Pathogenesis of cupping of the optic disc

SOHAN SINGH HAYREH

Department of Ophthalmology, University of Iowa, U.S.A.

Optic disc cupping (ODC) is a classical feature of chronic simple glaucoma. In attempts to explain the pathogenesis of ODC, a very large volume of literature has accumulated since its discovery over 120 years ago, but the mechanism is still far from clear. The presence of ODC with no rise in intraocular pressure (IOP), first described by von Graefe (1857), has further contributed to the confusion on the subject. Various theories attempt to explain the pathogenesis of the changes in the optic disc (OD) in these cases, postulating either a mechanical or a vascular basis, in addition to many more theories concerning cavernous degeneration; the subject has been reviewed elsewhere (Hayreh, 1974d).

I recently found a very high incidence of ODC in anterior ischaemic optic neuropathy (AION) due to temporal arteritis (Hayreh, 1974b, d) identical in all aspects to that seen in glaucoma and low tension glaucoma. Thus, identical pathological ODC occurs in glaucoma, low tension glaucoma (pseudo-glaucoma), and AION. Since AION, being an acute process, has a much-telescoped natural history, resulting in marked cupping within 4 to 5 months after its onset, it has been possible to follow in patients its entire natural history with modern techniques, *e.g.* stereoscopic ophthalmoscopy, fluorescein fundus angiography, and histopathology. On the basis of these clinical studies and also of experimental studies, I have tried to explain the pathogenesis of ODC in AION, and also, presumably, of ODC in glaucoma and low tension glaucoma, since the three conditions present an ischaemic disorder of the anterior part of the optic nerve (ON)—AION being an acute process while the other two are chronic.

Present studies

Detailed ophthalmoscopic and fluorescein fundus angiographic studies were performed on 25 patients with AION (Hayreh, 1974b) in addition to other studies (Hayreh, 1974d), and the patients were followed up for periods varying from 3 months to 3 years, the majority being between 1 and 2½ years (mean 15 ± 9 mths). In this series it was decided to find out the relationship of ODC to AION and to learn more about the mechanisms of ODC in general. This was of particular interest for two reasons:

(a) Our previous studies indicated that AION, glaucoma, and low tension glaucoma are manifestations of ischaemia of the anterior part of the ON (Hayreh, 1969, 1970, 1972; Hayreh and Perkins, 1969; Hayreh, Revie, and Edwards, 1970; Hayreh and Baines, 1972), AION being an acute process while the other two are chronic. Therefore, OD changes in AION should throw a significant light on similar changes in glaucoma and low tension glaucoma.

(b) In all previous reports of AION there is hardly any mention of the incidence of ODC. This is somewhat surprising. Begg, Drance, and Sweeney (1970, 1971) reported the presence of notching on the neuro-retinal rim in patients with sectoral AION in chronic simple glaucoma, which occurred some 2 to 3 months after the original haemorrhage had disappeared. Drance (1972) commented that, after the usual AION, the ON becomes atrophic but rarely cupped. Miller (1972) mentioned the occurrence of ODC without exception in AION due to temporal arteritis but gave no other details.

In my series, ODC was present in thirteen eyes (Hayreh, 1974b, d). The cupping usually developed about 2 to 3 months after the onset of AION, sometimes in as little as 6 weeks. There was a rapid progress in cupping so that after 3 to 4 months it was at its maximum, and thereafter increased only minimally in eyes followed-up for 12 to 20 months (Fig. 1).

FIG. 1 *Right eye of a 72-year-old woman with temporal arteritis, anterior ischaemic optic neuropathy, and no perception of light in that eye. It shows cupping of the optic disc 13½ months after the onset of anterior ischaemic optic neuropathy. Fig. 2a shows the optic disc 3 days after the onset of neuropathy*

ODC was correlated with the following:

(1) *Intraocular pressure*

The pressure in all the eyes was within normal limits (less than 20 mm.Hg on applanation tonometry) and was no higher than in those with no cupping.

