Transient Monocular Blindness

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SUMMARY: *This paper is a review of the causes of intermittent monocular blindness. The nature of cholesterol and platelet retinal emboli is discussed. Their sources, the frequency with which they may cause transient or fixed blindness and the association between these emboli and pathology of the major cerebral vessels and other organs is discussed.*

Consideration is given to the equally important abnormalities of platelet behavior and to some of the physiology of retinal blood flow and non-embolic blindness.

The current treatment of this symptom may be anticoagulation, surgical correction of a stenotic artery or both. The effect of treatment is unpredictable and in some situations the rationale is suspect.

This review may provide a summary on which to base future studies of the effectiveness of various therapeutic agents.

RÉSUMÉ: *Le présent article revoit les causes principales de la cécité monoculaire intermittente. On y discute la nature des embolies de cholestérol ou de plaquettes au niveau de la rétine, leur origine, la fréquence avec laquelle ces embolies peuvent causer une cécité transitoire ou permanente et finalement l'association entre ces embolies et la pathologie des vaisseaux cérébraux principaux et des autres organes.*

Il est également fait mention de l'importance qu'il faut reconnaître aux anomalies de comportement des plaquettes et à la physiologie du flot sanguin rétinien et de la cécité non-embolique.

Le traitement actuel de ce symptôme peut être soit l'anticoagulation, soit la correction chirurgicale d'une artère sténotique ou l'association des deux approches. L'effet du traitement est imprévisible et parfois même on peut mettre en doute l'augmentation.

La présente revue du sujet devrait servir de base pour les études futures de l'efficacité de nouveaux agents thérapeutiques.

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INTRODUCTION

The purpose of this paper is to review the known and suspected causes of transient monocular blindness. There is current interest in the merits of various therapies, i.e. aspirin, warfarin, extracranial artery surgery, and in order to have a basis for therapeutic comparison perhaps the etiologies of the symptom should be restated.

About thirty years ago, the syndrome of transient monocular blindness became popular and widely acknowledged in clinical medicine. It acquired a half-Greek, half-Latin name, "amaurosis fugax". Some descriptions of the syndrome suggested the temporary blindness might be followed or accompanied by temporary ipsilateral cerebral dysfunction. One of the explanations for these two lesions was the passage of embolic material up one carotid artery with some of it into or over the origin of the ophthalmic artery and the rest of it into the middle cerebral artery. This combination of ocular and ipsilateral cerebral symptoms is uncommon and the blindness may have other mechanisms. Of 205 patients with internal carotid artery stenosis and signs of cerebral ischemia only 4 had episodes of transient blindness. In a group of 153 patients with similar complaints, but with carotid artery occlusion, only one had episodes of blindness (Gurdjian et al., 1962).

However, the symptom of transient one-eyed blindness alone is common and is probably more common in the stroke age group (Hollenhorst, 1960). It is more frequent with carotid artery stenosis as opposed to occlusion. Hollenhorst reported the symptom in 56% of 86 patients with stenosed arteries versus a 5% incidence in 38 patients with occluded arteries. The natural

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history is variable and is probably a reflection of different etiologies plus unknown factors. Marshal and Meadows (1968) followed 80 patients with repeated attacks of one-eyed blindness for 24 to 55 months and found that 5 developed hemiplegia and 9 permanent visual loss. On the other hand, Hollenhorst (1966) examined 208 patients with retinal emboli and stated that 69% of these had fixed or transient cerebral symptoms within 10 days of the embolus being observed. Only 7% of 208 had a history of amaurosis fugax, however.

Amaurosis fugax occurs in association with many different clinical situations (Fisher, 1959). These include cholesterol and platelet retinal emboli (Hollenhorst, 1966; Russell, 1963), cranial arteritis, migraine, papilledema, global retinal ischemia (Dyll et al., 1966; Sanders, 1939; Harbridge, 1906; Bruner, 1921), orthostatic retinal hypotension (Hollenhorst, 1960) and in young females unrelated to oral contraception medication and with a variety of extracranial artery pathology.

Treatment of the symptom has provided some information but this aspect is not complete. There is no doubt warfarin was effective when given to Fisher's patient (1959) and at least one patient in the group reported by Marshal and Meadows (1968). The information on the long-term benefits of aspirin is not available. The surgical correction of internal carotid artery stenosis in the neck has been used as treatment and also has caused the emboli (Russell, 1961; McBrien, 1963; Hollenhorst, 1961).

Cholesterol Emboli

Hollenhorst (1961) provided one of the earlier descriptions of these lesions and speculated that the "bright-plaques", orange yellow or copper colored at various retinal artery bifurcations were cholesterol crystals. David et al. (1963) provided the proof. Their patient had an atheromatous internal carotid artery lesion treated surgically. Postoperatively he suffered an ipsilateral cerebral infarction and a shower of shiny copper-yellow plaques was seen in the retinal arterioles on the same side. At post-mortem, material from the carotid, the obstructed cerebral artery and the retinal arterioles was found to be composed of doubly refractile crystals which contained cholesterol esters.

