Occlusion of the posterior ciliary artery

II. Chorio-retinal lesions

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The clinical picture of central retinal artery occlusion is well-known. Little is known, however, about the clinical picture of occlusion of the posterior ciliary arteries (PCAs). We have, therefore, carried out experimental occlusion of the various PCAs individually or together in rhesus monkeys. The effects of such occlusions have been investigated in the choroid, pigment epithelium (PE), and retina of these monkeys over a period of time, ophthalmoscopically, by intravenous fluorescence fundus angiography (IVFA), and (after death) by histology. The study has revealed fundus lesions the nature of which has hitherto been obscure.

There are usually two to three PCAs, arising from the ophthalmic artery, which supply the posterior half of the choroid up to the equator of the eye. These are designated medial (MPCA) and lateral (LPCA), depending upon their relationship to the optic nerve near their site of entry into the sclera. A detailed account of the anatomy of the PCAs is given elsewhere (Hayreh, 1962, 1970).

The effects of occlusion of the various PCAs on the choroidal circulation have already been described in detail (Hayreh and Baines, 1972). Briefly, the distribution of the PCAs in the choroid was seen to be segmental, so that occlusion of one PCA resulted in non-perfusion of the choroid in that region during the transit of the dye in IVFA. However, a very late and sluggish patchy filling of the choroid via the various collaterals took place; this improved with time, so that in 2 to 4 weeks the choroidal circulation was restored.

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.

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

(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. gluteraldehyde via the left ventricle. All except nine of the eyes which had been followed up for 24 hrs or longer were excised and submitted to histological examination.

Observations

Fundus Lesions

Ophthalmoscopic examination of the fundus at about 1 hr after the occlusion of the PCAs showed no detectable fundus lesion.

The next examination of the fundus was made 18 to 24 hrs, or 2 days after the occlusion of the PCAs, when white patches were seen in the part of the fundus supplied by the occluded artery (Figs 1, 2a). These patches assumed a large variety of shapes and sizes. Their size varied from a tiny spot to a large area of the fundus. They were irregular in shape, many being elongated with pointed ends, and frequently tended to be triangular and sectoral. These patches were separated from one another by narrow strips of normal-coloured fundus and sometimes by the big visible choroidal vessels. The white patches gave an impression of being infarcts lying deep to the retina. Stereoscopic examination of the lesions also showed them to lie deep to the retina.

On follow-up, these lesions did not increase significantly in size. However, they became more clearly defined over the following few days. At the beginning of the second week they began to resolve. They became less white, assumed a granular appearance, becoming less dense and grey. After 2 to 3 weeks these lesions appeared as granular, greyish, depigmented scars in the fundus (Fig. 3). With the passage of time some of the patches tended to become ill defined (Fig. 2b).

Another interesting change appeared towards the end of the second week. The grey lesions became surrounded by a narrow zone, like a dark-coloured halo, which was darker than the surrounding fundus (Fig. 3). These patches became more marked with time and their size increased, extending to involve the adjacent normal-looking fundus. This was a slowly progressive phenomenon and the lesion was found to be still increasing in size when followed for more than 3 mths (Figs 2, 4), but became stationary by about 5 to 7 mths. Thus, the involved part of the fundus had large, irregular dark-brown areas, with steel-grey patches, in addition to the greyish-white granular depigmented patches scattered amongst them, and the pigmented areas encroached upon the normal-looking fundus. In the depigmented areas the main choroidal vessels were sometimes more conspicuous than in the normal fundus. Some of these patches, when associated with choroidal destruction, had a mottled, shining, greyish-white appearance, with prominently visible large choroidal vessels (Fig. 5, overleaf).

In addition to the characteristic fundus lesions seen in these eyes, a few eyes showed the following pattern:

(a) Instead of the ophthalmoscopically well-defined patches of the lesions mentioned above, only a diffuse scattered irregular motting of the pigment was visible in some areas. These patches were seen better on fluorescence angiography than by ophthalmoscopy.
FIG. 1 Fundus pictures showing white patches in (a) infero-temporal region 2 days after LPCA occlusion (in eye No. 36 in Fig. 4a) and (b) supero-temporal region 1 day after occlusion of all the PCAs (in eye No. 21 in Fig. 4c).

(b) In others no depigmented patches were seen, but large areas of dark brown discolouration (Figs 4, 6) of the fundus (similar to the haloes) were seen, usually situated in the region extending from the outer limits of the central part of the fundus (the central part includes the macular region, optic disc (OD), peripapillary choroid (PPC), and adjacent areas) to the equator of the eye. Examination of the peripheral fundus in some of the animals, which survived for a month or more, showed that in the equatorial region of the affected part of the fundus there was a scalloped border between the posterior dark-coloured fundus and the anterior normal fundus. This indicated that the pigmentary disturbance in the involved region was diffuse and extensive, and was associated with increased pigmentation of the fundus.

