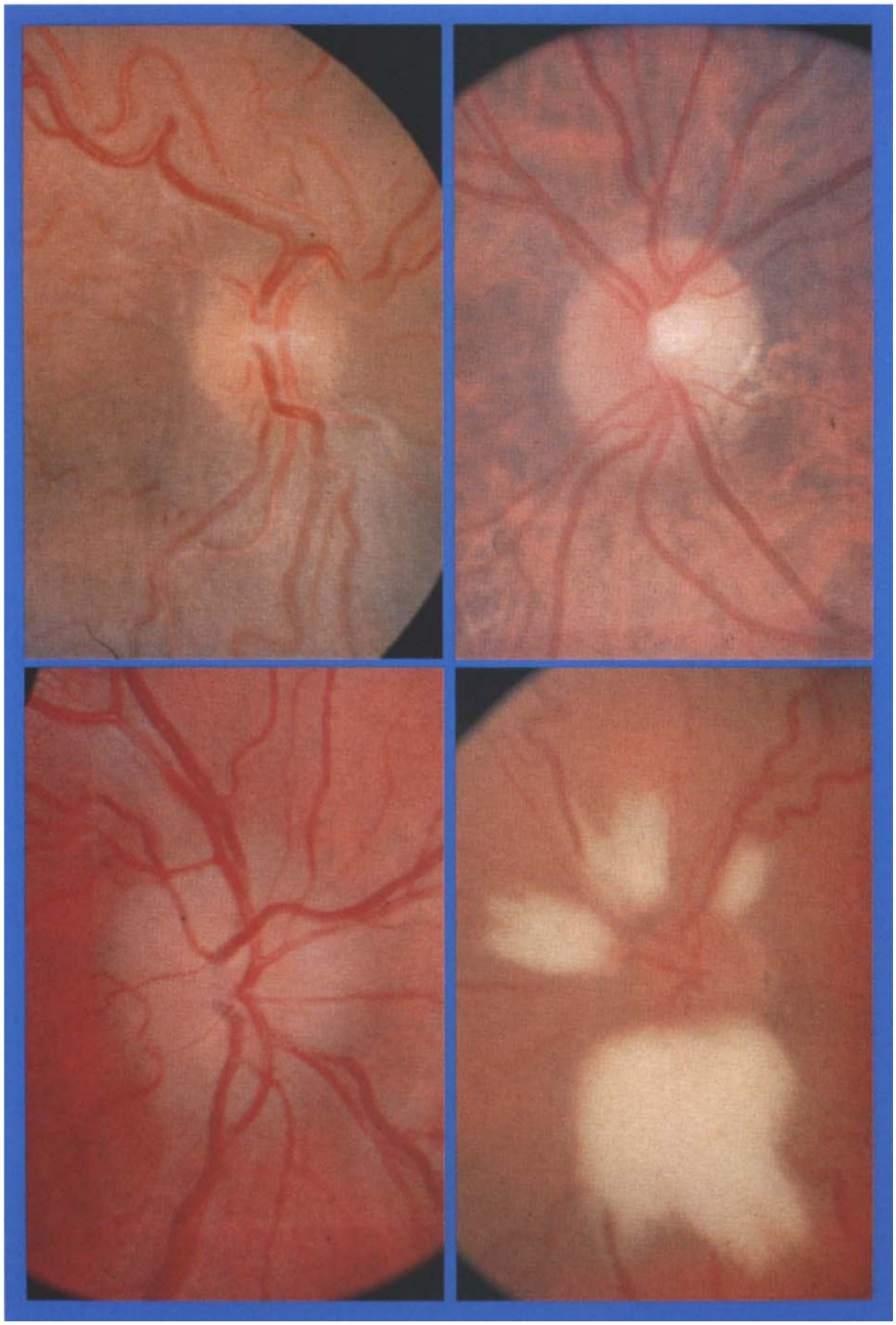


Fig. 4. *Pseudo-papilloedema. Top left: Small hypermetropic disc, with no pit and tortuous vessels. Top right: Myopic disc – a large disc with nasal fullness that often leaks fluorescein. Bottom left: Buried drusen, full and swollen disc with no pit, central emergence of vessels and late fluorescein leakage. Bottom right: Disc partially obscured by myelinated fibres.*

gested that they were due to deranged axons, with calcification of extruded mitochondria. There is only one pathological study of buried drusen,[30] which suggested that drusen seem to develop in perivascular spaces, and thus originate from the leakage of plasma constituents such as protein into the extravascular spaces with progressive calcification. The precise cause of drusen is unknown, but calcification when seen elsewhere in the central nervous system (CNS) is related to vessels, and extrusion of mitochondria from axons is not reported.[31] The diffuse leakage of fluorescein also suggests increased vascular permeability.

Local Causes of Disc Oedema

Local causes of disc oedema represent a wide variety of retrobulbar conditions – some systemic, some local – where in contrast to papilloedema the visual morbidity is high. They include inflammation, either within the eye or in the disc or the distal optic nerve; vascular conditions, either arterial or venous; tumours of the nerve or sheath; and infiltrations

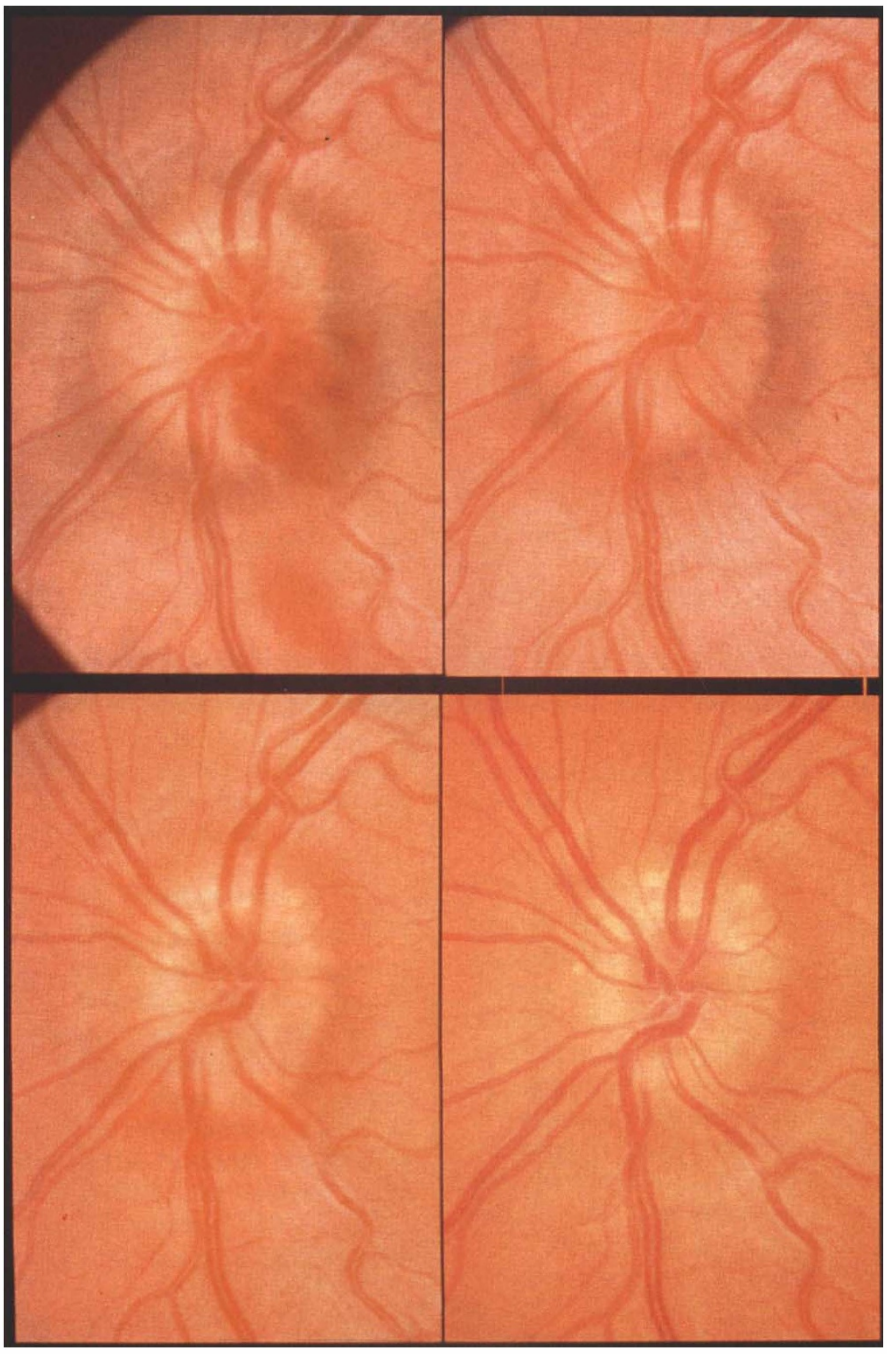


Fig. 5. *Drusen of the disc. Top left: Small disc with no cup, presenting with superficial haemorrhage. Top right: One month later this has cleared. Bottom left: Exposed drusen are seen developing 2 years later. Bottom right: After 3 years further increase in size of the drusen is visible.*

such as sarcoid, lymphoma, carcinoma and leukaemia (Table II).

The range and pattern of optic disc swelling is necessarily limited by the anatomical structure of the disc, the nature and mechanism of the imposed insult and the potential for swelling. Thus history, fields and full examination usually provide the vital diagnostic information. Major visual loss and pain on eye movements, with mild disc oedema, characterises optic neuritis, whereas sudden painless visual loss with asymmetric disc swelling characterises ischaemic optic neuropathy. Similarly, chronic

Table II. Local causes of disc oedema

INFLAMMATORY	Uveitis Papillitis
VASCULAR	Ischaemic Optic Neuropathy CRV Occlusion
TUMOUR	Primary or secondary of nerve or nerve sheath.
INFILTRATIONS	Sarcoid, Lymphoma, Carcinoma, Leukaemia
HAMARTOMAS and ANGIOMAS	

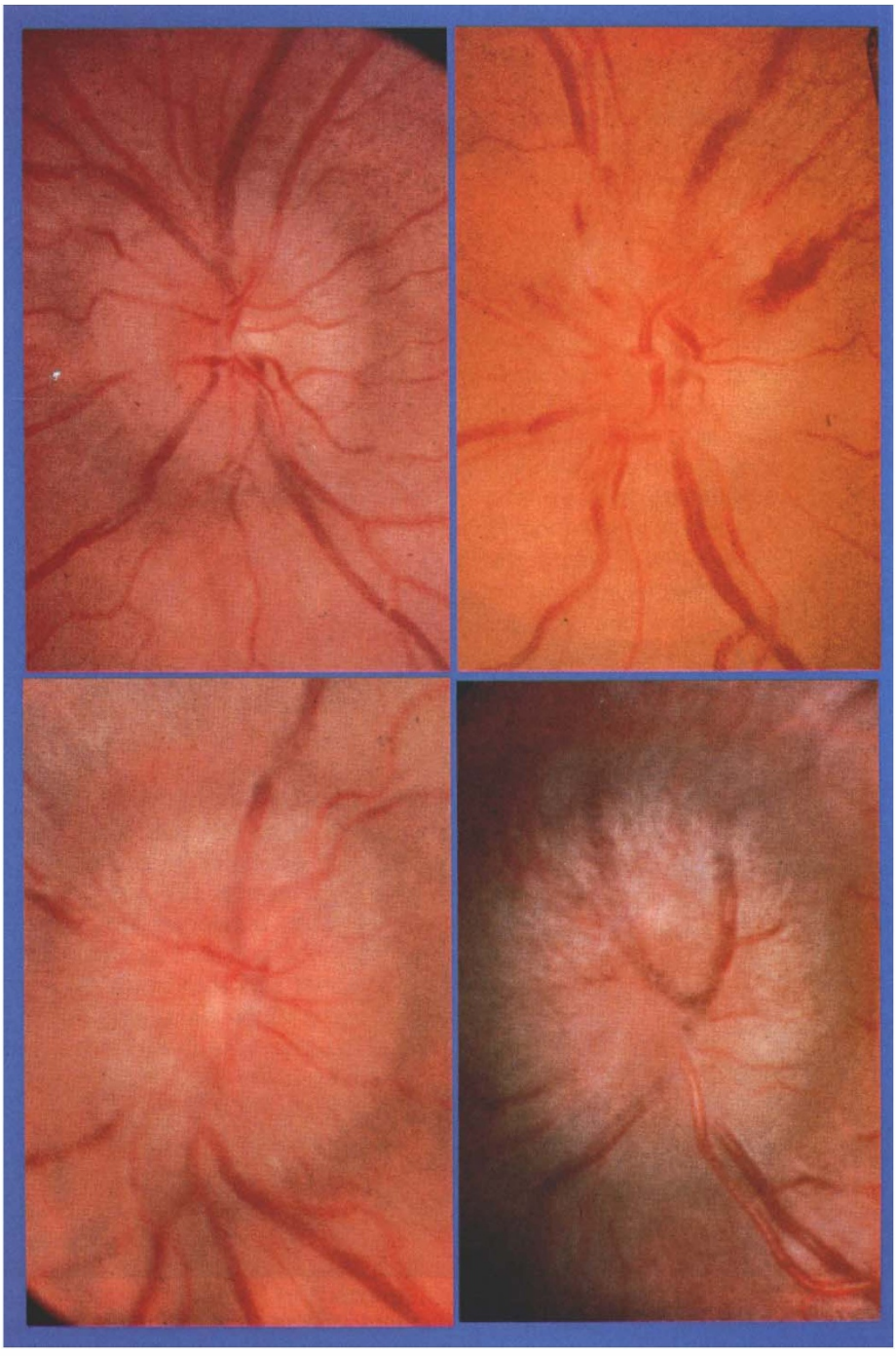


Fig. 6. *Local causes of disc swelling. Top left: Ischaemic optic neuropathy with sudden altitudinal loss and diffuse disc swelling with one or two haemorrhages. Top right: Optic neuritis. Sudden visual loss and pain on eye movements with diffuse low-grade disc swelling. Bottom left: Chronic disc swelling and visual loss due to optic nerve glioma. Bottom right: Sarcoidosis.*

disc swelling may be identical whether due to sarcoid or an optic nerve glioma, and radiological and medical studies are necessary to indicate the precise cause (Fig. 6).

