OCULAR MANIFESTATIONS OF INSUFFICIENCY OR THROMBOSIS OF THE INTERNAL CAROTID ARTERY

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THE SYNDROME of thrombosis of the internal carotid artery only recently has been accorded the attention it deserves as a cause of disability and death. The realization that most cases of occlusive-thrombotic disease of the carotid and the vertebral-basilar arterial systems have a premonitory period of several weeks to several years, and that permanent occlusion with cerebral infarction may be prevented by anticoagulant therapy, has led to a renewed interest in this condition.

The literature pertaining to the carotid arteries is very ancient. Chevers (1) in 1845 published an extensive review of the literature prior to that time and described fourteen cases of unilateral carotid occlusion. He found reports describing five cases in which both carotid arteries had been occluded without ill effects. However, he decried the opinion repeatedly voiced in those days that the carotid arteries could be safely tied in every patient. He quoted results in a large series of experimental procedures carried out on the carotid arteries of animals in the past, calling attention to the Arabian literature in which the carotid arteries were considered as "the apoplectic veins." He noted that there is evidence in the account of Rufus of Ephesus suggesting that the result of compressing the carotid arteries was known to the ancients prior to the time of Galen (130–200 A.D.). Chevers quotes a report by Davy (2) of a patient who died from a large aortic arch aneurysm and occlusion of the left carotid, subclavian, and vertebral arteries, and of another patient who died from occlusion of a left carotid artery. Other early reports were those of Kussmaul (3), Penzoldt (4), and Elschnig (5–7).

Considerable impetus was given to the study of thrombosis of the carotid vessels when arteriography proved to be a practical method of

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diagnosing this condition in human beings. Sjöqvist (8) apparently reported the first arteriographically demonstrable occlusion of the internal carotid artery in a patient who had an occluded central artery and optic atrophy of the left eye. Egas Moniz (9) reported thrombosis in the internal carotid artery in 4 of 537 patients on whom he had performed arteriography. Johnson and Walker (10) described 6 cases of their own and collected 84 cases reported in the European literature and 17 in the American literature up to 1951. The ages of these 107 patients ranged from 21 to 60 years. In 35 percent of the patients the onset was rapid with loss of consciousness, sudden onset of hemiplegia, and with or without aphasia. In 25 percent the onset was slow with headaches, mental regression, and impairment of speech with or without paresthesia and paresis. The remaining 40 percent had transient attacks of headache, hemiparesis, and aphasia. Of the 107 patients 65 had no visual signs at all; 97 patients had thrombosis of the internal carotid artery; 2 had thrombosis of both internal carotid arteries; 2 had thrombosis of both common carotid arteries, and 6 had thrombosis of the common, external, and internal carotid arteries on one side.

Gurdjian and Webster (11) reported 4 cases. Fisher (12) reviewed the problem completely in 1951, reporting 8 cases of his own with verification at necropsy in 4 of them. In a later paper (13), he reported 45 cases found at necropsy during a 2-year period. Berry and Alpers (14) reviewed 21 necropsy specimens.

The important contributions of Millikan and Siekert (15) and of Millikan, Siekert, and Shick (16) emphasized the necessity of recognizing the earliest signs of impending thrombosis before actual infarction had taken place in the brain. They applied to these signs the appropriate term, "the syndrome of intermittent insufficiency of the carotid arterial system." They showed that transient episodes of neurologic deficit may occur suddenly and remain for 2 to 15 minutes; the patient then slowly returns to normal without demonstrable physical signs of the episode. Such episodes are nearly always unilateral, and the pattern of the attack is usually similar during each repetition. Transient paresis of one arm or one leg, or, more usually, of both the arm and the leg, may occur. Hemianesthesia occurs more commonly in the hand or forearm of the affected side, if at all. Sometimes both hemiparesis and hemianesthesia develop, with paresis or numbness of one side of the face or of the lip on one side. If the lesion is in the left internal carotid artery, there may be transient attacks of aphasia too. The visual pathways are often affected, and there may be transient brief diminution or loss of vision (amaurosis fugax) in the

eye on the side of the affected artery, or there may be a transient homonymous hemianopsia to the opposite side. These episodes may recur as often as eight to ten times daily, although an interval of a month or two between attacks is not unusual. Such attacks may go on for weeks or years, but at some time probably most of them eventually terminate in thrombosis of the carotid artery and infarction of the brain. Unfortunately, not all impending thromboses give advance warning, and a sudden onset of "stroke" may be the first indication that atherosclerotic or embolic changes have occurred.