The appearance of a cholesterol embolus in the retina is characteristic. It is often oval, rice-grain in shape, highly reflective, lodged at a bifurcation, yellow or orange and variable in mobility. A patient may have 1 to 25 of these objects in the retinal arterioles at any one time (Hollenhorst, 1966). Digital pressure on the eye or the weight of the ophthalmodynamometer may make them move or disappear. Alternatively, they may stick at the same retinal arteriole bifurcation for months (Russell, 1963), and be followed by a soft white exudate. They often appear to be fatter than the vessel containing them. This may be an optical illusion.

They usually do not disturb vision. One or more cholesterol emboli may be found in the retina of an elderly arteriopathic patient with no visual complaints and no objective change in vision. As Hollenhorst (1966) has said, "In most cases these small crystals seem to be relatively innocuous, for usually when they appear in the retinal arterioles they cause little or no damage." However, they can infarct the retina (Russell, 1963; Hollenhorst, 1961). The frequency of amaurosis fugax due to these lesions is not known.

The incidence of this material in the retinal arterioles in a group of patients with carotid or vertebral-basilar artery disease is not high. Of 235 patients (80% male, average age 61 years) with carotid artery disease, 27 (11%) had one or more retinal cholesterol emboli and of 93 patients with vertebral-basilar disease 4 (4%) had these lesions (Hollenhorst, 1961).

Of these 31 patients only 11 had a history of amaurosis fugax, while 65 (65/328) other patients, without evidence of retinal emboli, had the same symptom. An additional 23 patients (23/328) had fixed occlusions of the central retinal artery or one of its branches. This group also had no evidence of retinal emboli.

The embolic material, in most patients, was mobile and transient. It changed position in the retina, fragmented, appeared in showers and disappeared. It is impossible to say that any one episode of transient blindness was or was not due to cholesterol retinal emobli when the patient is examined at a later date.

Although the relationship between amaurosis fugax and retinal cholesterol emboli is uncertain, there is a high association between these emboli and major pathology elsewhere.

Hollenhorst (1966) followed 208 consecutive patients seen over 5 years. They all had one or more cholesterol crystals and human atheromatous material into the infor selection. Two hundred of the group had crystals in one eye and 9 in both. Males comprised 85% of the group and the average age was 62 years. The reasons for seeking medical attention varied but 85% of the patients had a presenting complaint related to arteriosclerosis somewhere. Twenty percent were diabetic and 70% had some degree of hypertension. The signs of advanced generalized arteriosclerosis were frequent and serious. Sixty-three percent of the group had new or old strokes or transient ischemic attacks. Sixty percent had ischemic heart disease, 50% peripheral obliterative atherosclerosis, 16% abdominal aneurysms and 12% retinal arteriolar occlusions. However, only 7% of the patients had a history of amaurosis fugax. One of these patients had a white embolus as well as cholesterol crystals in the intermittently blind eye.

Again, there is no firm evidence to suggest that amaurosis fugax and the cholesterol crystals are related. Numerically, they are unrelated, i.e. 93% of the group with retinal arteriolar cholesterol crystals does not have amaurosis fugax and 7% of the group does — then there is probably another or additional explanation for the symptom. Marshal and Meadows (1968), who followed 80 patients with amaurosis fugax, saw yellow refractile emboli in only three of their patients.

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These retinal lesions are most common after and during surgery to the carotid artery in the neck, the aortic valve and possibly after vascular surgery for atheroma anywhere. The cholesterol crystal will fragment into particles 1 or 2 microns in diameter and circulate widely. Hollenhorst (1958) injected cholesterol crystals and human atheromatous material into the internal carotid artery of a monkey, and observed showers of transient and fixed bright orange-yellow plaques in the ipsilateral retina within seconds. When the opposite retina was looked at 10 minutes later the same lesions were present there.

Thirty-five of 235 patients with carotid artery disease were subjected to endarterectomy and 7 of these had retinal emboli. Five of the seven developed the emboli during surgery, one 6 weeks later and one patient before and after surgery. Two of these 7 patients sustained infarction of the retina (Hollenhorst, 1961).

Two of these 35 endarterectomized patients provide interesting examples. Case No. 25 — a 46-year-old male with right temporal lobe seizures had an occluded right internal carotid artery and normal pre-operative retina. After an unsuccessful right internal carotid endarterectomy, 15 cholesterol emboli were seen in the right retina with 2 occluded arterioles and none in the left eye suggesting that even if blood flow is not established at endarterectomy, the manipulation of the vessel may release cholesterol into the blood stream. Case No. 28 — a 58-year-old man with attacks of coma had an occluded right internal carotid artery and normal retinae pre-operatively. After a successful right internal carotid endarterectomy many cholesterol emboli were seen in both eyes suggesting that mobilized cholesterol will fragment into pieces less than 5 microns in size and circulate widely.

In summary, one can say the following about yellow, cholesterol crystal retinal emboli; they may arise from an atheromatous lesion anywhere in the body, the crystals and the fragments of crystals will circulate through the lung and peripheral circulation; they are usually benign in the retinal circulation although they may cause retinal infarction. They may cause amaurosis fugax although how often is not known. They are less common in the eye on the side of a carotid artery thrombosis than on the side of a stenosed or normal artery. Their presence in the retina has a high association with advanced arteriosclerotic disease elsewhere.