Vascular Conditions. Reduction of perfusion in the laminar region produces disc swelling, whether it is due to either arterial or venous involvement. Optic disc oedema due to presumed arteriolar constriction of the laminar vessels in a patient with accelerated hypertension and a blood pressure of 240/140 mmHg is demonstrated in Fig. 7 (top). In contrast, a patient with a central retinal vein occlusion also has marked disc swelling but with leakage extending into the macula (Fig. 7, bottom). Reduction of perfusion pressure below a critical level therefore produces disc oedema whether arteriolar[32,33] or venous in origin.[34] In the most severe form of ischaemic optic neuropathy, that is with giant cell arteritis, pallid swelling of the discs is diagnostic, with a paucity of

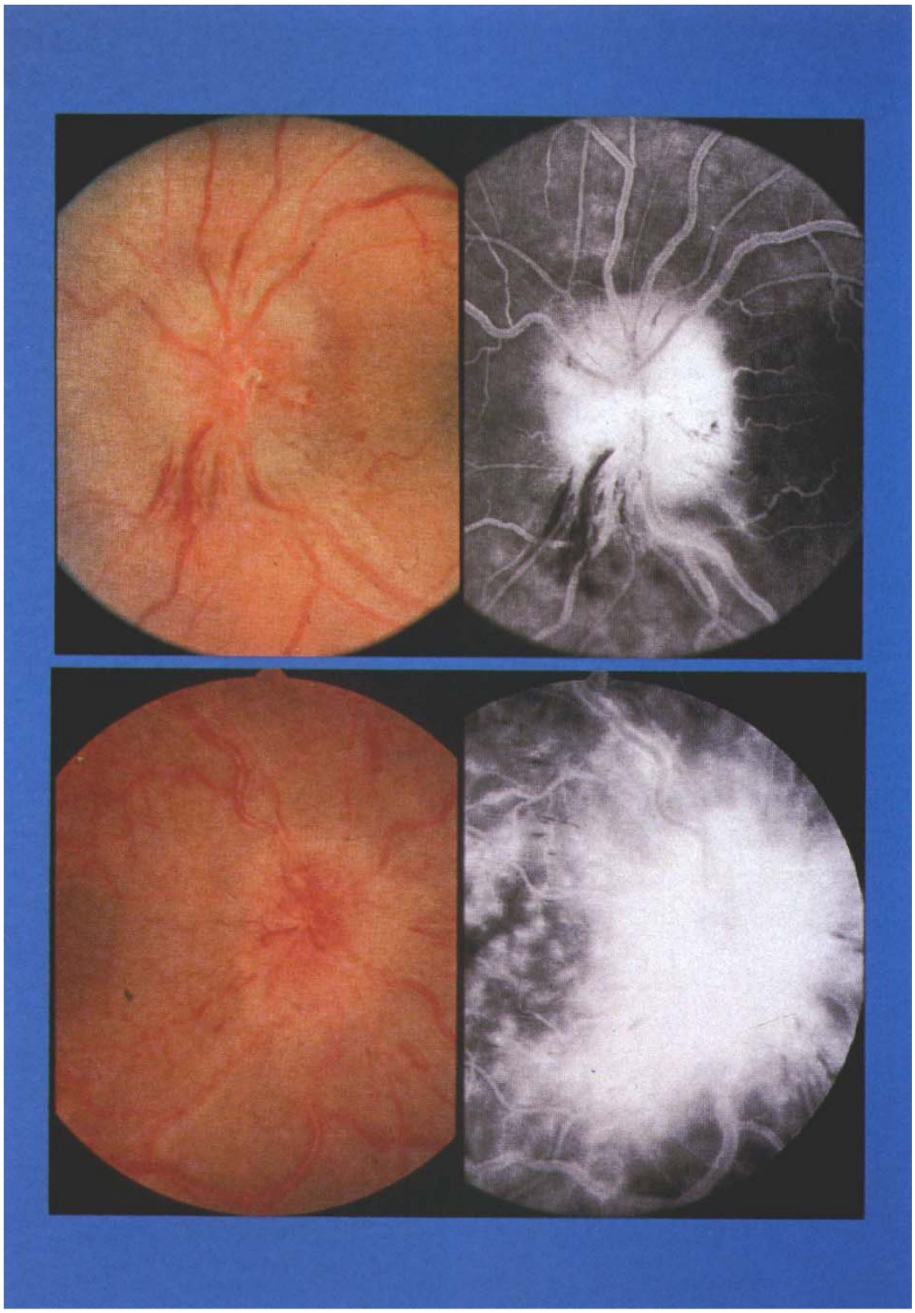


Fig. 7. *Vascular causes of disc oedema. Top: Disc oedema due to arteriolar disease of the laminar vessels in accelerated hypertension. Bottom: Venous occlusion in the proximal portion of the intraneural central retinal vein producing marked disc swelling with fluorescein leakage extending into the retina.*

dilated capillaries on the disc surface. Profound visual loss occurs and often a characteristic peripapillary infarct. Several pathological studies have provided localisation to the retro-laminar region and I am indebted to Barry Cullen for a study of the pathology of arteritic ischaemic optic neuropathy. Disc swelling is visible with inflammation of the short ciliary arteries, and a retro-laminar infarct is precisely localised to the retro-laminar region (Fig. 8). Thus local disc oedema is always due to laminar or retro-laminar ischaemia, inflammation or infiltration and is of localising value.

The aetiology of papilloedema has been debated over the years[35–37] and I would like to describe the salient features of this very large National Hospital series, which includes photography of all patients and fluorescein angiography of the majority. We have found fluorescein angiography a useful adjunct for both diagnosis[38] and continued observation. I will then present a classification and describe some of the visual problems and correlate them with the pathology. Finally I will explore the factors determining the pathogenesis of papilloedema.

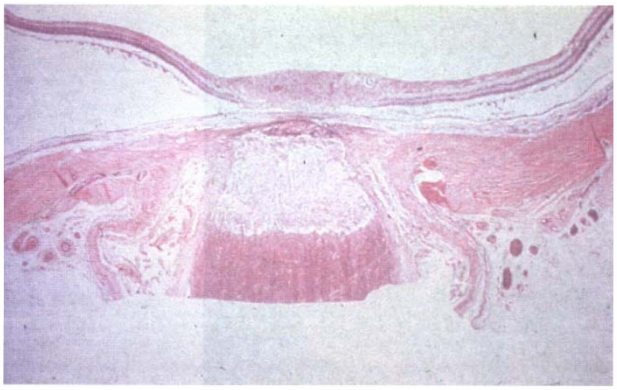


Fig. 8. *Arteritic ischaemic optic neuropathy. Disc swelling due to a retrolaminar infarct in giant cell arteritis. Note the inflammatory changes in the ciliary arteries. (Courtesy of Mr B. Cullen.)*

CLASSIFICATION

Staff at the National Hospital have contributed to the subject and[10,39–41] the first classification of papilloedema was by one of my predecessors, Marcus Gunn, in the *British Medical Journal* in 1907.[42] My tutor, mentor and friend Bill Hoyt arbitrarily classified papilloedema in his book on *The Ocular Fundus in Neurologic Disease*.[43]

In 1969 at the Ophthalmological Society of the United Kingdom[44] I presented 69 cases using a classification which I think is of value: early, acute, chronic, vintage and atrophic. The non-medical term 'vintage' is to highlight this important though rare sub-group. A woman patient was first seen at the High Holborn branch of Moorfields Eye Hospital in 1964 with swollen discs and small white superficial punctate dots on the disc and debate ensued as to whether this was papilloedema or drusen. She was admitted to the National Hospital, her meningioma removed and surprisingly her vision improved, the disc swelling subsided and the white spots disappeared. Similar diagnostic dilemmas have been faced by others.[45]

To emphasise the longevity and gravity of the condition, the terminology of 'antique' or 'baroque' papilloedema was discussed with Professor William Hoyt, but the final choice was 'vintage', with its convivial associations, and an illustrious beverage emanating from the town of Oporto in Portugal.

Early Papilloedema

Early papilloedema is disc swelling without haemorrhages or exudates (Fig. 9a). Sixty-six cases were seen with good vision (98% had a visual acuity of 6/9 or better), CNS tumours were a prominent cause (54%), obscurations occurred (20%), and CSF pressure was elevated (with an average of 300 mm H_2O) (Fig. 9b). Visual acuity is good in papilloedema, visual fields are normal, and enlargement of the blind spot an early and diagnostic feature. Other important signs are nerve fibre opacification around the disc, mild oedema and prominent veins with diminished or absent pulsation. Fluorescein shows dilatation of the disc capillaries in the arterial phase and residual leakage of dye after 10 minutes, occurring maximally above, below and nasally.

Acute Papilloedema

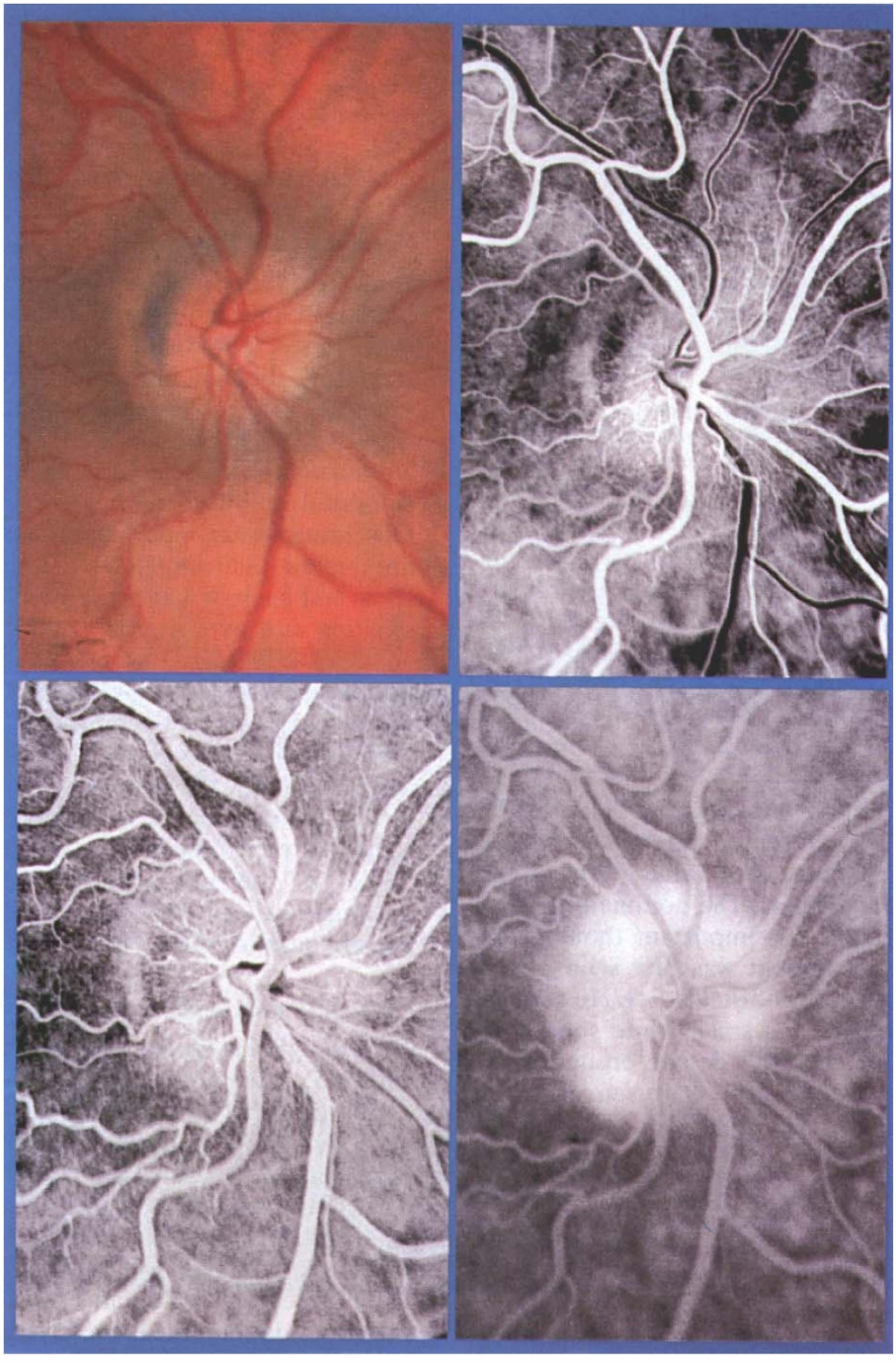
Acute papilloedema demonstrates signs of decompensation; this enables rapid diagnosis and was seen in 57 cases. The vision is again good (90% better than 6/9), benign intracranial hypertension a frequent cause (38%), and a wide variety of other causes (38%) outnumber CNS tumours (19%). Vascular problems such as haemorrhage (extra- or sub-dural or intracerebral) are usually responsible. Obscurations are more common and CSF pressures are higher (380 mmH_2O). Numerous cotton wool spots and haemorrhages are visible with marked disc swelling and extensive dilatation of the superficial capillaries (Fig. 10). In some patients pale linear prearteriolar transudates (PRATs) are visible and perivascular fibrin deposition can be seen on pathological examination. There is extensive leakage around the disc on fluorescein angiography but this never extends to the macular region. The visible signs therefore represent decompensation of perfusion to the pre-laminar tissues, with vascular decompensation (haemorrhages) and neuronal decompensation (infarcts).

