

Ocular Key Symptoms of Extracranial Cerebrovascular Disease

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Summary. Forty-six patients with stenosis or occlusion of the internal carotid artery were evaluated by direct Doppler sonography and ophthalmologic examination. A retrospective analysis showed the following secondary ocular manifestations of vascular disease: ischemic ophthalmopathy (9), amaurosis fugax (8), ischemic optic neuropathy (6), and retinal embolism ((5). Two patients had two ocular manifestations; three showed homonymous visual field defects. Results of the ophthalmologic examination were normal in seven patients. Eye changes not obviously related to extracranial vascular disease were present in ten patients. Ischemic ophthalmopathy was invariably due to an occlusive disease of the internal carotid artery.

Key words: Carotid stenosis – Ocular symptoms – Ischemic ophthalmopathy – Ischemic optic neuropathy – Retinal embolism

Zusammenfassung. Bei 46 Patienten mit einer durch direkte Dopplersonographie gesicherten Stenose oder einem Verschuß der A. carotis interna erfolgte eine ophthalmologische Untersuchung. Neun Patienten wiesen dabei eine ischämische Ophthalmopathie auf. Acht litten unter Amaurosis fugax, sechs unter einer ischämischen Opticusneuropathie, fünf unter retinaler Embolie und drei unter Gesichtsfelddefekten. Zwei der obengenannten Patienten hatten zwei verschiedene oculäre Manifestationen. Sieben Patienten waren ophthalmologisch unauffällig. Zehn Patienten wiesen Erkrankungen der Augen auf, die nicht offensichtlich in Beziehung zu dem Verschußprozeß der extrakraniellen Arterien standen. Eine ischämische Ophthalmopathie, gemäß augenärztlicher Primärdiagnose, war immer die Folge einer hochgradigen Stenose oder eines Verschlusses der A. carotis interna.

Schlüsselwörter: Carotisstenose – Augensymptome – Ischämische Ophthalmopathie – Opticusneuropathie – Retinale Embolien

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Introduction

Stenoses or occlusions of extracranial arteries frequently cause transient ischemic attacks (TIA) and strokes. Early diagnosis of extracranial arterial flow disturbances is essential, since stenoses of the internal carotid artery (ICA) are operable with thrombendarterectomy, occlusions of the ICA can be bypassed with an anastomosis between the superficial temporal artery and cortical branches of the medial cerebral artery (Yasargil 1969), and strokes can be prevented with anticoagulants and antiplatelet aggregation therapy. Noninvasive direct Doppler sonography is ideal for detecting a narrowing of hemodynamic relevance and for identifying the localization and extent of flow disturbances in extracranial vessels with a high (95%) validity (von Reutern et al. 1976; Diener and Dichgans 1979, 1980). A number of ophthalmologic symptoms occurring without neurologic manifestations may suggest an extracranial vascular disease and stimulate Doppler sonography prior to the occurrence of neurologic damage. These symptoms are reported in this paper.

Amaurosis fugax, a sudden attack of blindness of one eye with complete recovery of vision within some minutes or hours, is a symptom associated with retinal embolism, which is often combined with ulcerative plaques or occlusions of the internal carotid artery (Ehrenfeld et al. 1966; Hooshmand et al. 1974). Originally a local angiospasm was thought to be responsible for amaurosis fugax (Moore 1922). The detection of retinal cholesterol (Hollenhorst 1961) and platelet thrombi (Fisher 1959) after these attacks led to the understanding of the causal relationship between these thrombi or microemboli and arteromatous ulcerative stenoses of the extracranial carotid arteries. Subsequently some ocular diseases were described that were combined with extracranial arterial stenosis or occlusion. Kearns and Hollenhorst (1963) reported that venous stasis retinopathy, which consists of microaneurysms, small hemorrhages, and neovascularizations, is caused by retinal ischemia and hypoxia. Approximately 5% of patients with unilateral stenosis or occlusion of the internal carotid artery showed venous stasis retinopathy (Kearns and Hollenhorst 1963). In 1965 Knox described an ocular disease in five patients with occlusive brachiocephalic vascular disease that consisted of the following symptoms: amaurosis fugax, ocular pain, diffuse episcleral injection, corneal edema, iris atrophy, iris neovascularization, mid-peripheral retinal hemorrhages, and nervehead neovascularization. He called this disease ischemic ocular inflammation. Histopathological examinations of the eyes of a patient with Takayasu's disease revealed proliferative retinopathy, rubeosis iridis, anterior and posterior synechias, focal necrosis of the iris with pigment dispersion, and mature complicated cataract (Font and Naumann 1969). The term 'ischemic ophthalmopathy,' as coined by Ruprecht and Naumann (1980), subsumes the complete syndrome consisting of a venous stasis retinopathy, pseudouveitis anterior, unilateral cataract, rubeosis iridis, secondary glaucoma, and severe ocular pain.

