

Occlusion of the posterior ciliary artery

III. Effects on the optic nerve head

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The two or three posterior ciliary arteries (medial and lateral posterior ciliary arteries), which are the source of blood supply to the posterior choroid, are also the major source of blood supply to the optic nerve head (Hayreh, 1969, 1970) and have a segmental distribution (Hayreh, 1970, 1971b). The ciliary circulation is the only source of blood supply to the lamina cribrosa and prelaminar regions, and it is an important if not the only source of supply to the retrolaminar part of the optic nerve. Hayreh (1969, 1971a) put forward the view based on these studies that ischaemic optic neuropathy is produced by acute occlusion of the posterior ciliary arteries (PCAs).

The effects of acute occlusion of the PCAs on the optic nerve head have been investigated experimentally in rhesus monkeys. These produced a clinical and histopathological picture of ischaemic optic neuropathy. Intravenous fluorescence fundus angiography (IVFA) studies of patients with ischaemic optic neuropathy have further confirmed the presence of occlusion of the PCAs.

Material

The study was carried out in 85 rhesus monkey eyes.

Methods

By lateral orbitotomy, the PCAs were cauterized near their site of entry into the eyeball, leaving a small arterial stump close to the globe, as follows:

Lateral PCAs (LPCAs) in 31 eyes
Medial PCAs (MPCAs) in 17 eyes
All PCAs (APCAs) in 37 eyes

The following investigations were performed repeatedly during follow-up (see Table: Hayreh and Baines, 1972a).

- (a) Ophthalmoscopic examinations
- (b) Intravenous fluorescence angiography (IVFA)
- (c) Tonometry in some eyes.

At the end of the experiment, the carotid vascular tree was irrigated with 2 per cent. glutaraldehyde *via* the left ventricle. All except nine of the eyes followed up for 24 hrs or longer were excised and submitted to histological examination. In thirty of the experiments (21 eyes followed for up to 2 hrs; 9 for up to 3 mths), in which the eyes were not removed for histology, glutaraldehyde irrigation was followed by irrigation of the vascular tree with normal saline. Silicone rubber was then injected *via* the common carotid artery to perfuse the ocular vascular bed. The animal was stored in the deep freeze for 24 hrs or longer to "set" the silicone rubber, after which the eye and the optic nerve were removed and cleared, using the alcohol-methyl-salicylate clearing technique. The optic disc (OD) and optic nerve (ON) vasculature filling pattern was studied under the dissection microscope.

Observations

OPTIC DISC (OD) LESIONS

The following changes in the OD were observed after occlusion of the various PCAs:

(I) *After LPCA occlusion*

(a) *1 hour after occlusion* Ophthalmoscopic examination of the fundus at this time showed slight oedema of the disc in seven eyes. This oedema involved the lower part of the optic disc in three eyes, the temporal part in two, the nasal part in one, and the whole OD in the last. Eight eyes showed pallor of the disc, as compared to its previous appearance, the pallor being usually more evident on the temporal part of the disc.

IVFA studies at this stage revealed very faint or no fluorescence of the disc during the retinal arterial phase, and moderate fluorescence during the arterio-venous phase. The fluorescence was usually more marked on the nasal than the temporal part of the disc. This is interesting, because the pre-occlusion studies in these, and in normal eyes, mostly showed a more marked fluorescence on the temporal than the nasal part. Thus, occlusion of the LPCA reversed the fluorescence pattern in these discs. During the late phase, blurring of the disc margins was seen in seven eyes with oedema of the OD.

(b) *1 to 2 days after occlusion* Out of the twelve follow-up eyes, eight eyes were examined at this stage. Of these, five showed a mild degree of oedema of the OD, involving either the whole (Fig. 1) or a part of the disc. Three of the discs with pallor in (a) above remained pale at this stage. Two eyes were normal.

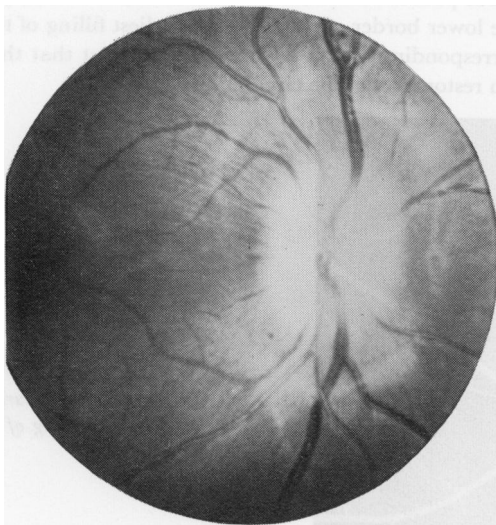


FIG. 1 *Fundus picture, showing oedema of the optic disc 2 days after occlusion of the LPCA*

IVFA studies revealed a slight fluorescence of the OD in the retinal arterial phase, largely uniform in distribution in the majority, which increased during the arterio-venous phase and again decreased in the venous phase. A mild degree of fluorescein leakage was seen in five eyes—usually along the temporal or lower margins.

