Hypoxic ocular sequelae of carotid-cavernous fistulae

Study of the causes of visual failure before and after neurosurgical treatment in a series of 25 cases

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The incidence of visual failure with carotid-cavernous fistula is high. It was impaired in 89 per cent. of the cases studied by de Schweinitz and Holloway (1908) and in 73 per cent. of those studied by Sattler (1920). The latter recorded blindness or near blindness in almost half of his patients. Treatment has reflected a clinical preoccupation with elimination of the bruit and reduction of the proptosis, and modern methods have become increasingly proficient at obtaining this by more extensive surgery (Dandy, 1935; Echols and Jackson, 1959; Hamby, 1966). However, in this condition, where the threat to life is small, preservation of vision becomes the major aim of therapy. Realisation of this goal has been lacking, though the ocular and cerebral hazards of surgery have recently been stressed by neurosurgeons (Walker and Allègre, 1956; Stern, Brown, and Allen, 1967).

Many articles and monographs have described the ocular complications of carotid-cavernous fistula both before and after surgery, but the patho-physiology of these changes has never received the detailed and systematic attention it deserves. We have approached this problem by analysing critically the preoperative and postoperative causes of impaired vision in a series of 25 carotid-cavernous fistulae studied and treated at the University of California Medical Center during the past 10 years. The changes that occurred in the eye, from the cornea to the optic nerve, were assessed in regard to:

- (1) Their effect on visual function.
- (2) Their appearance and resemblance to the hypoxic complications seen in other vascular diseases.
- (3) Their improvement or deterioration after neurosurgical procedures which alter the circulatory dynamics of the eye and orbit.

Abnormalities in ocular perfusion, circulation time, and vascular permeability were recorded in selected cases by ophthalmodynamometry or fluorescein angiography.

Review of cases

Aetiology and general manifestations

Trauma caused the carotid-cavernous fistula in eighteen patients and in the remaining seven the onset was spontaneous. Symptoms in the traumatic cases usually appeared soon after the head injury but occasionally there was a latent interval of days or even months.

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Seven patients with severe skull fractures were unconscious for several hours or days. Symptoms began more gradually in the patients with spontaneous fistula (although in one woman they developed immediately after a bout of severe vomiting) and the clinical manifestations were usually milder. Two of the spontaneous fistulae produced progressive changes over a period of several years; these lesions had unusual angiographic features which established them as external carotid-cavernous fistulae with dural shunts. One patient with a traumatic fistula had no symptoms for 8 months and neuro-radiological studies showed a dural arterio-venous shunt draining into the cavernous sinus.

Presenting complaints of the patients studied were:

- (1) Subjective bruit (75 per cent.)
- (2) Proptosis (64 per cent.)
- (3) Redness and swelling of the conjunctiva (36 per cent.)
- (4) Double vision (24 per cent.)
- (5) Ipsilateral blurred vision (16 per cent.)
- (6) Orbital pain (16 per cent.)

The most frequent ophthalmic sign was tortuous red and dilated vessels with thickened (arterialized) conjunctival veins of variable pattern (Fig. 1). Ipsilateral proptosis was seen almost as frequently. One patient had enophthalmos and ocular signs of an orbital blow-out fracture on the side of the fistula, and in two other patients there was no measurable exophthalmos. All patients with a rapid onset of ocular signs developed lid swelling and chemosis. Conjunctival changes and proptosis occurred bilaterally in three cases; the contralateral signs were less pronounced.

FIG. 1 Case 15 Conjunctival changes. Extreme tortuosity of conjunctival vessels, with dilatation and thickening "arterialization" of veins. Cornea demonstrates mild filamentary keratitis (see arrow)

Impaired visual function with carotid-cavernous fistula

Central visual acuity was recorded in twenty of the 25 patients* at the time of their admission to the hospital and in fourteen was found to be reduced. Two patients were blind, one because of traumatic optic atrophy and the other because of absolute glaucoma. Six patients had a visual acuity of less than 20/200; the retinal veins were dilated in all six cases and two manifested haemorrhages as well. Six patients had vision between 20/25 and 20/200 and four of these had dilated veins but no haemorrhages. In the remaining two patients in this group, one had a squint with amblyopia as a child, and the other had no recorded retinal findings. Finally, of six patients with normal visual acuity, four had