Chronic Papilloedema

Chronic papilloedema provides the largest group, with 555 cases in our series. Vision is still good (90% better than 6/9), CNS tumours (43%) and benign intracranial hypertension (42%) are the predominant causes and obscurations are common (62%). Disc perfusion just suffices, so that there are usually no haemorrhages or exudates; a capillary plexus derived from retinal vessels is visible on the disc surface (Fig. 11). Fluorescein angiograms show dilated capillaries, with often indolent leakage confined to the disc.

Vintage Papilloedema

Vintage papilloedema is rare, with 22 cases in our series. Signs of visual loss are apparent, with 86% having a visual acuity of 6/9 or better but 10% having vision of 6/24. Slow-growing CNS tumours are a preeminent cause (87%) and obscurations are almost the rule (75%). The characteristic features are small punctate white dots, resembling drusen and indicating long-standing neuronal degeneration (Fig. 12). The dots are smaller than drusen, lie in the nerve fibre layer, are not shown on a CT scan and resolve if the raised intracranial pressure is controlled. Long-standing compensatory vascular changes are also seen deflecting venous return from the central retinal



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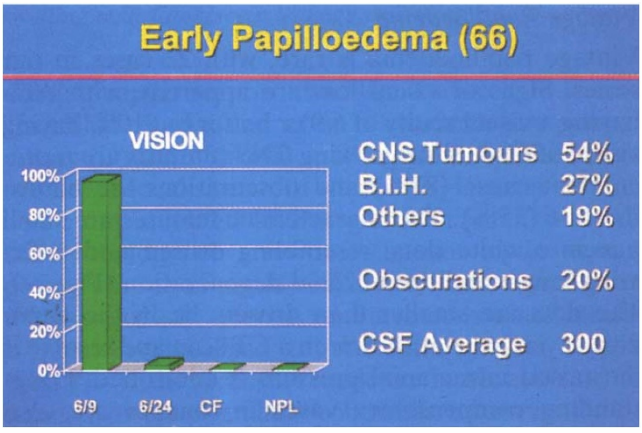
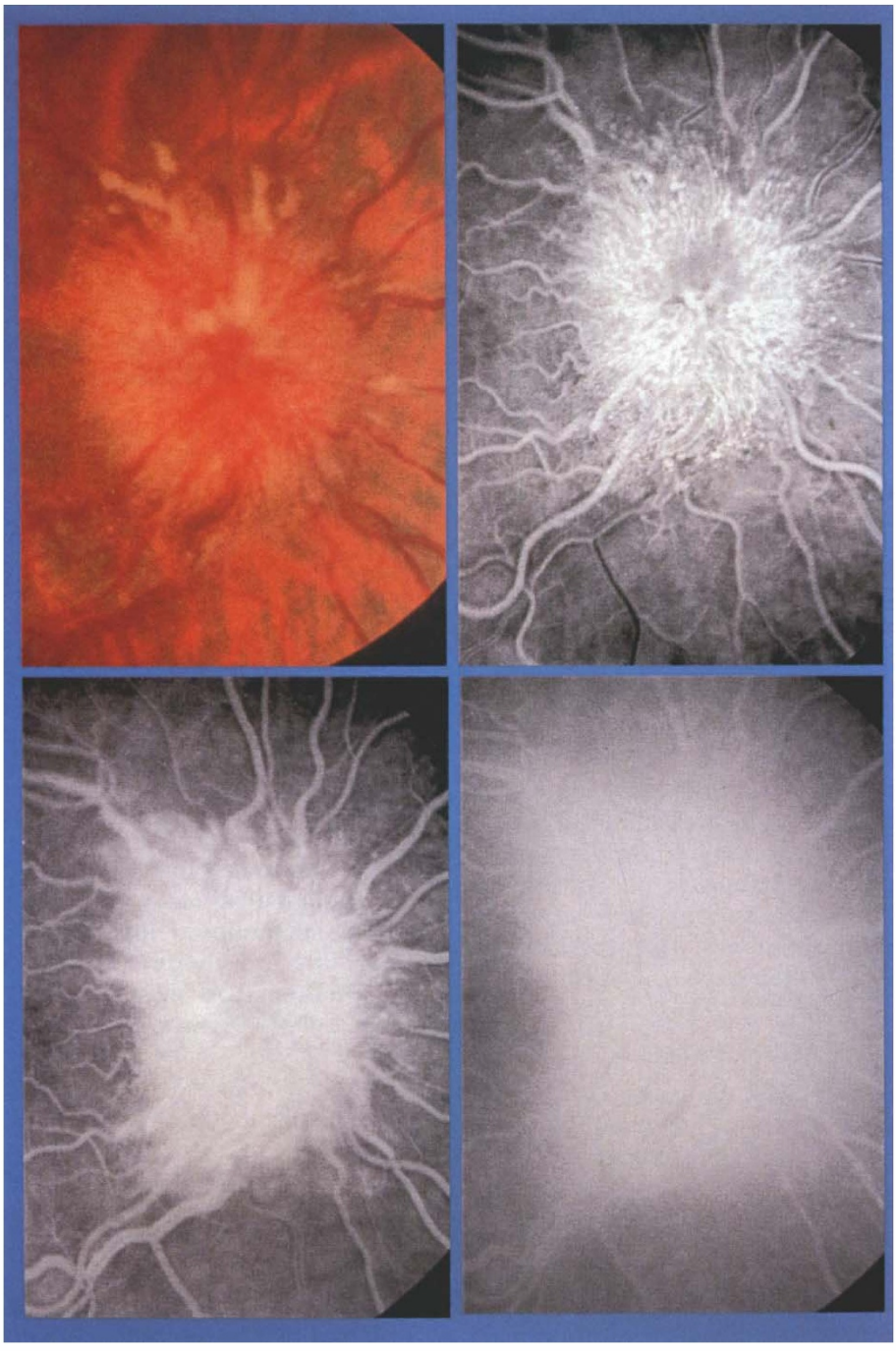


(b)

Fig. 9. *Early papilloedema. (a) Mild disc swelling, peripapillary neuronal swelling and hyperaemia (top left). Early fluorescein angiogram to show dilated capillaries (top right). Venous phase with early staining of disc (bottom left). Residual photograph at 10 minutes showing late leakage of fluorescein and indicating breakdown of the blood retinal barrier. (b) Table of early papilloedema (66 cases).*



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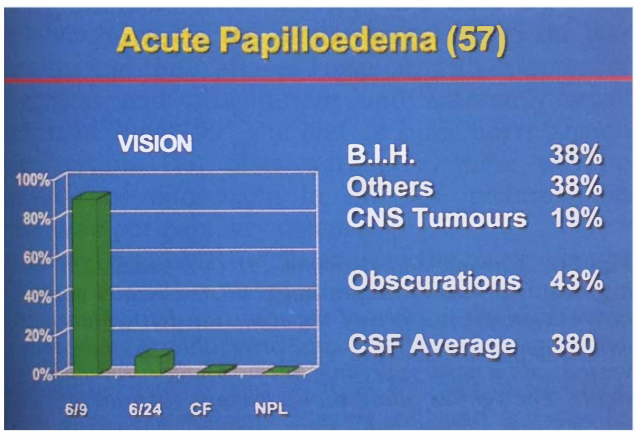
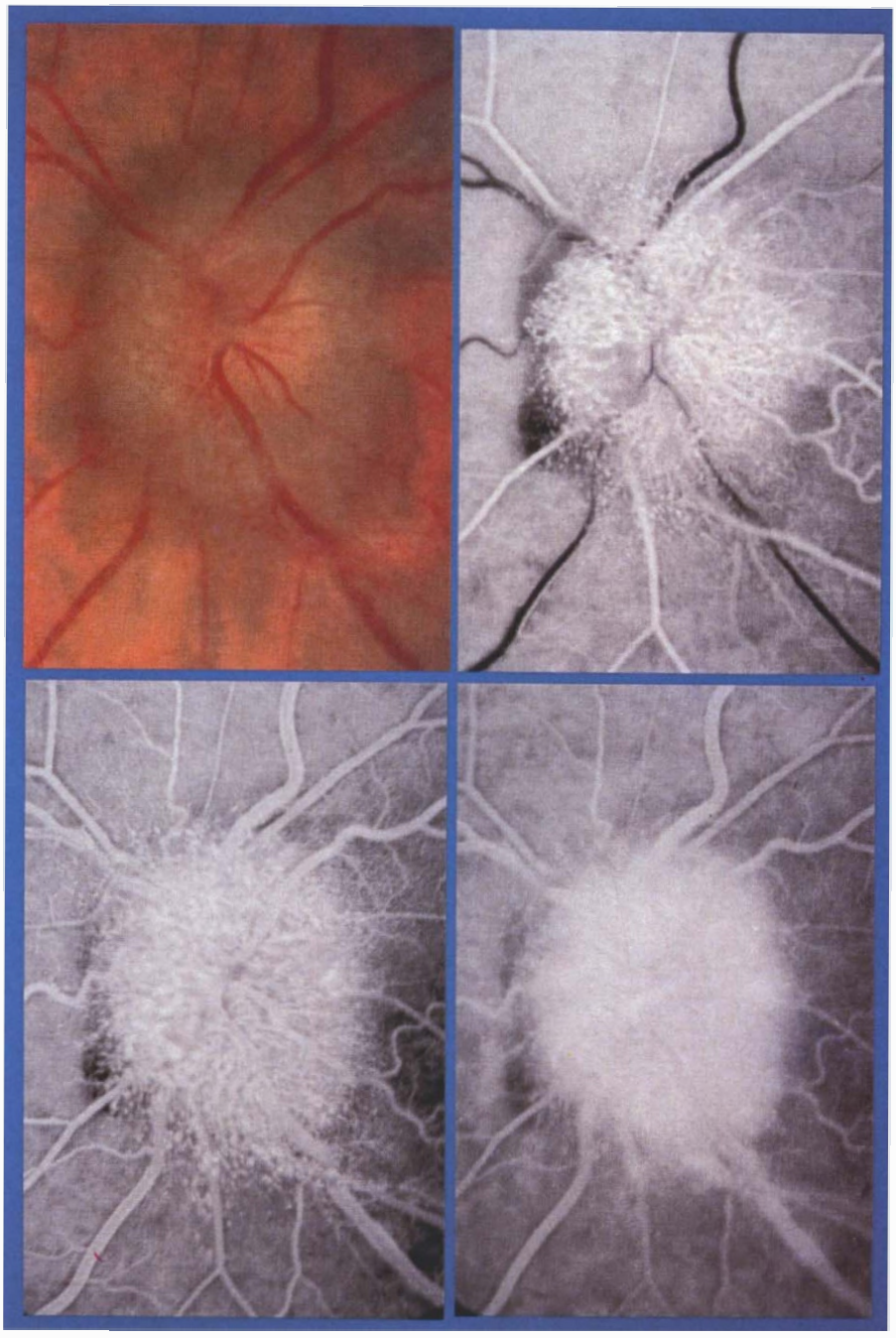


(b)

Fig. 10. *Acute papilloedema. (a) Acute neuronal decompensation with cotton wool spots and some preretinal arteriolar transudates (top left). Fluorescein angiography shows marked capillary dilatation (top right) more marked in the venous phase (bottom left) and marked leakage in the 10 minute residual photographs (bottom right). (b) Table of acute papilloedema (57 cases).*



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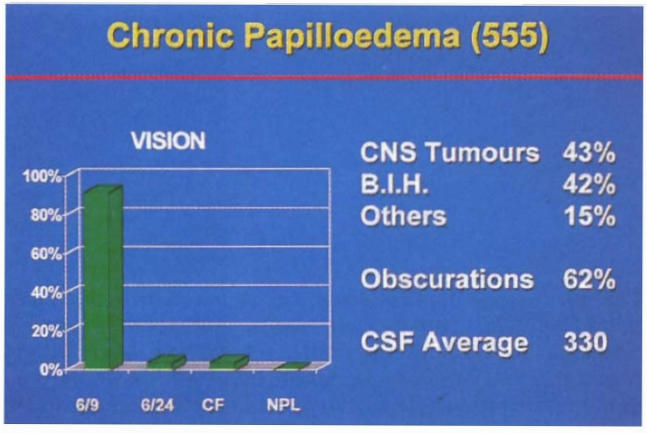
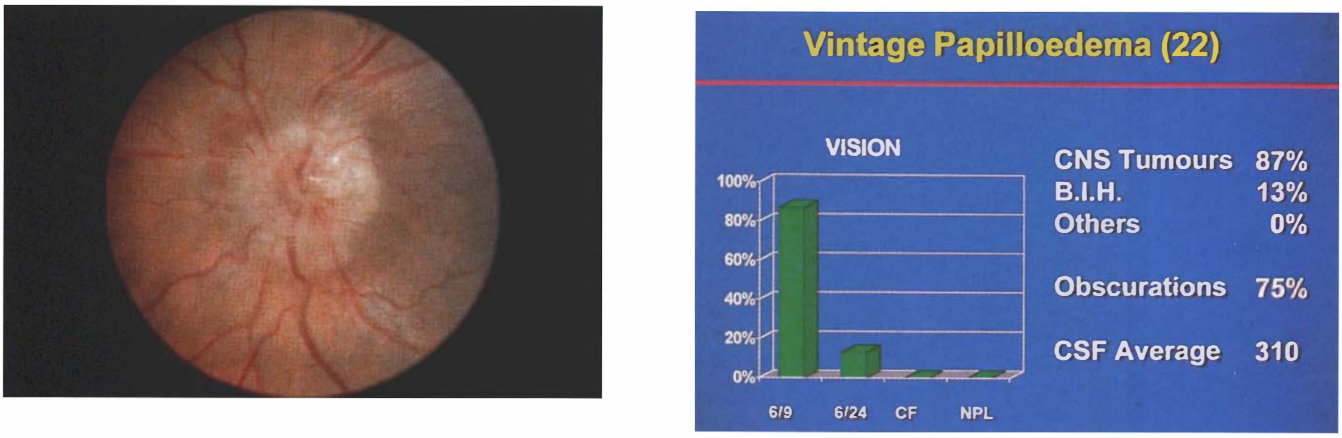