(2) *Temporal arteritis*

When AION was due to temporal arteritis (*i.e.* positive temporal artery biopsy for temporal arteritis), 80 per cent. of the eyes had definite ODC of variable size; in the remaining 20 per cent. the discs could not be evaluated satisfactorily because of lens opacities, although optic atrophy was present (visual acuity was no perception of light in two and counting fingers in one). In contrast to this, when AION was *not* due to temporal arteritis, cupping was seen in only 12.5 per cent. (Table I) and was comparatively of milder degree than in cases of temporal arteritis.

(3) *Size of physiological cup in the contralateral normal eye*

This was measured to rule out, firstly, pre-existing cupping due to so-called burnt-out high pressure glaucoma of a congenital nature, and, secondly, the possibility that a large physiological cup may predispose to ODC, as compared to discs with normal physiological cups.

Table I Correlation of optic atrophy, cupping of optic disc, temporal arteritis, and final visual acuity

Optic atrophy	No. of eyes	Cupping of optic disc	Temporal arteritis		Final visual acuity								
			Present	Absent	NPL	PL	HM	CF	6/60	6/36	6/12	6/9	6/6
Diffuse	10	Present	9	1*	8**	0	1	0	1	0	0	0	0
	7	Absent	0	7	0	0	2	1	0	2	0	0	2
Sectoral	3	Present†	2	1	0	0	0	2‡	0	0	0	1	0
	7	Absent	0	7	0	0	0	3	0	0	1	0	3

* This eye had a very shallow saucer-shaped cupping as compared to the other eyes with cupping.

** In one of these, optic atrophy was more marked in the temporal than the nasal part, and so was the cupping

† Atrophy and cupping involved upper one-half to two-thirds of optic disc in two eyes

‡ One eye also had central retinal artery occlusion

The size of the physiological ODC in the fellow eye was studied on the assumption that it would reflect the state of affairs before the affected eye developed AION, since for all practical purposes both eyes normally have identical ODCs.

The findings (Table II) indicate that there is no significant relationship between the development of pathological ODC after AION and the original size of the cup as judged from the fellow normal eye. In fact in two eyes with maximum generalized cupping, the fellow normal eye showed no physiological cup; similarly, the affected eye whose fellow eye had the biggest cup of the series (C/D 0.5) showed no pathological cupping. In any case all eyes either had no physiological cup or one within normal limits; none of them showed a large cup in the fellow eye.

Table II Correlation of pathological cup with size of physiological cup in contralateral normal eye

Type of optic atrophy	Pathological cupping	No. of eyes	Size of physiological cup in normal fellow eye	Bilateral involvement
Diffuse	Present	10	No cup seen = 3 eyes C/D 0.2 = 2 eyes C/D 0.3 = 1 eye	Four eyes of two patients
	Absent	7	No cup seen = 3 eyes C/D 0.5 = 1 eye	Three eyes of two patients*
Sectoral	Present	3	No cup seen = 3 eyes C/D 0.2 = 1 eye C/D 0.3 = 1 eye	Nil
	Absent	7	No cup seen = 6 eyes	One eye of patient marked * above

(4) Type of optic atrophy (Table I)

This indicates that there is a much higher incidence of ODC with diffuse optic atrophy than with sectoral atrophy, which in turn may be related to a higher incidence of temporal arteritis in diffuse optic atrophy.

(5) *Visual acuity*

Table I also summarizes the relationship of the final visual acuity with the cupping. This shows that the more marked the cupping, the worse is the visual acuity.

(6) *Haemorrhages on the OD and near its margins*

Half of the eyes with haemorrhages developed cupping, while the other half showed no evidence of it, thereby indicating no definite relationship between the two. Begg and others (1970), on the other hand, used these haemorrhages as their sole criterion of the presence of AION in glaucoma and recorded the development of notching of the involved neuro-retinal rim.

Pathogenesis of optic disc cupping

In our understanding of pathogenesis of ODC, particularly in AION, and also in glaucoma and low tension glaucoma, the following have provided very important information:

- (a) Pattern of arterial supply to the anterior part of the ON (Hayreh, 1969, 1970, 1974c).
- (b) Fluorescein fundus angiographic findings in patients with AION (Fig. 2), glaucoma (Fig. 3), and low tension glaucoma (Hayreh, 1972, 1974b, d; Hayreh and others, 1972).