* The failure to obtain measurements of visual acuity in five patients may have been due to the patients' being obtunded.

dilated veins (one with haemorrhages) and one showed anterior segment signs. Thus blindness caused by retinopathy alone was not encountered, and although severe retinopathy was often associated with marked visual loss, some of these patients still had normal vision. Of the patients with normal visual acuity on the side of the fistula, two complained of difficulty in seeing. They described intermittent uniocular dimness (related to posture in one) or a sense of constriction in the field of the affected eye, slowness of adaptation to changes in illumination, particularly to bright lights, and lingering of after-images. Similar complaints were also expressed by several patients with central depression of vision, and these symptoms were considered strongly suggestive of hypoxic involvement.

Changes in the anterior segment of the eye

GENERAL CONSIDERATIONS Seven of the 25 patients had preoperative changes in the cornea, iris, aqueous humour, or lens which conformed to the clinical criteria for anterior segment ischaemia (Crock, 1967). These manifestations of untreated carotid-cavernous fistulae appeared in the ipsilateral eye and usually in the presence of marked proptosis, chemosis, conjunctival hyperaemia, and lid swelling. In each instance the anterior segment signs were accompanied by hypoxic alterations in the fundus. Usually the changes appeared within days or weeks of the onset of the fistula. The findings listed in Table I exemplify the variety of hypoxic signs that occurred, but do not represent a comprehensive review of the problem. Many of the patients were not examined with the slit lamp either initially or during the course of their disease. It is possible that many other subtle corneal and anterior chamber signs would have been added to Table I if these examinations had been routinely performed.

Vision was impaired in four of the seven cases but was more often attributable to the current hypoxic retinal changes (present in each case) than to the anterior segment signs. Of the six patients with visible anterior segment signs, only two had normal visual acuity, while four had vision of 20/200 or less and two of these were blind. Three patients were treated surgically and in two of these aggravation of the anterior segment signs occurred (Cases 15 and 18) (see Tables I and II, opposite).

CORNEA Most of the corneal changes occurring in this series were the result of hypoxia. Severe glaucoma occurred in two patients and proptosis, though often present, did not prevent lid closure. Mild epithelial oedema was the most frequent finding. It resembled the postoperative hypoxic corneal changes that O'Day, Galbraith, Crock, and Cairns (1966) found after encircling procedures for retinal detachment. Corneal filaments and epithelial blebs, reported by the same writers, occurred in two of our cases (Cases 15 and 16); one (Case 15) had an anaesthetic and hypoxic cornea, the other (Case 16; Fig. 9, overleaf) developed extraordinary neovascularization of the cornea after multiple carotid occlusive procedures which failed to close the fistula but caused severe ocular hypoxia. Changes of this severity never occurred before treatment in our patients. Stromal haze or folds in Descemet's membrane are signs of an acute "ischaemic" keratopathy (Crock, 1967). One of our patients (Case 18) developed a mid-stromal opacity but folds in Descemet's membrane were not seen.

AQUEOUS HUMOUR The slit lamp revealed aqueous flare and occasional cells in five eyes. On two occasions the significance of this finding was misinterpreted and the patient was treated for uveitis. Knox (1965) drew attention to similar diagnostic confusion that may arise when flare and cells are discovered in a patient with brachiocephalic occlusive

Table I Anterior segment involvement before operation

Case No.	Visual acuity	Cornea	Conjunctiva	Anterior chamber	Iris	Lens	Intraocular pressure
1	20/200	Epithelial haze	Marked chemosis	—	Pupil large and fixed	Normal	Normal
6	20/400	—	Marked venous dilation	Moderate flare	Pupil fixed Iris vessels dilated Iris atrophy Blood in aqueous veins	Early nuclear changes	Normal
7	20/20	Epithelial haze	Extreme chemosis	—	Normal	Normal	Normal
12	No light perception	Epithelial haze (bilateral)	Extreme chemosis	—	Pupil fixed, mid-dilated	Normal	Absolute glaucoma
15	20/200	Epithelial haze, filaments No sensation	Veins dilated and tortuous	Moderate flare	—	Normal	Mild elevation
20	20/20	—	Veins dilated	—	Normal on slit lamp Fluorescein sectoral leak (See Fig. 4)	Normal	Normal
18	20/20	Epithelial mid-stromal haze	Marked chemosis	Mild flare and cells	Iris oedema Pupil irregular, fixed, dilated	Normal	Moderate elevation