After 1 week There was no significant change.

After 3 to 4 weeks In the three eyes with oedema of the OD which were followed for more than one week, the oedema subsided in about 3 to 4 weeks. Subsequently, these three eyes developed pallor, more marked on the temporal than the nasal part, and showed varying degrees of optic atrophy. None of these three eyes showed any immediate post-occlusion pallor of the OD, though two showed a degree of oedema. IVFA at the end of the follow-up revealed reduced fluorescence in the atrophic discs.

(2) *After MPCA occlusion*

(a) *1 hour after occlusion* One disc was oedematous in its lower part. No hyperaemia was seen. Five ODs showed a mild degree of pallor.

On IVFA the discs showed faint to moderate fluorescence in the retinal arterial phase, with the temporal part usually more fluorescent than the nasal. Fluorescence increased in intensity during the arterio-venous phase and was reduced in the venous phase. In the disc showing oedema inferiorly, fluorescein leakage was seen in the same area.

(b) *After 2 days* Mild oedema of the OD was seen in two eyes involving the upper part in one, and the lower part in the other. Half of the discs showed a mild degree of hyperaemia.

(c) *After 1 week* The oedema of the OD cleared.

(d) *After 2 months* One of the previously oedematous discs developed a moderate degree of optic atrophy with pallor, more marked in the nasal part than the temporal part (before the occlusion, the temporal part of the OD had been paler than the nasal part).

(3) *After APCA occlusion*

(a) *1 hour after occlusion* The discs showed uniform pallor in about a quarter of the eyes involved.

On IVFA, during the retinal arterial phase, usually only a faint OD fluorescence was seen, with some discs showing no fluorescence at all (Fig. 2). A uniform fluorescence of moderate to marked degree was seen during the arterio-venous phase. The late phase showed, in a third of these eyes, a leak of fluorescein with blurring of the lower border of the OD; the earliest filling of the peripapillary choroid (PPC) occurred in the corresponding sector. This would suggest that the fluorescein had leaked from the ischaemic vessels on restoration of the circulation.

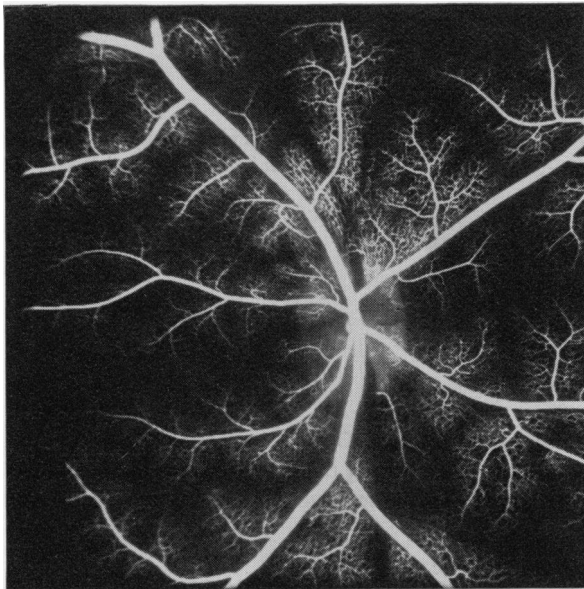


FIG. 2 *Angiogram 1 hr after occlusion of APCAs, showing, during the retinal arterial phase, no filling of the choroid*

(b) *2 days after occlusion* A mild degree of oedema of the OD with fluorescein leakage was seen in most of these eyes; this usually subsided in about a fortnight.

(c) *After more than 5 weeks* Of the thirteen eyes followed for more than 5 weeks, eleven showed optic atrophy of variable extent (Fig. 3). In four eyes with optic atrophy, enlarged collateral vessels on the OD, connecting the retinal vessels on the disc surface with the PPC, were seen—

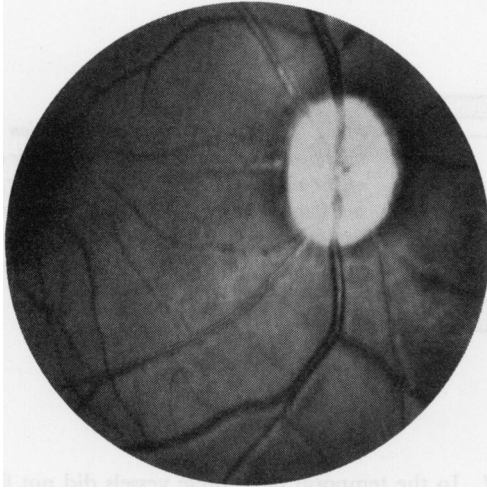


FIG. 3 *Fundus picture, showing optic atrophy 45 days after occlusion of APCAs*

an attempt at cilio-retinal anastomosis. These were on the temporal side in three (Fig. 4), and on the nasal side in one. No such vessels were seen before occluding the PCAs in these eyes. Their exact significance is not known, because they were not seen in other eyes with or without optic atrophy.

