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Submacular Choroidal Vascular Pattern

Experimental Fluorescein Fundus Angiographic Studies

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Summary. The submacular choroidal vascular pattern was investigated by experimental occlusion of either one of the temporal short posterior ciliary arteries (SPCAs) or 1, 2, 3 or all of the vortex veins in 87 rhesus monkey eyes and evaluation of their filling defects and anastomoses by fluorescein fundus angiography (FFA). No special artery supplying the submacular choroid was seen. All the temporal SPCAs entered the eyeball in the macular region and each artery supplied a segment of the choroid, with no anastomoses between the adjacent segments. Most of the segments of the choroid supplied by the temporal SPCAs and their watershed zones met in the macular region. Similarly the four quadrants of the uveal tract drained by the four vortex veins and their watershed zones met in the macular region. Since an area where numerous watershed zones meet is most vulnerable to ischaemic disorders, the macular region is likely to show special vulnerability to any generalized chronic ischaemic disorder of the choroid. This, however, would not hold good in occlusion of a single SPCA, because the latter supplies only a small segment of the macular region. It is postulated that senile macular degeneration, senile disciform macular degeneration and allied macular disorders are most probably due to this unusual pattern of the submacular choroid and its special vulnerability to suffer in generalized chronic choroidal ischaemia as compared to the rest of the choroid.

Zusammenfassung. Das Gefäßsystem der Aderhaut unterhalb der Macula lutea wurde experimentell untersucht. In 87 Affenaugen wurden entweder eine der temporalen kurzen hinteren Ciliararterien (KHCA) oder 1, 2, 3, oder alle 4 Vortexvenen unterbunden. Die gestörte Füllung und Anastomosen wurden dann im Fluo-Angiogramm studiert. Alle temporalen KHCA penetrieren den Bulbus in der Makulagegend. Jede dieser Arterien versorgt einen Teil der Aderhaut und benachbarte Segmente anastomosieren nicht. Die 4 Segmente der Aderhaut, die von den jeweiligen Vortexvenen drainiert werden, haben ihre Grenzen auch in der Gegend der Makula. In der Makula treffen sich daher viele Grenzen der Blutversorgung und dies macht dieses Gebiet besonders für allgemeine Gefäßstörungen anfällig. Der Verschluß einer einzigen KHCA würde allerdings nur ein kleines Segment der Makula stören. Wir nehmen daher an, daß die senile Degeneration der Makula (die trockene und die feuchte Form) durch diese eigenartige Gefäßverteilung in der Aderhaut bedingt ist. Die Makulagegend ist daher besonders empfindlich bei diffusen Gefäßstörungen der Aderhaut.

The localized involvement of the macular region is well known in a large number of conditions, e.g., senile macular degeneration, disciform macular degeneration, central serous retinopathy, central choroidal sclerosis, central areolar choroidal atrophy, toxoplasmosis, histoplasmosis, macular cyst and hole, various heredo-macular dystrophies, etc. There has naturally been a good deal of interest and curiosity about the factors responsible for this notable vulnerability of the macular region to degenerative and inflammatory diseases. Attempts have been made in the past to define some anatomical pecularities in the macular zone, as compared to the rest of the fundus, which would account for this. These anatomical peculiarities may be of the retina, pigment epithelium or choroid.

A. The Retina. The macular region of the retina comprises an area with a diameter of 5.5 mm in man, with its center at the fovea centralis (Hogan *et al.*, 1971). The retina in this zone has special histological features, e.g., large numbers of cones, Henle's fiber layer, thick inner and outer nuclear layers and more than one layer of ganglion cells. There is no evidence to suggest that this retinal structure has any bearing on the particular disposition of the macula to the above-mentioned lesions. In addition, the macular region, for unknown reasons, shows an exaggerated pathological response in some generalized and other localized retinal disorders, e.g. in occlusive disorders of the central retinal vein, uveitis, hypertensive retinopathy, angioid streaks, diabetic retinopathy, non-specific circinate retinopathy, etc. (Wise and Wangvivat, 1966; Wise *et al.*, 1971).

B. The Pigment Epithelium. In the macular region it shows no apparent difference when compared to that found elsewhere (Potts, 1966); however, fluorescein angiography reveals that it exercises a much greater masking effect on the background choroidal fluorescence than elsewhere. No definite information is yet available on the true nature of the pigment in the pigment epithelium in different parts of the fundus; the pigment epithelium may well be of importance in the production of some pigmentary degenerative disorders of the macula.