OCULAR MANIFESTATIONS

This report concerns 124 patients, of whom 38 had thrombosis of one or both internal carotid arteries, 80 had symptoms or signs of intermittent insufficiency of one or both internal carotid arteries, and 6 had symptoms of amaurosis fugax only. Although later I will review several excellent reports of fairly large series of cases of thrombosis of the carotid artery, I cannot find any publications in the literature that call attention primarily to the ocular signs and symptoms of intermittent insufficiency of these vessels and to the effect of anticoagulants on the course of amaurosis fugax. As will be seen, the incidence of ocular abnormality is high among patients with both conditions if all the pertinent observable phenomena are included.

I have personally conducted the neuro-ophthalmologic examination in more than 100 of the 124 patients. I am indebted to two of my colleagues who saw many of these patients with me and extended to me the benefit of their experience and advice, and who also examined the patients whom I did not see personally. I am indebted to members of the Section of Neurology who called these problems to my attention, conducted the diagnostic examinations, and directed the therapy.

In the group of 124 patients, only 1 case of intermittent insufficiency and 13 cases of thrombosis of the carotid arteries were proved by angiography. However, the symptoms and clinical signs exhibited by most of the other patients were so characteristic that exposing the patients to the hazards of angiography did not seem justified. The excellent therapeutic response obtained when anticoagulant therapy was given bore out the accuracy of the diagnosis. It was not possible, understandably, to be sure as to the exact extent and site of the occlusive process in the carotid vessels. Reasonable assurance that the diagnosis was correct was obtained by comparing signs and symptoms of these patients with those encountered among patients in whom

insufficiency or thrombosis of the carotid artery had been verified by necropsy or angiography, or both.

Table 1 shows that ocular signs and symptoms are seen more frequently in patients having intermittent insufficiencies of the carotid artery than in patients having thrombosis of the carotid artery. The criteria used for dividing the group were more or less arbitrary and

TABLE 1. OCULAR ABNORMALITIES IN 124 CASES OF THROMBOSIS OR INSUFFICIENCY OF THE CAROTID ARTERIES

	INTERMITTENT INSUFFICIENCY		THROMBOSIS	
Ocular abnormalities	*Number of cases*	*Percent*	*Number of cases*	*Percent*
With ocular signs and symptoms	58	67	22	58
Without ocular signs and symptoms	28	33	16	42
TOTAL	86		38	

so there may be some overlapping in so far as clinical data are concerned. The 86 patients who were classified as having intermittent insufficiency of the carotid artery were those who complained of transient episodes of visual loss, hemiparesis, hemianesthesia, or aphasia. The 38 patients classified as having thrombosis of the carotid artery were those who had experienced sudden onset of severe hemianesthesia, hemiplegia, homonymous hemianopsia, or aphasia from which they did not recover or else recovered slowly over a period of months.

The frequency with which left and right sides were affected was about equal as is seen in Table 2. In a small group of patients both sides were thought to be affected. The age distribution was essentially similar in the two groups. The ages ranged from 41 through 78 years, with the greatest incidence of insufficiencies occurring among patients 50 to 69 years of age. Thrombosis of the carotid artery seemed to

TABLE 2. LATERALITY OF THROMBOSIS OR INSUFFICIENCY OF THE CAROTID ARTERIES

	INSUFFICIENCY			THROMBOSIS		
Proof	*Right*	*Left*	*Both*	*Right*	*Left*	*Both*
	41	37	8	19	17	2
By angiography	0	1	0	7	5	1
By necropsy	0	0	0	1	3	0

occur with about equal frequency in each decade among patients 41 to 69 years of age. Approximately half of each of the two groups of patients had hypertensive cardiovascular disease, all of Keith-Wagener groups I and II, and none of group III or IV.

A summary of the incidence of the ocular signs and symptoms which appeared in these two groups is given in Table 3.