We found differences in the distribution of the fundus lesions in occlusion of the LPCA, MPCA, or APCA (Fig. 4a-c, overleaf).

(i) After LPCA occlusion
The lesions involved the temporal part of the fundus in every eye (Figs 1, 2, 4a). In two eyes they also encroached upon the adjacent part of the inferior nasal sector (Fig. 4a). In no eye did the lesions involve the PPC, or the area extending from the OD to the nasal margin of the macula. The macula was involved in three eyes (Fig. 4a). The temporal lesions were of extremely varied distribution, but were usually situated in the supero-temporal, temporal, and infero-temporal parts of the fundus in the area between the equator and the central region (Fig. 4a). In the macular region, particularly the region between the OD and the macula, horizontal retinal folds were frequently seen for the first 2 to 3 weeks.

(2) After MPCA occlusion
The lesions appeared in the nasal part of the fundus in one-half of the eyes, no lesion being seen in the rest. Their distribution was also very varied, and they were situated in the
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FIG. 2 Fundus drawings showing lesions after LPCA occlusion after (a) 5 and (b) 90 days of occlusion.

FIG. 3 Fundus pictures showing the lesions after occlusion of all the PCAs (in eye No. 12 in Fig. 4c) situated in (a) supero-nasal and (b) supero-temporal sectors 93 days after occlusion.

area between the equator and the central region of the fundus (Fig. 4b). In almost all cases the lesions seen in MPCA occlusion were much smaller in size and more localized than those seen in LPCA occlusion (Fig. 4).

(3) After APCA occlusion
The PCA supply to the eye was completely cut off. Much more extensive lesions were seen than in either of the previous groups (Fig. 4). In this group the lesions were seen in every eye and involved many parts of the fundus (Fig. 4c). In eyes in which a small short PCA escaped cutting, no fundus lesions were seen in the corresponding sector.
FIG. 4. Diagrammatic representation of the various fundus lesions seen in the monkey eyes of the present series after (a) LPCA, (b) MPCA, and (c) all PCAs occlusions. Dark areas represent the distribution of white patches and the shaded areas that of subsequent discolouration of the fundus.

X = position of the macula.
Fluorescence fundus angiographic pattern of the fundus lesions

As already mentioned, these lesions were followed up by IVFA. During the transit of the dye through the eye, no background choroidal fluorescence was seen in the region of the white patches during the initial stages of their appearance; these patches, however, showed fluorescence a few minutes after the transit (Fig. 7a) because the fluorescein stained the necrotic material, of which they consisted.

The white patches progressed to become thin, and unmasking of the choroidal fluorescence became evident, indicating a thinning of the PE (Fig. 7b). This unmasking became more prominent with the passage of time and was at its greatest when the lesions assumed
the granular depigmented greyish-white appearance (Figs 8, 9). The marginal parts of the lesion showed a bright granular fluorescence, which appeared with the filling of the choroid. The central part of the lesion showed evidence of reduction of choroidal vessels and some granular fluorescence as well. In these patches the main choroidal arteries showed a distinct filling and unmasking (Fig. 9). This fluorescence of the patches persisted only during the transit of dye through the choroid and faded off thereafter. There was no staining of the lesions after about 3 weeks.
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The steel-grey patches in the haloes around the depigmented choroidal lesions usually slightly masked the choroidal fluorescence (Figs 3a, 8). In the eyes showing no depigmented patches but large areas of dark brown discolouration, IVFA showed no abnormality. Similarly, when such a discolouration was associated with typical depigmented lesions, no fluorescence angiographic abnormality corresponding to the dark brown patches was evident.

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FIG. 9 Angiograms 58 days after occlusion of all PCAs (in the eye shown in Fig. 5) during retinal arterio-venous phase, showing marked destruction of choroid nasally with choroidal unmasking along the borders.

No other fluorescence angiographic abnormality was detected in the fundus. The findings suggested a degeneration of the PE in the areas of the patches with some destruction of small and medium-sized choroidal vessels in the central part of these lesions (Fig. 8). The retina showed no abnormality. In areas with marked choroidal degeneration (Fig. 5), apart from a few big choroidal vessels, no other choroidal vessels were seen (Fig. 9), except at their margins.

HISTOLOGICAL STUDIES
The various fundus lesions showed histological changes. These changes never involved the anterior part of the choroid nor the overlying retina, which is supplied by the anterior ciliary arteries.

