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The Choriocapillaris

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Summary. Based on present fluorescein fundus angiography and correlated with the previous neoprene latex and other injection studies, a pattern for the choriocapillaris has been worked out. It reveals that each terminal choroidal arteriole supplies an independent segment of choriocapillaris, with the arteriole joining the segment in its centre; the draining venules lie around the periphery of this segment. Each segment is an independent unit of a polygonal shape, with no anastomosis with the adjacent segments *in vivo*. The various segments are arranged like a mosaic, the borders of the mosaic being formed by the venous channels. This picture of the pattern of the choriocapillaris helps to explain the localized nature of various inflammatory, metastatic and degenerative lesions.

Zusammenfassung. Ein Modell der Gefäßverteilung in der Choriocapillaris konnte aufgrund von fluoreszein-angiographischen Untersuchungen und von Gefäßinjektionen mit Neopren ausgearbeitet werden. Jede Endarteriole der Gefäßhaut versorgt einen bestimmten Gewebsbezirk. Die Arterie liegt im Mittelpunkt dieses Gewebsbezirkes. Die Venen liegen in der Peripherie. Jeder Bezirk stellt eine unabhängige Einheit dar. Anastomosen zwischen benachbarten Bezirken gibt es am lebenden Auge nicht. Die verschiedenen Bezirke formen ein Mosaik, wobei die äußeren Grenzen immer von den Venen gebildet werden. Dieses Modell der Gefäßverteilung der Choriocapillaris erlaubt es, das lokalisierte Auftreten verschiedener entzündlicher, metastatischer und degenerativer Veränderungen zu erklären.

Capillaries of the choroid were first described by Hovius in 1702 and called "choriocapillaris" by Eschricht in 1838. According to Passera (1896), the smallest choroidal arteries descend perpendicularly and break up at once into a star-shaped formation of capillaries radiating out in all directions. Winslow, as far back as 1733, described this layer composed of "vascular stars". A large number of studies of the choroidal vascular bed have been conducted over the last century, using various injection media, such as Indian ink, neoprene latex, silicone, etc. Almost all the workers have agreed on the main features of the choriocapillaries. It has been mentioned that the characteristic feature of the choriocapillaris is a sudden transition from large choroidal vessels to the choriocapillaris, without the usual gradual change through arterioles and venules.

According to Ruskell (1961) the efferent venules of the choriocapillaris travel a short distance, draining several capillaries, before turning away obliquely and quickly joining neighbouring venules, and the resulting stem shortly joins the nearest large vein.

The classical textbook description is that the choriocapillaris is arranged in one plane as a single continuous layer of capillaries forming a network on the Bruch's membrane; the capillaries have a very wide lumen (18–38μ—Sattler, 1876; 10–36μ—Leber, 1903; 18–50μ—Hogan *et al.*, 1971) so that several red blood corpuscles can pass through them side by side (ordinary capillaries have room for hardly one red blood corpuscle) and form a continuous anastomotic network over the entire choroid, with no segmental distribution. Although Rohen (1965) stated that "the entire choriocapillaris network unboubtedly has a continuity by capillary anastomoses" he did find that "the finer branches of the choroidal arteries run in relatively delimited sectors of the choriocapillaris." *In vivo* studies, involving embolization of choroidal arteries in dogs (Gay *et al.*, 1964; Goldor and Gay, 1967) and in cats (Henkind, 1967), have also suggested segmental distribution of the choroidal arteries and choriocapillaris; however, Henkind in these studies stated that "blocking a choroidal artery leads to diminished or absent flow in a large segment of the choriocapillaris; this is in spite of the fact that the choriocapillaris seems to be a continuous anastomotic network over the entire choroid." Dollery *et al.* (1968), on fluorescein angiography of pig's eyes with experimentally raised intraocular pressure, recorded the filling of the choriocapillaris in the form of dots which later enlarged and coalesced. Based on these studies, they stated that "this would indicate that the choriocapillaris fills as small independent segments rather than as a continuum over the entire surface" and that "the segmental filling of the choriocapillaris resembles a pattern of patchy choroiditis or multiple drusen."