Platelet Emboli

In 1959 Fisher made precise and lengthy observations of the retina of an intermittently blind man and suggested that the transient intra-arterial material was embolic.

This amazing patient was an obese, middle-aged, hypertensive male who experienced from 700 to 1000 attacks of one-eyed blindness over 18 months without permanent compromise of his vision. The episodes were all in the same eye and there had been two short episodes of probable cerebral ischemia in the ipsilateral hemisphere. The patient's retina was examined in four attacks of blindness lasting from one to 60 minutes.

The embolic material had the following characteristics. Vision was lost before any abnormality was seen in the retina. The material was white with a square end at the leading and trailing edges. The containing artery was the same diameter, proximal, distal and in the portion holding the material. The material was adhesive to itself and at times to the arteriole containing it. It arrested for minutes at bifurcations, it moved both proximally and distally when the arteriolar flow was arrested. It was seen, early in an attack of blindness, at the division of the central retinal artery with four fingers extending a short distance into the four major branches of this artery. As it moved into the two superior branches, the fingers in the inferior branches withdrew, joined the main body of material and advanced into the superior branches. It was compressable and also fragmented. The same extension into and withdrawal from, small arterioles in the peripheral retina was also probably seen. Apparently, the material always appeared first in the central retinal artery and not more distally in the peripheral branches.

The pathology of the white body embolus has been established by McBrien et al. (1963). Their patient had an internal carotid artery stenosis, a thrombo-endarterectomy followed by carotid thrombosis. After this event embolic material was seen passing through the ipsilateral retinal arterioles every few minutes for several hours. The passage time was 3-5 minutes and at one time any vessel might have had 3 or more emboli separated by columns of blood. Post-mortem examination of retinal arterioles revealed the material consisted mostly of platelets, a few leucocytes, some lipid, no fibrin and no red blood cells. The condition of the internal carotid, ophthalmic and central retinal arteries was not stated.

This type of embolic material does not always cause transient blindness. Skovborg and Lauritzen (1965) have photographed white body emboli which took less than two minutes to pass from the nerve head to the peripheral retina while the patient was free of visual symptoms. In my experience two patients have been examined while transiently blind. Both had repeated attacks of blindness with irregular frequency over many months. The intra-arterial embolus resembled an air bolus travelling through a plastic intravenous tube. Vision had started to fail before it appeared, passage time was less than one minute and vision did not recover until 30-45 seconds after it had disappeared. Other observers have mentioned the short passage time of the material, unlike Fisher's patient who had one episode of 30 minutes duration and another of 60 minutes.

The frequency of attacks varies enormously. Marshal and Meadows (1969) reported a 44-year-old female patient with loss of vision once for 2 hours. The same day a white body embolus was seen at an arteriolar retinal bifurcation and 3 days later it was gone. She was followed for over

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6 years with no further signs or symptoms.

These emboli are not always benign. Gerstenfeld's (1964) patient had about 20 episodes of blindness over 24 hours due to transient white body emboli and then infarcted a segment of the retina.

Any observer is lucky to examine a single patient during an attack of amaurosis fugax. Marshal and Meadows studied a group of 80 patients with this symptom and more than half the group had histories of blindness from 2 to 10 years in duration although the attacks varied in frequency. They saw emboli in only 5 of their 80 patients. Two of these were white and the other three yellow, presumably cholesterol crystals.

In a few recorded cases in which the cause of blindness was known, the state of the arterial system, particularly the internal carotid, was varied and unpredictable.

Fisher's patient (1959) had internal carotid stenosis at the sinus. McBrien's patient (1963) had postoperative thrombosis of the carotid and Russell's first patient (1961) had spontaneous thrombosis of the carotid and ophthalmic arteries and probably the central retinal artery. These latter patients suggest the in situ formation of the embolic material in the central retinal artery proximal to the globe. Gerstenfeld's patient (1964) had a thrombosed internal carotid distal to the origin of the ophthalmic artery. All of these patients had white body emboli. There is a similar variability of artery pathology in the reports of patients with amaurosis fugax in whom the mechanism of the blindness is unknown.

Of the 80 patients with amaurosis fugax reported by Marshal and Meadows, 21 had angiography. Ten had normal arteries. Seven had carotid stenosis and 4 had carotid occlusions.

In a group of 234 patients with amaurosis fugax (some of whom also had cerebral ischemic episodes), Lemak and Fields (1976) found angiographically normal carotid arteries in 22%, stenosis in 64% and total occlusion in 14%. Ramirez-Lassepas et al. (1973) found one angiographically normal carotid artery, 20 stenosed and 6 occluded arteries in a group of 27 patients with amaurosis fugax with or without ischemic cerebral symptoms. In Hollenhorst's (1960) 86 patients with carotid stenosis, 48 (55%) had a history of amaurosis fugax and of 38 patients with carotid occlusion, 2 (5%) had the same symptom.

From angiographic studies it appears that amaurosis fugax, without reference to the mechanism of blindness, is most commonly associated with a stenosed internal carotid artery, next most commonly with a normal artery and least common with an occluded artery.