FIG. 2 *Right eye of a 72-year-old woman with temporal arteritis, anterior ischaemic optic neuropathy, and no perception of light in that eye.*

- (a) *Fundus photograph 3 days after onset of anterior ischaemic optic neuropathy, showing chalky-white swelling of the disc*
- (b) *Fluorescein fundus angiogram of (a) during the retinal venous phase, showing no filling of the optic disc and peripapillary choroid, with filling of rest of the choroid (Compare Fig. 4b)*

FIG. 3 Fluorescein fundus angiograms of left eye of a 47-year-old woman with chronic simple glaucoma and deeply-cupped optic disc.

- (a) At 60 mm.Hg IOP Retinal arteries fill without choroidal filling except for a few large choroidal arteries.
 (b) At 20 mm.Hg IOP 2 days later Retinal arterial and choroidal filling normal.

The disc fluorescence seen in (a) and (b) is due to a preliminary test dose of fluorescein and not to disc filling

- (c) Fluorescein fundus angiographic findings in experimental ocular hypertension (Fig. 4) and systemic arterial hypotension (Hayreh, 1972; Hayreh and others, 1970).

FIG. 4 Fluorescein fundus angiograms of right eye of cynomolgus monkey (after experimental central retinal artery occlusion at 70 mm.Hg IOP).

- (a) Early phase of choroidal filling, showing very slow and patchy filling of the choroid in the temporal half (supplied by the lateral posterior ciliary artery), with only a very early localized filling in the superior nasal choroid but no filling of the peripapillary choroid, superior choroidal watershed zone, inferior nasal choroid, and optic disc.
 (b) 12 sec. after (a), showing complete filling of the choroid, though less than normal, no filling of the peripapillary choroid and optic disc, and patchy filling of the choroid watershed zones above and below (compare Fig. 2b).

Fluorescence of the optic disc in (a) and (b) is due to previous fluorescein angiography done a few minutes before these pictures to determine the filling pattern at normal IOP when the entire choroid and optic disc filled normally

(d) Experimental production of AION in rhesus monkeys by occlusion of PCAs and consequent histopathological changes in the ON (Fig. 5) (Hayreh and others, 1972).

FIG. 5 Photomicrograph of optic nerve head and retrolaminar optic nerve in a rhesus monkey 36 days after occlusion of all the posterior ciliary arteries (Masson's trichrome stain), showing marked degeneration of neural tissue in retrolaminar region, producing an appearance resembling cavernous degeneration

(e) Histopathological changes in the ON in patients with AION (p. 870) (Fig. 6).

(f) Pathogenesis of AION (Hayreh, 1974a, d).

A complete knowledge of the anatomy and blood supply of the anterior part of the optic nerve, consisting of the optic nerve head (ONH) and retrolaminar optic nerve, is an essential prerequisite to an understanding of the pathogenesis of AION and ODC. As far as the arterial supply of the optic nerve is concerned, the ONH and retrolaminar region form a single unit. The ONH (from the front backwards) is composed of:

- (i) The surface nerve fibre layer, continuous with the nerve fibre layer of the retina,
- (ii) The prelaminar region, composed of nerve fibres and glial tissue septa,
- (iii) The lamina cribrosa, containing nerve fibres and dense compact connective tissue septa.

In the retrolaminar region the nerve fibre bundles lie in large polygonal spaces formed by connective tissue septa; the septa are attached to the lamina cribrosa in front (Fig. 7). The structure of the anterior part of the ON is discussed in detail elsewhere (Hayreh, 1974c). *The posterior ciliary arteries (PCAs) are the only source of blood supply to the lamina cribrosa and prelaminar region, and the main (if not the only) source to the retrolaminar region, and they may*

FIG. 6 Photomicrograph of optic nerve head and retrolaminar optic nerve of a 67-year-old woman 4 months after onset of temporal arteritis and anterior ischaemic optic neuropathy and no perception of light, showing atrophy of prelaminar tissue and fibrosis and gliosis of lamina cribrosa and retrolaminar tissue (Verhoeff elastic stain). (Reproduced by courtesy of Dr. Paul Henkind and the Amer. J. Ophthalm.)