In my fluorescein angiographic studies in occlusion of the various main posterior ciliary arteries (PCAs) (Hayreh and Baines, 1972a) and short PCAs (Hayreh, 1974b) in rhesus monkeys, I found no direct extension of filling from the normally filling sector of the choroid to the adjacent empty choroid. Similarly watershed zones and spatial geographical filling defects were seen in normal human choroid (Hayreh, 1974a) and monkey choroid (Hayreh, 1969a, b; Hayreh *et al.*, 1970) on angiography. These phenomena were difficult to explain on the prevalent concept that the choriocapillaris forms a freely communicating vascular network.

The present studies have revealed that the choriocapillaris has a segmental distribution and the choroidal arteries behave as end-arteries.

Present Study

To have a better understanding of the choriocapillaris pattern, the choroidal filling pattern in fluorescein fundus angiograms of good quality was critically evaluated in the following conditions:

a) Normal human and monkey eyes.

b) After experimental occlusion of the main PCA, short PCA, long PCA and vortex veins, in rhesus monkeys.

c) After experimental ocular hypertension in monkeys.

d) In patients with high intraocular pressure and anterior ischaemic optic neuropathy.

These studies revealed some interesting findings which helped to shed an entirely new light on the subject of the choriocapillaris. The prevalent classical concept, based on some excellent postmortem injection studies, is that the choriocapillaris forms a freely communicating vascular network. My studies suggested that this does not hold good *in vivo*. Thus the postmortem injection studies, although extremely useful, have misguided us to some extent about the actual haemodynamics in the choroid in general, and in the choriocapillaris in particular. This is in no way a reflection upon those who undertook the earlier postmortem injection studies and made the very best use of the tools then available to them.

The following account is based on fluorescein fundus angiographic findings in the above-mentioned material, comprising about 250 eyes of rhesus monkeys and a similar number of human eyes.

Fluorescein Fundus Angiographic Pattern of Filling of the Choriocapillaris

Ordinary intravenous fluorescein fundus angiograms usually give no significant information on the subject because of the very fast flow of blood in the choriocapillaris. It is well known that to get the best resolution of vessels in the fundus on angiography, it is absolutely essential to cause a very small bolus, consisting of as high a concentration of fluorescein as possible, to reach the eye, giving a sharp and bright dye-front in the ocular vessels. This is particularly so for the choriocapillaris. Also the ordinary fundus camera cannot take pictures frequently enough to catch the different phases in the fast transit of the dye through the choriocapillaris. These limitations of ordinary intravenous fluorescein angiography in outlining the choriocapillaris have been overcome in the present study by the following methods:

1. Intracarotid injection of fluorescein gives a small bolus of high concentration and a sharp dye-front which outlines the choriocapillaris (of course this was done only in the monkeys).

a

Fig. 1a—e. Fluorescein fundus angiograms of two normal eyes of rhesus monkeys ('*a*', '*e*' from one eye, and '*b*', '*c*', '*d*' from another—the same area, nasal to the optic disc, in all pictures) after intracarotid injection of fluorescein (reproduced by courtesy of British Journal of Ophthalmology). (a) Very early filling phase of choriocapillaris. Choriocapillaris is seen as bunches of very tiny fluorescent spots (like microaneurysms) at the ends of terminal choroidal arterioles. In order to outline and photograph this phase with ordinary fundus camera, the intraocular pressure was elevated so as to slow down the choroidal circulation. Figure *e* is the first picture possible with the normal intraocular pressure in the same eye. (b) Early filling phase of choriocapillaris. This phase is next after (a). Each bunch of choriocapillaris (supplied by the terminal choroidal arteriole) now forms a big spot. Each spot is surrounded by a polygonal unfilled zone, producing a mosaic pattern in the choriocapillaris. (c) This shows a further stage in the filling of the choriocapillaris. Note the extraordinary well-defined mosaic pattern, with each unit of the mosaic an independent entity, and the isolated non-filling or slow filling of some of the units clearly visible. It suggests that there is no communication between adjacent units. (d) Early emptying phase of choriocapillaris. The pattern is like a honeycomb and the fluorescent pattern is the reverse of that seen in (b), i.e., the fluorescent areas are non-fluorescent and vice versa. (e) Complete filling phase of choriocapillaris. The choriocapillaris fills uniformly in the distribution of the medial PCA during the pre-retinal arterial phase with no outlines of individual choriocapillaris visible. The area of the choroid supplied by the lateral PCA is still not filled. Note the very fast filling of the choriocapillaris at normal intraocular pressure in this angiogram as compared to the comparatively slow filling in the same area in Fig. *a* at elevated intraocular pressure which allowed different phases to be photographed with the ordinary fundus camera