(b)

Fig. 11. *Chronic papilloedema. (a) Low-grade disc swelling, with no haemorrhages but a dilated retinal capillary network on the surface of the disc (top left). Fluorescein angiography shows dilated capillaries filling from the retinal vessels, and a nasal subretinal haemorrhage is revealed (top right). The venous phase shows leakage (bottom left) and the residual photographs show defined leakage (bottom right). (b) Table of chronic papilloedema.*



(a) (b)

Fig. 12. *Vintage papilloedema. (a) Multiple small white nodules on the surface of the disc, indicating chronic neuronal degeneration. A nasal subretinal haemorrhage is visible. (b) Table of vintage papilloedema.*

vein to the choroidal system (retino-choroidal collaterals). Vintage papilloedema continues to be misdiagnosed as drusen, so close scrutiny is necessary.

Atrophic Papilloedema

Atrophic papilloedema is a sign of diagnostic or therapeutic failure and fortunately rare, contributing only 32 cases in our series. Vision is devastated, with almost half the patients having vision of 6/36 or worse. Benign tumours (29%) and benign intracranial hypertension (38%) are the predominant causes, and most surprisingly obscurations can still occur (15%) despite the absence of disc oedema. The CSF pressure remains very high (365 mmH_2O), indicating the failure of treatment. There are two points to note. Firstly, if the degree of disc swelling reaches such proportions as to exceed the blood supply, then whatever intervention is used, atrophy is likely to develop. Thus, marked disc swelling must be treated with urgency. Secondly, most patients progress slowly over a year to the atrophic state, but, despite marked pallor, visual recovery is still possible.

A 48-year-old woman had headaches in 1990, normal vision and a CSF pressure of 420 mmH_2O. Benign intracranial hypertension was diagnosed and in 1992 the vision was diminishing. In 1995 she was first seen at the National Hospital, with episodes of fogginess and obscurations and extremely small fields. In June 1995 she had an optic nerve sheath fenestration. Her discs were pale, there was no leakage of fluorescein in the late pictures, but extensive peripapillary damage.

T2-weighted MRI scans showed the nerve sheaths filled with CSF, an expanded sella and CSF visible around the optic nerves on axial scans. Postoperatively at 1 week, there was CSF diffusing into the medial part of the orbit, at the site of fenestration. The obscurations disappeared and a dramatic improvement occurred in the visual fields, with trebling in size of the I4 isoptres (Fig. 13). Expansion of the fields may be dramatic and immediate and occurs in the contralateral eye as well, suggesting a general reduction in CSF pressure. Thus improved retro-laminar perfusion, even with pale and flat discs, may produce some visual rewards.

The pale flat disc, and the presence of obscurations, suggest that the site of axonal disturbance involves laminar or retro-laminar perfusion, rather than the more anterior layer of the disc. It is interesting to speculate on the efficacy of the drainage procedure of the optic nerve sheath, and compare it with the rarity of improvement after glaucoma drainage surgery.

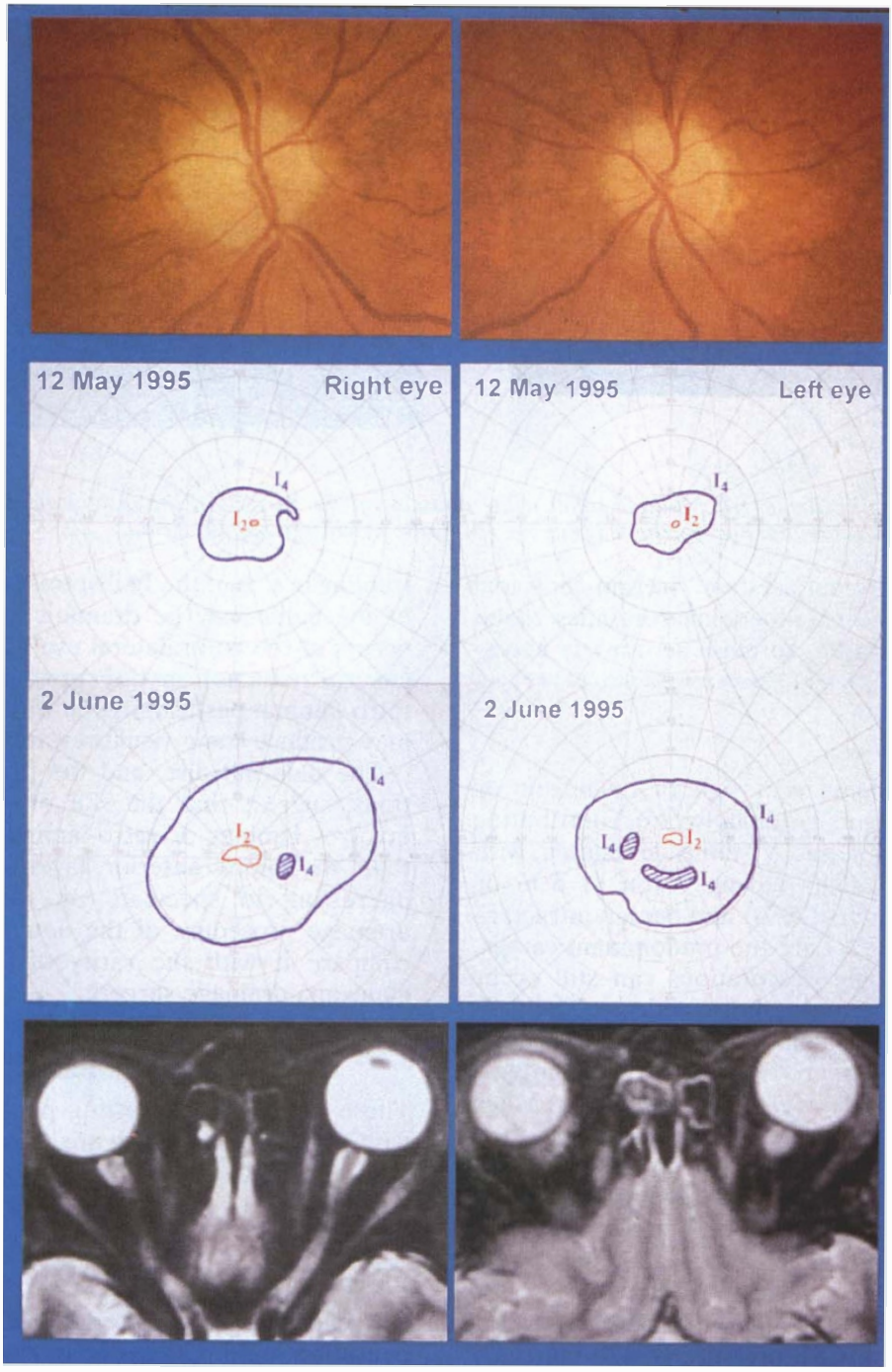
CLINICAL FEATURES

There are some interesting phenomena associated with papilloedema which are of diagnostic value but also contribute to our thoughts on the pathogenetic mechanisms.

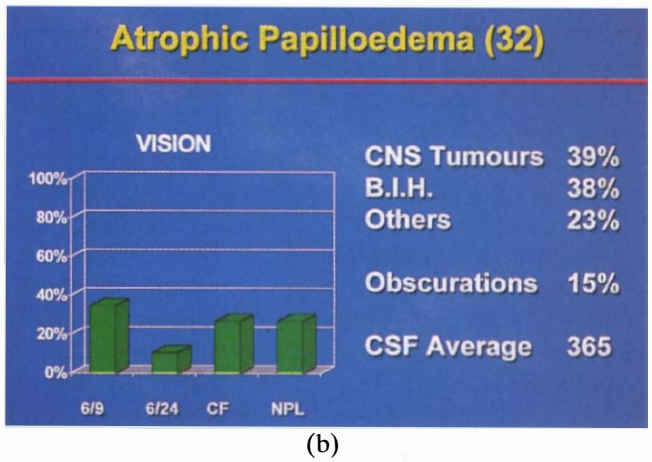
Vascular Changes

Vascular changes occurred either with acute decompensation in 36 patients or as chronic long-standing compensatory changes in 13 patients (Fig. 14). These findings are of particular importance in relation to the pathogenesis of papilloedema, as they indicate elevation of retinal venous pressure as a subsidiary rather than as a primary factor.[46]

The *acute changes* consisted of central retinal vein occlusion in 8 patients, usually with very high CSF pressures and often with metastatic cerebral disease.[47] The remainder had small punctate haemorrhages scattered in the mid-periphery and peripheral retina (28 cases). Therefore significant signs of elevated retinal venous pressure may occur in papilloedema, in addition to the frequent finding of venous dilatation, venous tortuosity and absence of pulsation.



(a)



(b)

Fig. 13. *Atrophic papilloedema. (a) Pale discs without disc swelling and peripapillary irregularity are seen (top). Visual fields are shown prior to nerve sheath decompression (top) and after nerve sheath decompression (below). T2-weighted MRI scans of optic nerves show CSF in the subarachnoid space before surgery (bottom left) and CSF leaking into the medial part of the orbit after optic nerve sheath decompression (bottom right).*

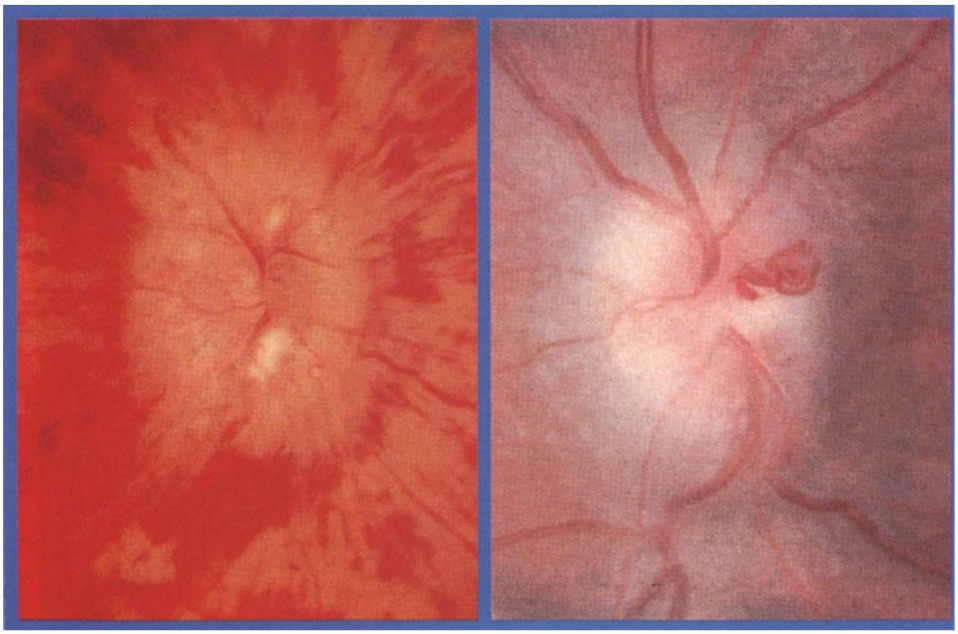


Fig. 14. *Signs of elevated central retinal venous pressure. Left: Central retinal vein occlusion. Right: Chronic papilloedema with pallor and multiple nasal retino-choroidal collaterals.*

The *chronic changes* consisted of retino-choroidal collateral vessels, which occurred in 13 patients and serve to confirm and remind us that raised retinal venous pressure occurs in papilloedema.[48] Previously termed optico-ciliary shunts these vessels are in fact collaterals between the central retinal vein and the choroidal veins and indicate past disc oedema. They are usually associated with central retinal vein occlusion, but are also seen with distal nerve sheath meningiomas,[49] distal optic nerve gliomas[50] and drusen of the disc.[51] The presence and size of the collateral vessels depend on the CSF pressure in the dilated optic nerve sheath, so that when the pressure is high they are functioning and when the pressure is low they disappear.[52,53] The fact that so few patients developed these collaterals suggests the rarity of venous collaterals between the central retinal vein at the disc and the choroidal vasculature. Thus any discussion on the pathogenesis of papilloedema must place some emphasis on elevation of central retinal venous pressure as a contributory factor.