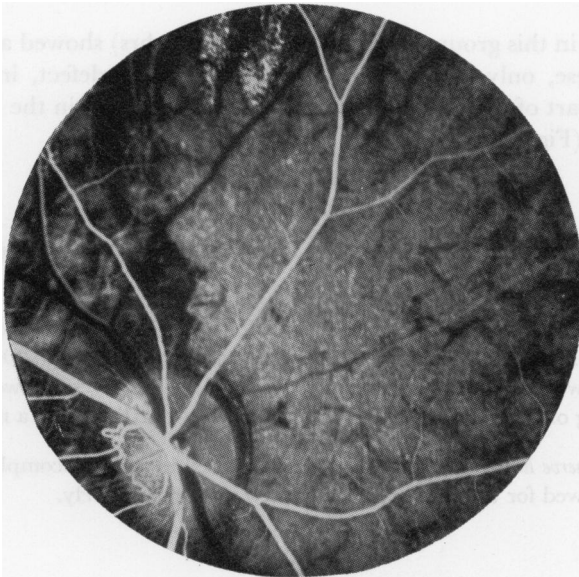


FIG. 4 *Angiogram 45 days after occlusion of APCAs showing, during the retinal arterial phase, filling of the choroid and retino-ciliary collaterals on the temporal part of the optic disc*

SILICONE RUBBER PERFUSION STUDIES

The extent of filling of small vessels in the retrolaminar part of the ON and of the ciliary vessels in the optic nerve head was studied after the occlusion of the various PCAs.

(1) *After LPCA occlusion*

There were nine eyes in this group (seven followed for up to 2 hrs and two for up to 7 and 14 days).

(i) *Retrolaminar region of the ON* In eyes followed for up to 2 hrs, the vessels in this part of the ON did not fill in three specimens (Fig. 5, overleaf), though the nerve posterior to this region filled well. In the eyes followed for 7 and 14 days, no such filling defect was seen.

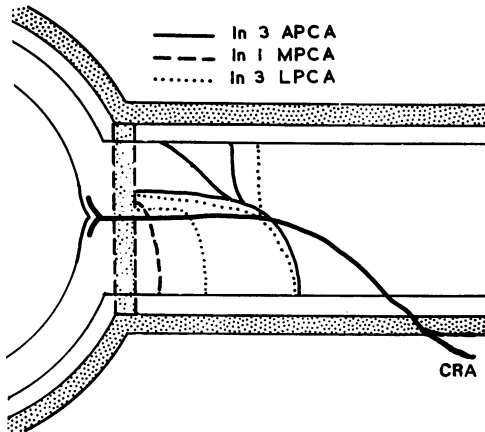


FIG. 5 Diagrammatic representation of non-filling of the vascular bed in the retrolaminar optic nerve in occlusion of the various PCAs in some of the eyes followed up to 2 hrs (based on silicone rubber perfusion studies). The non-filling area extended from the lamina cribrosa to the various lines indicating the posterior limits. CRA = central retinal artery

(ii) *Ciliary vessels in the optic nerve head* In the temporal part, these vessels did not fill in four discs followed for up to 2 hrs. In the eye followed for 14 days, the temporal part showed reduction in the number of vessels.

(2) *After MPCA occlusion*

Three of the five specimens in this group (all followed for up to 2 hrs) showed a satisfactory filling of the ON. Of these, only one specimen showed a filling defect, involving the ciliary vessels in the nasal part of the optic nerve head and a small area in the inferior part of the retrolaminar region (Fig. 5).

(3) *After APCA occlusion*

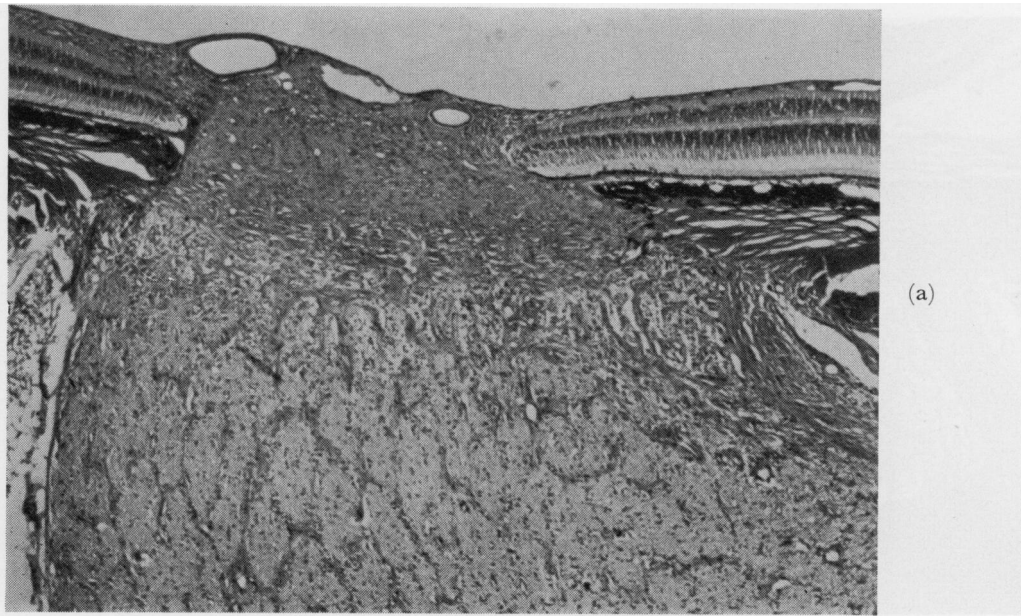
There were sixteen eyes in this group (nine followed for up to 2 hrs, three for up to 2 weeks, and four for 3 mths).