The condition of the arterial tree was approximately similar in a matched age group of patients with only cerebral ischemic symptoms. Of 394 patients with exclusively cerebral ischemic symptoms, 49% had stenotic arteries, 43% normal and 8% occluded arteries (Lemak and Fields, 1976). In another group of 267 patients with transient cerebral ischemic attacks, 75% had stenotic arteries, 18% normal and 5% occluded arteries (David et al., 1973). In another group of 265 patients without ocular or cerebral symptoms, all of whom had neck bruits, angiography revealed internal carotid stenosis in 65%, normal in 28% and occlusion in 5%.

It is difficult to reconcile the embolic theory of amaurosis fugax with the variations in the state of the carotid artery listed above. No doubt potential embolic material can arise on a stenotic and atheromatous area in the cervical portion of the carotid artery and migrate into the ophthalmic, and then the central retinal artery. However, one might reasonably expect embolic material from this source to flow into the middle cerebral artery as often or more often than into the ophthalmic artery. The middle cerebral artery is a direct anatomical extension of the internal carotid and receives a high proportion of the volume of blood in the internal carotid artery. Both of these factors make it a preferential embolic target. The ophthalmic artery leaves the carotid at an angle usually greater than 100 degrees and receives a relatively small proportion of the volume of blood in the internal carotid artery (Clay and Vignaud, 1971). These factors make the ophthalmic and central retinal arteries non-preferential embolic targets. One would expect patients with transient cerebral ischemic attacks to have infrequent episodes of amaurosis fugax and one might similarly expect virtually all patients with amaurosis fugax to have ipsilateral cerebral hemisphere symptoms. This is not the recorded experience. How may the symptom be explained with an occluded or normal internal carotid artery? Ligation of the internal carotid artery does not interfere with vision in the ipsilateral eye (Mount, 1959; Poppen, 1960; Smith, 1962). Ligation of the ophthalmic artery does not interfere with vision (Dandy, 1935; Adson, 1942). Thrombus in a carotid artery at the bifurcation in the neck may extend as high as the origin of the ophthalmic artery or beyond. In the former case, the ophthalmic artery usually has a retrograde flow into the carotid, and in the latter, usually no flow from its origin as far as the first major intraorbital branch. In these circumstances the central retinal artery is filled by a retrograde flowing ophthalmic which in turn is filled by one of its numerous anastamotic branches (Clay and Vignaud, 1971).

This circuitous route of blood supply to the retina in the presence of carotid and/or ophthalmic artery thrombosis makes migrant emboli an improbable explanation for amaurosis fugax. It is more likely that platelet material aggregates in the central retina artery at its origin from the ophthalmic.

This is further supported by the fact that in the patients described by McBrien (1963) and Russell (1961) platelet emboli were seen in the retina after the ophthalmic and carotid arteries were occluded. Also, in the 24 of 208 patients described by Hollenhorst (1966) in whom both cholesterol and platelet emboli were seen at the same time, all had central retinal artery thrombosis.

In some reported cases there is a mild inference that gravity or some

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unique anatomical feature influences the direction of embolic material into a particular retinal vessel. Fisher's (1959) patient suggested that if he was sitting at the start of an attack of blindness he usually lost his lower vision and the white embolic material was seen to enter the superior temporal or nasal or both arterioles. If he was supine he might go blind in any segment or the whole eye. McBrien's patient (1963) had the majority of his embolic material in the superior nasal artery. Russell's (1961) first patient had white emboli in all directions and his second patient probably had them mostly in superior retinal vessels. With respect to cholesterol crystal emboli, Hollenhorst (1958) usually saw them in the superior or inferior temporal arterioles and only occasionally in the nasal vessels.

Apart from the state of the vascular tree supplying blood to the eye, the behavior of the platelets forming the embolic material must be of great importance. What determines the aggregation of platelets and the disintegration of the aggregate repeatedly over months and years, with a small incidence of permanent vascular occlusion and minimal evidence of the same process occurring elsewhere? Why does warfarin appear to halt the process?

The growing interest in platelets is evidenced by the Cumulated Index Medicus which listed 190 citations on the subject in 1973 and 350 in 1975. Deykin (1974) has said, "these are palmy days for those of us concerned with platelet research." One wonders when some of the palminess will filter down to the clinician and change the present situation which might be described as the blind treating the intermittently blind.

It is known that the platelet aggregation process may start if flowing blood comes in contact with subendothelial tissues. The platelets then change their shape and the release reaction occurs. The released substances include serotonin, calcium, adenosine triphosphate and adenosine diphosphate (ADP). The ADP is a powerful promotor of further secondary aggregation and release as are prostaglandin E2, serotonin and thrombin. Prostaglandin E1 inhibits aggregation. If the ADP is below a critical level platelets will dissociate and regain their normal shape. The change in platelet shape which precedes release allows reorganization of the surface membrane and accelerates the reactions of some of the blood clotting proteins. This clot accelerating property, platelet factor 3, is not an extruded property of the platelet. Possibly this is the effective site of warfarin.