FIG. 7 Histological sections of optic nerve head and adjacent retrolaminar optic nerve in rhesus monkeys. (a) Longitudinal section (LC = lamina cribrosa; PL = prelaminar region; RL = retrolaminar region). (b) (c) (d) Transverse sections in (b) prelaminar, (c) lamina cribrosa, and (d) retrolaminar regions

supply the temporal part of the surface nerve fibre layer (Hayreh, 1969, 1970, 1974c). The extremely important role played by the PCAs in the blood supply of the anterior part of the ON is the crucial factor to be recognized before one can understand the pathogenesis of ODC.

There are many histopathological studies on patients with AION; most of these have been reviewed by Henkind, Charles, and Pearson (1970). The area of greatest involvement in the ON is at the retrolaminar and ONH (mentioned as lamina cribrosa in reports which pertain to the lamina cribrosa and prelaminar regions). The lesion begins with infarction and evolves through liquefaction necrosis in 4 weeks (MacMichael and Cullen, 1972), reactive increase in astrocytes and lymphocytes in 8 weeks (Crompton, 1959), and finally to retrolaminar fibrosis in 4 months (Henkind and others, 1970—Fig. 6). The involved part of the ON is usually well-defined and circumscribed. All but two of these reports are of patients with temporal arteritis and the remaining two are of AION due to arteriosclerosis (Cogan, 1966; Knox and Duke, 1971). The latter reported focal necrosis of the temporal half of the ONH and the retrolaminar ON, with some distension of the lamina cribrosa in that region, in a patient with occlusion of the left common carotid artery and generalized arteriosclerosis, 2 weeks after the onset of visual disturbance. Cogan (1966) also reported a case of AION with well-defined infarction of the retrolaminar ON in the entire temporal half. The pathogenesis of these changes in the ON in AION is discussed in detail elsewhere (Hayreh, 1974a, d). Experimental production of AION in rhesus monkeys by occlusion of the PCAs (Hayreh and Baines, 1972) and a study of the arterial supply to the anterior part of the ON showed that the above-mentioned histopathological changes and their localization to the anterior part of the ON are due to interference with the PCA circulation to the ON.

Infarction of the anterior part of the ON in AION destroys maximally all the neural tissue and to some extent the fibrous connective tissue. Since the entire ONH except for the superficial nerve fibre layer is supplied by the PCAs, occlusion of the PCAs produces massive infarction of the ONH; the capillaries in the surface nerve fibre layer of the OD, though derived from the retinal arterioles, may also become obliterated due to secondary associated oedema of the nerve fibre layer. The neural tissue of the prelaminar part of the ONH forms the main part of the ONH in front of the lamina cribrosa (Fig. 8). An idea of the normal thickness of this region can easily be gained from the depth of the normal physiological cups in cases in which the lamina cribrosa forms their floor. Complete destruction of this neural part of the ONH will result in a significant amount of cupping. Central retinal artery occlusion with patent PCAs would not produce so much destruction of the neural tissue in the ONH because:

- (i) The retinal arterioles supply only a thin superficial nerve fibre layer of the ONH and not the main part of the ONH;
- (ii) It has been noticed in most of the cases of central retinal artery occlusion that the capillaries in the surface nerve fibre layer, which are of retinal arterial origin, fill profusely through their deep communications with the PCA prelaminar vessels (Fig. 9) so that the surface layer does not suffer significant ischaemia, unlike the marked ischaemia seen in the prelaminar region in AION;
- (iii) In central retinal artery occlusion, infarction of the inner layers of the retina and retinal nerve fibre layer would produce an ascending degeneration of the nerve fibres, so that in the ONH there is ultimately degeneration involving the ON fibres only without involvement of the glial tissue. Similarly, other conditions involving degeneration of the ON fibres alone in the ONH, *e.g.* after ascending or descending degeneration of the ON,

FIG. 8 *Longitudinal section of a normal human optic nerve head, showing normal thickness of neural prelaminar region. ×60*

FIG. 9 *Fluorescein fundus angiogram of patient with fresh central retinal artery occlusion, showing filling of vessels of posterior ciliary artery origin in the optic disc and choroid with no filling of the central retinal artery or any other retinal vessel*

could not be expected to produce the same amount of destruction of the prelaminar neural tissue as in AION.