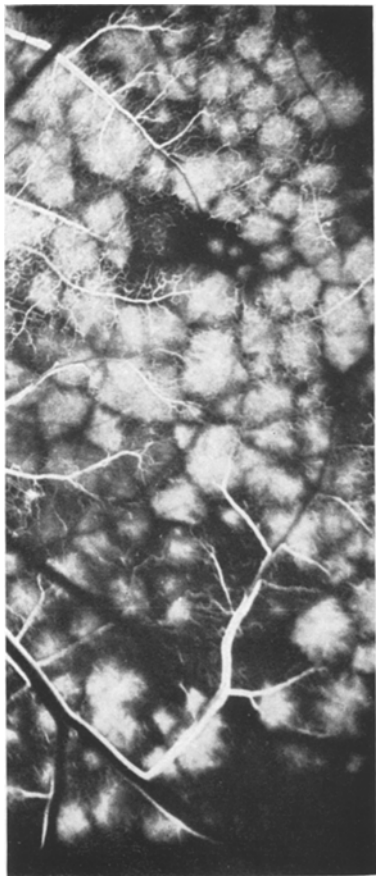

Fig. 1 b

2. The choriocapillaris can also be outlined on intravenous injection if the speed of blood flow in the capillaries is significantly slowed. This was achieved in the present study by choroidal vascular occlusion or raised intraocular pressure.

3. Spatial variations in the filling of the choroidal vascular bed provided additional information.

Cineangiography would be very useful in outlining the filling pattern of the choriocapillaris because of the very fast transit of dye through it, but was not available to me.

I observed the following phases in the filling of the choriocapillaris on fluorescein fundus angiography:

a) Early Filling or Arterial Phase. The earliest fillings of the choriocapillaris recorded by me have constituted a filling of the terminal