Aspirin appears to be an anticoagulant by impeding the release reaction, possibly by interfering with prostaglandin formation. By inhibiting release both the primary and secondary platelet aggregates can be prevented.

Walsh (1972) has written extensively on the mechanisms of initiation of intrinsic platelet coagulation and more recently (1976) has studied platelet activity in 22 patients with transient cerebral ischemia. Twelve had normal serum lipids and 10 had type IV hyperlipoproteinemia.

Platelet aggregation and release were normal in all patients. However, "platelet coagulant activities concerned with initiation and early stages of intrinsic coagulation were increased two to three times in the 12 patients with normal serum lipids." In the other 10, with abnormal lipids, these factors were normal.

Platelet factor 3 was the same in the two groups and the control groups.

Carvalho (1974) also demonstrated normal platelet behavior in patients with type IV hyperlipoproteinemia and abnormal aggregation in platelets from patients with type II hyperlipoproteinemia.

In spite of sophisticated angiography of cerebral and retinal vessels, intermittent blindness and cerebral ischemia will not be well understood or intelligently treated until all factors influencing coagulation changes in the elderly, hypertensive, hyperlipemic, hyperuricemic and diabetic are known. The same comment can be made about the nature and abnormalities of local blood flow and its autoregulation to the eye and brain.

In summary, we know the following about white-body retinal emboli. Their occurrence may be frequent or solitary. They are usually benign, may cause no symptoms or may infarct part or all the retina. They are made of platelets. They occur in the presence of a normal carotid system, internal carotid stenosis and occlusion of the carotid, ophthalmic and central retinal arteries. They may form in the carotid artery or elsewhere in the circulation and migrate into the retinal circulation, but there is evidence they commonly arise in the ophthalmic or central retinal arteries. Warfarin appears to stop their development.

Abnormalities of platelet aggregation are probably as important as the state of the artery in which the aggregates are formed.

Global Retinal Ischemia

There is evidence that transient monocular blindness occurs on a non-embolic basis. It is not known if this is a common mechanism relative to embolic episodes.

Recognition of the unique blood supply of the eye and orbit is important in understanding the mechanisms of this type of blindness. The ophthalmic artery usually arises from the internal carotid artery in its infraclinoid portion. It may arise from the intracavernous portion or directly from the middle cerebral artery. It may have a double origin from the internal and external carotid or arise exclusively from the middle meningeal. Inside the orbit it gives rise to 15 branches half of which form substantial anastamoses with vessels having other origins (Clay and Vignaud, 1971). It is not surprising that ophthalmic artery ligation or obstruction does not interfere with vision.

Blood supply to the retina and choroid is physiologically distinct and interference with either will produce blindness. The choroid has 20 to 25 times the blood flow of the retina and autoregulates poorly. In the cat, 20% of the oxygen supply of the retina comes from retinal vessels and 80% from the choroid (Alm and

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Bill, 1972). In monkeys, the proportions are 35% and 65% (Alm and Bill, 1973). Both sources are necessary for the retina to function and survive (Buettner et al., 1973).

Alm and Bill (1973) have used radioactively labelled microspheres in the monkey to study the effects of increased intraocular pressure (IOP) on ocular blood flow. They defined ocular perfusion pressure as mean arterial pressure less intraocular pressure because the latter is usually the same as venous pressure. Clinically, reductions in perfusion pressure might occur due to a drop in systemic blood pressure or an increase in intraocular pressure.

Increasing IOP to 41 cm H_2O in the test eye versus 13 cm H_2O in the control eye reduced choroidal blood flow by 29% and by a similar amount to the prelaminar part of the optic nerve. In contrast, blood flow to the retina was either not significantly reduced or increased. The autoregulation of the retina is highly efficient.

Retinal Blood Flow

Retinal blood flow is affected little by changes in perfusion pressure, in cats, monkeys (Alm and Bill, 1972, 1973), and pigs (Ffytche et al., 1974).

Bulpitt and Dollery (1971) have found the same retinal blood flow in normal and hypertensive patients. The hypertensive patients had blood pressures 50% higher and were about 20 years older than the normotensives.

The mechanisms of retinal autoregulation are not clear. Myogenic factors are probably important and CO_2 is known to influence blood flow (Tsacopoulos et al., 1973). At a pCO_2 of 25 mm/Hg the retinal blood flow has been measured at 15 mg/min (in cats) and maximum vasodilatation produced at a pCO_2 of 75 mm/Hg and a flow of 50 mg/min (Alm and Bill, 1972).

In premature babies high arterial oxygen causes retinal artery contraction, degeneration and new vessel growth into the vitreous with permanent eye damage (Ashton, 1968). In the adult, retinal vessels contract when the oxygen tension is increased and reductions seem to cause vasodilation. Part of the constriction of high tensions is probably due to an increase in the O_2 supply to the retina from the choroid (Dollery et al., 1969).