C. The Choroid. This special vulnerability of the macular region to involvement in localized degenerative and other lesions has been generally attributed to the many choroidal features peculiar to the submacular region. These include:

1. Increased Arterial Supply to this Part. Sattler (1876), Leber (1903), Nettleship (1903), Wolfrum (1908), Salzmann (1912), Hepburn (1912), Lauber (1931), Wolff (1948), Mörike (1949), Potts (1966), Gass (1967), Ring and Fujino (1967), Amalric (1973) and others have described the submacular choroid as being much thicker than elsewhere and containing an aggregation of the largest of the short posterior ciliary arteries (SPCAs). Alm and Bill (1973) found a higher blood flow in the submacular choroid

than elsewhere in the choroid. In view of all this it has been assumed that the submacular choroid has a more abundant arterial supply than other parts of the choroid and that this increased arterial supply is a response to the high metabolic demands of the macular retina.

2. Maximum Density of Choriocapillaris in Macular Region. This has been mentioned by a large number of workers (Passero, 1895–6; Wolfrum, 1908; Salzmann, 1912; Wolff, 1948; Mörike, 1949; and others). Mörike (1949) reported that in the bifoveal eye of the sea swallow the choriocapillaris is thickest in the macular regions despite the fact that the SPCAs perforate the sclera in an area remote from either macula. Wolff (1948) mentioned that the choriocapillaris has its widest bore in the macular region, to ensure the richest blood supply to this part, a view not shared by all workers.

3. Very High Arterial Pressure in the Submacular Choriocapillaris. This has been speculated by Passero (1895–6), Ring and Fujino (1967) and Gass (1967). It has been thought to be due to the fact that the SPCAs are concentrated in the macular region and have rich anastomoses (Gass, 1967); the large arteries also enter the choriocapillaris abruptly and perpendicularly (Passero, 1895–6; Ashton, 1952; Podesta *et al.*, 1961; Ring and Fujino, 1967). Potts (1966) postulated that since the ciliary nerves form a neural garland around the macular area, they provide a neural portion of a homeostatic apparatus which, by supplying the precapillary arterioles, can control the flow in the choriocapillaris; if this neural controle is abolished, since pressure is greatest in the macular area, fluid leak from the choriocapillaris is caused. According to Potts, because of the higher arterial pressure in the macular region, narrowing of arterioles must be maximum in this area; this would provide a higher chance of emboli lodgement, thus making the macular region a predilection site for embolic diseases. According to Gass (1967) a high blood pressure and more rapid flow produce significantly greater haemodynamic stress in the choriocapillaris and lead to permeability changes.

4. A Special Macular Artery Supplying the Submacular Choroid. Hepburn (1912), on no anatomical basis, postulated the existence of a macular artery because he thought the vascular supply in the choroid has three distinct sections = macular, mid-peripheral and extreme peripheral. Heimann (1970, 1972), in a study of foetal choroidal vessels has stated that the branches of the SPCAs that supply the submacular choroid branch out in star-shaped tufts and thus differ from other choroidal arteries, which divide dichotomously in antero-posterior direction, and this may explain the particular disposition of this zone to various degenerative and inflammatory processes. Amalric (1973) feels that the blood supply of the submacular choroid is quite different from that of the rest of the choroid and is probably independent; that it cor-

responds to an arterial and venous retinal vascular pattern peculiar to the macular region and has an oval shape.

The present study was conducted to investigate the normal vascular pattern *in vivo* in the submacular choroid. It revealed findings which had been totally missed in post-mortem injection studies and other studies on the submacular choroid.

Material and Methods

By lateral orbitotomy in rhesus monkeys the following vessels were cauterized outside the sclera:

A. One of the temporal SPCAs in 47 eyes. These included:
   i. Superior temporal SPCA in 12 eyes.
   ii. Mid-temporal SPCA in 20 eyes.
   iii. Inferior temporal SPCA in 15 eyes.

B. One or more vortex veins in 40 eyes. These included:
   i. One vortex vein in 5 eyes.
   ii. Two vortex veins in 12 eyes.
   iii. Three vortex veins in 9 eyes.
   iv. Four vortex veins in 14 eyes.

Intravenous fluorescein fundus angiography was performed about one hour after the occlusion of these vessels to find out the filling defects, vascular distribution and anastomoses of these occluded vessels.

Observations

Size of the Macular Region in Rhesus Monkeys. This was determined in histological sections of 10 eyes by micrometry, using the criterion of Hogan *et al.* (1971); i.e., the area around the fovea centralis containing more than one layer of ganglion cells. The outer limit of the macular region from the fovea was 2.5 mm on the nasal and 2.75 mm on the temporal side on the average, with the center of the fovea situated 2.8 ± 0.45 mm from the temporal border of the optic disc, the optic disc diameter being 1.1 ± 0.009 mm horizontally and 1.5 ± 0.045 mm vertically.