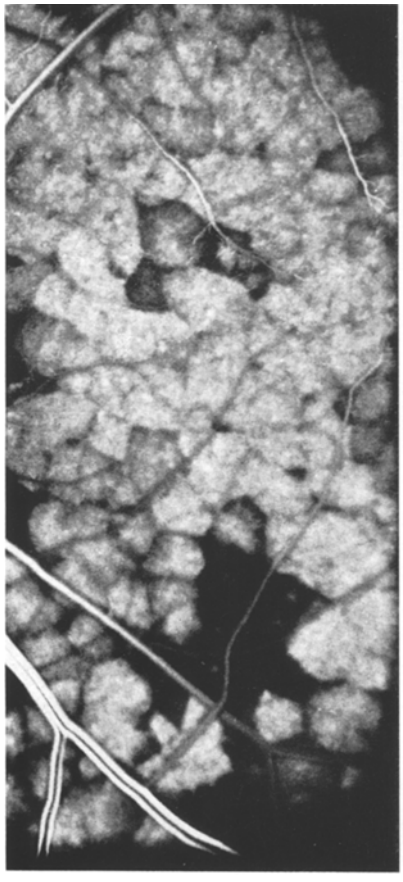

Fig. 1c

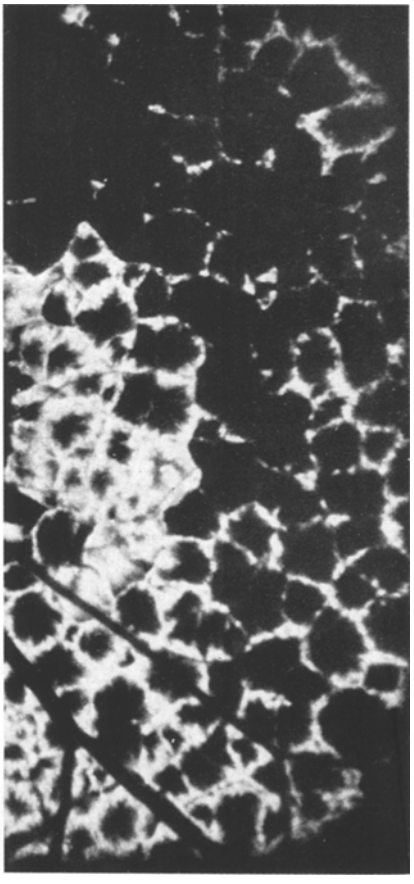

Fig. 1d

choroidal arterioles and a large number of fluorescent spots resembling tiny microaneurysms, clustered at the end of each arteriole, like a bunch of grapes at the end of a stalk (Fig. 1a, 2a). Each bunch of choriocapillaris forms a discrete collection which is separated from other similar bunches. Soon the tiny fluorescent spots fuse together to form big discrete spots (Fig. 1b, 2). Each big spot is about a quarter or less of the size of the optic disc and is surrounded by a polygonal non-fluorescent zone. This ultimately gives the appearance of a mosaic to the choriocapillaris; each unit of the mosaic is polygonal in shape and is well-defined (Fig. 1c, 2). Due to spatial variation in the filling of the choriocapillaris some units of the mosaic may not fill synchronously with the rest, so that well-defined empty or partially filled units may be seen,

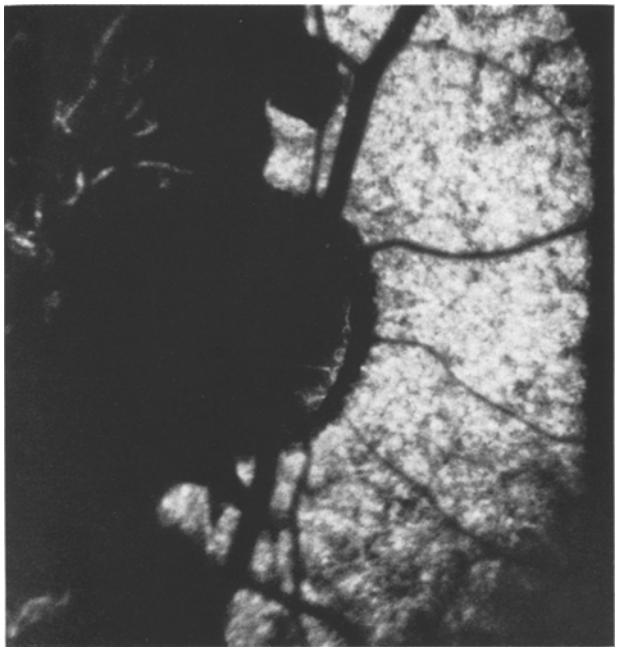

Fig. 1e

surrounded by discrete, fully-filled units (Fig. 1c). This suggests that there is no free communication between the adjacent units of the choriocapillaris mosaic.

b) Complete Filling Phase. The entire choriocapillaris bed is uniformly fluorescent and no mosaic pattern is now visible (Fig. 1e; 2b—inferior nasal quadrant). It is not uncommon to find well-defined geographical filling defects of variable size and shape in the otherwise diffusely filled choriocapillaris bed, due to the normal spatial variation in their filling (Hayreh, 1974a). These areas fill late and remain well-defined. Their filling sequence seems slightly delayed as compared to that of the main bed.

c) Early Emptying or Venous Phase. The fluorescent pattern at this stage is the reverse of the arterial phase (Fig. 1d), i.e., a central non-fluorescent zone (corresponding to the fluorescent zone in the arterial phase—Fig. 1b) surrounded by a polygonal girdle composed of very tiny fluorescent spots of about the size of microaneurysms. This produces a well-defined honeycomb pattern (Fig. 1d) which is reproducible on repeated fluorescein fundus angiography, indicating that these are not artefacts. The honeycomb pattern may not always be polygonal and show variations in size, shape and pattern (Fig. 3).