Table II Anterior segment involvement after operation

Case No.	Visual acuity	Procedure	Cornea	Anterior chamber	Iris	Lens	Intraocular pressure
10	Blind	Internal carotid ligation	—	—	Pupil irregular Iris atrophy Posterior synechiae	Early opacity	Hypotony
15	Counting fingers	"Trapping" procedure	Recurrent corneal erosion	Mild flare	Normal	Normal	Normal
16	20/50	Two stage carotid ligation Signs 1 year later	Haze Filamentary keratitis Severe neo-vascularization	Mild flare	Pupil irregular Posterior synechiae	Normal	Hypotony
18	Hand movements	"Trapping" procedure	Epithelial oedema Stromal haze	Hyphaema	Pupil irregular Iris atrophy and vessels markedly dilated Posterior synechiae	Mild opacity	Absolute glaucoma

vascular disease. The sign results from hypoxic alteration of the iris and ciliary vessels with a resulting increase in their permeability. These vessels also may bleed into the anterior chamber as was seen in two of our patients (Cases 6 and 18).

FIG. 2 Case 16 Corneal changes. Striking vascularization of cornea with a dependent filament visible centrally

IRIS Oedema of the iris was present in one patient, iris atrophy in three, ischaemic paralysis of the pupillary muscles in seven, posterior synechiae in three, and (visible) dilated iris vessels in three. Patients with pupillary dilatation often had other signs of ischaemia which favoured this mechanism rather than an internal ophthalmoplegia (see Fig. 3).

FIG. 3 Case 7 Anterior segment changes. Extreme chemosis and conjunctival vascular changes. Pupil irregularly dilated and fixed

Changes in iris vessels, which had not been evident in one eye during a routine slit-lamp examination, caused a clearly visible and abnormal sector-shaped extravasation of dye following the intravenous injection of fluorescein (Fig. 4, opposite). Crock (1962) mentioned many of the iris changes also noted in our series.

LENS Changes in the lens were rarely encountered as a complication of carotid-cavernous fistula or its treatment. Cataract occurred as a late development in only two patients after carotid ligation, and both had other ocular signs. One patient had neovascular glaucoma and the other had ischaemic changes and hypotony.

FIG. 4 Case 20 *Iris changes.* Fluorescein angiogram of iris vessels, taken 10 minutes after intravenous injection of 10 per cent. fluorescein. Excessive leakage of dye visible in upper temporal segment, where iris vessels are abnormally permeable. Slit-lamp examination of this patient was normal

INTRAOCULAR PRESSURE Intractable glaucoma and blindness occurred in three patients; one elderly patient lost vision in both eyes (Case 12) from a unilateral spontaneous fistula, and in the other two the glaucoma became absolute in the ipsilateral eye after surgery. A carotid ligation was performed in the first patient, and a "trapping" procedure in the second (Case 18) with the development of severe neovascularization of the angle. This case has been reported elsewhere (Weiss, Shaffer, and Nehrburg, 1963). Mild and reversible elevation of intraocular pressure related to increased episcleral venous pressure was recorded in 5 patients with untreated carotid-cavernous fistulae and may have been overlooked in others. This type of glaucoma is related to the venous pressure and is not caused by hypoxia of the anterior segment.

Changes in the posterior segment of the eye

RETINAL SIGNS WITH UNTREATED FISTULAE We have already remarked on the correlation between visual acuity and the retinal findings. Dilated retinal veins were the most frequent ophthalmoscopic finding in this series and were present in nineteen of the 25 cases. This change may be subtle and easily overlooked, as undoubtedly occurred in some of our patients. Dilatation was found in all patients who complained of constriction of the visual fields and dimming in the involved eye.

More severe retinal vascular changes occurred in three patients (Cases 6, 20, and 23; Table III, overleaf), all of whom had marked venous dilatation and tortuosity, and scattered punctate haemorrhages; two also had multiple microaneurysms. In one of the three, an elderly man (Case 6), the retinal signs appeared after 3 months and included haemorrhages along the course of the veins, several exudates, and moderate disc swelling. This was the only instance of definite disc swelling in this series. This patient refused surgery and the chemosis and retinopathy resolved spontaneously. In the second patient, a 53-year-old man (Case 20), symptoms of a fistula had been present for 8 months and involved his only eye (see Figs 5A-F, overleaf).