TABLE 3. OCULAR SIGNS AND SYMPTOMS OF INSUFFICIENCY OR THROMBOSIS OF THE CAROTID ARTERY IN 124 CASES

Ocular signs and symptoms	*Insufficiency* (86 cases)	*Thrombosis* (38 cases)
Amaurosis fugax	48	2
Unilateral retinopathy	11	4
Unequal retinal hypertensive vascular changes in the two eyes	8	2
Homonymous hemianopsia		
Transient	2	1
Permanent	2	6
Homonymous hemianopic hallucinations	3	0
Occlusion of retinal artery	8	6
With contralateral homonymous hemianopsia	4	2
Pupil smaller on affected side	1	1

The pressures in the retinal arteries were measured with the ophthalmodynamometer of Bailliart in all patients except some who had sustained occlusion of a branch artery. Pressures were not determined in these latter patients because of fear (perhaps unfounded) that the exertion of pressure on an eye which had already sustained partial occlusion might produce a greater loss of vision. The results of these measurements are given in Table 4.

TABLE 4. RETINAL ARTERY PRESSURES AMONG PATIENTS WITH INSUFFICIENCY OR THROMBOSIS OF THE CAROTID ARTERY

Location of pressure	*Insufficiency* (86 cases)	*Thrombosis* (38 cases)
Pressure lower on side of affected carotid	58	25
Pressure higher on side of affected carotid	5	1
Pressure equal on the two sides	20	7
Not measured	3	5

AMAUROSIS FUGAX

The incidence of transient unilateral loss of vision was found to be much higher among patients having intermittent insufficiency than among those having thrombosis. The symptoms of six patients consisted solely of transient episodes of visual loss. All six had noted these attacks for several months; the frequency varied from ten or twelve attacks daily in several patients to one or two attacks monthly in others. Five of the six were treated with anticoagulants (Dicumarol), and all five had immediate relief for the duration of treatment. Termination of treatment resulted in recurrence of symptoms in two patients; so treatment was resumed. Three had right-sided and three had left-sided involvement. Three patients had significantly lower pressure in the retinal artery on the affected side and the other three had equal pressures on the two sides. The case of one of the three patients having equal pressures on the two sides is interesting and is presented herewith:

CASE 1. In December, 1956, a 54-year-old man was seen who complained of attacks of transient visual loss in the left eye three to six times daily for the previous three weeks. Each attack consisted of sudden complete loss of vision of the left eye unaccompanied by other symptoms; the vision usually returned to normal within five minutes. Physical exertion often precipitated an attack. Changes of posture were of no importance. No abnormality was found on general physical examination. The blood pressure was 130 mm. of mercury systolic and 70 mm. diastolic, and there were no signs of postural hypotension. Ocular examination gave completely negative results. The diastolic pressure in the retinal artery measured 25 mm. of mercury in each eye. One day he was examined 30 minutes after an attack; the eyes appeared to be normal, but the retinal artery pressures measured 40 mm. of mercury in the right eye and 32 mm. in the left eye.

The patient was asked to remain for observation and about two hours later an attack developed which was observed from its onset. Some ten seconds after the eye became blind, the pupil of the eye was completely nonreactive to direct light, but it reacted consensually when light was thrown into the right eye. Ophthalmoscopically, the retinal vessels of the blind left eye were completely normal in all respects. Pressures in the retinal artery of the right eye were 80 mm. of mercury systolic and 22 mm. diastolic, but when the left eye was just barely touched with the ophthalmodynamometer the entire arterial vascular tree was observed to collapse completely. This indicated a systolic and diastolic pressure of approximately zero, since the pressure was too low to register on the instrument. The circulatory system of the eye instantaneously refilled when the pressure was released. Five

minutes after onset the vision had returned completely and pressures in the retinal artery had returned to normal. After Dicumarol therapy was begun, the attacks immediately ceased. Pressures in the retinal artery after ten days of anticoagulant therapy were recorded as: right eye 70/38; left eye 60/22.