The other important factor in the pathogenesis of ODC in AION is the change in the retrolaminar part of the ON, which at first undergoes infarction and ultimately fibrosis (Fig. 6). Since all the retrolaminar fibrous septa are firmly attached to the posterior surface of the lamina cribrosa (Fig. 7a), fibrosis of the retrolaminar ON would pull the lamina cribrosa backwards by contraction of the fibrous tissue. Histopathological studies demonstrated fully developed retrolaminar fibrosis by about 4 months after the onset of AION (Henkind and others, 1970), and similarly the maximum cupping of the OD in the present study was seen by about 4 months (p. 864). Moreover, the normal neural tissue occupying the wide spaces between the fibrous septa of the ON (Fig. 7d) undergoes liquefaction necrosis and produces a collapse of the spaces, which in turn collapses the posterior support to the lamina cribrosa. Thus, a combination of these two factors would result in a bowing backwards of the lamina cribrosa which is seen on histopathology in ODC. The other factor which may play a further part in the bowing backward of the lamina cribrosa could be the effect of marked ischaemia on the lamina cribrosa itself. The lamina cribrosa is composed partly of connective tissue and partly of neural tissue and could be weakened and thinned by ischaemia.

Thus, a combination of the following three factors may be responsible for ODC in AION:

- (a) Destruction of the neural tissue in the prelaminar region of the ONH. As mentioned above, it is a thick tissue composed almost entirely of neural tissue.
- (b) Bowing backwards of the lamina cribrosa due to retrolaminar fibrosis, and disappearance of normal support of lamina cribrosa posteriorly due to loss of normally large amounts of neural tissue in the retrolaminar ON.
- (c) Destruction of the neural tissue in the lamina cribrosa and possible weakness of the connective tissue part of the lamina cribrosa (as a part of infarction) would further aggravate the bowing backwards of the lamina cribrosa.

I do not feel that the intraocular pressure in itself has any significant role to play in cupping in AION as there is no evidence in this study to suggest it.

Miller (1972) postulated that, for ODC to develop in AION, it is essential to have occlusion of both retinal arteries and PCAs. All the studies, as discussed in pathogenesis of AION (Hayreh, 1974a, d), clearly show that AION is due to occlusion of the PCAs with no involvement of the central retinal artery. In fact, according to the basic definition of AION, there is no involvement of the central retinal artery in this condition. Similarly, in all but two cases of my series, fluorescein angiography demonstrated no evidence of central retinal artery occlusion (Hayreh, 1974b, d); the rest had only occlusion of the PCAs. In the two eyes with associated central retinal artery occlusion, the retinal artery was arising in common with the PCAs (Hayreh, 1974b, d). Moreover, Miller (1972) tried to differentiate AION from ischaemic papillopathy, but it is not clear from the description exactly what is his concept of the latter. Sanders (1971) had in fact used the term "ischaemic papillopathy" synonymously with AION.

A comparatively low incidence of ODC was seen in AION due to arteriosclerosis in the present series. It is not possible to give a satisfactory explanation for this difference. All the evidence in the present study suggests that, in arteriosclerotic AION, the ischaemic process

is not as marked and massive as in temporal arteritis. It is possible that in arteriosclerotic AION, the ischaemic neuropathy is the result of a single transitory haemodynamic crisis in the PCAs, unlike the complete or marked occlusion of the PCA by arteritis in temporal arteritis. Since in arteriosclerotic cases the ischaemia is in all probability temporary and transient with a single vascular insult, the ischaemic changes in the ONH and retrolaminar part are presumably not as marked and extensive as in temporal arteritis. This would explain the better visual acuity, better prognosis, and lower incidence of ODC in arteriosclerotic AION as compared to temporal arteritic AION (Hayreh, 1974d). This fact has also been pointed out by Drance, Morgan, and Sweeney (1973).