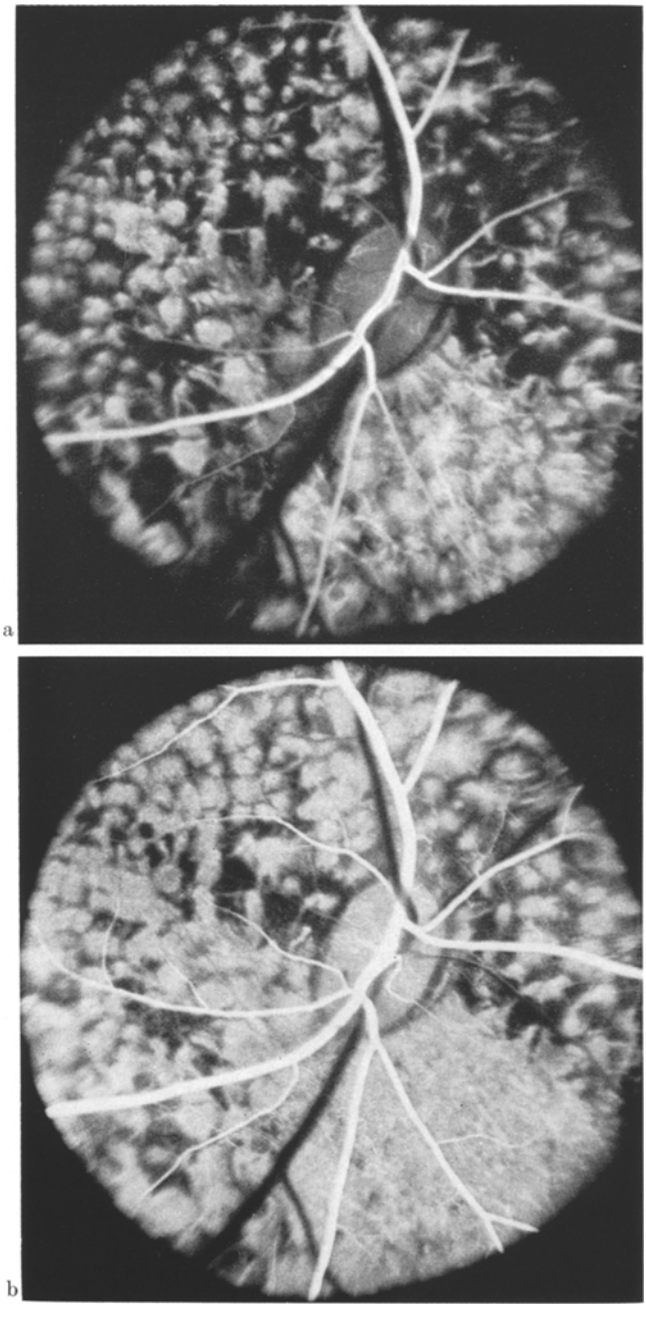

Fig. 2a and b

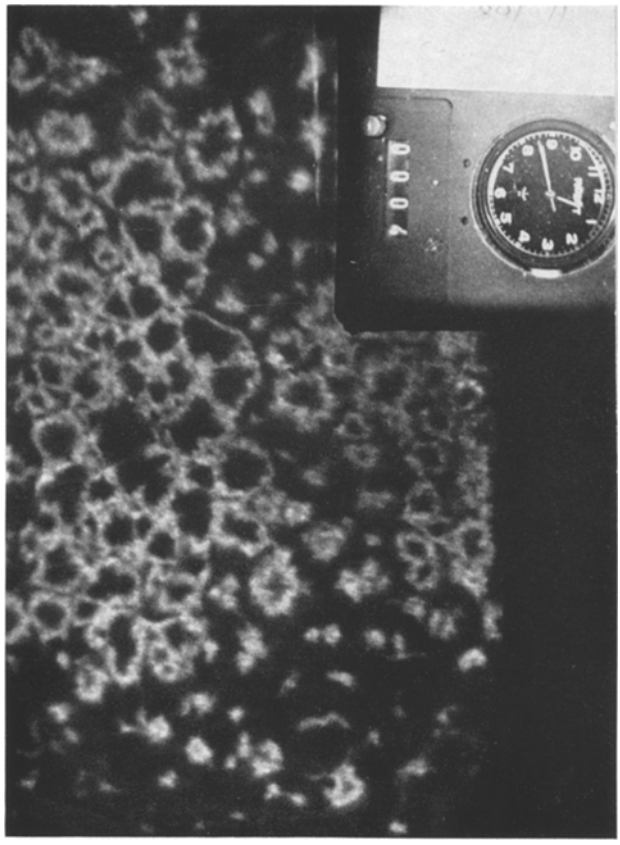

Fig. 3. Fluorescein fundus angiogram in a rhesus monkey during the venous phase of filling of the choriocapillaris. The eye had elevated intraocular pressure. It shows some of the possible variations in size, shape and pattern of the venous channels and segments of the choriocapillaris

Fig. 2a and b. Fluorescein fundus angiograms of the right eye of a rhesus monkey after occlusion of superior temporal, superior nasal and inferior temporal vertex veins. (a) In the occluded segments the phases of filling of the choriocapillaris correspond to those shown in Fig. 1*a*, *b*, while in the inferior nasal unoccluded quadrant filling corresponds to that in Fig. 1*c*. (b) In the unoccluded inferior nasal quadrant there is complete uniform filling of the choriocapillaris while in the rest it mainly corresponds to Fig. 1*c*. Note the well-defined horizontal water-shed zone between the superior and inferior vortex veins which passes through the optic disc

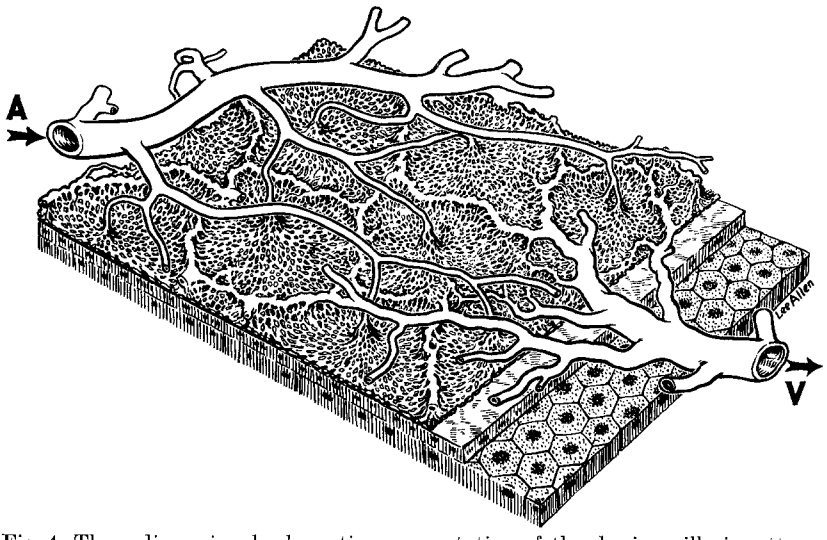

Fig. 4. Three dimensional schematic representation of the choriocapillaris pattern. *A* choroided arteriole; *V* choroidal vein