In this study the results of ophthalmologic examinations in patients with severe stenosis or occlusion of the internal carotid artery, as detected by Doppler sonography, are reported. Special emphasis is given to the question of collateral

vascular supply of the orbit and the results of operative desobliteration, whenever possible.

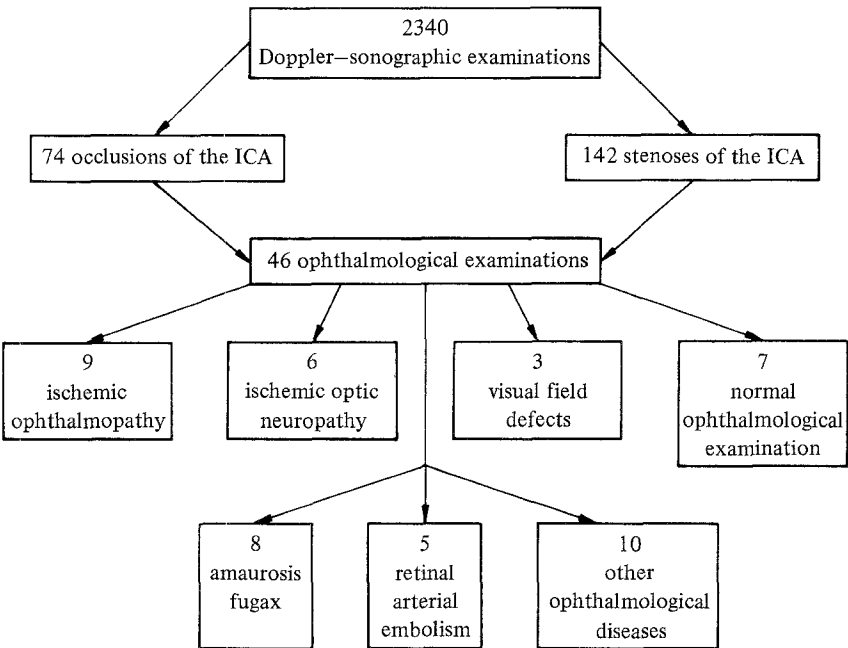
Methods of Examination

We investigated only patients with severe (more than 50%) stenoses or occlusions of the internal carotid or common carotid arteries. The diagnosis was initially based on Doppler sonography. Some of the patients were investigated with cerebral angiography, which was performed only if a thrombendarterectomy was envisaged. Doppler sonography was performed with a directional Doppler system; the emitting frequency was 4 MHz. In a routine examination the supratrochlear, common carotid, internal and external carotid, vertebral, and subclavian artery were investigated. Flow signals were monitored acoustically and recorded on a strip chart. By means of these recordings a comparison of the diastolic and systolic flow velocities of corresponding arteries on both sides of the neck was possible. Methods for identifying the arteries and diagnosing a stenosis or occlusion are described elsewhere (Büdingen et al. 1976; von Reutern et al. 1976; Diener and Dichgans 1979). All patients were given a thorough ophthalmologic examination, including perimetry, at the Department of Ophthalmology of the University of Tübingen. Pathologic findings at the fundus and the anterior segments of the eyes were photographed.