Since in glaucoma and low tension glaucoma, the primary defect is the interference with the PCA circulation to the ONH and retrolaminar ON (Hamasaki and Fujino, 1967; Ernest and Potts, 1968; Hayreh and Perkins, 1968, 1969; Hayreh and others, 1970; Hayreh, 1969, 1972; Blumenthal, Best, Galin, and Gitter, 1971a; Blumenthal, Best, Galin, and Toyofuku, 1971b; Best, Blumenthal, Galin, and Toyofuku, 1972), either because of a rise in IOP (glaucoma) or a fall in perfusion pressure in the PCAs (low tension glaucoma), the above-mentioned mechanism of ODC in AION would also hold good for glaucoma and low tension glaucoma. In glaucoma and low tension glaucoma, the factors responsible for production of ischaemia are ongoing factors and, unlike those of arteriosclerotic AION, are not transitory in nature; therefore they would develop far more ischaemic changes (and associated changes) than in arteriosclerotic AION. This factor was very well illustrated by the studies of Drance and others (1973). In considering ODC in low tension glaucoma, it is interesting to note that Ellenberger and Netsky (1968) examined forty ONs in persons above 45 years of age for atherosclerosis and arteriosclerosis and found that the changes in the ON vessels were similar to those seen elsewhere in the body, thus suggesting a constant involvement of ON vessels in systemic atherosclerosis and arteriosclerosis. In AION the vascular changes in the ON show little or no correlation with those in the retina (Igersheimer, 1929; Peters, 1958).

Thus it seems that ODC in AION due to temporal arteritis, glaucoma, and low tension glaucoma is due to combined ischaemic degenerative changes in the neural tissue of the prelaminar region of the ONH, the retrolaminar ON, and the lamina cribrosa, with retrolaminar fibrosis and bowing backwards of the lamina cribrosa. Individual variations in the pattern of blood supply of this region of the ON may be responsible for variations in the response to ischaemia (acute or chronic) of the anterior part of the ON in different individuals. For example, the central retinal artery, during its intraneural course within the ON, gives no branch in 25 per cent. of cases, one branch in 26.6 per cent., two branches in 20.3 per cent., three branches in 10.9 per cent., four branches in 10.9 per cent., six branches in 1.6 per cent., and eight branches in 1.6 per cent. (Singh and Dass, 1960; Hayreh, 1963b), and these branches may be located anywhere between the point where the artery enters the optic nerve and the retrolaminar region; their size varies greatly. These branches of the central retinal artery, when and where present, constitute an axial centrifugal vascular system in this part of the ON. The major blood supply to the ON comes from the centripetal branches from the pial plexus; the latter is formed by recurrent pial branches from the peripapillary choroid and branches of the short PCAs, and collateral branches from the ophthalmic artery and its branches (Hayreh, 1963a), with marked variations in the amount of contribution from different sources. From this brief account of the blood supply of the intraorbital part of the optic nerve, it is evident that there is a very great variation in the blood supply of the retrolaminar and intraorbital ON. In some cases the retrolaminar part of the ON may have its major blood supply from the central retinal