The autonomic nervous system has an influence on retinal blood flow. The ophthalmic artery and extraocular part of the central retinal artery have a rich sympathetic innervation, but not the intraocular retinal vessels (Ehinger, 1966; Laties, 1967). Sympathetic stimulation produces a slight reduction in retinal O_2 tension suggesting that vasoconstriction outside the eye may reduce retinal blood flow (Alm and Bill, 1973). A marked vasoconstriction occurs in the choroid. The reduced nutrition via the choroid causes vasodilatation in the outer parts of the retinal vessels and the net change in retinal vessels and retinal flow may be a slight reduction, slight increase or no change. Whether the marked reduction in choroidal blood flow interferes with vision is not known.

Choroidal Blood Flow

Choroidal vessels show no evidence of autoregulation (Alm and Bill, 1972, 1973A) and are strongly affected by the sympathetic nervous system. Sympathetic nerves to the choroid consist only of vasoconstrictor fibers (Bill, 1962). Sympathetic stimulation in cats has produced a 60% reduction in choroidal blood flow. The oxygen content of the venous blood from the choroid is very high at 95% of that in the arterial blood (Alm and Bill, 1970). Reduced choroidal blood flow results in increased O_2 extraction and the total extraction in the choroid is unchanged until very low flow rates are reached. Carbon dioxide is a potent dilator of choroidal vessels in cats (Alm and Bill, 1972; Friedman and Chandra, 1972), while moderate variations in arterial O_2 tension have no effect on the vascular resistance.

There are cholinergic fibers from the pterygopalatine ganglion to the choroidal vessels (Ruskell, 1971) and as these vessels dilate when acetycholine is given intra-arterially (Chandra and Friedman, 1972), the choroidal nerves are probably vasodilatory. The effect of stimulation of these nerves is unknown (Bill, 1975).

Epinephrine and other adrenergic drugs cause contraction of the choroidal vessels indicating alpha adrenergic receptors (Chandra and Friedman, 1972), while the same substances have no effect on the retinal arterioles (Alm, 1972).

Thus, there are two circulatory systems — retinal and choroidal, both necessary for vision and with a common origin. The former has a superb autoregulatory capacity and is immune to the effects of the autonomic nervous system and almost all drugs. The latter autoregulates poorly, and is subject to autonomic influence and drugs.

Albert Alm has posed an important possibility. "The fact that the choroidal vascular bed, which has a normal blood flow 25-50 times that through the retina and lacks autoregulation, should make the retina unusually susceptible to an 'intraocular steal syndrome'. Drugs that dilate the choroidal vessels will cause marked increases in blood flow through the ophthalmic artery and thereby reduce the arterial pressure at the point of origin of the retinal artery, which tends to reduce retinal blood flow" (Alm, 1972). Possibly the highly efficient autoregulatory function of the retina can be overcome if the changes in choroidal blood flow are great enough.

There are some clinical observations of non-embolic ischemia causing transient monocular blindness. Saunders (1939) reported a 60-year-old man with multiple short attacks of monocular visual loss occurring while the patient strained in a bent over position. He could reproduce the attacks at will. When the blind eye was examined during an attack, the retinal arterioles were thin white threads, the disc was pale, the retina hazy and there was no red spot on the macula. Retinal photographs were made. The veins were normal during an episode and dilated and distended for 10 minutes after an attack. The attacks occurred twice while at rest, following forced hyperventilation and particularly after performing the Valsalva man-

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oeuvre. The act of straining while in a bent forward position is probably an effective form of Valsalva manoeuvre. This procedure, producing a drop in systemic blood pressure plus a marked increase in sympathetic outflow might well disturb ocular blood flow sufficiently to produce transient blindness in an arteriopathic patient.

Harbridge (1906) reported a similar patient with repeated intermittent monocular blindness whose attacks occurred only if the patient was bending forward.

In contrast, Bruner (1921) reported a 34-year-old man with up to 10 attacks of monocular blindness per day unrelated to postural change or straining. During the blindness an ischemic retina was observed without embolic material. The attacks seemed to stop after the intraocular pressure was reduced with eserine.

Dyll et al. (1966) reported a 68-year-old man with repeated attacks of transient blindness in one eye. Some of these were accompanied by syncopal symptoms. Ophthalmodynamometry gave equal readings in the two eyes, his blood pressure was 110/70, and arm to retina circulation times were equal on the two sides. The internal carotid artery on the side of the blindness revealed roughness and narrowing of the carotid siphon. Retinal photographs at the time of an attack of blindness showed similar global retinal ischemia described above and no embolic material.

Hollenhorst has also observed global retinal ischemia and has pertinent comments on the measurement of ocular blood pressure. "Most authors, including myself, have used the term 'retinal artery' pressure to designate the findings on ophthalmodynamometry. Many years ago Duke-Elder showed that the readings reflected the pressure within the ophthalmic artery and not the central retinal artery. Therefore, I recommend the term ophthalmic artery pressure."

One of the patients, with intermittent blindness, reported by Hollenhorst is particularly informative (1960). The eye was blind, during an attack, with no direct pupil response. The fundus and retinal vessels were normal before, during and after the episodes. The ophthalmic artery pressures were normal and equal before the episode, but during the blind attack, merely touching the sclera with the ophthalmodynamometer caused the retinal arterial tree to collapse.

A number of his patients had amaurosis fugax only on standing and had a marked ocular orthostatic hypotension in this position. Three-quarters of his patients with carotid occlusive disease had lower ophthalmic artery pressure on the affected side and of these, half had significantly lower pressure when standing as opposed to lying.