Arterial Supply. These studies showed that the vast majority of the temporal SPCAs pierce the sclera in the region corresponding to the macular area. This produces a large aggregation of SPCAs in the submacular choroid, as has been noticed by previous workers.

The temporal SPCAs, for descriptive purposes, can be divided into superior temporal, mid-temporal and inferior temporal groups, according to their location at the site of penetration of the sclera. Each group may contain more than one SPCA.

In the present study, it was found that each SPCA supplied a small sector of the choroid, of irregular shape and size, with well-defined edges; each sector extending from the posterior part of the choroid to its periphery (Fig. 1). No anastomoses were seen between the adjacent

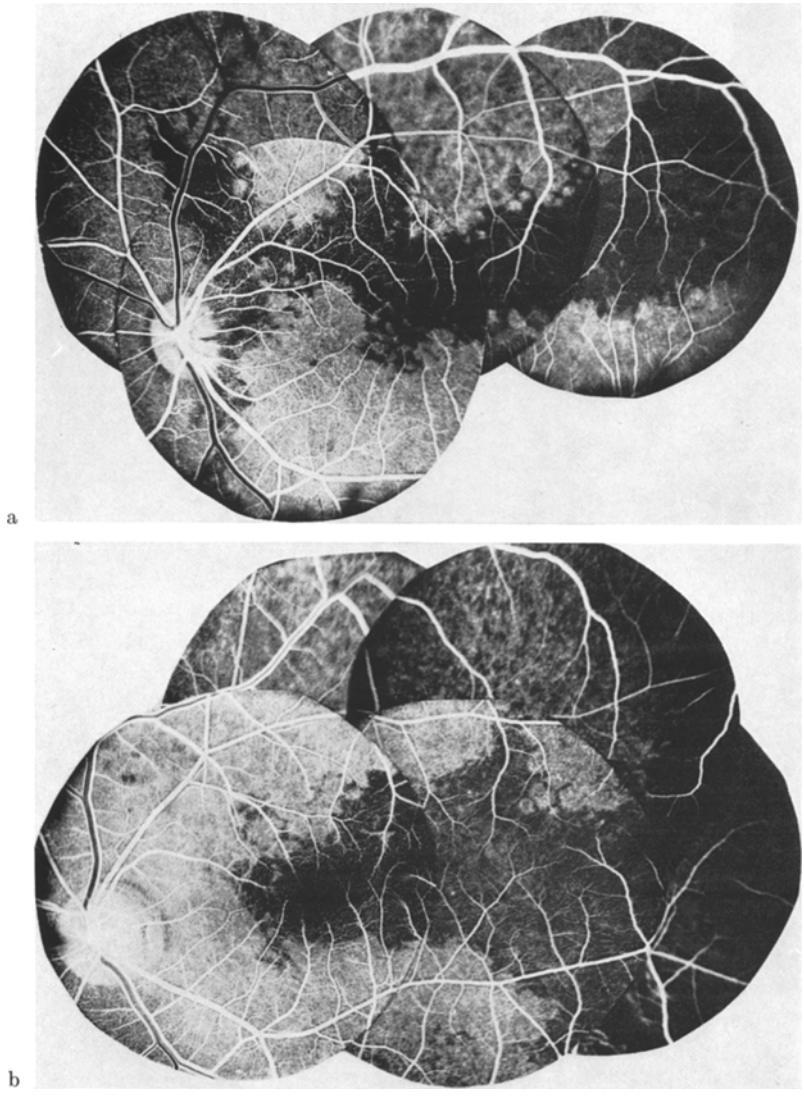

Fig. 1a—e. Fluorescein fundus angiograms after occlusion of one of the temporal SPCAs showing filling defects in the choroid in the region of the occluded SPCA. After occlusion of one of the mid-temporal SPCAs (a—c) and superior temporal. SPCA (d)

SPCAs, so that the filling defect in the choroid produced by the occlusion of one SPCA showed no signs of filling by direct extension from the adjacent choroid. Contrary to the prevalent concept that choriocapillaris