(1) Retina
In eyes with white patches necrotic material was present between Bruch’s membrane and the inner layers of the retina in the region of the patches (Fig. 10). The necrotic material consisted of dead PE, rods, cones, and to a variable degree the outer nuclear layer. The pigment granules of the PE were irregularly scattered in the necrotic mass. The latter varied in thickness and structure, depending upon its age, and disappeared completely in older lesions.

In old lesions the commonest change observed was the loss of visual cells and outer nuclear layer in the area of the lesion (Figs 11; 12). A few nuclei of the outer nuclear layer might still be seen (Fig. 13, overleaf). Rarely, the inner nuclear layer was somewhat involved and disorganised but not significantly.

FIGS 10 to 14 Microphotographs showing microscopic changes after the PCAs occlusion
FIG. 10 Section through a white patch in the fundus, showing necrosis of the pigment epithelium, rods, cones, and outer nuclear layer, 11 days after occlusion of all the PCAs. Haematoxylin and eosin. ×277
FIG. 11 Section through an area with normal (right side) and degenerate (left side) retina, 41 days after all PCAs occlusion. Haematoxylin and eosin. ×42
FIG. 12 21 days after all PCAs occlusion (in eye No. 29, Fig. 4c). Haematoxylin and eosin. ×234
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FIG. 10

FIG. 11

FIG. 12
Chorio-retinal adhesions were frequently seen in ophthalmoscopically well-marked lesions (Figs 12; 13). In these adhesions, the PE and Bruch’s membrane were often absent or disorganized. In a few instances some big pigmented cells were seen to have invaded the retina close to the choroid (Fig. 12). No migration of the pigment into the deeper layers of the retina was seen.
(2) Pigment epithelium

This was involved significantly in the vast majority of these eyes. There were, however, instances where, with the retina showing absence of the visual cells and outer nuclear layer, no significantly demonstrable changes in the PE could be seen. The reverse was also true (Fig. 14b).

The changes in the PE varied from mild degeneration (Fig. 14b) to complete disorganization (Figs 12; 13) or even to the complete absence of the PE. Usually the degeneration of the PE was more widespread than the changes in the overlying retina (Fig. 14b). The normal PE is thin, uniform in thickness, light brown, having regularly arranged cells and a very finely granular appearance (Fig. 14a). The changes in the PE seen in the region of the white patches have already been mentioned under 'retina'. In old lesions, the PE might be represented by very dark (sometimes even black) clumps or granules. In others the epithelium might be irregular in thickness, with coarse granules (Fig. 14b). Some of these granules were discrete, rounded, of varying size, and black. At some places a few of these isolated granules were the sole evidence of the PE (Fig. 12). Big, round, pigmented cells were seen lying over Bruch's membrane in some areas (Fig. 12), or even invading the adjacent layers of the retina. These were considered to be grossly hypertrophied PE cells. Sometimes localized hypertrophy of the PE was seen around the area of the destruction of the PE (Fig. 13).

In eyes where the ophthalmoscope showed pigmented fundus lesions, e.g. brownish discoloration of the fundus—the only histological evidence was roughening and some thickening of the PE (Fig. 14b).

(3) Bruch's membrane

Usually Bruch's membrane showed no demonstrable changes in mild fundus lesions. Where chorio-retinal adhesions were seen, the membrane was generally absent (Fig. 12). A possible thickening and hypertrophy of Bruch's membrane was seen in some places and frequently in areas close to chorio-retinal adhesions. In some eyes, however, a normal Bruch's membrane was present, even in the presence of the adhesions (Fig. 13).

(4) Choroid

Usually no demonstrable change was seen in the choroid, except for some obliteration of the chorio-capillaris. In some of the areas which showed evidence of absence of choroidal vessels on IVFA, there was localized atrophy of the choroid. In the eyes irrigated with gluteraldehyde, normally no blood was seen in the choroidal vessels if adequate circulation was present, but in eyes with freshly occluded PCAs, the choroid was full of blood on the side of the occlusion.