Observations in Patients

Between February 1978 and 1980, 2340 patients were examined by Doppler sonography. The method detected occlusions of the internal carotid artery in 74 patients. Thirty-four patients had an additional occlusion or a stenosis on the contralateral side. A stenosis of the internal carotid artery of more than 50% (a stenosis of less than 50% cannot be detected by direct Doppler

Table 1



sonography) was found in 142 patients; among them, 51 exhibited a stenosis bilaterally. Forty-six of the 216 patients (21%) with stenosis or occlusion detected by Doppler sonography were investigated in the Department of Ophthalmology. This group probably overrepresents patients with ocular manifestation of ischemia. Thus, 18 patients were referred first to Doppler sonography by the ophthalmologist, among them eight of the nine patients with ischemic ophthalmopathy. The patients (37 males, 9 females) were 30–83 years of age, with a mean of 62.6 years. In 29 (63%) of the 46 ocular findings were pathologic and presumably caused by the extracranial flow obstruction (Table 1). Nine patients suffered from ischemic ophthalmopathy, and eight from amaurosis fugax. (One patient had an additional ischemic ophthalmopathy, and another had an occlusion of a branch of a retinal artery, which brings the number of patients in Table 1 to 48.) Six patients showed an ischemic optic neuropathy, five retinal arterial occlusions, and three a visual field defect of central origin. In seven patients ophthalmologic findings were normal. Ten patients demonstrated pathologic findings that could not be causally related to the extracranial vascular disease.

Results

1. Ischemic Ophthalmopathy

Seven of nine patients with ischemic ophthalmopathy had venous stasis retinopathy (Fig. 1), six rubeosis iridis, six secondary glaucoma, and three a unilateral cataract. In one patient, the retinal fundus could not be seen because of a mature

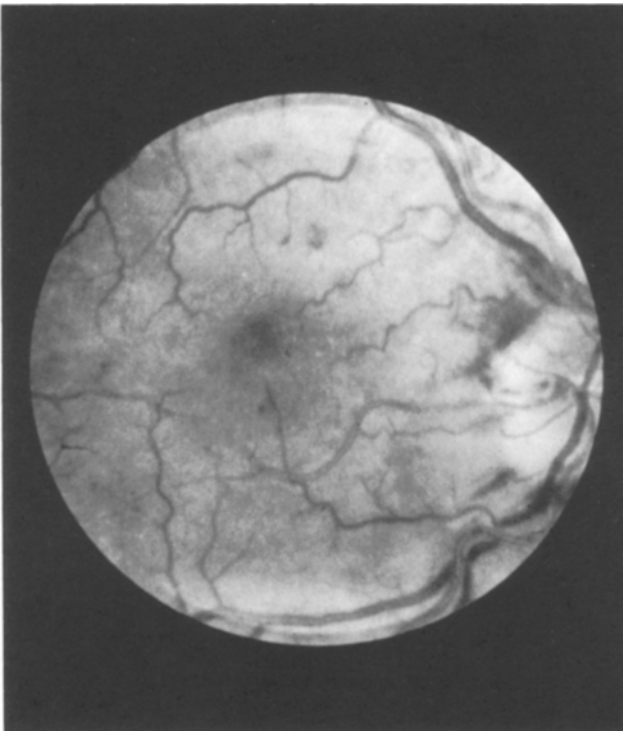


Fig. 1. Venous stasis retinopathy in a 57-year-old man with a severe stenosis of the right internal carotid artery. Fundoscopy shows midperipheral microaneurysms and small hemorrhages

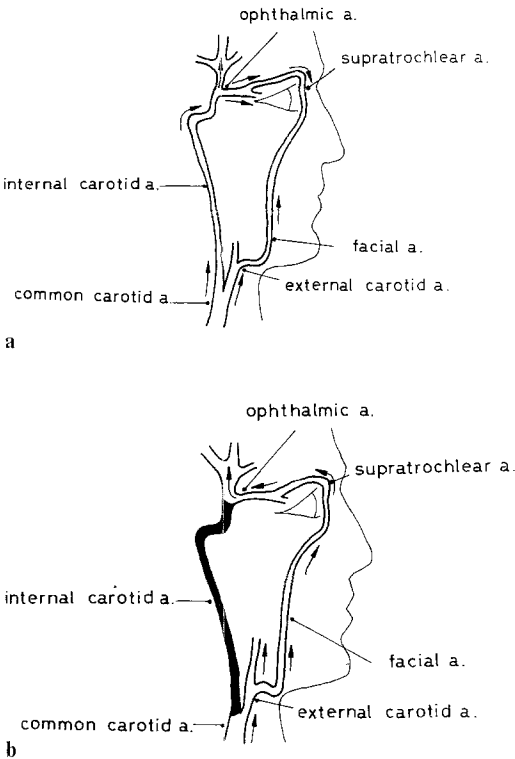


Fig. 2. a shows the physiologic orthograde flow in the supratrochlear artery, a branch of the ophthalmic artery. In the case of an occlusion of the internal carotid artery (b) the corresponding cerebral hemisphere may be supplied by the external carotid artery via retrograde flow in the supratrochlear and ophthalmic artery