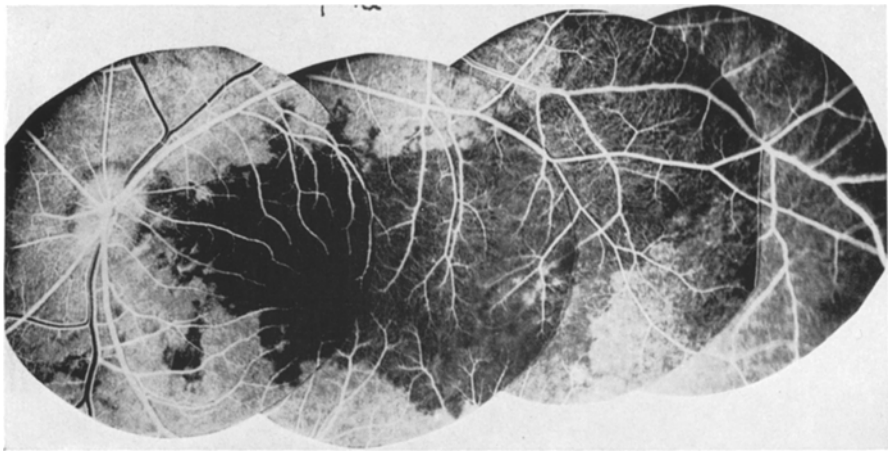

Fig. 1c

freely communicate in the choroid, my studies showed that the choriocapillaris had a segmental supply with no direct communication between the adjacent sectors (Hayreh, 1974a, b). Thus the watershed zone between the patent and occluded SPCAs usually showed no filling by direct extension from the normally filling choroid.

The superior temporal SPCAs supplied mainly the superior temporal choroid (Fig. 1d), inferior temporal SPCAs the inferior temporal choroid, and the mid-temporal SPCAs in the intervening middle temporal zone of the choroid (Fig. 1a, b, c). The distribution of these three groups of the SPCAs was usually not only localized to the corresponding part of the choroid, but also there was a good deal of extension into the adjacent zones, particularly near the optic disc. The superior and inferior temporal retinal vessels in the fundus lie roughly along the boundaries between these three zones.

Thirty-four of the 47 temporal SPCAs in this series showed a contribution to the submacular choroid, this being seen in all of the mid-temporal group and in about half of the others (i.e., superior and inferior temporal SPCAs). The watershed zone of the mid-temporal group of SPCAs, although sinuous and very variable in location, was always situated at or near the central part of the macular region (Fig. 2a); this also occurred in half of the superior (Fig. 2b) and inferior temporal groups.

No special macular artery in the choroid was found in any specimen.

Venous Drainage. Our findings on the effects of vortex vein occlusion on the choroidal circulation and areas of distribution by the various vortex veins in the choroid are described in detail elsewhere (Hayreh

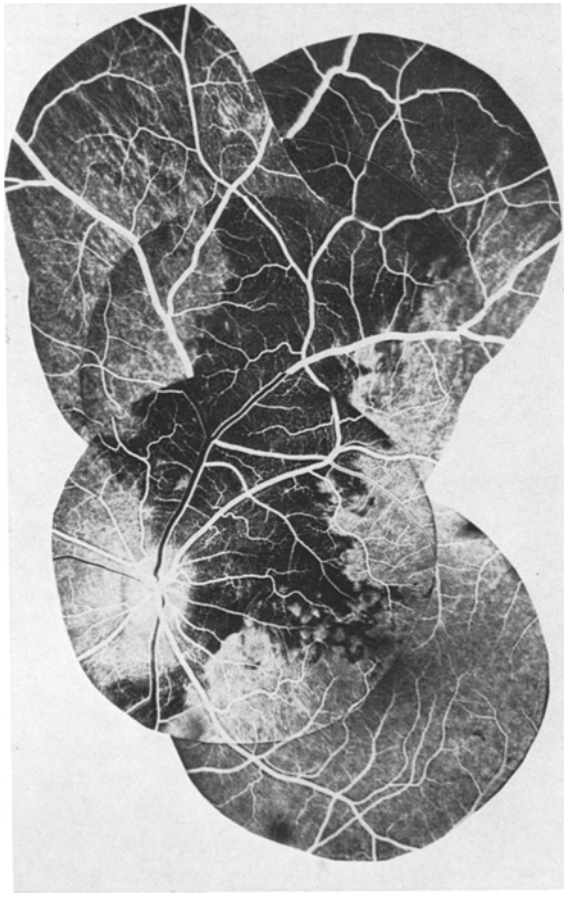

Fig. 1d

and Baines, 1973). These studies showed that the vortex veins had a segmental distribution in the choroid (Fig. 3), with poor communication between the adjacent veins. The watershed zones between the four vortex veins formed a cross, with its horizontal limb passing through the center of the macula and the vertical limb through the nasal part of the macular region (Fig. 4). Unlike the watershed zone of the temporal SPCAs, this was fairly consistent in location and shape.