Based on these observations, Fig. 4 has been constructed to represent schematically the pattern of the choriocapillaris. This shows that each terminal choroidal arteriole joins a small segment of choriocapillaris near the middle; this is strongly suggested by fluorescein angiograms of the arterial phase (Fig. 1a, b; 2a). The radiating arrangement of the choriocapillaris from the terminal arteriole resembles somewhat the description by Winslow (1733) and Passera (1896) of a star-shaped pattern. The venous draining channels surround each of these segments of the choriocapillaris and thus usually help to drain adjacent segments, as suggested by fluorescein angiograms of the venous phase (Fig. 1d, 3). Although I have been aware of this pattern of the choriocapillaris for the last five years, I found it hard to reconcile the angiographic pattern with the neoprene latex pattern (Ashton, 1952; Wybar, 1954; Ruskell, 1961; Ring and Fujino, 1967; and many others) which has been clearly demonstrated by excellent studies by very experienced and reliable researchers. In an effort to correlate the two patterns, I speculated some time ago that the choriocapillaris consisted of separate alveoli, each served by an arteriole and a venule (Hayreh, 1973a). This possible alveolar concept of the choriocapillaris was further prompted by flat or tangential histological sections of the choriocapillaris showing sac-like or local widening, and afferent and efferent vessels often entering the choriocapillaris layer at somewhat oblique angles (Hogan *et al.*, 1971).