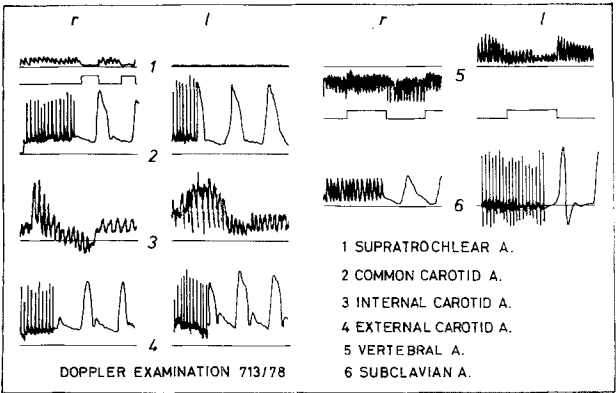


Fig. 3. Doppler sonographic recordings of a 59-year-old man with TIAs from the right hemisphere and amaurosis fugax. The supratrochlear artery shows reversed flow on the right and no flow on the left. The internal carotid artery shows a severe stenosis with increased flow velocity and turbulences on both sides. An occlusion of the right subclavian artery with subclavian steal was also found. Some recordings have been taken at 2.5 and 25 mm/s paper speed



Fig. 4. Ischemic optic neuropathy of the left eye in a 59-year-old man with a bilateral stenosis of the internal carotid artery, a stenosis of the left external carotid artery, and an occlusion of the left subclavian artery. Note the swelling and pallor of the papilla and the discontinuities within the proximal retinal arteries

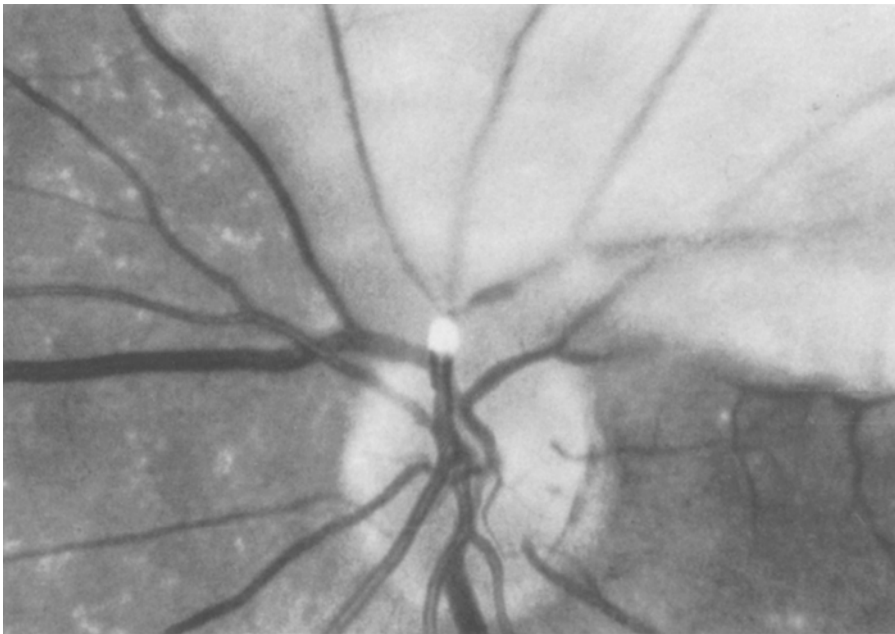


Fig. 5. Occlusion of the superior branch of the retinal artery by a cholesterol embolus in a 69-year-old man with an occlusion of the corresponding internal carotid artery