Discussion

These studies as well as others after experimental occlusion of the various choroidal vessels, and in normal eyes of rhesus monkeys, have shown a segmental distribution of blood supply in the choroid (Hayreh,

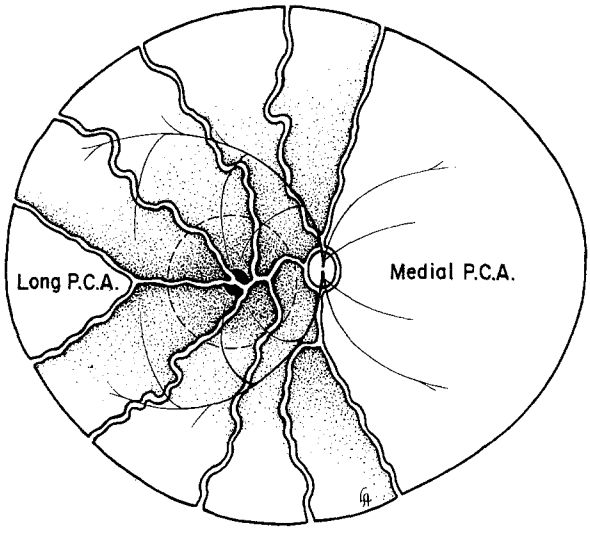

Fig. 1e. Diagrammatic representation of the distribution by various temporal SPCAs and their watershed zones in the posterior part of the fundus. Dotted circle in the region of the distribution of the temporal SPCAs represents the macular region. Areas of supply by the medial PCA and temporal long PCA are also shown

1974a, b; Hayreh and Baines, 1972a, 1973). This segmental distribution is seen not only in the distibution of the main posterior ciliary arteries (PCAs) arising from the ophthalmic artery (Hayreh and Baines, 1972a) and vortex veins (Hayreh and Baines, 1973) but also in the SPCAs, and right down to the choriocapillaris (Hayreh, 1974a, b). *In vivo* studies studies involiving embolization of choroidal arteries in dogs (Gay *et al.*, 1964; Goldor and Gay, 1967) and in cats (Henkind, 1967), and experimental ocular hypertension in pigs (Dollery *et al.*, 1968), have also suggested segmental distribution of the choroidal arteries and choriocapillaris. These *in vivo* results contradict previous anatomical studies in post-mortem eyes (demonstrating that post-mortem appearances are not always consistent with the *in vivo* condition). The watershed zone of each segment is well-defined.

These studies have shown that the area of the choroid supplied by each SPCA extends from the posterior pole to the periphery and varies greatly in size, shape and location. When plotted, these segments supplied by the temporal SPCAs resemble a jig-saw puzzle in the distribution of the lateral PCA (Fig. 1e). There are no anastomoses between the adjacent segments. Each piece of the jig-saw pattern has a well-defined margin which forms the watershed zone between the adjacent SPCAs. All the temporal

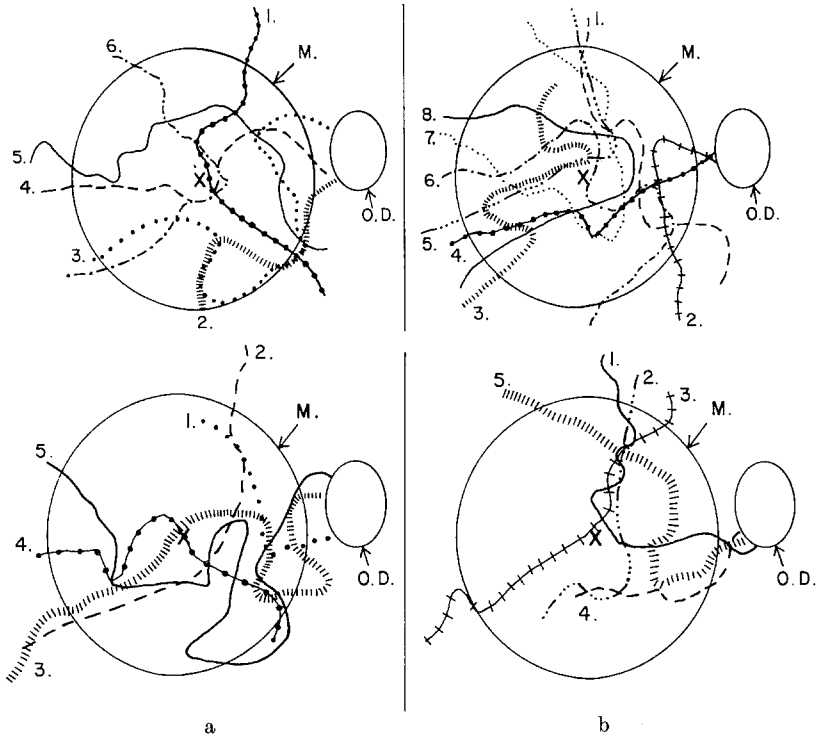

Fig. 2a and b. Diagrammatic representation of some of the watershed zones of mid-temporal (a) and superior (b) SPCAs. Note the sinuous and inconsistent pattern of the watershed zones except for their passing through or near the center of the macula. *M* macular region; *X* fovea; *OD* optic disc