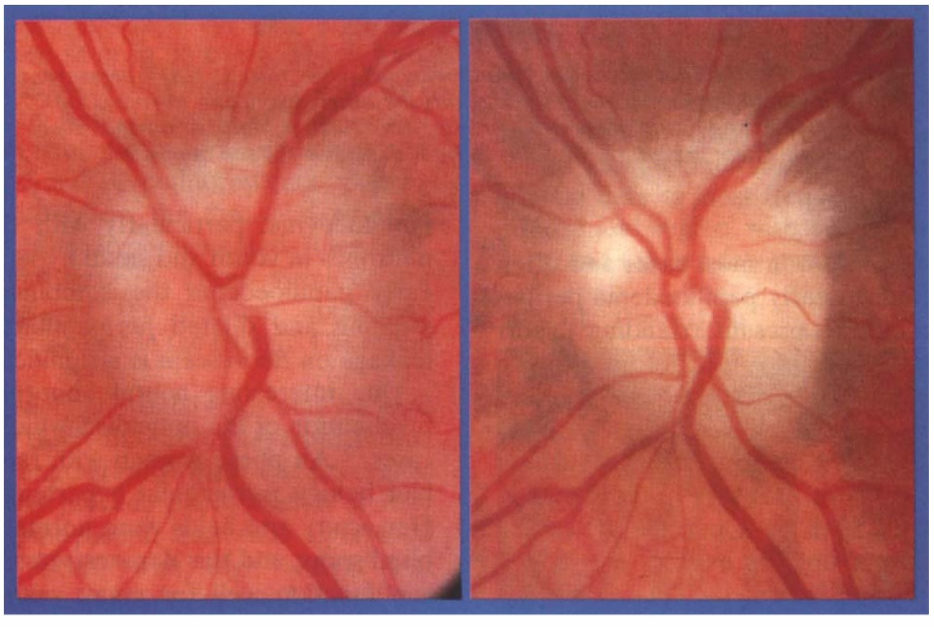
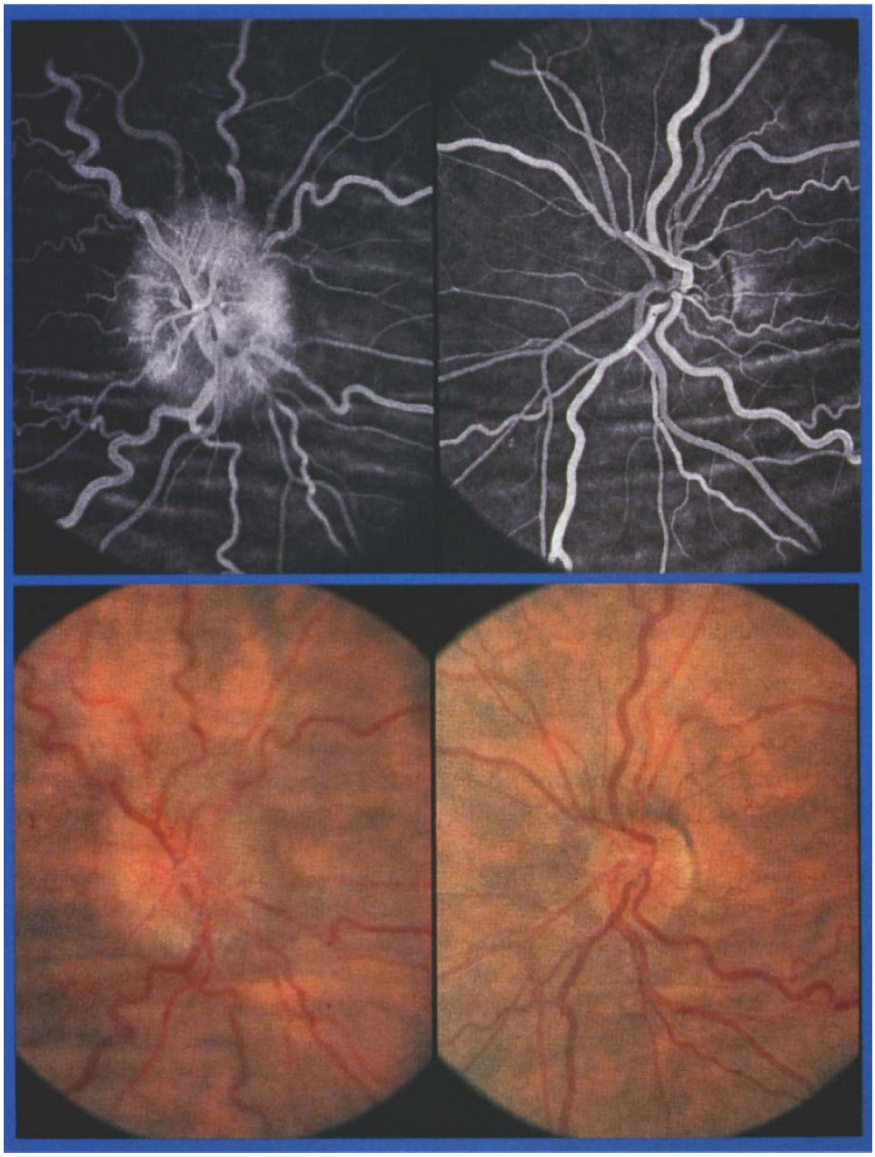


Fig. 15. *Acquired myelination of nerve fibres. Benign intracranial hypertension was observed in this patient for 21 years and there is a period of 8 years between these photographs showing chronic papilloedema (left) and myelination of fibres (right).*



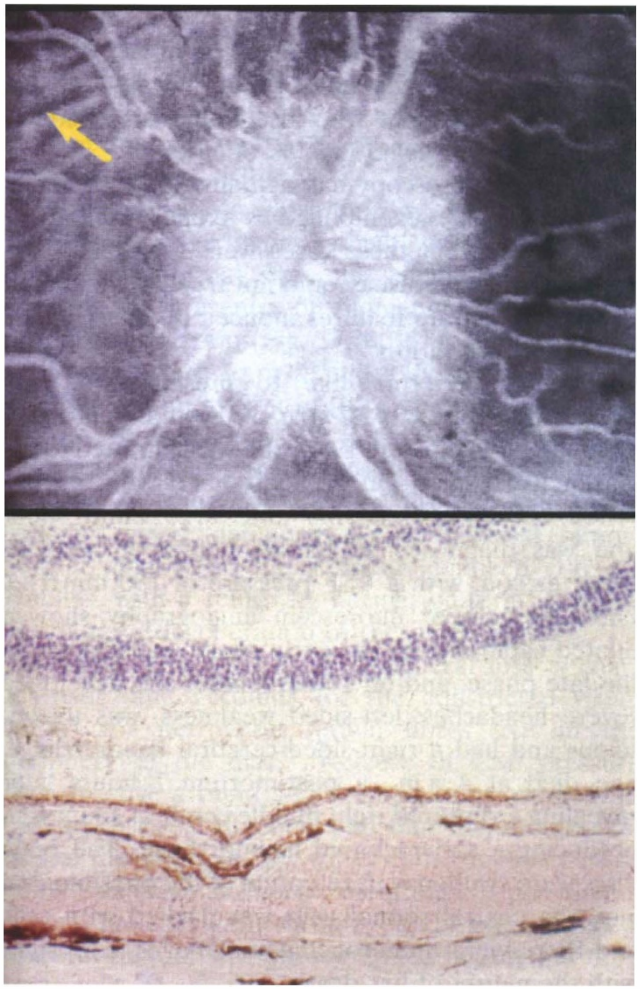
(a)

Fig. 16. *Choroidal folds in papilloedema with raised CSF pressure. (a) Unilateral papilloedema is visible with the other disc being normal (top). Fluorescein angiography shows chronic disc leakage, and a normal disc (bottom). There are choroidal folds in both eyes. For (b) see opposite.*

Neural Changes

Neural changes are present in most cases and often fail to be recognised. In early papilloedema peripapillary neuronal swelling is present extending a short way (½ disc diameter) into the retina due to presumed orthograde axoplasmic hold-up. Ophthalmoscopically mild pallid swelling is seen, usually above and below the disc. The neurones some distance from the disc are probably normal, and in the experimental situation with peripheral nerves, orthrograde axoplasmic hold-up extends only a few millimetres.[54] In some cases the neurones are excessively prominent, particularly the arcuate fibres, and may extend into the mid-periphery. Similar though not identical changes may be seen in pseudopapilloedema, particularly with the abundance of neurones in youth and small hypermetropic discs. In early papilloedema the combination of neuronal swelling and dilated peripapillary capillaries with leakage on fluorescein is a significant finding.

One interesting neural abnormality is acquired myelination of the optic disc, which I have seen in 2 cases.[55] An obese woman with raised CSF pressure had benign intracranial hypertension for 21 years. Her acuity and fields were normal apart from large blind spots, and this demonstrates that swollen discs can function well for many years. The increasing myelination is well demonstrated (Fig. 15) and evidence suggests this is derived from Schwann cells and not oligodendroglial cells.



(b)

Fig. 16 *(contd). (b) Choroidal wrinkles with chronic papilloedema (top; see arrow) and histological correlation (below), with a wrinkle in the pigment epithelium and a flat retina.*

Choroidal Folds

Choroidal folds were seen in 56 cases. These were first described with orbital tumours,[56] and they indicate compression and distortion of the globe.[57] There are two characteristic patterns: wide bands of alternating hyper- and hypofluorescence passing obliquely above and below the disc, and wrinkles which present as fine hypopigmented lines with hyperfluorescent borders.[13,58] These wrinkles are due to indentation of the pigment epithelium producing hypofluorescence in the trough. The retina is normal.

Ophthalmoscopically choroidal folds may be hard to detect, and for their differentiation from retinal folds fluorescein angiography may be necessary. Choroidal folds may precede papilloedema or may occur without papilloedema, and thus signify an expanded nerve sheath with high sheath and intracranial pressure. It is not uncommon to see unilateral papilloedema with bilateral choroidal folds (Fig. 16). The precise mechanical and hydrostatic reasons why some patients develop choroidal folds prior to the development of papilloedema is not clearly understood, but if the high sheath pressure indents the globe before the vascular supply is compromised this situation would occur; evidence supporting this is the frequent association with acquired hypermetropia.

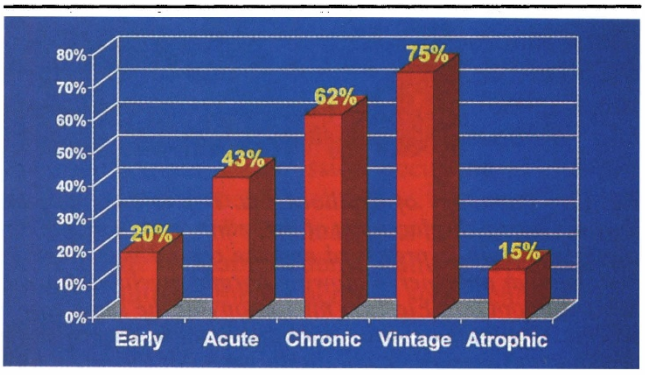
VISUAL IMPLICATIONS

Having described the clinical features of papilloedema it is appropriate to consider its visual implications.

Obscurations of vision are pathognomonic for papilloedema. They may be unilateral or bilateral, last only a few seconds[59] and are precipitated by movement, postural changes, Valsalva manoeuvres, and in a female opera singer whilst singing a long aria. They increase in frequency with increasing duration of papilloedema, reaching their zenith in vintage papilloedema (75%), and yet they still occur in atrophic papilloedema (Table III). The whole visual field is lost rapidly and recovers rapidly, usually accompanied by a negative scotoma. The rapidity of the process, the relationship to alterations of CSF pressure, and the resolution of obscurations following lumbar puncture or nerve sheath decompression suggest a transient vascular process in the laminar region, precipitated by a sudden rise in CSF pressure in the nerve sheath. The occasional occurrence of obscurations with other conditions at the disc, including drusen, meningioma and Fuchs' coloboma, again supports the concept of critical perfusion of the laminar region,[60] though others favour impaired perfusion of the pre-laminar region.[61]

Visual loss has been studied most extensively in benign intracranial hypertension. Two papers in the 1980s showed visual loss in almost 50% of cases,[62,63] though 75% of patients showed visual field defects with Goldmann perimetry.[64] The visual field defects are of three types: (1) peripheral constriction, which is the most common and appears reversible, (2) arcuate defects most frequently commencing in the infero-nasal region with sudden onset and permanent, and (3) in a few patients (6%) an unexplained

Table III. Obscurations



central scotoma, without retinal changes. All patients have an enlarged blind spot and this occurs early and is a diagnostic feature. The ophthalmologist as guardian of the visual fields has a vital role in this condition, and I would now like to try to explain the nature of the field defects by an understanding of the pathology.

PATHOLOGY

Clinical and experimental studies in papilloedema abound in the literature, though there has been a paucity of reports in the past 30 years. The classic paper by Paton and Holmes[40] emphasised essential features from the study of 60 globes. Samuels[65] subsequently confirmed many of these findings, after studying 50 globes.

Essential features are:

1. Oedema of the disc as a major factor.
2. Neuronal swelling, especially in the periphery of the nerve.
3. Vascular changes with venous and capillary distension and the central retinal vein dilated in the nerve. Capillaries show endothelial proliferation.
4. Emphasis of the lateral bulge – a constant and important finding producing marked lateral displacement of the retina.
5. Preservation of the physiological cup.

The vascular features were emphasised by Fry,[66] who emphasised the concept of elevated central venous pressure, but who also found distension of the optic nerve sheath in 77% of cases.