(i) *Retrolaminar region of the ON* Three of the eyes followed for up to 2 hrs showed no filling of the vessels in this region, in spite of a normal filling of the nerve posterior to it (Fig. 5). One of the eyes followed for up to 2 weeks showed a poor filling in this region. Of the four eyes followed for 3 mths, three showed poor or no filling of this part of the nerve, although the fourth showed a normal filling.

(ii) *Ciliary vessels in the optic nerve head* These were either not filled at all or incompletely filled in four, one, and three eyes followed for up to 2 hrs, 2 wks, and 3 mths respectively.

HISTOLOGICAL STUDIES

In the OD showing ophthalmoscopic evidence of atrophy, histological examination revealed the presence of atrophic changes in the OD and the retrolaminar part supplied by the PCAs (Fig. 6a, b, opposite). In some eyes, the atrophic area had a well-marked border with the normal ON (Fig. 6a). This well-marked infarction of the ON is also seen in patients with ischaemic optic neuropathy (Fig. 6c, overleaf). In other monkey eyes the junction between the two was not so well-defined, although the distribution of atrophic changes was similar. In some of these, the atrophic changes were more marked in the peripheral part of the ON. There was a localized patch of optic atrophy in the peripheral part of the retrolaminar ON on the occluded side in a significant number of these nerves.

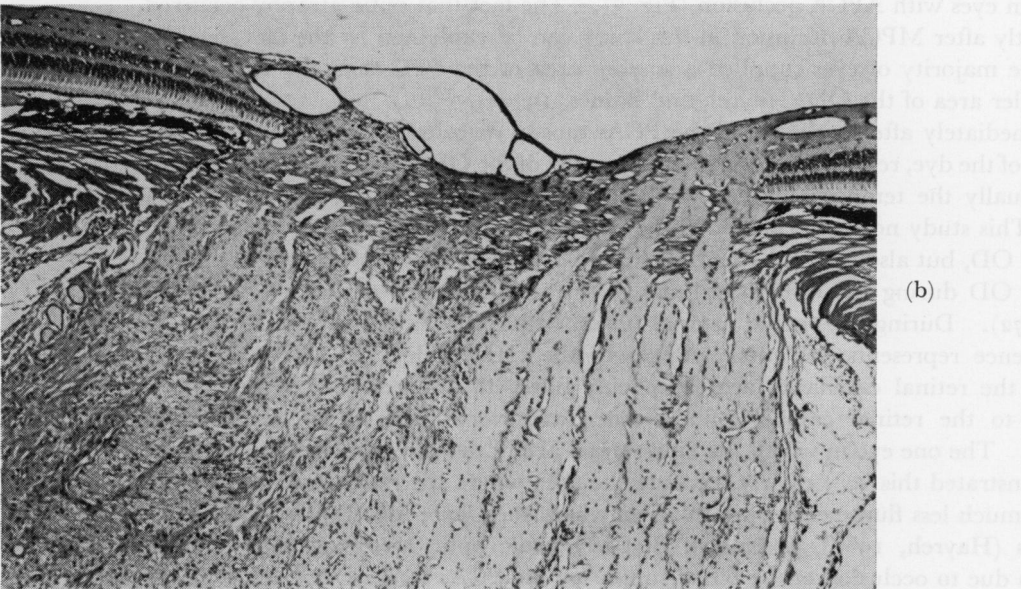


(a)

FIG. 6 Photomicrographs of optic disc and optic nerve

- (a) 36 days after APCA occlusion (Masson's trichrome stain). $\times 38$;
- (b) 42 days after LPCA occlusion (Masson's trichrome stain). $\times 38$;
- (c) in a patient with ischaemic optic neuropathy (Verhoeff's modified elastic stain). $\times 6$.