Patients who had recently undergone carotid thromboendarterectomy demonstrated the orthostatic drop in ophthalmic artery pressure even more markedly. Ophthalmic artery pressure may be equal in the two eyes when lying and significantly different when the patient is sitting or standing.

In addition to arterial pathology and platelet behaviour, the dynamics of retinal blood flow, systemic blood pressure, intraocular pressure and the possibility of a choroidal "steal" of retinal blood all deserve consideration in any patient with intermittent monocular blindness.

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REFERENCES

ADSON, A. W. (1942). Surgical Treatment of Vascular Diseases Altering the Function of the Eyes. Am. J. Ophthalmol., 25: 824-838.

ALM, A. (1972). Effects of Norepinephine Angiotensin, dihydroergotamine, Papaverine, isoproterenol, histamine, nicotinic acid, and xanthinol nicotinate on retinal oxygen tension in cats. Acta Ophthalmol., 50: 707-719.

ALM, A. and BILL, A. (1970). Blood flow and Oxygen extraction in the cat uvea at normal and high intraocular pressures. Acta Physiol. Scand. 80: 19-28.

ALM, A. and BILL, A. (1972). The Oxygen Supply to the Retina II. Effects of High Intraocular Pressure and of Increased Arterial Carbon Dioxide Tension on Uveal, and Retinal Blood Flow in Cats. Acta Physiol. Scand. 84: 306-319.

ALM, A. and BILL, A. (1973a). Ocular and Optic nerve Blood Flow at Normal and Increased Intraocular Pressures in Monkeys (Macaca Irus): A Study with radioactively labelled microspheres including flow determinations in brain and some other tissues. Exptl. Eye Res. 15: 15-29.

ALM, A. and BILL, A. (1973b). The Effect of Stimulation of the Cervical Sympathetic Chain on Retinal Oxygen Tension and on uveal retinal and cerebral blood flow in cats. Acta Physiol. Scand. 88: 84-94.

ASHTON, N. (1968). Some Aspects of the Comparative Pathology of Oxygen Toxicity in the Retina. Br. J. Ophthalmol., 52: 505-531.

BILL, A. (1962). Autonomic Nervous Control of Uveal Blood Flow. Acta Physiol. Scand. 56: 70-81.

BILL, A. (1975). Blood Circulation and Fluid Dynamics in the Eye. Physiol. Rev. 55: 383-417.

BRUNER, A. B. (1921). Spasm of the Central Retinal Artery. Am. J. Ophthalmol., 4: 503-506.

BUETTNER, H. R., MACHEMER, S., ANDERSON, C. and et al. (1973). Experimental Derivation of Choroidal Blood Flow. Retinal Morphology, early receptor potential and electroretinography. Am. J. Ophthalmol., 75: 943-952.

BULPITT, C. J. and DOLLERY, C. T. (1971). Estimation of the Retinal Blood Flow by Measurement of the Mean Circulation Time. Cardiovas. Res. 5: 406-412.

CARVALHO, A. C. A., COLMAN, R. W. and LEES, R. S. (1974). Platelet function in hyperlipoproteinemia. N. Engl. J. Med., 290: 434-438.

CHANDRA, S. R. and FRIEDMAN, E. (1972). Choroidal Blood Flow II. The effects of autonomic agents. Arch. Ophthalmol., 87: 67-69.

CLAY, C. and VIGNAUD, J. (1971). Vascularisation de l'orbite. Encyclopedie medico-chirurgicale, Paris. 21: 006.

Cumulated Index Medicus (1973). 14: 7641-7643.

Cumulated Index Medicus (1973). 16: 5195-5198.

DANDY, W. E. (1935). The Treatment of Carotid Cavernous Arteriovenous Aneurysms. Ann. Surg., 102: 916-926.

DAVID, N. J., KLINTWORTH, G. K., FRIEDBERG, S. J. and DILLON, M. (1963). Fatal Atheromatous Cerebral Embolism Associated with Bright Plaques in the Retinal Arterioles. Neurology (Minneap.) 13: 708-713 (1963).

DAVID, T. E., HUMPHRIES, A. W., YOUNG, J. R. et al. (1973). A correlation of neck bruits and arteriosclerotic carotid arteries. Arch. Surg., 107: 729-731.

DEYKIN, D. (1974). Emerging Concepts of Platelet Function. N. Engl. J. Med., 290: 144-151.

DOLLERY, C. T., BULPITT, C. J. and KOHNER, E. M. (1969). Oxygen Supply to the retina from the retinal and choroidal circulations at normal and increased arterial

https://doi.org/10.1017/S0317167100025208 Published online by Cambridge University Press

oxygen tensions. Invest. Ophthalmol., 8: 588-594.

DYLL, L. M., MARGOLIS, M. and DAVID, N. J. (1966). Amaurosis Fugax. Neurology (Minneap.) 16: 135-138.

EHINGER, B. (1966). Adrenergic nerves to the eye and to related structures in man and in the cynomolgus monkey. Invest. Ophthalmol., 5: 42-52.