There was a moderate dilatation of the conjunctival veins, marked dilatation and tortuosity of the retinal veins with punctate haemorrhages, and numerous microaneurysms. (see Fig. 5A). He noted intermittent blurring of vision but the visual fields were normal, the visual acuity being 20/25. Fluorescein angiograms demonstrated the greatly reduced

Table III *Posterior segment involvement before operation (excluding dilatation of veins)*

Case No.	Onset	Veins	Micro-aneurysms	Retinal haemorrhage	Vitreous haemorrhage	Optic disc	Follow-up
6	Acute	Marked dilatation and tortuosity	Numerous	Scattered punctate and perivenous haemorrhages Exudates	—	Moderate swelling	Resolution
14	Chronic	Moderate dilatation	Several	—	—	—	Post-operative transient blurring
17	Chronic	Mild dilatation	Occasional	—	Two episodes	—	No recurrence
20	Chronic	Marked dilatation and tortuosity	Numerous	Scattered punctate and flame-shaped	—	—	No recurrence 9 months
23	Chronic	Marked dilatation and tortuosity	—	Scattered punctate	—	? blurred margins	Post-operative deterioration

blood flow through the vessels, particularly evident in the arterial phase (Fig. 5B and C). The capillary phase revealed multiple dilatations and microaneurysms (Fig. 5D and E). The impaired rate of flow was well demonstrated in the venous phase, and perivenous leakage was visible in relation to some of the large venous trunks (Fig. 5F). Ophthalmic dynamometry in this man showed reduction of the mean arterial pressure and elevation of the venous pressure. He refused treatment and no progression of his signs or symptoms were noted during the 9 months that he was observed. The third patient (Case 23) with a traumatic fistula had dilated and tortuous veins and multiple punctate haemorrhages. Carotid ligations (internal and external) were followed by absolute glaucoma and blindness. Two patients (Cases 14 and 17) with external carotid-cavernous sinus shunts and mild chronic ocular changes showed dilated retinal veins and occasional microaneurysms. One of these patients had two episodes of vitreous haemorrhage from a peripheral clump of microaneurysms; the blood was reabsorbed and one year later she developed proptosis and

FIG. 5A Case 20 *Fundus changes. Arterial narrowing, venous dilatation, and numerous punctate (intra-retinal) and streak haemorrhages*

FIG. 5B *Fluorescein angiogram. Arterial phase (9 seconds after injection). Impaired arterial filling with irregularity in the calibre of the vessels*

FIG. 5C *Arterial phase (11 seconds after injection). Marked arterial stasis, with some early filling of capillaries below disc*

FIG. 5D *Capillary phase (14 seconds after injection). Dilatation of veins and capillaries with numerous microaneurysms*

FIG. 5E Capillary phase (Enlargement of 5d). Dilated capillaries visible on the right side, though absent capillary filling on the left is notable. Numerous microaneurysms visible

FIG. 5F Venous phase (10 minutes after injection). Marked perivenous leakage along larger vessels and some residual dye in microaneurysms

subjective awareness of a bruit. Her ocular signs did not progress after operation. The second patient had a ligation of the external carotid artery with satisfactory results.

The clinical entity of chronic hypoxic retinopathy has been well established and amply described in patients with brachiocephalic occlusive vascular disease (Takayasu, 1968; Kearns and Hollenhorst, 1963). As the flow of blood is reduced, several compensatory mechanisms are initiated by the hypoxia and the retention of metabolites. This results in capillary and venous dilatation with an associated increase in permeability. Prolonged changes may induce the formation of capillary microaneurysms.

The preservation of reasonable vision in eyes with marked hypoxic vascular signs, as exemplified in Cases 6 and 20, attests to the remarkable capacity of the retina to function despite significant slowing of the circulation.