Electron microscopy has demonstrated the major neuronal changes exemplified by axonal swelling and degeneration, but these cases were associated with malignant orbital disease and not true papilloedema, and may illustrate features induced by local inflammation or infiltration.[67]

I would therefore like to present two well-documented cases. A 37-year-old woman had headaches and a fall in July 1982. She was admitted to the National Hospital on 6 September with normal vision, mild papilloedema and large blind spots. She was diagnosed as having benign intracranial hypertension, with a CSF pressure of 280 mmH_2O. On 7 September fluorescein angiography showed dilated capillaries in the early phase and leakage in the late phase, and on 10 September she developed severe headaches, left-sided weakness, was unconscious and had a right-sided cerebral haemorrhage. She died at 4 a.m., a post-mortem 7 hours later revealing a ruptured right middle cerebral aneurysm, producing a subarachnoid haemorrhage. The optic discs were swollen with retention of the physiological cup, the central retinal vein was packed with cells and there were numerous haemorrhages, consistent with the nature of her death.

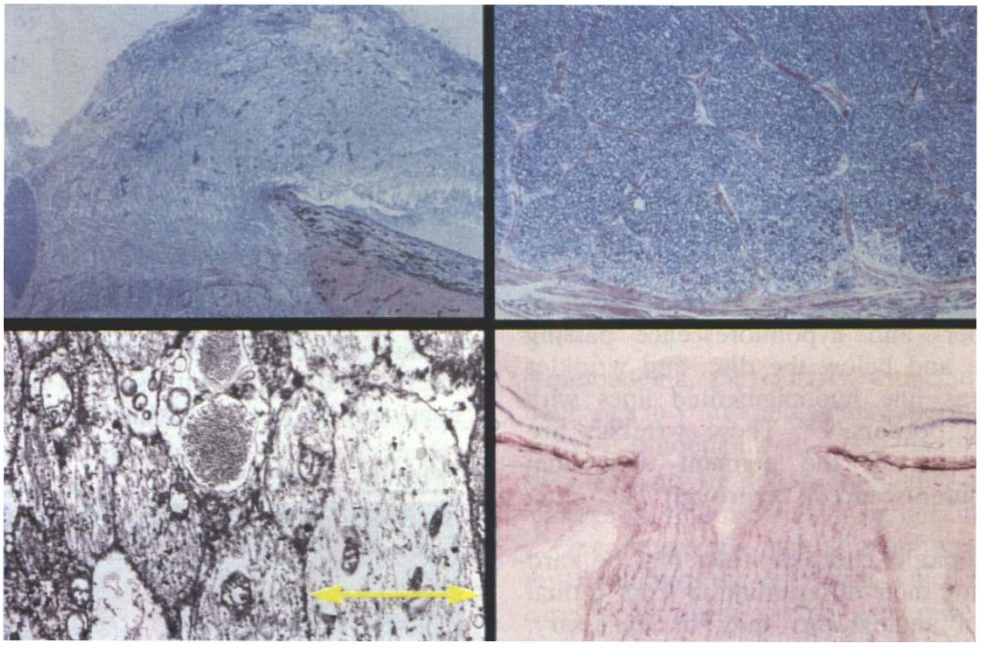


Fig. 17. *Pathology of papilloedema. Top left: Acute papilloedema with massive pre-laminar swelling and haemorrhages. Note the lateral displacement of the retina, and marked compression of peripheral fibres adjacent to Bruch's membrane. The physiological pit is preserved and the central vein filled with red cells. Subretinal fluid is visible (MAB stain). Top right: Retrolaminar optic nerve showing normal myelinated axons centrally but with marked degeneration in the periphery (MAB stain). Bottom left: Electron microscopy of the same case to show massive swelling of axons (arrow), without extracellular oedema. Glycogen deposits and mitochondria are visible (×5.0). Bottom right: Chronic papilloedema. Note the chronic disc swelling, and marked lateral displacement of the retina by the 'lateral bulge'. Note also the marked distension of the sheath.*

Deep staining occurred at the periphery of the nerve, particularly in the region adjacent to Bruch's membrane, where the axons were maximally compressed and damaged (Fig. 17, top left.) Subretinal fluid was clearly visible.

The major cause of disc swelling was the marked distension of the axons, which were probably 10 times their normal size, and electron microscopy showed the presence of filaments which suggest axoplasmic hold-up (Fig. 17, bottom left). Thus if 1 million fibres are 10 or 20 times their normal size, a vascular system may have to compensate maximally to prevent ischaemia and infarction of neurones. Corpora amylacea and cytoid bodies were also present. A transverse section through the retrolaminar region demonstrated in contrast almost normal myelinated fibres within connective tissue bundles, with a relatively normal pattern centrally, but marked degeneration in the periphery (Fig. 17, top right). This pattern of peripheral loss is characteristic, and accounts for the constricted visual field,[68] for peripheral retinal fibres exit in the periphery of the disc.[69] Release of CSF pressure may produce a rapid and dramatic improvement in peripheral visual function, and thus major compression of the axons as they traverse the tightest part of the scleral canal at Bruch's membrane is postulated.

One patient with chronic papilloedema and a cerebral tumour was photographed in July but died in August. There was chronic disc swelling, marked distension of the nerve sheath, whose distal end is adjacent to the circle of Zinn, and marked lateral displacement of the retina by the 'lateral bulge' (Fig. 17, bottom right). This tissue has no nuclei and its origin is unknown, but it is an established feature of papilloedema[40,65] and probably accounts for the enlarged blind spot. Correlation of the field defects with the observed pathology leads me to suggest: (1) The enlargement of the blind spot is related to the lateral displacement of the retina by the 'lateral bulge' produced by the distended axons. (2) The constriction of the visual field is due to the severe damage to the peripheral neurones in the optic nerve, as these are presumably compromised against the tightest part of the disc margin (i.e. Bruch's membrane). (3) Arcuate and infero-nasal defects result from vascular compromise of branches from the circle of Zinn, because they are sudden, permanent and conform to established arterial patterns.[70]

What happens to the neurones in papilloedema? In 1944, Weiss produced the first functional evidence of axonal transport with the damming of axoplasm in a constricted nerve.[71,72] By the 1960s this was being used to study axonal transport in the eye, and in 1977 Tso and Hayreh[73] showed that following the intravitreal injection of tritiated leucine, autoradiographic studies demonstrated accumulation of both the fast component and slow components of axoplasmic transport. The grain count in the layers of the optic nerve was greatest at the level of the scleral portion of the lamina cribrosa, suggesting that this served as an important primary focus of damage to the optic nerve. Pathological and axoplasmic studies led these authors to state that axonal swelling was the main cause of the disc swelling not only in papilloedema but in ocular hypotony and other disc causes of disc oedema. Despite the many excellent papers on papilloedema from clinicians (Fry,[74] Leinfelder,[75] Glew,[76] Gunn,[42] Hedges and Weinstein,[77] Wirtschafter *et al.*[36]) and researchers (particularly the dedicated work of Hayreh) a clear hypothesis has not emerged, though most authors have contributed shrewd observations. 'The exact mechanism by which the raised pressure in the sheath produced oedema of the disc still remains a mystery' wrote Hayreh in 1968,[35] whereas Miller in Walsh and Hoyt in 1982[37] suggested that 'despite continued advances, we still do not have a clear and concise scheme for the pathogenesis of papilloedema'.

PATHOGENESIS

I would therefore like to review some of the evidence we have for the pathogenesis of papilloedema, emphasising that my views will of necessity be clinical ones, utilising extensive and valuable experimental work but introducing Todd's axiom that a 'correct physiology must ever be the foundation of rational medicine'. I will consider this in three parts: optic nerve sheath pressure, effects of CSF pressure elevation on the venous system, and local factors in the laminar region.

A. Optic Nerve Sheath Pressure

The clinical features that have to be assimilated in any hypothesis include mechanisms for (1) transient unilateral or bilateral visual loss (obscurations), (2) swelling localised to the optic disc, (3) mechanical distortion of the globe and (4) venous distension, lack of pulsation with retinal haemorrhages and retino-choroidal collaterals. Evidence has been presented that localises the primary site to the retrolaminar region and shows that ischaemia, either arterial or venous, produces disc oedema. The pathology of papilloedema indicates prominent disc oedema and pre-laminar axonal distension, with maximal axonal compression occurring in the disc at the level of Bruch's membrane.[72]

High pressure in the sheath has been a recognised prerequisite for papilloedema[77] and is dependent on the continuity of the intracranial subarachnoid space with the subarachnoid space surrounding the nerve sheaths (Fig. 18, top left). When the subject is in the

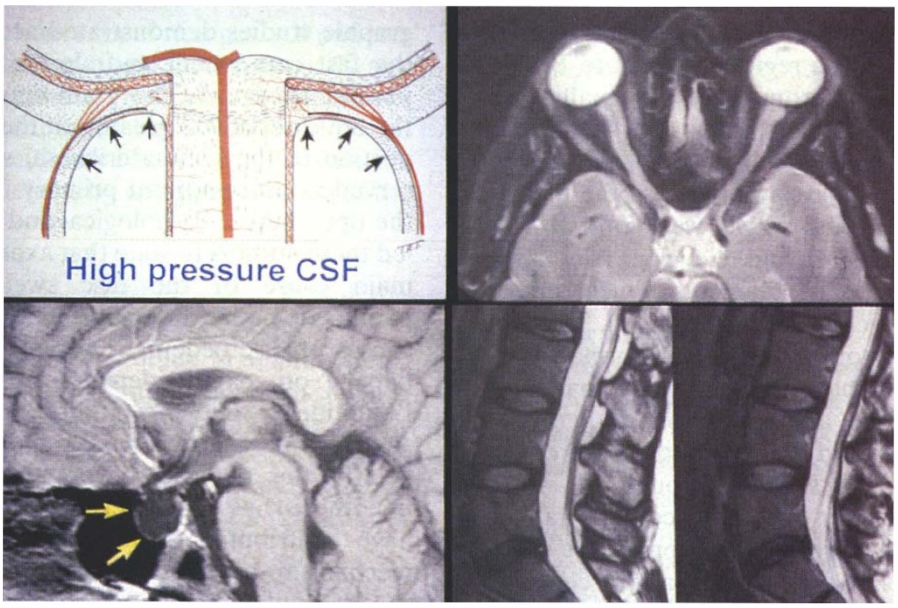


Fig. 18. *High CSF pressure and the optic nerve sheath. Top left: High CSF pressure distends the distal sheath and fluctuations in pressure can affect branches of the circle of Zinn. Top right: Distended sheath with distal dilatation, acting as an 'expansion vessel', shown on T2-weighted axial MRI scans. Bottom left: Distended pituitary fossa, containing CSF and termed the 'empty sella syndrome'. Bottom right: CSF in the main expansion vessel the 'lumbar sac'.*

erect position, the normal sheath in the normal person probably contains very little CSF, but if the sheath is patent and raised CSF pressure occurs, the sheath has potential for limited expansion. In the early part of this century, Cushing and Bordley[79] emphasised the dilatation of the distal subarachnoid nerve sheath and the variable pattern of distension in raised intracranial pressure. The sheath is dilated in 75% of cases of papilloedema and as dilatation progresses the vital blood vessels supplying the laminar region become vulnerable. The optic nerve can now be visualised with T2-weighted magnetic resonance imaging (MRI), when the CSF appears white, and extends down both nerve sheaths with a distended appearance at the distal end of the sheath (Fig. 18, top right), which Paton and Holmes[40] described as resembling 'a leek'. If, however, CSF fails to enter the sheath on either axial or coronal views, due to a failure of communication of the subarachnoid space, then papilloedema does not develop. However, one patient in her thirties should have had severe papilloedema, as she had a venous thrombosis due to activated protein C resistance and a CSF pressure of over 1000 mmH_2O. Three manometers were necessary to measure the pressure and this is the highest pressure I have seen in a patient without papilloedema.

I would therefore like you to join me in a journey down the corridors of clinical speculation, which started when I was at Great Ormond Street Hospital for Sick Children. I was puzzled by the tendency for children with meningomyelocoele, meningocoele or spina bifida to progress, after closure of the fistula, to hydrocephalus. When I joined the National Hospital I was similarly interested in those patients with spinal cord tumours who had papilloedema with or without a high CSF protein. One patient with a sacral cyst of Tarlov had acute papilloedema.[80] Another patient who had presented to her gynaecologist with a sacral cyst detected on pelvic examination was blind 1 month after its removal from untreated and sadly unrecognised papilloedema.

I became interested in the spinal sac and the CSF, for as mammals attained the erect posture major pressure adaptations were necessary. There are 150 ml of CSF and about 500 ml are produced in 24 hours. Fifty per cent of the CSF is below the level of the foramen magnum and almost half is absorbed in the spinal sac. Weed,[81] at Johns Hopkins University in the 1930s, first recognised the importance of the spinal sac and its elastic component and thus amended the Monro–Kellie doctrine. He stated that 'within this rigid bony container there is a complex elastic element, constituted of the spinal dural sac and also of the blood vascular channels within the nervous system and the meninges'. More recently myelography has confirmed dynamically the expansion of the sac on changes of posture,[82] on Valsalva manoeuvres and on abdominal compression. Further fluctuations of arterial blood, capillary blood, venous blood and CSF have been demonstrated by spin echo MRI sequences.[83] The pressure of the CSF in the sac on standing probably approximates 600 mmH_2O and the CSF pressure in the head might be below atmospheric. A British neurosurgeon had an intracranial bolt inserted and

recorded pressures of zero when he was standing upright but 600 mmH_2O whilst standing on his head.[84]

The spinal sac is therefore an important aspect of CSF dynamics, and Davson in 1982 said that 'the spinal compartment may be characterised as an expansion vessel, coupled to the rigid skull cavity, moderating the intracranial pressure and volume changes[85] (Fig. 18, bottom right). We know that with elevated CSF pressure the pituitary fossa expands, earning the erroneous appellation of the empty sella syndrome (Fig. 18, bottom left), and CSF may also be forced into Meckel's cave. It is my suggestion that the optic nerve sheath also functions as an 'expansion vessel'. In addition, we now know that the CSF pressure varies greatly and that the insertion of an intracranial intraparenchymal bolt provides constant CSF pressure monitoring. Thus in a patient with raised CSF pressure, when the patient is sitting up the pressure is 250 mmH_2O, but on lying flat the CSF pressure elevates to 700 mmH_2O; thus the pressure goes up almost 500 mgH_2O when lying flat, which is almost 40 mmHg (Fig. 19). There can therefore be very wide fluctuations in the CSF pressure, and the higher the pressure, the less the compliance or elasticity.