FFYTCHE, T. J., BULPITT, C. J., KOHNER, E. M. et al. (1974). Effect of changes in Intraocular Pressure on the Retinal Microcirculation. Br. J. Ophthalmol., 58: 514-522.

FISHER, C. M. (1959). Observations of the Fundus Oculi in Transient Monocular Blindness. Neurology (Minneap.) 9: 333-347.

FRIEDMAN, E. and CHANDRA, S. R. (1972). Choroidal Blood Flow III. Effects of Oxygen and Carbon Dioxide. Arch. Ophthalmol., 87: 70-71.

GERSTENFELD, J. (1964). The Fundus Oculi in Amaurosis Fugax. Am. J. Ophthalmol., 58: 198-205.

GURDJIAN, E. S., HARDY, W. G., LINDER, D. W. et al. (1962). Occlusive cerebrovascular disease. Diagnostic evaluation and treatment. Tr. Am. Acad. Ophthalmol. & Otolaryngol., 66: 149-165.

HARBRIDGE, D. F. (1906). Monocular Visible Spasm of the Central Artery of the Retina. Ophthalmol. 2: 647-653.

HOLLENHORST, R. W. (1958). Ocular Manifestations of Insufficiency on Thrombosis of the Internal Carotid Artery. Trans. Am. Ophthalmol. Soc., 56: 474-506.

HOLLENHORST, R. W. (1960). The Ocular Manifestations of Internal Carotid Arterial Thrombosis. Med. Clin. North Am., 44: 897-908.

HOLLENHORST, R. W. (1961). Significance of Bright Plaques in the Retinal Arterioles. JAMA 178, 23-29.

HOLLENHORST, R. W. (1962). Carotid and Vertebral Basilar Arteriole Stenosis and Occlusion: Neuro-Ophthalmologic Considerations. Tr. Am. Acad. Ophthalmol. & Otolaryng., 66: 166-180.

HOLLENHORST, R. W. (1966). Vascular Status of Patients who have Cholesterol Emboli in the Retina. Am. J. Ophthalmol., 61: 1159-1165.

LATIES, A. M. (1967). Central retinal Artery Innervation. Arch. Ophthalmol., 77: 405-409.

LEMAK, N. A. and FIELDS, W. S. (1976). The Reliability of Clinical Predictors of Extracranial Artery Disease. Stroke 7: 377-378.

MARSHAL, J. and MEADOWS, S. (1968). The Natural History of Amaurosis Fugax. Brain 91: 419-433.

McBRIEN, D. J., BRADLEY, R. D. and ASHTON, N. (1963). Retinal Emboli in Stenosis of the Internal Carotid Artery. Lancet 1: 697-699.

MOUNT, L. A. (1959). Results of treatment of Intracranial Aneurysms using the Selverstone Clamp. J. Neurosurg., 16: 611-618.

POPPEN, J. L. and FAYER, C. A. (1960). Intracranial Aneurysms: Results of Surgical Treatment. J. Neurosurg., 17: 283-296.

RAMIREZ-LASSEPAS, M., SANDOK, B. A. and BURTON, R. C. (1973). Clinical Indicators of Extracranial Carotid Artery Disease in Patients with Transient Symptoms. Stroke 4: 537-540.

RUSKELL, G. L. (1971). Facial Parasympathetic Innervation of the Choroidal Blood Vessels in Monkeys. Exptl. Eye Res. 12: 166-172.

RUSSELL, R. W. Ross (1961). Observations on the Retinal Blood Vessels in Monocular Blindness. Lancet 2: 1422-1428.

RUSSELL, R. W. Ross (1963). Atheromatous Retinal Embolism. Lancet 2: 1354-1365.

SANDERS, T. E. (1939). Intermittent Occlusion of the Central Retinal Artery. Am. J. Ophthalmol., 22: 861-869.

SKOVBORG, F. and LAURITZEN, E. (1965). Symptomless Retinal Embolism. Lancet 1: 361-362.

SMITH, P. (1962). Differential Carotid Ligation for Supraclinoid Arterial Cerebral Aneurysms. J. Neurosurg. 19: 787-792.

TSACOPOULOS, M., BAKER, R. and JOHNSON, M. (1973). The Effect of Arterial pCO_2 on inner retinal oxygen availability in monkeys. Invest. Ophthalmol. 12: 449-455.

WALSH, P. N. (1972). The Role of Platelets in the contact phase of blood coagulation. Br. J. Haematol. 22: 237-254.

WALSH, P. N. and BIGGS, R. (1972). The Role of PLatelets in intrinsic factor Xa formation. Br. J. Haematol. 22: 743-760.

WALSH, P. N., PARETI, F. I. and CORBETT, J. J. (1976). Platelet Coagulant Activities and serum lipids in Transient Cerebral Ischemia. N. Engl. J. Med., 295: 854-858.

WEITER, J. J., SCHACHAR, R. A. and ERNEST, J. (1973). Control of Intraocular Blood Flow. Effects of Sympathetic Tone. Invest. Ophthalmol., 12: 332-334.

https://doi.org/10.1017/S0317167100025208 Published online by Cambridge University Press