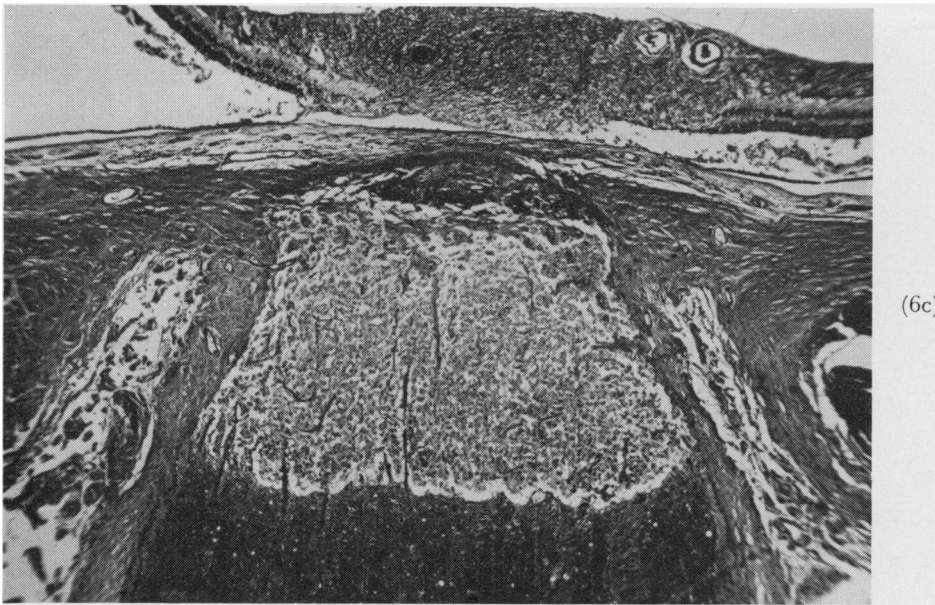
(a and c) show generalized well-demarcated involvement of the optic disc and retrolaminar part, while (b) shows the atrophy involving only the temporal half of this region. (Fig. 6c is reproduced by kind permission of Dr. I. M. MacMichael.)



(b)

Discussion

In the present study, the OD was not involved in all the eyes. A mild to moderate degree of oedema of the OD following the occlusion of the PCAs was seen (Fig. 1); less frequently in LPCA than in APCA occlusion, and least frequently in MPCCA occlusion. This



represents ischaemic optic neuropathy. About one-quarter of the eyes in each group showed immediate post-occlusion pallor of the OD; the pallor of the OD was usually more marked on the temporal than the nasal side in LPCA occlusion, more on the nasal than the temporal side in MPCA occlusion, and uniform in APCA occlusion. When the course was followed for over 5 to 6 weeks, evidence of optic atrophy was seen in three out of five eyes with LPCA occlusion, in one out of six eyes with MPCA occlusion, and in eleven out of thirteen eyes with APCA occlusion (Fig. 3). The fact that optic atrophy occurred least frequently after MPCA occlusion in this study can be explained by the fact that the MPCA in the majority of eyes supplied a smaller area of the PPC than the LPCA and hence a smaller area of the OD (Hayreh and Baines, 1972a).

IVFA immediately after occlusion of the PCAs mostly revealed, during the early part of the transit of the dye, reduced fluorescence of the part of the OD supplied by the occluded PCA, *e.g.* usually the temporal part in LPCA occlusion and the nasal part in MPCA occlusion. This study not only confirmed the role of the ciliary circulation in the blood supply of the OD, but also helped by giving more information about the origins of fluorescence of the OD during the different phases of the retinal transit of the dye in IVFA (Hayreh, 1972). During the retinal arterial phase, before the retinal capillaries fill, the disc fluorescence represents the ciliary supply to the OD, while in the arterio-venous phase when the retinal capillaries are completely filled, the fluorescence of the OD is due mainly to the retinal capillary fluorescence and very little to the deep ciliary fluorescence. The one eye in which the cilio-retinal artery did not fill on occlusion of the LPCA demonstrated this very clearly, because the area where the retinal capillaries were missing was much less fluorescent than the area where they were full (Fig. 7).

One of us (Hayreh, 1969), postulated that ischaemic optic neuropathy, as seen in patients, was due to occlusion of the blood supply by the PCAs to the OD. This view is supported by the fact that, on IVFA, the eyes of patients with ischaemic optic neuropathy show very slow and poor filling of the choroid or, on occasion, complete absence of filling (Fig. 8, overleaf).