artery and only a minor contribution from the PCAs to its peripheral part (*via* the recurrent pial branches from the peripapillary choroid); such an ON would suffer only minor peripheral ischaemia in AION. In contrast to this, in 25 per cent. of eyes, the central retinal artery gives out no branches within the nerve, and the entire blood supply to the anterior part of the ON comes from the PCAs; such a nerve would suffer massive retrolaminar destruction in the event of AION. Between these two extremes lies a whole spectrum of variations in blood supply to the anterior part of the ON. Moreover, the contribution by the peripapillary choroid to the pial plexus also varies considerably. Indeed, the pattern in the two eyes of the same individual may show a wide variation. An ischaemic disorder of the PCA would thus show all sorts of variation in the distribution of degenerative lesions in the ON. I feel this variation in the pattern of blood supply is an important factor in determining the dissimilar development of ODC in different eyes in response to identical PCA ischaemia. The involvement of the retrolaminar part of the ON in glaucoma, low tension glaucoma, and AION has always intrigued workers in the field because it has been difficult to explain how raised IOP could influence the extraocular part of the ON. Various mechanisms have been postulated to explain this, including the forcing of the vitreous or toxic intraocular fluid from the eye into the retrolaminar part of the ON, and the existence of a special artery ("the central artery of the optic nerve"—François and Neetens, 1954, 1955; François, Neetens, and Collette, 1956) supplying this region. From this description of the arterial supply of the anterior part of the ON we now know that for the retrolaminar part of the ON the peripapillary choroid is usually the main, if not the only, source of blood supply; the peripapillary choroid in turn is not only subjected to the IOP and any imbalance between the IOP and perfusion pressure in the PCAs, but also shows a higher vulnerability to obliteration under these circumstances than the rest of the choroid (Figs 2b, 3, 4). Thus, although the retrolaminar part of the ON is not directly subjected to the IOP, its blood supply is very much influenced by it.

In glaucoma and low tension glaucoma, the presence of cavernous degeneration in retrolaminar ON, which is again the result of ischaemia, is well established (Hayreh, 1972). Spencer and Hoyt (1960) pointed out that the changes in the retrolaminar ON seen by them in their histopathological study of AION due to temporal arteritis resembled cavernous degeneration. Fig. 5 shows experimentally produced cavernous degeneration after PCA occlusion in rhesus monkeys. Various locations for cavernous degeneration in the ON are given in the literature. In my study of the distribution of cavernous degeneration on histopathology in patients, I have seen all these variations. In the light of the above-mentioned variations in the contribution by the PCA to the retrolaminar ON, these variations are no surprise. Ischaemia of the ON in the region of blood supply by the recurrent pial branches of the peripapillary choroid would produce cavernous degeneration and I agree with Wolff (1947) as to the mechanism of neural degeneration although he could not explain the factors responsible for such an ischaemia.

These findings lead us to believe that ODC, cavernous degeneration, and visual field defects in AION, glaucoma, and low tension glaucoma are vasogenic in origin. In the production of vascular disturbances not only is IOP important, but the perfusion pressure in the PCAs is even more important; in fact, it is the balance between the two pressures which is crucial. This helps towards clearing up some of the age-old mysteries concerning the occurrence of ODC and cavernous degeneration without any rise in IOP.

Summary

Recent information derived from (a) clinical and experimental studies on anterior ischaemic optic neuropathy (AION), (b) the pattern of the arterial supply to the anterior part of the optic nerve (ON), and (c) fluorescein fundus angiographic studies related to glaucoma has suggested further progress in the elucidation of the pathogenesis of optic disc cupping (ODC) and cavernous degeneration.

Most probably a combination of three factors may be responsible for ODC:

- (1) Destruction of the neural tissue in the prelaminar region;
- (2) Backward bowing of the lamina cribrosa which is due to retrolaminar fibrosis and absence of the normal support of the lamina cribrosa posteriorly because of the disappearance of retrolaminar neural tissue;
- (3) Weakness of the lamina cribrosa.

ODC, cavernous degeneration and visual field defects in AION, glaucoma, and low tension glaucoma are considered to be ischaemic and vasogenic in origin, and to be due to interference with the posterior ciliary artery (PCA) supply to the anterior part of the ON either through the rise in intraocular pressure (in glaucoma) or through the fall in perfusion pressure in the PCAs (acute in AION, and chronic in low tension glaucoma).

I am grateful to my wife Shelagh for help in preparation of the manuscript and to Mrs. Maria Warbasse for secretarial assistance.