An identical sequence of events was noted in a patient who, while undergoing neck dissection for a large carcinoma, had a severe spastic contraction of the internal carotid artery brought on by slight traction on the vessel while a piece of tape was being passed around it. The retinal vessels were ophthalmoscopically normal but collapsed when a minute unmeasurable amount of pressure was exerted on the eye. Pressures in the retinal artery returned to normal after the carotid spasm relaxed, and there were no residual visual defects.

Another patient, not included in this series, had noted transient loss of vision in the lower field of the right eye about once weekly for eight years. While the retinal artery pressure was being measured, the superior retinal arteriole was noted to empty completely of blood for a few minutes. During this time the patient had complete inferior anopsia.

Of the 80 patients who had transient episodes of hemiparesis, facial weakness, hemianesthesia, or aphasia, 42 had concomitant attacks of amaurosis fugax. Of these, 10 had retinopathy consisting of 1 to 10 cotton-wool patches scattered sparsely over the perimacular and peripapillary retina. Of the 42, 33 had diastolic retinal artery pressure from 20 to 75 percent lower on the affected side; 5 had equal pressures on the two sides. One patient who probably had bilateral carotid insufficiency had a higher pressure in the eye on the side causing the symptoms. In three patients the pressure was not measured. Five patients who had hypertensive cardiovascular disease showed an interesting phenomenon in the eye on the side of the compromised carotid artery: the hypertensive arteriolar narrowing and focal constrictions were either absent or less intense than in the opposite eye. All five patients had appreciably lower pressures in the retinal artery on the side of the affected carotid artery.

Thirty-eight patients who had intermittent insufficiency of the carotid artery did not complain of amaurosis fugax. One of these had unilateral retinopathy. Pressures in the retinal artery were higher on the side of the affected carotid artery in four patients who presumably had bilateral lesions, but were lower on that side in twenty-two patients and equal on the two sides in twelve patients. Three patients, all of

whom had lower pressures in the retinal artery on the side of the affected carotid artery, also had fewer and less severe hypertensive arteriolar changes in that eye.

One of the two patients in the group with thrombosis of the carotid artery who had amaurosis fugax complained for four months of this symptom in the left eye and then suddenly right hemiplegia and right homonymous hemianopsia developed; both conditions gradually abated. This patient had a diastolic pressure in the retinal artery of 50 mm. of mercury on each side until hemiplegia and hemianopsia appeared; the pressures then changed to 55 mm. of mercury in the right eye and 38 mm. in the left eye. After the right homonymous hemianopsia cleared, the pressures in the retinal artery of each eye returned to 50 mm. of mercury.

Of the thirty-six patients who did not have amaurosis fugax associated with carotid artery thrombosis, four had unilateral retinopathy on the side of the affected carotid artery. Twenty-three patients, of whom seven had angiograms, had a lower pressure in the retinal artery on the side of the thrombosis. In one patient, proved by angiography to have bilaterally occluded carotid arteries, the pressure in the retinal artery was higher in the eye on the side of the cerebral infarction. Seven patients, of whom two had angiograms, had equal pressures in the retinal arteries on the two sides.

UNILATERAL RETINOPATHY

This interesting phenomenon, which will be discussed later, was encountered in 15 of the 124 cases (Table 3). In the literature the occurrence of this phenomenon has been reported when a carotid artery was ligated, but I have not found it described in any reports pertaining to spontaneous thrombosis in the carotid artery. Since retinopathy occurred among 12 percent of the cases in this series, it is difficult to understand why the phenomenon has not been observed before. Reports of two illustrative cases follow:

CASE 2. On September 28, 1955, a 55-year-old man reported that he had been having intermittent numbness, tingling and weakness of the left arm and leg for nearly five years. The attacks lasted for a few minutes and recurred at irregular intervals. The visual acuity and visual fields were normal and he had no ocular symptoms. The results of general and neurologic examinations were normal. Blood pressure was 140 mm. of mercury systolic and 80 mm. diastolic. Ophthalmoscopy showed several cotton-wool

patches in the right retina but none in the left (Figure 1). The arterioles and veins of the right eye were larger than those of the left eye. Diastolic pressure in the retinal artery was less than 10 mm. of mercury in the right eye and was 35 mm. in the left eye. Diagnosis of intermittent insufficiency of the right carotid artery was made. Anticoagulant therapy ended his attacks.