RETINAL CHANGES AFTER FISTULA OPERATIONS The presence of hypoxic retinopathy did not signify imminent blindness in patients who refused surgical treatment. In fact, the visual outcome after operation in some patients with relatively mild retinopathy was unsatisfactory and occasionally disastrous (Cases 10 and 18). In three cases a florid retinopathy followed surgical attempts to restrict or trap the fistula (Table IV, opposite).

Table IV *Posterior segment involvement after operation*

<i>Case No.</i>	<i>Operation</i>	<i>Veins</i>	<i>Retinal haemorrhage</i>	<i>Vitreous haemorrhage</i>	<i>Ophthalmic artery pressure</i>	<i>Vision</i>
8	"Trapping" procedure	Immediate marked dilatation	Punctate haemorrhages Microaneurysms Soft exudates	—	Marked decrease	Postural amaurosis
10	Carotid ligation (cervical)	Fundus obscured suddenly 2 months after operation		Marked haemorrhage	Marked decrease	Blind
18	"Trapping" procedure	Immediate marked dilatation	Punctate and perivenous haemorrhages	Pre-retinal and vitreous	Marked decrease	Hand movements Glaucoma

Vitreous haemorrhage with permanent blindness occurred 2½ months after carotid ligation in the neck in one patient (Case 10) and acute hypoxic retinopathy followed "trapping" procedures in two others. One of the latter had definite preoperative signs of ocular hypoxia (Case 18), and visual loss and glaucoma occurred postoperatively. The second (Case 8) had no preoperative signs, but a disturbing postural amaurosis postoperatively.

POSTOPERATIVE DETERIORATION OF VISION Sixteen of 25 patients in this series had single or multiple arterial ligations to "protect vision", reduce proptosis and swelling, and eliminate the bruit caused by the fistula. These procedures included cervical ligation of the internal carotid artery (6 cases), cervical ligation of the external carotid artery (1 case), cervical ligation of the internal and external carotid arteries (4 cases), two-stage cervical and intracranial carotid and ophthalmic artery ligations (3 cases), and simultaneous cervical and intracranial ligation of carotid and ophthalmic arteries (2 cases). Two patients were hemiplegic after operation and two had symptoms of transient cerebral ischaemia. The proptosis and conjunctival swelling was greatly improved or eliminated in almost all cases, but the outlook for vision was far less satisfactory. Ten patients had deterioration of vision immediately or (in a few cases) several months after treatment. In six cases there was no record of the postoperative visual status; The critical tissue alterations causing visual loss were hypoxic. (See previous sections.) Of seven patients with preoperative vision of at least 20/40, two had repeated attacks of amaurosis fugax associated with postural change. Two had postoperative vision of 20/200 with constriction of the visual field in the involved eye and three were barely able to count fingers. Of three patients with preoperative vision of 20/200 or less, two eventually lost all vision on the operated side and one could only count fingers.

Contrasting with these results, nine patients were not treated, either because of the surgical risks involved or because they refused treatment. Follow-up information obtained in four of them recorded no visual deterioration. The duration of follow-up was 4 years, 2 years, and 9 months in three of the patients, and the fourth had been blind since onset of the fistula. Spontaneous cure did not occur in any patients in this series.

Ophthalmic artery pressures (ophthalmodynamometry); their relation to hypoxic ocular complications

Data on ophthalmic (central retinal artery) pressure in members of this series are incomplete, but some of the ophthalmodynamometric studies in selected patients deserve comment. Without exception depressed visual acuity, constricted monocular field of

vision, intermittent or persistent dimness of vision, and acute or subacute forms of hypoxic retinopathy occurred in the eyes with significant reduction in diastolic (ophthalmic artery) pressures. In two patients with monocular constriction of the visual field, the diastolic pressures were only 40 and 30 per cent. of the values recorded in the normal eye. In one patient with acute onset and vision reduced to hand movements, the ipsilateral diastolic pressure was 30 per cent. of the value noted in the contralateral eye. Similar ipsilateral reduction of diastolic pressure was noted in *every* patient whose vision deteriorated after surgery. Arterial and venous pressure were recorded in one patient (Case 20) with marked and chronic hypoxic retinopathy; his arterial (diastolic) pressure was 45 mm. Hg, but the venous pressure was elevated at 30 mm. Hg.