References

- BEGG, I. S., DRANCE, S. M., and SWEENEY, V. P. (1970) *Canad. J. Ophthalmol.*, **5**, 321
 ——— (1971) *Brit. J. Ophthalmol.*, **55**, 73
 BEST, M., BLUMENTHAL, M., GALIN, M. A., and TOYOFUKU, H. (1972) *Ibid.*, **56**, 6
 BLUMENTHAL, M., BEST, M., GALIN, M. A., and GITTER, K. A. (1971a) *Amer. J. Ophthalmol.*, **71**, 819
 ———, and TOYOKUFU, H. (1971b) *Arch. Ophthalmol. (Chicago)*, **86**, 31
 COGAN, D. G. (1966) "Neurology of the Visual System", p. 185. Thomas, Springfield, Ill.
 CROMPTON, M. R. (1959) *Brain*, **82**, 377
 DRANCE, S. M. (1972) In "The Optic Nerve: Proc. 2nd Wm. Mackenzie Memorial Symposium, J. S. Cant, Glasgow, 1971", ed. p. 339. Kimpton, London
 ———, MORGAN, R. W., and SWEENEY, V. P. (1973) *New Engl. J. Med.*, **288**, 392
 ELLENBERGER, C., and NETSKY, M. G. (1968) *J. Neurol. Neurosurg. Psychiat.*, **31**, 606
 ERNEST, J. T., and POTTS, A. M. (1968) *Amer. J. Ophthalmol.*, **66**, 380
 FRANÇOIS, J., and NEETENS, A. (1954) *Brit. J. Ophthalmol.*, **38**, 472
 ——— (1956) *Ibid.*, **40**, 45
 ———, and COLLETTE, J. M. (1955) *Ibid.*, **39**, 220
 GRAEFE, A. VON (1857) *v. Graefes Arch. Ophthalm.*, **3**, abt. 2, 484
 HAMASAKI, D. I., and FUJINO, T. (1967) *Arch. Ophthalmol. (Chicago)*, **78**, 369
 HAYREH, S. S. (1963a) *An. Inst. Barraquer*, **4**, No. 1, p. 7
 ——— (1963b) *Brit. J. Ophthalmol.*, **47**, 651
 ——— (1969) *Ibid.*, **53**, 721
 ——— (1970) *Ibid.*, **54**, 289
 ——— (1972) *Ibid.*, **56**, 175
 ——— (1974a) *Ibid.*, **58** (December)
 ——— (1974b) *Ibid.*, **58** (December)
 ——— (1974c) *Trans. Amer. Acad. Ophthalm. Otolaryng.*, **78**, OP-240

- (1974d) "Anterior Ischemic Optic Neuropathy". Springer, New York (In press)
- and BAINES, J. A. B. (1972) *Brit. J. Ophthalm.*, **56**, 754
- and PERKINS, E. S. (1968) "Proc. Wm. Mackenzie Centenary Symposium: The Ocular Circulation in Health and Disease", ed. J. S. Cant, p. 71. Kimpton, London
- (1969) "Proc. Int. Symp. Fluorescein Angiography, Albi", ed. P. Amalric, p. 323. Karger, Basel
- , REVIE, I. H. S., and EDWARDS, J. (1970) *Brit. J. Ophthalm.*, **54**, 461
- HENKIND, P., CHARLES, N. C., and PEARSON, J. (1970) *Amer. J. Ophthalm.*, **69**, 78
- IGERSHEIMER, J. (1929) *Z. Augenheilk.*, **69**, 47
- KNOX, D. L., and DUKE, J. R. (1971) *Trans. Amer. Acad. Ophthalm. Otolaryng.*, **75**, 1065
- MACMICHAEL, I. M., and CULLEN, J. F. (1972) In "The Optic Nerve: Proc. 2nd Wm. Mackenzie Memorial Symposium, Glasgow, 1971", ed. J. S. Cant, p. 108. Kimpton, London
- MILLER, S. J. H. (1972) *Trans. ophthalm. Soc. U.K.*, **92**, 563
- PETERS, W. (1958) *Klin. Mbl. Augenheilk.*, **132**, 363
- SANDERS, M. D. (1971) *Trans. ophthalm. Soc. U.K.*, **91**, 369
- SINGH, S., and DASS, R. (1960) *Brit. J. Ophthalm.*, **44**, 280
- SPENCER, W. H., and HOYT, W. F. (1960) *Arch. Ophthalm. (Chicago)*, **64**, 862
- WOLFF, E. (1947) *Trans. ophthalm. Soc. U.K.*, **67**, 133