I would like to suggest that the nerve sheath pressure is constantly fluctuating and when elevated may reach levels where laminar or retro-laminar perfusion is reduced or halted, which would adequately explain the mechanism of obscurations of vision. In addition the nerve sheath was not designed as an expansion vessel, because the central retinal vein is placed *within* the subarachnoid space. In the spinal sac the veins are placed *outside* the dura, so that they are not subjected to constant alterations in CSF pressure. Studies with Professor Ian Whittle in Edinburgh on the rat glioma model showed that though CSF pressure was raised and the nerve sheath distended, papilloedema failed to develop because the blood supply to the disc was outside the nerve sheaths, so that neither the laminar and retro-laminar microcirculation nor the central retinal veins were subjected to a high CSF pressure.

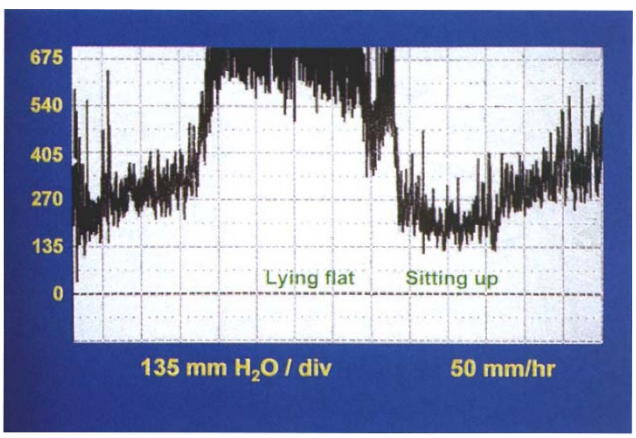
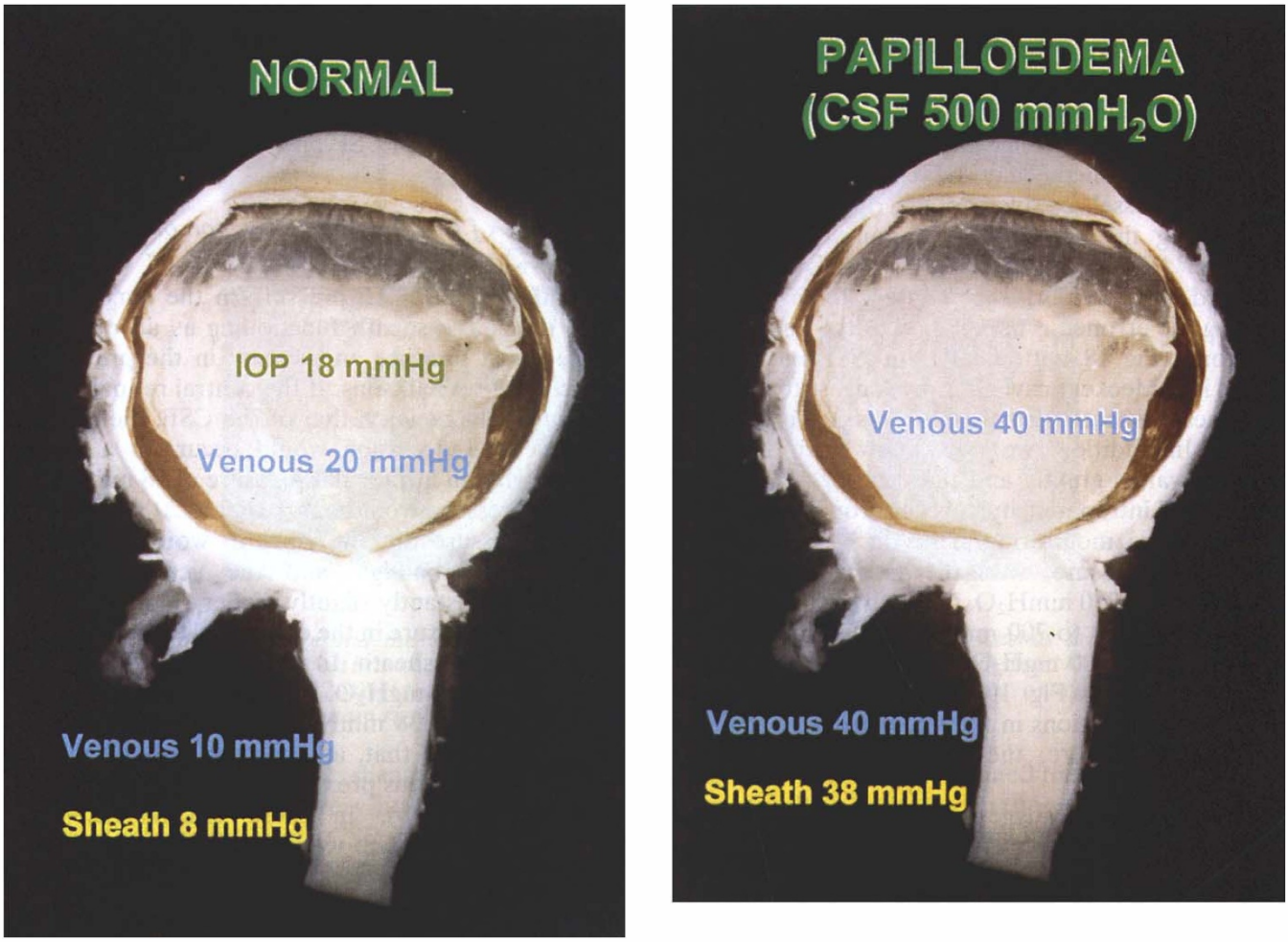


Fig. 19. *CSF intracranial pressure monitoring with an intraparenchymal bolt in a patient with raised intracranial pressure. The graph shows the elevation of CSF pressure on lying flat: CSF pressure is 250 mmH_2O sitting up, but 750 mmH_2O on lying flat.*

B. Effects of CSF Pressure Elevation on the Venous System

Elevation of the CSF pressure in the nerve sheath with the nerve sheath functioning as an expansion vessel must produce an increase in the pressure in the central retinal veins. If the central retinal venous pressure falls beneath that of the CSF, then venous collapse and occlusion would occur. In a normal person with an intraocular pressure of 18 mmHg, the venous pressure would approximate 20 mmHg. The tissue pressure in the sheath would, however, average 8.5 mmHg[86] and the venous pressure would be constantly slightly higher (Fig. 20a). Thus the venous pressure in the eye would be at least twice that within the sheath. In papilloedema with a CSF pressure of 500 mgH_2O, the pressure in the sheath would be about 38 mmHg and the venous pressure would be above that, at approximately 40 mmHg, and thus the venous pressure in the eye would be 40 mmHg (Fig. 20b). In these circumstances the pressure in the sheath would be double that within the eye, which would account for the acquired hypermetropia, the choroidal folds, the apparent shortening of the globe seen on MRI scanning, and the bowing forwards of the lamina cribrosa on pathological examination.[87,88] Venous pulsation would also not be visible, which accords with our clinical findings.

Thus is the high venous pressure the cause of papilloedema (Fig. 21)? Clinically and experimentally this has been an old chestnut, originating with von Graefe who thought papilloedema was due to elevated cavernous sinus pressure.[89] However, experiments in dogs showed that raised cerebral venous pressure produced by neck tourniquet resulted in venous congestion but no disc oedema.[78] Similarly, experiments on the monkey showed that occlusion of the central retinal vein failed to produce papilloedema, only congestion in the retinal veins.[35] In the present series central retinal venous occlusion was rare, but other signs of elevated venous pressure were evident, including: (1) absent venous pulsation, (2) distension and increased tortuosity of veins, (3) elevated venous pressure on ophthalmodynanometry, (4) peripheral haemorrhages and (5) retinochoroidal collaterals. Much debate has therefore centred on the crucial local mechanisms at the disc which would account for the local nature of the changes. These include raised pressure in the laminar veins[42] or capillaries,[75] CSF infiltration into the perivascular lymphatic space[74] or optic nerve,[90] or the obstruction



(a) (b)

Fig. 20. *Relationships of venous pressure to fluid pressures in the nerve. (a) Normal. The intraocular pressure is 18 mmHg with the venous pressure slightly above (e.g. 20 mmHg). In contrast the CSF pressure is much lower at 8 mmHg, with the venous pressure slightly higher (e.g. 10 mmHg). (b) Papilloedema with CSF pressure of 550 mmH_2O. The sheath pressure is now 38 mmHg and the venous pressure just above this at 40 mmHg, so that the venous pressure in the eye is also about 40 mmHg, and thus venous pulsation is absent. (The intraocular pressure is unaltered at 18 mmHg.).*

of lymph drainage from the optic nerve.[40] A comprehensive summary has been provided by Hayreh.[35]

C. Local Factors in the Laminar Region

Factors emphasising the crucial role of the laminar region in the production of papilloedema include: (1) an explanation for obscurations, (2) the localised nature of papilloedema, (3) local causes of disc oedema which have been localised to the retrolaminar region and (4) pathological and experimental studies, showing maximal hold-up of axoplasmic flow at the lamina cribrosa.

Elevated CSF pressure in the optic nerve sheath (functioning as an expansion vessel) produces elevation of the central retinal venous pressure, resulting in a reduced perfusion pressure. Hence the disc and retina are even more vulnerable to further ischaemic insult.[91]

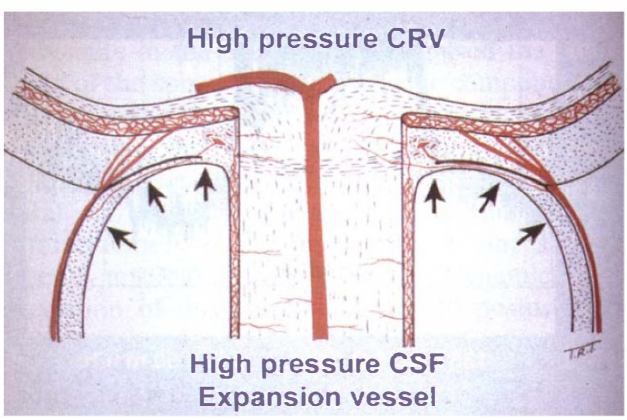


Fig. 21. *Elevated central venous pressure as a result of high CSF pressure. The venous pressure is always above the CSF pressure to avoid occlusion, and thus in papilloedema the venous pressure is elevated.*

Studies of the disc microcirculation show a scleral arterial anastomosis (circle of Zinn–Haller) supplying the laminar and pre-laminar region,[19,20] but marked variability occurs, so that in about 15% of specimens the circle is absent. The disc blood supply is essentially pial and retinal, and not choroidal.[92] We have studied the position of the circle of Zinn in relation to the distal subarachnoid optic nerve sheath in 29 eyes. The circle was anterior to the nerve sheath in 86.2% of cases and posterior in 13.8%. The variability in pattern was again confirmed and the circle of Zinn narrowed or incomplete in 37.9%.[93] The distance between the terminal nerve sheath and the circle of Zinn was about 200 μm, the circle measured 200 μm in diameter and precapillary arteriolar branches of 50 μm were visible supplying the lamina cribrosa (Fig. 22). These small vessels were closely related to the distal nerve sheath.