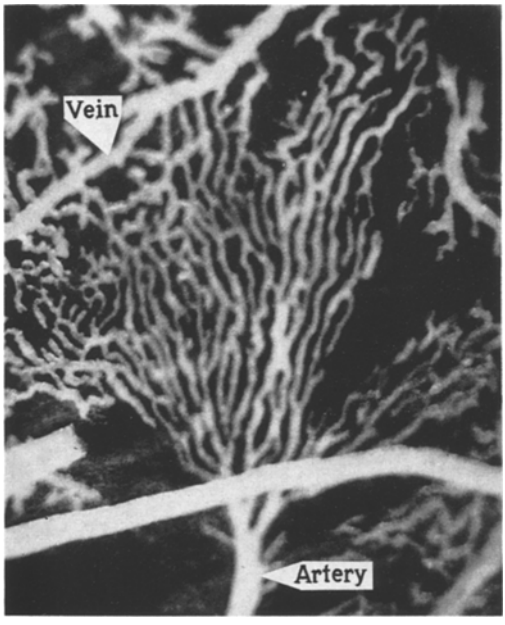

Fig. 5. A neoprene latex cast of the choriocapillaris, with its feeding artery and the draining vein, made by Professor Norman Ashton (1952). In his original picture the artery was labelled as vein and vice versa. Such an error is possible and not uncommon because of the difficulty in differentiating those vessels in an isolated cast. (Reproduced by the kind courtesy of Professor Ashton and British Journal of Ophthalmology)

However, further studies convinced me that this concept was wrong (Hayreh, 1974b). The present concept shown in Fig. 4 correlates fully the angiographic (Figs. 1–3) and neoprene latex (Fig. 5) patterns. A critical retrospective analysis of most of the published neoprene latex and other injection studies, in the light of Figure 4, reveals a good correlation. My present concept on the choriocapillaris, as shown in Fig. 4, has been further confirmed recently by examination of flat preparations of the human choriocapillaris by Torczynski and Tso (1974). In their excellent study they found a distinct lobular arrangement in the choriocapillaris, with the feeding choroidal arteriole in the centre of the lobule and the draining venule at the periphery of the lobule (Fig. 6)—a pattern having some resemblance to the pattern of a liver lobule.

Thus Fig. 4 represents a pattern of the choriocapillaris which agrees not only with fluorescein fundus angiographic findings (Figs. 1–3) but also with histological (Fig. 6) and neoprene latex (Fig. 5) and other injection studies.