INTRAOCULAR PRESSURE STUDIES

This was measured by Schiötz tonometer in some of the long-term experiments. It was found to be unrecordably low on examination 1 or 2 days after the occlusion in all the eyes. It started to recover very slowly after at least 3 to 4 weeks, and did not recover to the normal level during the period of follow-up in the present study—three months in most cases.
Discussion

(1) EXPERIMENTAL STUDIES

Fundus lesions

In PCA occlusion, patchy fundus lesions are seen in the region between the equator and the outer limits of the posterior pole, in the temporal part in LPCA occlusion, in the nasal part in MPCA occlusion, and in both temporal and nasal parts in occlusion of all the PCAs (Fig. 4). The patches are of all shapes and sizes, usually triangular and sectoral, and varying from tiny spots to ones involving a large area, while the intervening fundus may appear normal. The patches are more extensive in LPCA than in MPCA occlusion, and most extensive in APCA occlusion. Their colour depends upon their stage—fresh patches are well-defined and homogeneously white in colour (Fig. 1), but after resolution they assume a granular, greyish, depigmented appearance (Figs 3; 5). Around these patches are areas of hyperpigmentation, with dark brown or steel-grey pigmentation (Figs 2; 3; 4); occasionally no depigmented patches may be visible and the fundus may show areas of hyperpigmentation only (Figs 4; 6). In the depigmented patches choroidal vessels may be prominently visible and some have a mottled, shining, greyish-white appearance because of the sclera shining through the thinned choroid (Fig. 5).

On IVFA, no background choroidal fluorescence is usually seen during the transit of the dye in areas of the white patches during the early changes of the lesion, because the choroid in and around the patches does not fill at this stage. We feel that the masking effect of the necrotic tissue in the white patches is not a significant factor in the absence of this background choroidal fluorescence. This is because (a) the filling defects tend to be more extensive than the white patches, (b) non-perfusion of the choroidal vascular bed in that region has been demonstrated less than 24 hrs before the development of the white patches, and (c) later on, as the choroidal circulation improves, choroidal filling can be seen in the region of the patches. A few minutes after the injection of fluorescein, the white patches show late fluorescence (Fig. 7a) associated with an abnormal leakage of fluorescein into the eye. The late fluorescence is due to staining of the necrotic tissue of the white patches by the fluorescein very slowly perfusing into that part of the choroid (Hayreh and Baines, 1972) and its profuse leakage from the choroid into the overlying tissue. The various factors responsible for the abnormal leakage of fluorescein into the eye have already been discussed (Hayreh and Baines, 1972).

On angiography the depigmented patches show thinning or absence of the PE (Figs 7b; 8). In the central part of big patches most of the small choroidal vessels are absent and only the big vessels are outlined which, ophthalmoscopically, may look white but still have blood flowing in them (Figs 5; 9)—a condition similar to choroidal sclerosis. No leakage of fluorescein is seen from the depigmented patches. The brown patches usually show no abnormality on IVFA. The steel-grey patches tend to mask the choroidal fluorescence (Figs 3a; 8). The retinal vasculature and circulation is normal.

Correlation of site of lesion with choroidal ischaemia

In the majority of the eyes, the site and extent of the lesions after PCA occlusion depended to a great extent upon the extent of the choroidal filling, either via the posterior episcleral arterial plexus or retrograde filling via the vortex veins (Hayreh and Baines, 1972). The lesions usually appeared in areas devoid of choroidal filling from these sources immediately after the occlusion, as revealed by non-perfusion of the area of the choroid during the transit of the dye in IVFA studies. In some, however, it was difficult to be definite about
the exact area of non-perfusion in the choroid. On follow-up studies, a delayed filling of the choroid in the areas of the lesion was usually evident. It is, again, difficult to explain the occurrence of elongated pointed lesions with narrow intervening strips of normal-looking fundus.

Fundus lesions after the section of the PCAs in the rabbit have been described in the literature (Wagenmann, 1890; Krückmann, 1899; Capauner, 1893; Nicholls, 1938). Nicholls (1938) recorded three types of changes, depending upon the number of vessels cut:

(a) No change.
(b) Phthisis bulbi.
(c) Localized area of retinal degeneration: this was seen in the region supplied by the bulk of the vessels.

Degeneration was produced only after cutting at least two-thirds of the PCAs, although Wagenmann (1890) noticed these changes on section of only a few ciliary arteries. Nicholls (1938) found extreme pallor in the area immediately after occlusion, spreading fan-wise from the optic nerve head out to the ora; in a few hours these were less pale but swollen. In about a week, two changes were noticed:

(i) A normal appearance returned to certain areas with the restoration of circulation;
(ii) Where circulation was not restored, the pale area gradually became spotted here and there with round sharply-circumscribed dense accumulations of pigment (mostly in the equatorial region), which progressively changed over several weeks to stabilize in 4 to 5 months, when a contraction of the degenerate area, with shallow folds in the normal areas, was seen.

The changes seen by these authors resemble some seen in our present study. In none of our animals did a circumscribed dense accumulation of pigment or phthisis bulbi develop.