SPCAs enter the eyeball in the macular region and spread out to the periphery of the fundus to supply the temporal half of the choroid. It is, therefore, natural that most of the segments of the choroid supplied by the temporal SPCAs and their watershed zones meet in the macular region. Not only that, but also the four quadrants of the uveal tract drained by the four vortex veins and their watershed zones meet in the macular region. It was indeed surprising to see consistency of this pattern in all the eyes. It is well established that an area where numerous watershed zones meet is usually an area of comparatively poor vascularity and in the event of circulatory disorders, most vulnerable to ischaemia. Thus the location of the macular region on the meeting points of arterial as well as of venous watershed zones of the choroid must surely make it more vulnerable to vascular disorders than any other part of the posterior choroid. This would be particularly so in eyes suffering from

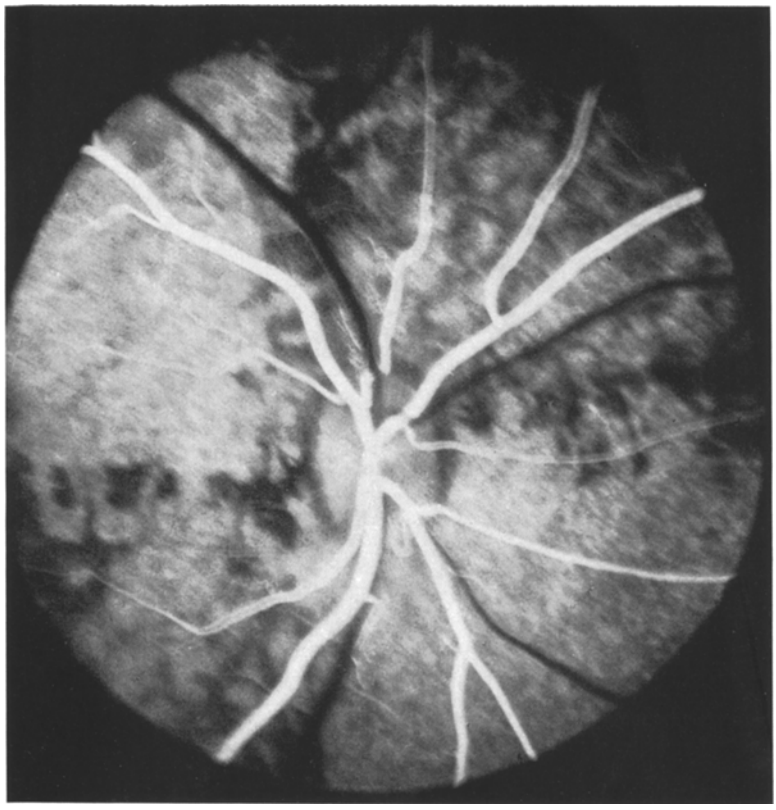

Fig. 3. Fluorescein angiogram of the right fundus after occlusion of superior nasal and inferior temporal vortex veins showing normal and poor filling of the choroid in the regions of the normal and occluded vortex veins respectively, with well-defined watershed zones

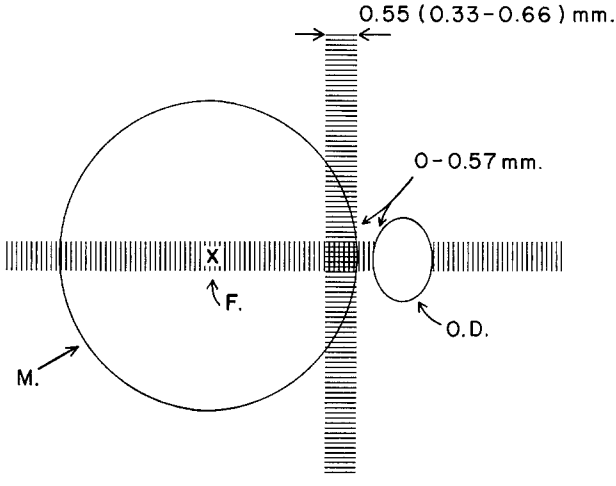

Fig. 4. Diagrammatic representation of the watershed zones of the vortex veins. *F* and *X* Favea; *M* macular region; *OD* optic disc