cataract. In two other patients a cataract developed in the follow-up time. Eight patients with ischemic ophthalmopathy had a severe stenosis or occlusion of the ipsilateral internal carotid artery. In patients with a bilateral occlusion or stenosis, the ophthalmic disease was also bilateral. With one exception, all patients showed retrograde flow in the supratrochlear artery, as tested by Doppler sonography, on the affected side. This artery connects to the ophthalmic artery, which then retrogradely supplies the corresponding cerebral hemisphere via the external carotid artery (Fig. 2a and b). Doppler sonographic findings were confirmed by angiography in six patients. The others were not subjected to angiography. One patient exhibited orthograde flow in both supratrochlear arteries. No extracranial stenosis or occlusion was found by Doppler sonography. X-rays of the skull showing severe calcifications of the intracranial part of the internal carotid arteries suggested a stenosis. Four patients exhibited a slight hemiparesis and two showed mental dysfunction. Thrombendarterectomy was performed in four patients with a severe stenosis. After operation, rubeosis iridis and ocular pain improved dramatically in one patient; in three patients the disease did not improve or progress within the short follow-up. In four patients the secondary angle-closure glaucoma was successfully treated by cyclocryotherapy. In one patient the cataract was extracted.

2. *Amaurosis Fugax*

Among the six patients with amaurosis fugax, three had a severe stenosis and three an occlusion of the internal carotid artery always on the ipsilateral side. Two patients also had cataracts which were accentuated on the side of the vascular lesion. In three patients the supratrochlear artery showed a retrograde flow, in one patient no flow was demonstrable, and in two patients flow was orthograde. One patient also suffered from cerebral TIAs (Fig. 3). Two patients had a hemiparesis. Endarterectomy was performed in two patients after angiography. Both experienced no further attack of amaurosis fugax. TIAs were also remedied. The clinical course of the remaining four patients was unknown.

3. *Ischemic Optic Neuropathy*

Six patients showed an ischemic optic neuropathy (Fig. 4). Doppler sonography detected an occlusion of the internal carotid artery in two cases and one severe, two mild, and one slight stenosis at the bifurcation. Endarterectomy was performed in three patients suffering from TIA. Neurologic examinations of the three patients without TIAs were normal. Since the erythrocyte sedimentation rate was invariably normal, no biopsy of the superficial temporal artery was performed to exclude temporal arteriitis. Within the follow-up period none of the patients developed symptoms in the contralateral eye.

4. *Occlusions of Retinal Arteries*

Three patients had an occlusion of the central retinal artery. In these cases the corresponding internal carotid artery was invariably occluded. Two additional

patients presented an occlusion of a branch of the central retinal artery (Fig. 5). One of them was later endarterectomized (because of a stenosis) after appearance of amaurosis fugax. In the other the internal carotid artery was occluded. Four of the five patients within this group had no neurologic deficits.

5. Visual Field Defects

Two patients showed a homonymous hemianopia to the right and the left side. Another patient had a homonymous field defect in the lower left quadrant. Doppler sonography showed an occlusion of the internal carotid artery in one, and a severe stenosis of the ICA in two patients. Endarterectomy was performed in one patient with a slight hemiparesis and mental disturbance. The remaining two patients had no other neurologic deficit.

6. Unrelated Ophthalmological Symptoms

Of the remaining ten patients (eight with stenosis and two with occlusion) five had a bilateral cataract. Two patients showed a hypertensive retinopathy. The remaining three showed a hemorrhage into the vitreous body, an atrophy of the choroid, and an uveitis of unknown etiology, respectively. Seven of the ten patients suffered from TIAs or permanent neurologic deficits.

7. Normal Ophthalmologic Examination

Ophthalmologic examination was normal in seven patients. All of them had a severe stenosis of the internal carotid artery, often combined with a contralateral stenosis. In contrast to the patients with ischemic ophthalmopathy, retrograde flow in the supratrochlear artery occurred only twice. Five of the seven patients had neurologic deficits. In four patients an endarterectomy was performed.

Discussion

The ophthalmologic examination of 46 patients with an occlusion of the internal carotid artery or a stenosis of more than 50% revealed pathologic changes in roughly 60% which could be causally related to the extracranial vascular disease. The frequency of ophthalmopathy among patients with extracranial vascular diseases, based on our data, is at least 13%. Since a thorough ophthalmologic examination is often impossible in these patients, we estimate that it is even higher: at least 25% of patients with occlusive disease suffer from ophthalmologic consequences.