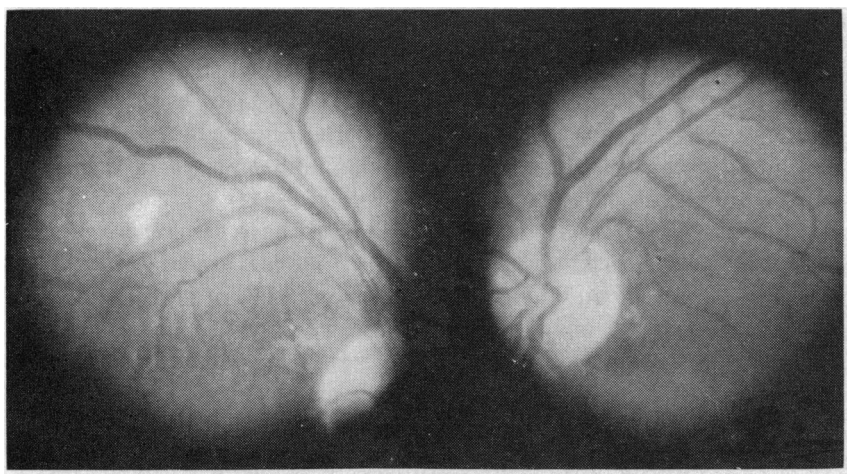

FIGURE 1. CASE 2

Right eye: cotton-wool patches and dilated vessels. Left eye: normal. Result of insufficiency of internal carotid artery, right side.

CASE 3. On March 6, 1957, a 58-year-old man reported that he had had attacks of blurred vision in both eyes two to three times daily for nine months, sometimes accompanied by vertigo and numbness of the left hand and left leg. Examination showed paresis of the left arm and leg and absence of the radial pulses. Pulsation was felt only in one leg. A diagnosis of aortic arch syndrome with occlusion of the subclavian arteries and the right carotid artery was made. He had a cotton-wool patch in the right eye (Figure 2) and pressures in the retinal artery measured 55 mm. of mercury systolic and 30 mm. diastolic in the right eye and 95 mm. and 52 mm. respectively in the left eye.

The retinal findings in the other 13 patients were similar (Figure 3). In all 11 cases of unilateral retinopathy encountered among the 86 patients with intermittent insufficiency of the carotid system, pressures in the retinal artery were much lower on the side of the affected carotid artery. In 3 of the 4 patients in whom thrombosis was diag-

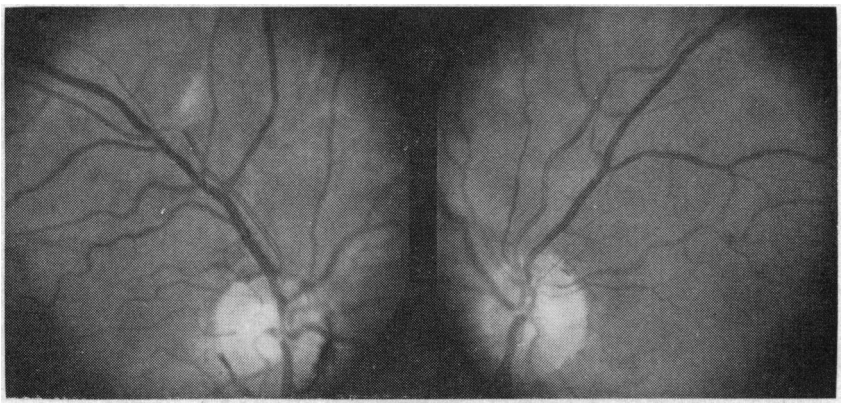

FIGURE 2. CASE 3

Right eye: cotton-wool patches and dilated vessels. Left eye: normal. Result of thrombosis of internal carotid artery, right side.