Discussion

Carotid cavernous fistula with its alarming physical signs and perplexing therapeutic problems has stimulated monographs and detailed clinical reviews in numbers rivalled by only a few subjects in the history of surgery. Paradoxically, the preoccupation of more than a century with improved methods to divert, trap, or obliterate the fistula has increased the morbidity and mortality of the disease, without reducing the incidence or severity of visual deterioration. Fatal or disabling cerebral involvement from untreated carotid-cavernous fistulae is rare, but catastrophic complications of carotid occlusive procedures are common (Walker and Allègre, 1956; Stern and others, 1967).

The character and frequency of hypoxic ocular sequelae of carotid-cavernous fistulae are well exemplified in the data from our cases. Complete lists of these eye signs appeared in the classic monographs of de Schweinitz and Holloway (1910) and Sattler (1920), but these writers did not recognize the hypoxic nature of the ocular changes. Most reviews cite cases in which ipsilateral visual loss or even blindness resulted from surgical attempts to obliterate the fistula, even when these were successful. The intracranial circulatory alterations related to carotid occlusive procedures for fistula have been carefully analysed by various workers including Dandy (1935), Sweet and Bennett (1948), and Stern and others (1967), but the concurrent alterations in the orbital and ocular circulations have been neglected.

The therapeutic objectives in the patient with a carotid-cavernous fistula deserve re-examination. The disease itself seldom justifies operation, particularly if the risks of death or cerebral damage are high. Preservation or restoration of visual function therefore warrants top priority in the therapeutic management, and reduction of proptosis and elimination of the bruit should be regarded as secondary objectives. Rational treatment requires consideration of certain unique features of the ocular circulation that account for its selective vulnerability in carotid-cavernous fistula.

Physiology of the ocular circulation

The retinal and choroidal (uveal) vascular systems are perfused by blood from separate branches of the ophthalmic artery. The retinal vessels supply the inner retinal layers and the choroidal vessels supply the high metabolic demands of the outer retinal layers (photoreceptor cells and pigment epithelium). The main volume of blood is contained in the choroidal vessels and, though both systems function under similar hydrostatic conditions, there are certain noteworthy anatomical differences. The rigid sclera encloses the retinal and choroidal vessels, which are thus subjected to the intraocular pressure (extra-vascular pressure) which is approximately 16 mm. Hg. This unique situation results in a high-

pressure circulatory system, the integrity of which depends on maintaining the intra-luminal pressure in all vessels above the intraocular pressure. The rate of blood flow in the eye depends essentially on the arterio-venous pressure gradient, and as the venous pressure is high the gradient is the lowest in the carotid tree. (The venous pressure at the optic disc is equal to the intraocular pressure, whereas in all other cephalic veins it is below 10 mm. Hg and approaching zero.) However the rate of flow is rapid (choroidal greater than retinal) with a particularly sensitive regulatory control in the retinal capillary network.

Any condition that reduces the arterio-venous gradient will embarrass the circulatory system of the eye. This may occur when the arterial pressure is reduced either centrally (fall in blood pressure) or peripherally (carotid-cavernous fistula), or when the venous pressure is raised (*e.g.* by glaucoma, congestive cardiac failure, or carotid-cavernous fistula). The blood flow is related to two factors:

$$\text{Blood flow} \propto \frac{\text{Blood pressure}}{\text{Peripheral resistance}}$$

Thus, when the gradient is reduced, the vascular bed compensates by reducing the peripheral resistance through opening of precapillary shunts and dilatation of the venules. When the capacity of the retinal and choroidal capillary net to adjust (or compensate) for a reduced arterio-venous gradient is expended, the ocular perfusion rate is reduced (flow per unit tissue per unit of time). If the reduction in blood flow reaches a level that fails to meet the local metabolic demands of the retina, the retinal tissue becomes hypoxic and retinal function begins to fail. Visual acuity is impaired and the field of vision constricts. Continuing inadequacy of retinal blood flow causes punctate intraretinal and superficial retinal haemorrhages, with microaneurysmal formation at the capillary level.