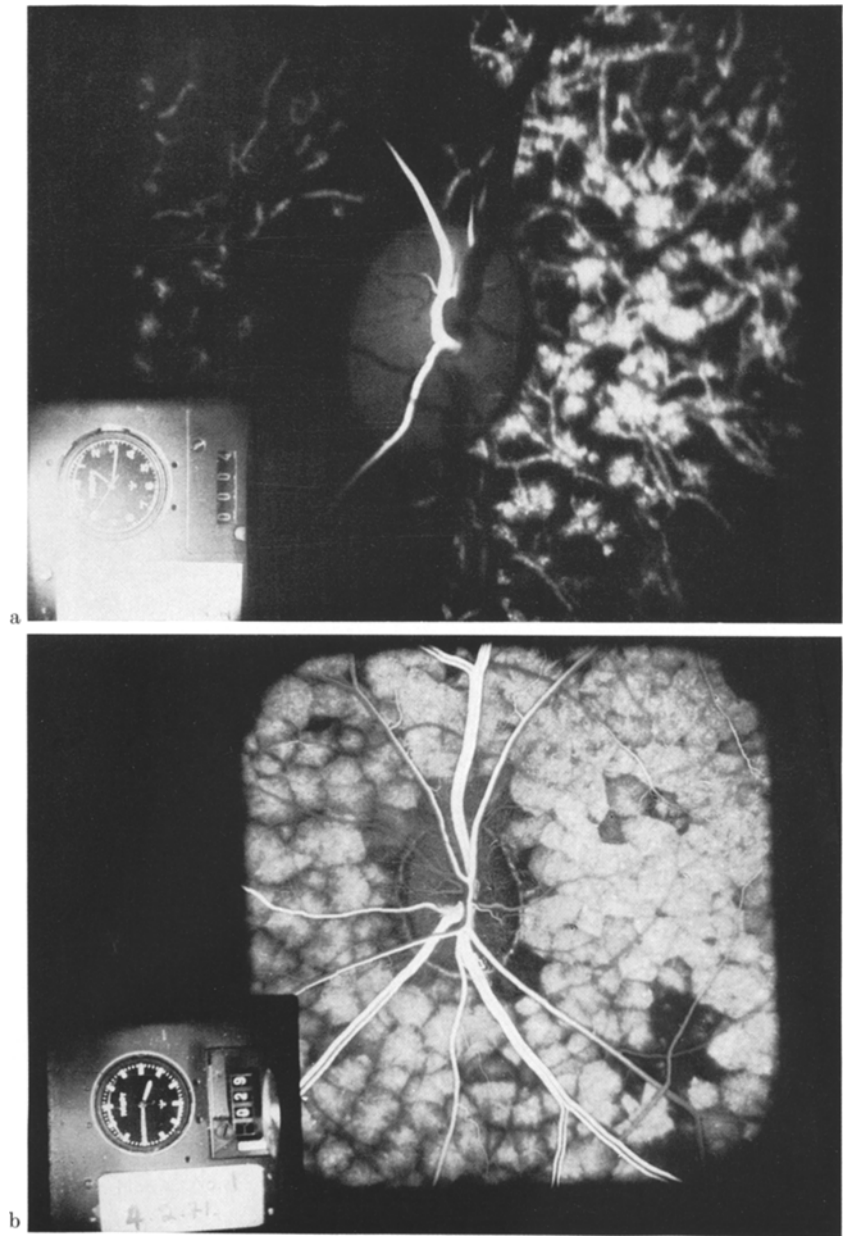

Fig. 5a and b. Fluorescein fundus angiograms showing. (a) Filling of the terminal choroidal arterioles and the choriocapillaris supplied by them. (b) Various units of the choriocapillaris mosaic (each unit supplied by a terminal choroidal arteriole), note the presence of some empty units amongst normally filled units

generalized chronic ischaemia due to arteriosclerotic changes in the main PCA and generalized choroidal arteriosclerosis. These findings are again in sharp contrast to the previously expressed views that submacular choroid is the most vascular zone (p. 50, 51). It is true large numbers of SPCAs, having pierced the sclera in the macular region, are aggregated together in this zone, but that does not mean that they all supply this part of the choroid. Similarly, increased blood flow mentioned in this region (Alm and Bill, 1973) in all probability also represents the increased blood flow in the large number of SPCAs aggregated in the submacular choroid. Wybar (1954) rightly pointed out that a mere increase in the number of arteries does not affect the nutrition of an area of the choroid. Maximum density of choriocapillaris in the macular region is mentioned (p.); 51 however, Wybar (1954) and Ring and Fujino (1967), in their detailed studies, found no difference in the structure and density of the choriocapillaris in the macular region and other areas equidistant from the optic disc. No special macular artery was seen in this study.