Wagenmann (1890) and Nicholls (1938), in their histological studies in rabbits, found massive degeneration of all layers of the retina, with degeneration of the PE in these areas, which was absent at other places. At the border of this complete degeneration of the retina, a gradual thinning of rods, cones, and outer nuclear layers was seen, with little or no change in the PE. When the external limiting membrane was involved in the border area, pigment migrated to the retina rather than to the choroid, and later spread throughout the retina, but the changes were not like those of retinitis pigmentosa. The choroid did not show marked changes except some thinning here and there; the choroidal changes had no relationship to the retinal changes. Our studies mostly confirm their findings, except that in the retina we saw degeneration only of the rods, cones, and the outer nuclear layer, and not of the entire thickness of the retina. The difference in the blood supply of the retina in rabbits and primates would account for this difference in our findings; in rabbits the entire thickness of the retina is supplied by the choroid, but in primates the choroid supplies only the outer layers of the retina. No migration of the pigment into the retina was seen in the present studies.

(2) Clinical studies

The primary object of any experimental study is to give a better understanding of a clinical condition, the pathogenesis of which is not very evident in a clinical study. With this in view, we have looked for clinical conditions which our experimental lesions simulate.
Hepburn (1912, 1935) described sectoral fundus lesions in patients, starting with an ill-defined area of oedema, and later resolving to sectoral pigmentary changes (fine granular pigmentary changes in the PE) with normal retinal vessels. In one of his cases the changes involved the lower half of the fundus. He rightly attributed these lesions to occlusion of the main PCA. Similarly, Amalric (1971) has described triangular sector-shaped areas of pigmentary disturbance in the fundus and ascribed these to PCA occlusion. Foulds, Lee, and Taylor (1971) also described similar cases. Acute posterior multifocal placoid pigment epitheliopathy (Fig. 15), originally described by Gass (1968), is in all probability an example of localized acute choroidal ischaemia produced by occlusion of small choroidal arteries. The lesions seen in all these instances have a great deal of resemblance to the fundus lesions seen in our experimental studies. We have seen similar sector-shaped pigmentary degeneration of the fundus in some of the cases investigated in our Retinal
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Unit. The two following cases are cited very briefly as examples, the first being of particular interest:

Case 1. In a 22-year-old female, after light coagulation to a cilio-retinal vascular anomaly in the peripapillary region, an area of chorio-retinal degeneration developed midway between the posterior pole and the equator of the eye (Fig. 16). We are of the opinion that this is due to occlusion of a small division of one of the short PCAs in the peripapillary region by light coagulation.

Case 2. A 25-year-old male, with vitreous haemorrhage in the left eye (diagnosed as Eales's disease), was found on routine examination to have multiple scattered depigmented lesions posterior to the equator in the right fundus. The patient gave no history of any trouble in the right eye. IVFA of one of the lesions, situated temporal to the macula, revealed poor and delayed choroidal
Condon (1971) recorded a chorio-retinal degeneration in two patients with sickle-cell disease. In both cases it involved the lower half of the fundus. There were irregular, thin, white granular lines and blotchy circles, with intermediate areas of normal retina. IVFA showed evidence of choroidal unmasking with degeneration of the PE and reduced filling of the chorio-capillaris circulation in patchy areas. These, again, very much resemble the lesions seen in the present experimental study, and are most probably due to PCA occlusion due to sickle-cell disease.

These few clinical studies reveal that lesions due to acute choroidal ischaemia are not rare, but their nature has not until now been clearly understood. Consequently, these lesions are either grouped in the large and ill-understood category of PE degenerations or described as “obscure and interesting” fundus lesions. Our present studies have given a
better insight into the nature and pathogenesis of this group of fundus lesions.

Summary

In 85 rhesus monkey eyes, various posterior ciliary arteries (PCAs) were cut outside the eyeball either individually or together. Within 24 hours after PCA occlusion, white patches of markedly varied shape, size, and distribution appeared in the parts of the fundus supplied by the occluded artery. After one week these patches began to change gradually, so that over a 2 to 3-week period they became greyish-white, granular, depigmented areas. During the evolution of the lesions, they became surrounded by deeply pigmented haloes, and the adjacent fundus showed similar pigmentation. In the greyish-white depigmented patches, intravenous fluorescein angiography revealed degeneration of the pigment epithelium and partial destruction of the choroidal vasculature. The sites of these white patches corresponded to post-occlusion non-perfusion areas in the choroid. The peripapillary choroid filled by sectors and not as one continuous vascular bed. Histological studies of the fundus lesions revealed destruction of visual cells and the outer nuclear layer, with degeneration of the pigment epithelium and Bruch's membrane, but with little change in the choroid. Clinical studies of similar fundus lesions in patients are discussed.

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