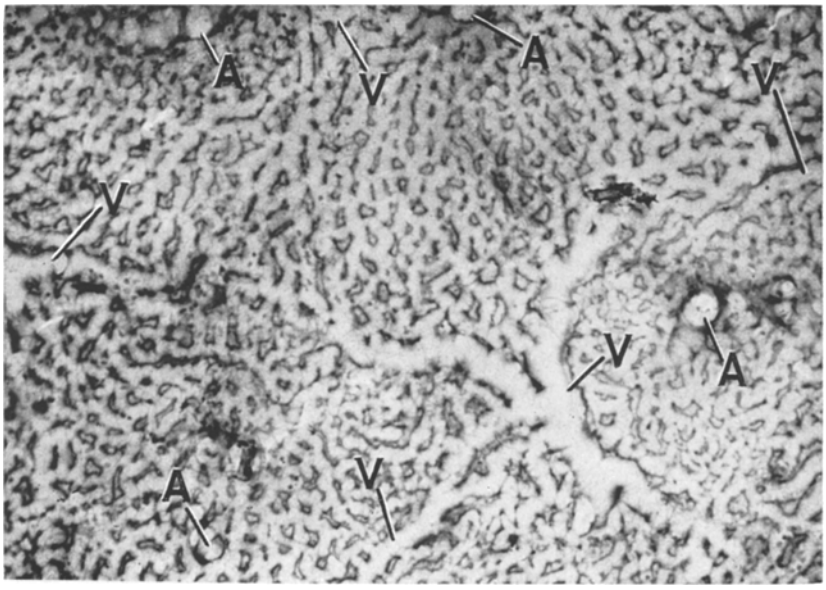

Fig. 6. Microphotograph of a flat preparation of the human choriocapillaris. (Reproduced by the kind courtesy of Drs. Torczynski and Tso from the Armed Forces Institute of Pathology, Washington, D.C.). *A* Terminal arteriole, *V* Venule

It shows that each segment of the choriocapillaris is supplied by a terminal choroidal arteriole and is independent. The various segments communicate only via the venous channels. In a living eye each segment acts as an independent functional unit. Because of haemodynamic factors in each segment, the blood does not flow from one segment to the other. The question could be posed: when the blood supply to a segment is cut off, why does it not fill from the adjacent segment via the common venous draining channel? My occlusive studies in a large series have shown that there is no such direct extension of filling between the various segments (Hayreh and Baines, 1972a, 1973; Hayreh, 1974c). I have no definite explanation for this well-established fact. I feel it is possible that the normal intraocular pressure obliterates the area of choriocapillaris supplied by an occluded arteriole because of its intraluminal pressure having fallen to nil, and the perfusion pressure in the adjacent venule is not high enough to force blood into the collapsed choriocapillaris.

My previous studies have suggested that there are no inter-arterial anastomoses in the choroid, so that it is an end-arterial system. The only way the choroid in the occluded artery can fill is by a retrograde

filling via the big choroidal veins (Hayreh and Baines, 1972a), presumably due to the pumping action by the intraocular pulsation.

Clinical Significance

It is well established that choroidal lesions tend to be localized, particularly inflammatory, metastatic and degenerative lesions. However, this was difficult to explain on the prevalent concept of the choriocapillaris as being a single continuous network of vessels with a very wide lumen (10–50 μ—p. 2). In malignant hypertension and associated diseases and in collagen diseases (e.g., polyarteritis nodosa) small isolated chorioretinal degenerative lesions have been well known, e.g., *Elschnig's spots* (black isolated flecks of pigment associated with a bright yellow or red halo—Elschnig, 1904), *Siegrist's streaks* (chains of pigmented spots with yellowish zones about them, arranged like a string of beads along a white sclerosed choroidal vessel—Siegrist, 1899), and spots no more than a third of the disc diameter in size containing central clumps of pigment surrounded by yellowish halos (Klien, 1968). Each lesion represents pigment epithelium degenerative changes over a segment of the choriocapillaris due to fibrinoid necrosis and obliteration of the choroidal arteriole and its segment of choriocapillaris. From the pattern of the choriocapillaris presented in this study, it is evident that inflammatory, metastatic and degenerative choroidal lesions must almost invariably be localized. This new information about the pattern of the choriocapillaris may also help to explain many other lesions of obscure aetiology. For example, I feel, so-called "acute posterior multifocal placoid pigment epitheliopathy" (Gass, 1968) represents an occlusive disorder of the terminal choroidal arteriole because each focus in this disease has a close resemblance in size and shape to that of a unit of choriocapillaris supplied by a terminal choroidal arteriole. The initial whitish focus in all probability represents pigment epithelial infarction and the later depigmented spots pigment epithelial degeneration overlying the occluded units of the choriocapillaris (similar to that seen in our experimental posterior ciliary artery occlusion—Hayreh *et al.*, 1972b; Hayreh, 1973b). However, the cause of the occlusion still remains obscure. Similarly the fluorescein-leaking spot seen on fluorescein angiography in central serous retinopathy, and multiple fluorescent spots in Harada's disease, seem to correspond to individual choriocapillaris units.

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