It is further confirmed by the histological demonstration of infarction of the

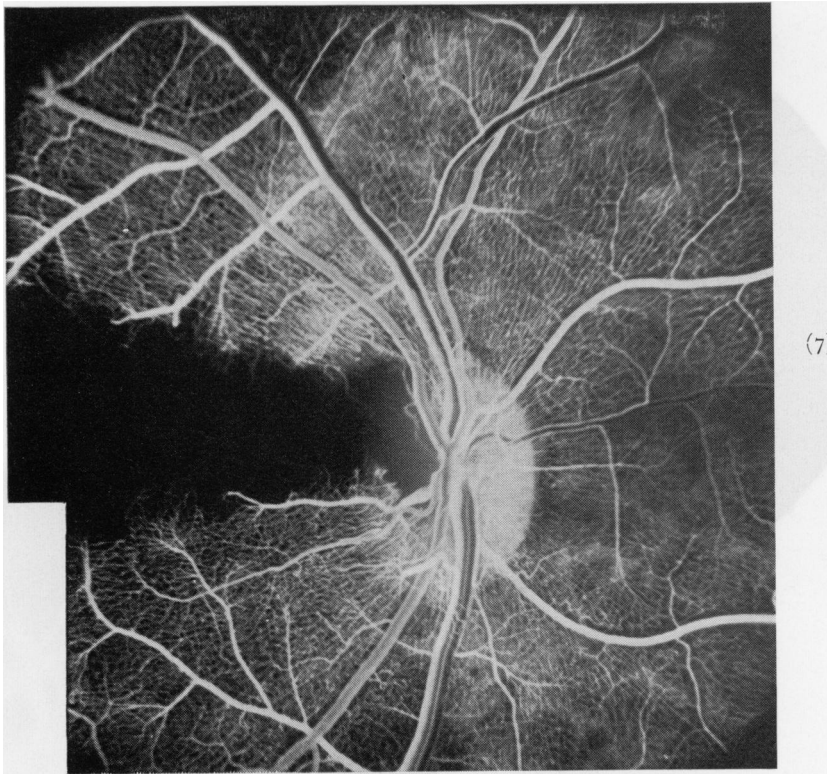


FIG. 7 Angiogram 1 hr after occlusion of the LPCA, showing a filling defect in the retinal vascular bed in an eye with a cilio-retinal artery supplying the unfilled part of the retina

retrolaminar part of the ON and OD in such cases (Fig. 6c). In the present experimental study some animals showed a similar ischaemic optic neuropathy, ophthalmoscopically (Fig. 1) as well as histologically (Fig. 6a,b). Other animals, however, did not show this phenomenon, but its absence can be explained easily: the monkeys of the present study were all young and healthy, and the majority of them had many collaterals available, e.g. via the pial branches of the PPC (Hayreh and Baines, 1972a), so that occlusion of the PCAs did not seriously disrupt the blood supply to their discs. Such a collateral circulation to the OD was seen on silicone rubber perfusion of the arteries. IVFA studies of the monkeys also showed filling of the PPC and frequently a mild degree of fluorescence of the OD during the arterial phase immediately after occlusion of the PCAs. The posterior episcleral collaterals (Hayreh and Baines, 1972a) would also help to maintain the circulation in some eyes. Hayreh, Revie, and Edwards (1970) demonstrated that the circulation in the optic disc is dependent upon the difference between the intraocular pressure and the perfusion pressure in the disc vessels (derived from the PCAs). The markedly low intraocular pressure seen in these experimental eyes within 24 hrs of the occlusion of the PCAs (Hayreh and Baines, 1972b) would assist the perfusion of the disc vessels, even if the perfusion pressure (maintained by the collateral circulation to the disc) is very low in the vessels. This will prevent the development of ischaemic optic neuropathy. On the contrary, patients suffering from ischaemic optic neuropathy are typically over 60 years of age, and have such a marked degree of arteriosclerosis that the collateral circulation is unlikely to be adequate; the normal intraocular pressure would further interfere with the disc circulation in these eyes with very low perfusion pressure in the disc vessels.