Thus sudden elevation of the CSF pressure might reduce perfusion through these vulnerable vessels and produce obscurations as an acute transient event, and papilloedema as a chronic event. The CSF pressure determines retro-laminar tissue pressure,[94] so that an elevated tissue pressure would further compromise the microcirculation. Events at the lamina cribrosa would lead to orthograde axonal swelling producing massive distension in the anterior optic disc, and hence the morphological changes already described. Thus primary ischaemic changes in the laminar region would produce secondary neuronal and vascular changes at the optic disc. The wide fluctuations in the CSF pressure have not previously been appreciated, and the variability induced by posture, movement, Valsalva manoeuvres, straining, etc., cannot hope to be reproduced experimentally. Thus though Hayreh accurately suggests axonal changes as the cause of the disc swelling, these are produced by compromise of the arteriolar branches of the circle of Zinn at the lamina cribrosa. Precise physiological understanding of cellular events is conceptual but breakdown of the blood–retinal barrier and failure of autoregulation seem contributory and, in experimental studies of peripheral nerves, a process of ischaemia and axonal stasis is followed by further oedema and nerve fibre degeneration,[95] and even the secretion of cytokines.[96]

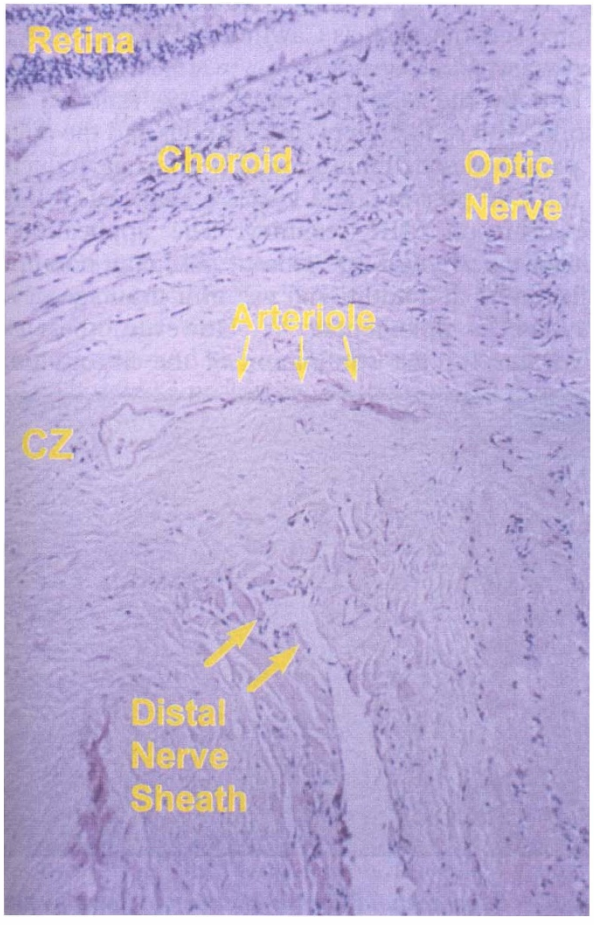


Fig. 22. *Circle of Zinn and distal nerve sheath. The distal nerve sheath is in close proximity to precapillary arterioles (50 μm) passing from the circle of Zinn to the lamina cribrosa and optic nerve.*

Furthermore, anatomical variability is built into the system, so that the size and configuration of the sheath, the angle of its insertion into the globe, the degree of patency at the canal and the vagaries of the vascular system will all have an effect on the morphological appearances.

In the myopic eye, for instance, the sheath is inserted into the sclera as a lateral fusion, whereas in the hypermetropic eye, insertion close to the nerve is apparent. The diameter of the canal is least at the level of Bruch's membrane (1.37 mm in 29 eyes measured), so maximum compression would occur here, whereas the myopic eye with a larger disc would be relatively protected. These factors may explain the relative protection of the myopic disc from the effects of raised intracranial pressure as first discussed by Marcus Gunn.[42]

The vital role of CSF pressure on the laminar arterioles in producing papilloedema could be confirmed by conducting an experiment in which the effects of a fistula fashioned in the distal nerve sheath were compared with a fibrous tissue subarachnoid band preventing direct contact between the CSF and the vessels. This would provide firm evidence that the third crucial factor necessary for the development of papilloedema is an interference with laminar perfusion.

SURGERY

In 1871 in London, Queen Victoria opened the new St Thomas' Hospital. William Bowman, now aged 56, with his beloved microscope, was as Johnson said 'living more in the broad sunshine of life than any other ophthalmologist'. He had fame, he had a family

Fig. 23. *Joldwyns, Sir William Bowman's country house at Holmbury St Mary near Dorking, designed by William Morris.*

of seven, he had a fortune and it was therefore appropriate that he should consider a small family retreat in the country. He built his country retreat on the Downs near Dorking, which housed the Bowman Tennyson painting and had an exotic garden. It subsequently become a Country Club, the Joldwyns Country Club in Holmbury St Mary (Fig. 23), but sadly it was finally ravaged by fire. The house was built by Philip Webb the architect, and William Morris, the famous designer whose centenary was celebrated in 1996.

The next year, in 1872, a German ophthalmologist, De Wecker, who practised in Paris came to London to the Quadrennial Ophthalmic Congress. He presented a new operation performed and instigated entirely on his own, in which he incised the optic nerve sheath in two patients with papilloedema, producing relief of headache, improvement of symptoms, and improvement of vision in one patient, without any side effects.[97] Using no anaesthetic he inserted a guide followed by a neurotome, and with these fine blades incised not only the sheath but the scleral ring, in order, as he said, 'to relieve the strangulated nerve'.[98] Power[99] and Brudenel Carter[100] repeated the operation in London; Carter, using an anaesthetic, performed the operation satisfactorily on 15 patients. Thus 90 years before Hayreh showed that incising the nerve sheath relieved papilloedema in the monkey, the operation had been performed in humans by De Wecker with proven efficacy. The operation is successful in about three quarters of cases and has become a useful adjunct to the current treatment of papilloedema.[101,102]

Most commonly used in benign intracranial hypertension, the procedure still needs improvement. A 23-year-old obese patient demonstrates the problem. She had been treated with 62 lumbar punctures, 10 lumbo-peritoneal shunts and an optic nerve sheath fenestration on each side. When first seen at the National Hospital she had an intravenous line administering an antibiotic to treat her infected shunt. Unfortunately after bilateral sheath fenestration a further lumbo-peritoneal shunt was necessary and this resulted in severe headaches, which were now due to tonsillar herniation. A foramen magnum decompression was then performed. The insertion of a 2 mm plastic tube from the spinal column subcutaneously to the peritoneal cavity leaves the way open for blockage, infection, excessive drainage and migration, so that CSF diversion procedures have become a nightmare for neurosurgeons. Rosenberg[103] reviewed the results in five American centres, in which 37 patients underwent 73 lumbo-peritoneal shunts and 9 ventricular shunts. Sixty-four per cent of shunts lasted less than 6 months. Re-operation for shunt failure occurred in 55% of cases, and low-pressure headache, more devastating than high-pressure headache, in 21%.[103]

Thus optic nerve sheath fenestration has an established and useful role, 125 years after its inception. A medial approach is used, the ciliary vessels are deflected, the dura and subarachnoid incised and a window 2 mm × 4 mm fashioned. Retractors are required to contain the orbital fat, and angled scissors, such as Cawthorne ENT scissors, are necessary.

Initially the operation appears to function as a fistula, with reduction of obscurations and the degree of papilloedema, diminution of headaches, reduction in the CSF pressure, and visible leakage of CSF into the orbit on MRI scanning. The application of mitomycin, though not without risk, may potentiate a fistula,[104] and additional use of a drainage device may be complementary.[105] However, there are advocates for the stimulation of the fibrous tissue

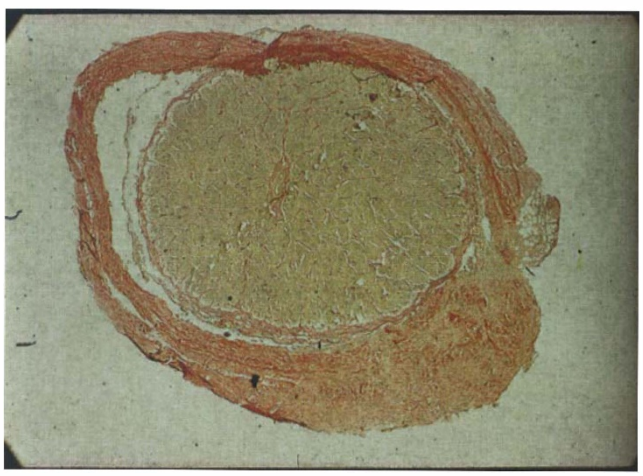


Fig. 24. *Subarachnoid fibrosis after nerve sheath fenestration. The site of incision shows fibrosis and there is also a fibrous reaction extending around the nerve in the subarachnoid space, protecting the vascular supply to the lamina from the high CSF pressure (Courtesy of Mr S. Davidson.)*

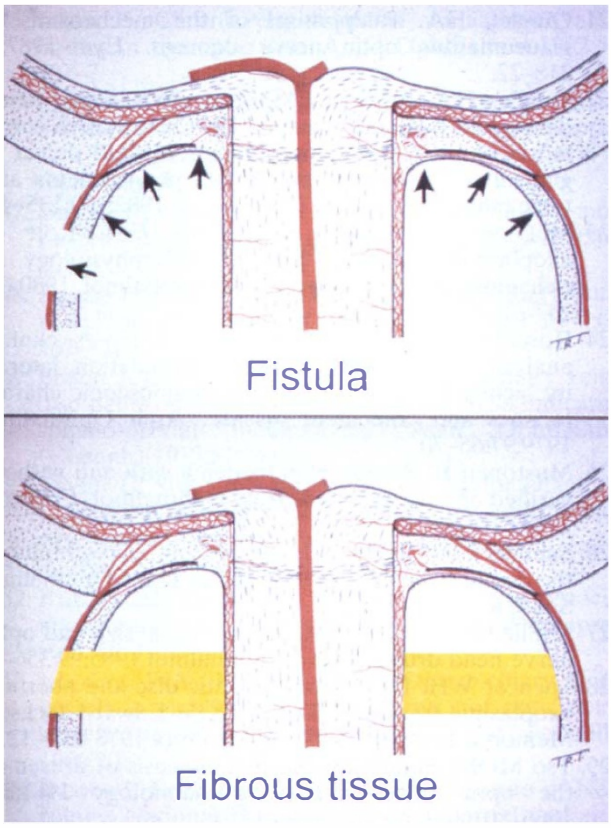


Fig. 25. *Mechanism of action of nerve sheath fenestration. Top: Functioning as a fistula, with leakage of CSF into the orbital fat. Bottom: Proliferation of fibrous tissue in the subarachnoid space. Both methods protect the laminar blood vessels supplying the disc from the effects of the elevated optic nerve sheath pressure.*

by the CSF, and the concept of drainage through an enclosed bleb of fibrosis.[106] Davidson[107] first demonstrated fibrous tissue at the site of incision and extending around the subarachnoid space (Fig. 24) and postulated a protective mechanism. Thus it is my belief that in the majority of patients the procedure functions as a fistula initially, with lowering of the CSF pressure, but ultimately adherence of orbital fat and the development of fibrous tissue either produces a very slow-flow fistula or the fibrous tissue functions as a protective meshwork (Fig. 25). Either of these results would be beneficial and the final verdict on the mechanism is still open, but the surgeon is left contemplating whether he is to encourage or discourage fibrosis.

The fact that both methods may be successful supports the concept that high CSF pressures impair perfusion of the laminar blood region and that this is crucial for the development of papilloedema. Restoration of the blood supply abolishes papilloedema.[108]

CONCLUSION

I have therefore provided a classification of papilloedema, reviewed the clinical spectrum and correlated this with the pathology, and suggested that there are three essential ingredients for the development of papilloedema: a high and volatile CSF pressure in the distal nerve sheath, an elevation of the pressure in the central retinal vein, and impaired perfusion of the neurones as they traverse the laminar cribrosa. Impaired functioning of these neurones produces orthograde axoplasmic hold-up and further compression at the pre-laminar disc, and this is responsible for the clinical appearances. The small precapillary arteriolar branches of the circle of Zinn are intimately affected by the rapid pressure changes in the distal nerve sheath functioning as an expansion vessel, and acute transient elevation of CSF pressure produces obscurations whereas chronic elevation produces papilloedema.

I would like to conclude this Bowman Lecture with two final thoughts. The first is that the ideals of Sir William Bowman are as necessary today as they were in his life-time. These were well summarised by Swanzy in his 1888 Bowman Lecture.[108] 'Bowman', he says, 'was conscientious in his relations with his patients, honourable in his relations with his professional brethren, careful not to put himself forward in any unrecognised manner. Not seeking notoriety, simple, kind, courteous and dignified, William Bowman is presented to our minds as the personification of the best of those qualities which go to make an English gentleman.' My second parting thought is that 'The bane of specialisation is isolation and the cure is co-operation.' Ophthalmologists choose their specialty to combine the practical dexterity of surgery with the mental artistry of medicine. The medical affiliations in our speciality are of crucial importance for the survival of ophthalmology, and of the past 56 Bowman Lectures less than a quarter have been on surgically related topics. Medical ophthalmology at the highest levels can only be performed by those firmly grounded in ophthalmology, and our future as an enlightened speciality will only be secure if we maintain close links with the exciting growth areas emerging in the basic sciences and the wider aspects of medicine. It is our duty to persuade our political masters to support specialisation and encourage academic excellence.

My heart will be warmed if this Lecture plays a small part in keeping the flames of neuro-ophthalmology burning, so that a new generation will not only be inspired but also supported in fanning those important flames.

Many devoted and talented ophthalmologists and neurologists over the years have helped with the clinical recordings, and my consultant colleagues at the National Hospital have been generous with their time and the referral of patients. Mr Burdon has been intimately involved, Dr Jean Jacobs and Professor Luthert have examined the pathology and the late Professor Hugh Davson has been generous with discussion. Dr Gauntt and

Mr Williamson have examined the optic discs in Professor Marshall's department. I would like to thank the following for advice: Mr P. Riordan-Eva, Dr E. Graham, Mr J. Acheson, Dr I. Moseley, Mr A. Crockard, Prof. G. du Boulay, Prof. I. Whittle, Mr W. Harkness, Dr M. Segal, Mr T. Matthews, Mr A. Casey and Dr M. Smith. Grateful thanks for financial support go to Mr and Mrs Salmonovicz, and the Iris Fund; the Frost Trust provided the original camera. I would also like to thank Dr and Mrs D. Collins, Mr T. Tarrant who helped with the illustrations, Mr Richard Dewhirst who nurtured the photography and Mrs Deborah Gibson who produced the spoken and written word, for without their invaluable help the project may have floundered.

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