The most frequent manifestation is ischemic ophthalmopathy. The dominant symptom of this disease is the venous stasis retinopathy (Kearns and Hollenhorst 1963) with microaneurysms, dark and dilated retinal veins, small retinal hemorrhages, and patches of neovascularization. Differential diagnosis against diabetic retinopathy considers the fact that venous stasis retinopathy is mostly unilateral

and that the location of the retinal changes is midperipheral. Differentiation from 'incomplete occlusion of the central retinal vein' is made by proving the occurrence of an extracranial flow obstacle (Kearns 1979). The frequency of venous stasis retinopathy in patients with carotid artery occlusive disease was roughly 5% in the study of Kearns and Hollenhorst (1963). Knox (1965) recognized additional symptoms of ischemic ophthalmopathy. He observed amaurosis fugax, ocular pain, diffuse episcleral vascular injection, corneal edema, rubeosis iridis, and iris atrophy in five patients with stenoses or occlusion of the internal carotid artery. Additionally some patients developed a cataract or glaucoma. The mature cataract in a patient with thrombotic occlusion of the innominate and both common carotid arteries was thought to be a consequence of the impaired ciliary blood flow (Font and Naumann 1969). Michelson et al. (1971) investigated the histopathology of the eyes of a man who died from bilateral occlusion of the internal carotid arteries. They found a rubeosis of the filtration angle, iris and ciliary body atrophy, mature cataract, and microaneurysms in the periphery of the retina. Our findings further support the assumption of ischemic ophthalmopathy as a syndrome pathognomonic for extracranial occlusive vascular disease.

Huckman and Haas (1972) observed rubeosis iridis and neovascular glaucoma in two patients with occlusion of the internal carotid artery. Carotid angiography showed retrograde collateral circulation through the ophthalmic artery on the ipsilateral side. In our study eight of nine patients with ischemic ophthalmopathy had retrograde flow. It may be speculated that the retrograde flow in the supratrochlear artery analogous to a Bernoucci vacuum pump (Wasserstrahlpumpe) causes a diminution of the ocular blood flow. This suggestion is supported by the fact that in patients without ophthalmopathology and equally severe extracranial flow disturbances the ophthalmic artery was orthograde in five of seven patients.

Ischemic ophthalmopathy with a severe stenosis of the internal carotid artery, in our opinion, requires endarterectomy, even if neurologic deficits or TIAs are absent. In our study the follow-up time after operation was too short to make a definite statement. However, we were able to show that the symptoms of ischemic ophthalmopathy did not progress after the operation in three patients and disappeared in one patient with painful rubeosis iridis. Similarly, Neupert et al. (1976) observed one patient in whom venous stasis retinopathy and neovascularization of the optic disc disappeared rapidly after the operation for severe stenosis of the internal carotid artery. They thought that the neovascularizations might have been caused by a vasoproliferative substance produced in the eye as a response to hypoxia.

In our study 17% of the patients had amaurosis fugax. Hollenhorst (1960) demonstrated that 88% of the patients with flow disturbances of the carotid artery showed amaurosis fugax. Angiography in 34 patients with amaurosis fugax of one eye revealed ulcerative plaques or stenoses in 32 patients (Hooshmand et al. 1974). Two patients had a heart disease with no carotid lesion. Amaurosis fugax, as well as TIA, should be interpreted as an urgent warning signal for stroke and requires immediate Doppler sonography.

Sometimes amaurosis fugax can precede occlusions of retinal arteries. In our study 13% of the patients had an occlusion of the central or peripheral retinal

artery. In an angiographic study, Meythaler et al. (1978) found in eight of fourteen patients with occlusion of the central retinal artery, homolateral stenoses of the internal carotid artery. One patient showed a bilateral occlusion of this artery. Pfaffenbach and Hollenhorst (1973) observed in a study of 208 patients with embolic cholesterol crystals in the ocular fundus, a reduction in the survival rate of roughly 50%. Liegl (1975) described a patient with bilateral occlusion of the internal carotid arteries after radiation of the neck. Here an ischemic ophthalmopathy as well as an occlusion of the central retinal artery was found.

Of our patients, 13% had an ischemic optic neuropathy. Although the most common cause of this disease is arteriitis temporalis, an extracranial stenosis or occlusion should be considered if the erythrocyte sedimentation rate is normal (Cullen 1967; François 1975; Hayreh 1978).

Ocular manifestations of an occlusive disease of the extracranial arteries may be the only key symptom. Ophthalmologists have become increasingly aware of this possibility and effectively help such patients by referring them to the neurologist for Doppler sonography. Careful exploration then frequently reveals TIAs or mental disability that neurologically justifies operation.

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