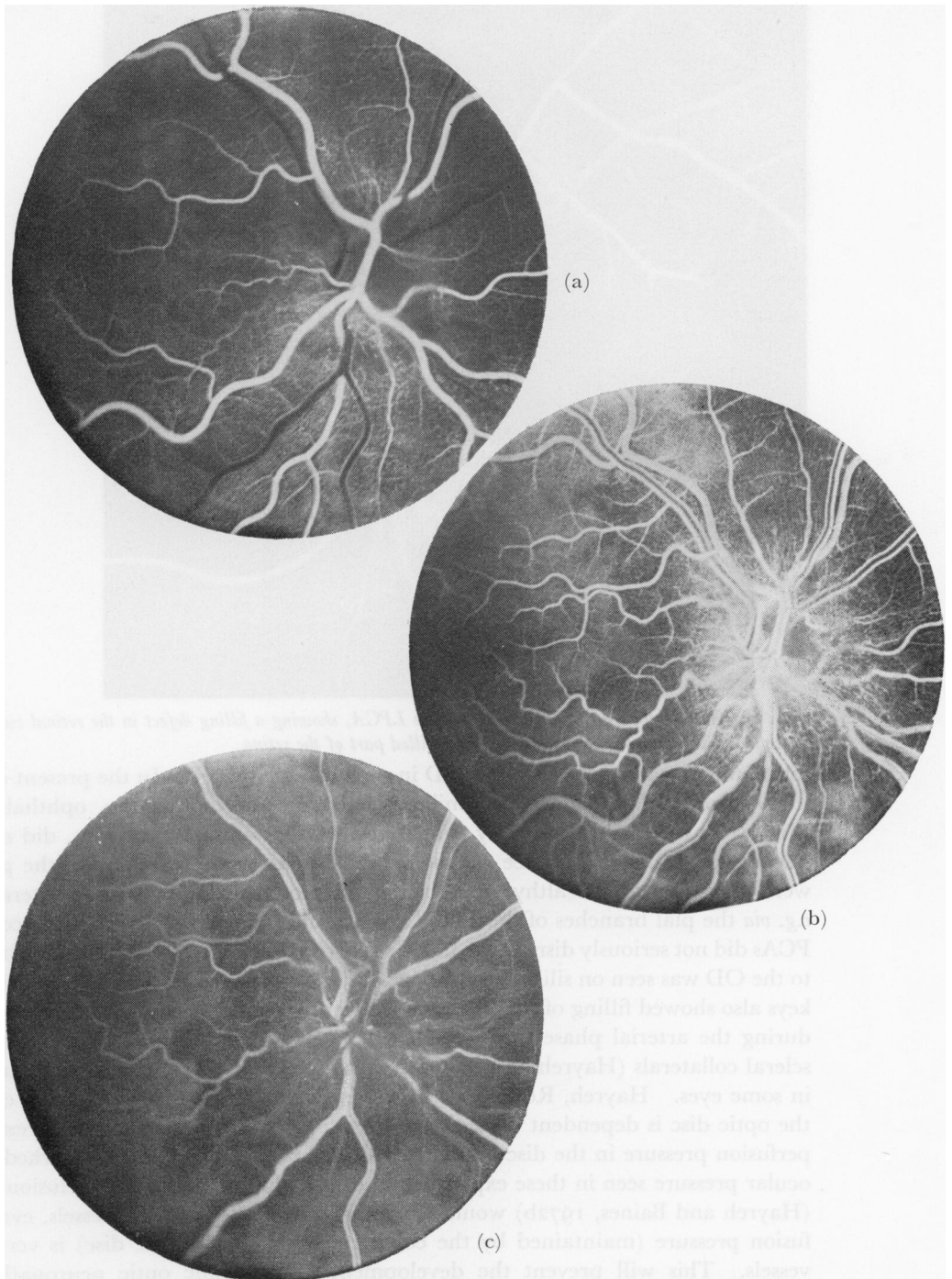


FIG. 8 Angiograms of right eye of 72-year-old patient with ischaemic optic neuropathy:
 (a) Early retinal arterio-venous phase, showing no choroidal filling (compare with Fig. 2);
 (b) Late retinal arterio-venous phase, showing filling of temporal choroid but not of peripapillary choroid (PPC) and optic disc;
 (c) Late retinal venous phase, showing filling of choroid but not of PPC and optic disc

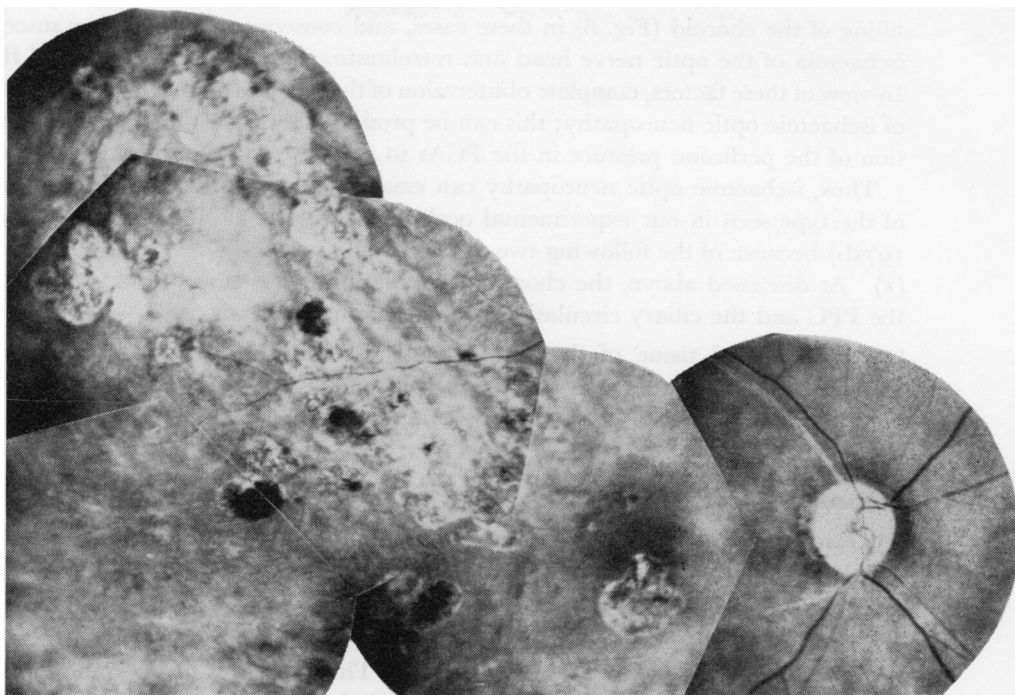


FIG. 9 Fundus photograph of right eye of 72-year-old patient who had had ischaemic optic neuropathy 9 months previously, showing optic atrophy (with cupping) and a sectoral chorio-retinal degenerative lesion