Since the macular region is the meeting place for the areas of supply by the majority of the temporal SPCAs and each artery supplies a sector of the macular region, it could be argued that the macular region is situated in the most favorable and safe position from the vascular point of view; because occlusion of one SPCA is likely to involve only a small sector of this region and not the entire macular region. This is certainly true if only one of the temporal SPCAs is involved. However, it does not hold good when there is a *generalized chronic choroidal ischaemia* or reduction of blood flow produced by arteriosclerosis of the *main PCAs (Please note that the main PCAs arise directly from the ophthalmic artery and the SPCAs are the multiple small branches of the main PCAs)* and generalized arteriosclerosis of *all the SPCAs* and choroidal arteries; in this case the macular region, being the only place in the choroid where many arterial as well as venous watershed zones meet, would be most susceptible to chronic ischaemia. *Thus, for the involvement of the macular region, it is the generalized chronic ischaemia of the choroid and not involvement of one of the temporal SPCAs which is essential.* Unless this important and basic fact is borne in mind, it may be difficult to comprehend the entire concept presented in this paper.

It could also be argued that in my previous studies involving experimental occlusion of the main lateral PCA (alone or in combination with medial PCAs), I did not record an unusually marked and frequent involvement of the entire macular region by the choroidal ischaemic lesions (Hayreh and Baines, 1972b). In these studies the peripapillary region and the area of the macula between the fovea and the optic disc was almost always spared although the macular region temporal to the fovea was frequently involved by ischaemic changes. The explanation

of such a disparity between my previous studies (Hayreh and Baines, 1972b) and the present hypothesis is fairly simple. Firstly, I was producing sudden acute ischaemia of the temporal choroid and not chronic ischaemia. Secondly, we were dealing with very young, healthy animals with no evidence of arteriosclerosis or any other arterial disease. Thirdly, a variable retrograde filling of the peripapillary choroid and the adjacent choroid, via the anastomoses between the peripapillary choroid and the pial vessels of the optic nerve, was seen in the vast majority of animals immediately after the occlusion, and improved within a few days. Moreover, filling of the macular region via other collateral routes was seen, as discussed in detail elsewhere (Hayreh and Baines, 1972b); whereas the areas showing ischaemic chorioretinal lesions showed no such restoration of choroidal circulation soon after the occlusion. Thus the situation seen clinically with macular lesions is totally different from these experimental acute ischaemic lesions and no parallels can be drawn between the two.

The present studies, therefore, suggest that the macular region is especially vulnerable to chronic ischaemic disorders and those disorders most likely to affect the watershed zone in any circulatory bed. A selective localization of senile choriocapillaris atrophy in old age in the submacular region has been reported (Kerschbaumer, 1892; Friedman and Smith, 1965; Ring and Fujino, 1967). Friedman and Smith (1965) have postulated that the tendency for the choriocapillaris atrophy to be more marked in the macular region appears to be consequent on the increased density of the SPCAs and branches of the vortex veins. Ashton (1953) showed, on neoprene injection, a well-demarcated avascular zone in the submacular choroid in central areolar choroidal sclerosis. Since this disease is of insidious onset and is seen only in middle age or later, he thought it was in keeping with an arteriosclerotic vascular occlusion.

In the light of my findings the frequent occurrence of senile macular degeneration is not at all surprising. In senile disciform macular degeneration, the well documented submacular neovascularization from the choroidal vascular bed (Teeters and Bird, 1973) may represent a response to chronic ischaemia, a phenomenon similar to that of neovascularization of the iris, trabecular area, and retina in patients with aortic arch syndrome (Pulseless disease), carotid artery occlusion and other conditions producing chronic ocular ischaemia. Each terminal choroidal arteriole supplies a bunch of choriocapillaris (Fig. 5a), occupying an area equal in size to about a quarter of the optic disc or less (Fig. 5b), and each bunch of these choriocapillaries has no direct communication with the adjacent choriocapillaris (Hayreh, 1974a, b). This has been further confirmed by histological examination of flat preparations of the human choriocapillaris where a distinct lobular pattern of the choriocapillaris

with the arteriole in the center and the venules in the periphery has been found (Torczynski and Tso, 1974). It is possible that a sudden occlusion of one or more of these terminal choroidal arterioles in the macular region could lead to overlying localized pigment epithelial disturbance which may vary from upsetting the normal "chorioretinal barrier" (Shakib *et al.*, 1972) associated with serous exudation, to the production of depigmented spots in the macular region. These are simply hypotheses based on the *in vivo* pattern of the submacular choroidal vascular bed.

Involvement of the macular region by toxoplasma is well-known. To explain this predilection by toxoplasma for the macular region, some authors feel that in these cases, contrary to the conventional view, the disease is primarily choroidal (Wollensak *et al.*, 1965; Potts, 1966; Heimann, 1970). Wollensak *et al.* (1965) and Heimann (1970) claim to have found a collection of toxoplasma organisms in the choroid besides the SPCAs. It is certainly a stimulating thought.

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