Pathophysiology of the orbital and ocular circulations in carotid-cavernous fistula

Carotid-cavernous fistula results in a marked pressure gradient between the intracavernous segment of the carotid artery and the surrounding venous sinus which creates a low resistance shunt. The velocity and size of the shunt will depend on the diameter of the fistula. The haemodynamic alterations as a result of the shunt fall into two main categories:

- (1) The arterial pressure is reduced in the supracavernous carotid artery (ophthalmic artery and intracranial carotid artery) and if the fistula is large, further arterial "steal" may occur. In some cases the direction of flow may be reversed in the ophthalmic artery.
- (2) The principal tributaries of the cavernous sinus are now exposed to an arterial pressure which results in slowing of flow and in some cases reversal.

Thus, the arterio-venous pressure gradient may be drastically narrowed by reduction of the arterial pressure and elevation of the venous pressure. The maximal circulatory disturbance will be in the eye because of the particular physiological circumstances already discussed, and to a lesser extent in the orbit. These will now be discussed with the compensatory mechanisms involved.

OCULAR CIRCULATORY DISTURBANCE The principal haemodynamic and pressure alterations are represented diagrammatically in Fig. 6. The normal relationships between the mean retinal artery pressure, the retinal venous pressure, and the intraocular pressure are indicated in Fig. 6A. The alterations with carotid-cavernous fistula include a reduced

arterial pressure, and an elevated venous pressure resulting in a diminished arterio-venous gradient and perfusion pressure in Fig. 6B. The intraocular pressure may also be slightly elevated. If the intraocular pressure is raised more, the venous pressure will also be raised and further reduction in the arterio-venous pressure gradient will occur (Fig. 6C). This additional insult may force an eye previously on marginal perfusion into severe vascular insufficiency. The eye adapts to a reduced perfusion pressure by lowering the peripheral resistance through microcirculatory changes consisting of capillary shunting, dilatation, and venous dilatation. The reduced perfusion pressure affects all tissues in the eye and, as our data show, the manifestations may be seen from the cornea to the optic disc. Marginal perfusion for long duration causes microaneurysms in the capillary network, and widespread intraretinal and superficial haemorrhages. These findings are exemplified by Case 20 where fluorescein angiograms indicate the slow arterial flow, the capillary dilatation and microaneurysms, and the venous dilatation and permeability. The iris vessels were also dilated and excessively permeable.

FIG. 6 Schema of changes in ocular arterio-venous pressure gradients
(A) Normal
(B) Carotid cavernous fistula
(C) Carotid cavernous fistula with raised intraocular pressure

ORBITAL CIRCULATORY DISTURBANCE The same conditions govern the orbital tissues but the changes are less severe because of two physiological differences.

- (1) In the absence of the intraocular pressure factor the venous pressure is lower, and thus the arterio-venous gradient is wider.
- (2) The collaterals, both arterial from the external carotid and venous from the facial channels, provide a wider vascular network. Pressure in the superior and inferior ophthalmic veins is elevated, and blood flow is slowed or even reversed. The venous channels in the orbit become dilated and the tissues are oedematous and hypoxic, these factors contribute to the proptosis and also mechanically restrict ocular mobility and may elevate the intraocular pressure. Long-standing pressure elevation produces secondary thickening or arterIALIZATION of these vessels. The raised pressure in the episcleral vessels, also elevates the intraocular pressure by disturbing the aqueous outflow.

Several compensatory orbital vascular changes gradually act to widen the arterio-venous gradient:

- (1) Collateral arterial circulation from branches of the external carotid artery may increase the orbital and ocular arterial pressure.
- (2) Dilatation of major venous channels in the orbit and other tributaries of the cavernous sinus reduces the outflow resistance, thus lowering the venous pressure. The beneficial effects of this will be transmitted to the smaller orbital veins, including the vortex and central retinal veins.

If the total effects of these events produces sufficient increase in the ocular perfusion pressure, vision may improve to normal or near normal levels.

VISUAL FAILURE AFTER SURGERY The arterio-venous pressure gradient is the critical factor for ocular perfusion. Any surgical procedure that lowers the arterial pressure without any concomitant reduction in the venous or intraocular pressure will further embarrass the ocular circulation. A frequent surgical approach to carotid-cavernous fistula consists of single or multiple ligations of the carotid or its branches, the ocular effects of which depend on the vascular status of the eye. "Trapping" procedures with multiple ligations can be particularly lethal to the visual system (Walker and Allegre, 1956; Jaeger, 1959). Acute vascular decompensation presents a characteristic appearance with "exudates", attenuated arteries, and haemorrhages (Swan and Raaf, 1951). These changes are more likely if the intraocular or the orbital pressure is elevated during or after surgery. Less severe reduction of the arterio-venous pressure gradient may expedite the chronic changes already in progress and previously described. The latter group may have more severe manifestations days or months after surgery, if the venous pressure is suddenly raised by re-opening of the fistula, or the intraocular pressure becomes elevated.