In contrast to the fundus lesions seen in our experimental occlusion of the PCAs (Hayreh and Baines, 1972b), patients with ischaemic optic neuropathy showed only rarely similar sectoral fundus lesions (Fig. 9), with disturbance of the pigment epithelium posterior to the equator (in five out of twenty eyes examined). This rarity could be explained by the fact that, in almost all the patients investigated by IVFA, some choroidal circulation from the PCAs was observed during the venous phase of the retinal circulation (Fig. 8c), although there was no choroidal filling during the arterial and early arterio-venous phases (Fig. 8a). However, no filling of the PPC, even in the venous phase, could be observed (Fig. 8). Thus, in these cases, the OD suffers most, while the poor and delayed circulation in the rest of the choroid in these eyes is sufficient to prevent the development of classical fundus lesions. This choroidal effect was also seen in our experimental study (Hayreh and Baines, 1972b). In almost all cases of ischaemic optic neuropathy, the presence of some choroidal circulation, however poor and delayed, seems to suggest either (a) that the main PCAs are markedly narrowed but not completely occluded, or (b) that the circulation in the occluded PCAs re-establishes itself very quickly. That such rapid re-establishment can occur is clearly demonstrated by angiographic findings in patients with central retinal artery occlusion (Hayreh, 1971c). Whether poor and delayed choroidal circulation is due to (a) or to (b), in either case the perfusion pressure in the PCA circulation would be significantly reduced. This would produce an imbalance between the perfusion pressure and intraocular pressure. Such an imbalance leads to defective perfusion and/or obliteration of vessels in the choroid and PPC, and depletes the PCA supply to the optic nerve head (Hayreh and others, 1970). Susceptibility to obliteration of the vessels in these circumstances is maximal in the OD, slightly less in the PPC, and least in the rest of the choroid. This explains the non-filling of the PPC and OD, with poor and delayed

filling of the choroid (Fig. 8) in these cases, and consequently the higher susceptibility to ischaemia of the optic nerve head and retrolaminar part of the ON than of the choroid. In view of these factors, complete obliteration of the PCAs is not necessary for the production of ischaemic optic neuropathy; this can be produced by any sudden and prolonged reduction of the perfusion pressure in the PCAs to a level below the intraocular pressure.

Thus, ischaemic optic neuropathy can exist in man without any chorio-retinal lesions of the type seen in our experimental occlusive studies of the PCAs (Hayreh and Baines, 1972b) because of the following two factors:

- (1) As discussed above, the choroidal circulation is less susceptible to obliteration than the PPC and the ciliary circulation in the optic nerve head.
- (2) The neural tissue of the ON is far more sensitive to anoxia than the pigment epithelium, as the latter can survive in spite of a very poor circulation (suggested by our experimental study—Hayreh and Baines, 1972b).

Summary

The effects of experimental occlusion of the various posterior ciliary arteries (PCAs) on the optic nerve head have been investigated in 85 rhesus monkey eyes. Optic atrophy developed after 5 to 6 weeks in 16 per cent., 60 per cent., and 85 per cent. of the eyes after occlusion of the medial, lateral, and all PCAs respectively. During the initial phases these eyes showed oedema of the optic disc. These changes in the optic disc are typical of ischaemic optic neuropathy. Patients with ischaemic optic neuropathy, on fluorescence angiography, showed evidence of occlusion of the PCAs. In both groups, histopathological studies revealed involvement of the optic nerve head and retrolaminar part of the optic nerve—the parts of the optic nerve supplied by the posterior ciliary circulation. The role of the intraocular pressure in ischaemic optic neuropathy is discussed.

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References

- HAYREH, S. S. (1969) *Brit. J. Ophthalm.*, **53**, 721
 ——— (1970) *Ibid.*, **54**, 289
 ——— (1971a) In "Proc. int. Symp. Fluorescein Angiography, Albi, 1969", pp. 510–530. Karger, Basel
 ——— (1971b) *Trans. ophthalm. Soc. U.K.*, **91**, 291
 ——— (1971c) *Amer. J. Ophthalm.*, **72**, 998
 ——— (1972) *Ophthalmologica (Basel)*, **165**, 100
 ——— and BAINES, J. A. B. (1972a) *Brit. J. Ophthalm.*, **56**, 719
 ——— (1972b) *Ibid.*, **56**, 736
 ———, REVIE, I. H. S., and EDWARDS, J. (1970) *Ibid.*, **54**, 461