Carotid ligation experimentally or in the treatment of aneurysm usually has no deleterious effects on vision (Elschnig, 1893; Walsh and King, 1942). The altered haemodynamics in carotid-cavernous fistula, and the fact that current methods of surgical treatment further reduce an often marginal perfusion pressure are the sole factors responsible for the postoperative visual demise in this condition. Judgements of the effects on the eye when the fistula is treated by muscle embolization (Brooks, 1931; Jaeger, 1949; Hamby, 1966), by gelfoam embolization (Ishimori, Hattori, Shibata, Shizawa, and Fujinaga, 1967), by occlusion with radio opaque measured beads (Kosary, Lerner, Mozes, and Lazar, 1968), or by direct approach on the cavernous sinus (Parkinson, 1967; Reichert, 1967) will be awaited with interest.

Conclusion

Strong evidence has been produced to support the hypoxic hypothesis as the major aetiological factor for the ocular signs of carotid-cavernous fistula. Consideration of ocular haemodynamics and their relation to ocular pressure enables a more rational interpretation of the ocular findings. The benign natural history of the disease contrasts with the severe ocular and cerebral hazards of surgery. The failure of angiography to detect preoperatively the potential patient with a poor surgical prognosis is disappointing (Stern and others, 1967). Visual preservation as the major objective is stressed, and we suggest that a thorough ocular evaluation may contribute information about the size of the shunt and the ability of collateral vessels to compensate. The gradual onset and paucity of ocular signs in cases with external carotid shunts should also be considered.

We therefore recommend a complete ocular examination, including corrected visual acuity, Goldmann perimetry, slit-lamp examination including gonioscopy, tonometry, tonography, and assessment of the retinal vascular system with ophthalmoscopy, ophthalmodynamometry, and fluorescein angiography. Additional tests of retinal function by photo-stress methods or electroretinography (Krill, Diamond, and Iser, 1962) may provide further quantitative information. These data are essential guidelines in planning therapy.

Preservation of visual function depends on the maintenance of an adequate ocular perfusion before, during, and after surgery. If the ocular arterial pressure is to be reduced (e.g. carotid ligation), the intraocular pressure and venous pressure must simultaneously be reduced by an equal amount in order to maintain the arterio-venous pressure gradient.

Intraocular pressure may be reduced by the administration of carbonic anhydrase inhibitors or osmotic agents, and the venous pressure may be lowered by occlusion of the major ophthalmic veins. The former method is simple and therapeutically effective. The latter method, recommended as a single procedure by de Schweinitz and Holloway (1908), deserves serious consideration either as a primary procedure or else in combination with arterial surgery. The importance of maintaining an adequate systemic blood pressure during surgery is a further factor. Utilizing these adjuncts, the surgeon has greater leeway, and if the fistula is not obliterated, visual catastrophe may be avoided. Practical application of these principles in a prospective study should yield valuable information and improved visual results.

Summary

A detailed review of the visual status of 25 patients with carotid-cavernous fistulae is recorded. The major physiological disturbance is hypoxia, and evidence for this includes clinical criteria from our patients, in conjunction with the similar manifestations reported in other "ischaemic ocular syndromes". The fistula produces haemodynamic changes resulting in a lowered arterial pressure and a raised venous pressure, particularly in the eye but also in the orbit. The resultant reduction in perfusion pressure determines the ocular signs and initiates compensatory mechanisms. The natural history of the condition is relatively benign when contrasted with the ocular and cerebral hazards frequently seen after carotid occlusive surgery. A re-examination of the criteria for surgery is proposed, and the importance of visual preservation as the major aim of therapy is stressed. All patients with carotid-cavernous fistulae require complete ophthalmic examination to detect the varied signs of ocular hypoxia and to estimate the retinal vascular pressures and perfusion. Clinical and therapeutic application of this information may improve the visual prognosis.

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