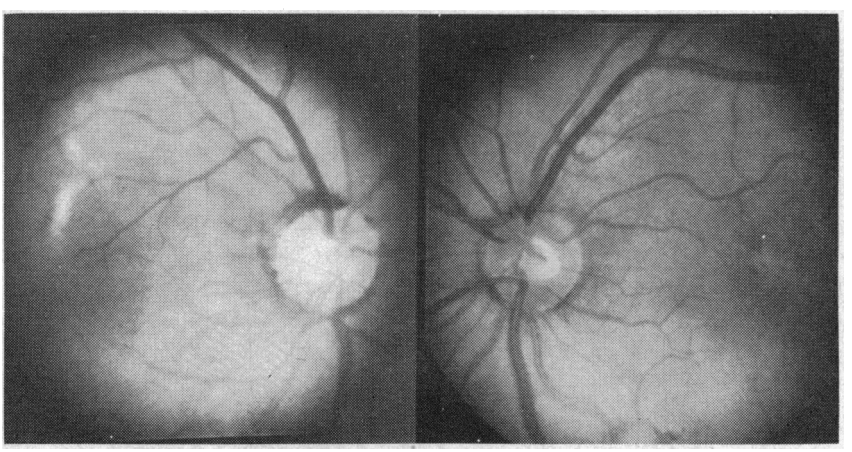

FIGURE 3.

Right eye: cotton-wool patches, retinal edema, and narrowed arterioles. Left eye: normal. Result of insufficiency of internal carotid artery, right side, caused by postural hypotension.

nosed the pressure was much lower on the affected side; in the fourth patient the pressures were equal on the two sides. These low pressures were usually in the range of 0 to 10 mm. of mercury diastolic, and the pressure on the side of the normal carotid artery might be at any level

from 30 to 90 mm. Mild to moderate hypertensive cardiovascular disease was reported in 9 of the 15 patients; in 3 of the 9, hypertensive retinal arteriolar changes were less severe on the side of the affected carotid artery. Eleven patients gave histories of attacks of amaurosis fugax in the eye with the retinopathy. One patient had arcuate field

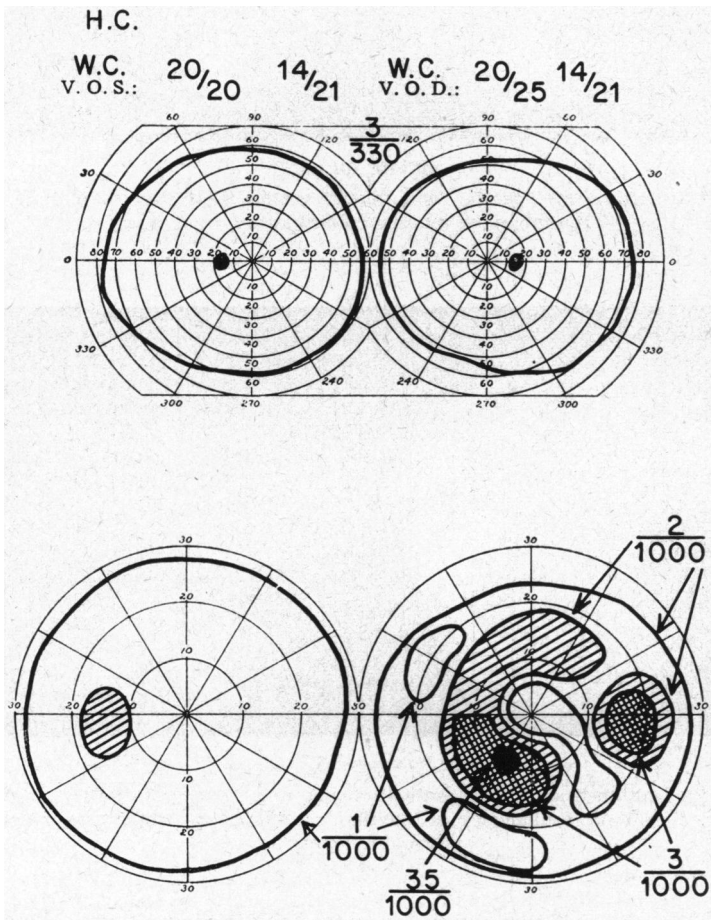

FIGURE 4. RIGHT EYE: RELATIVE AND VARYING FIELD DEFECTS; LEFT EYE: NORMAL

Other defects include retinopathy and amaurosis fugax, right eye. Result of insufficiency of internal carotid artery, right side.

defects (Figure 4), and another had a small scotoma (Figure 5). A third patient had arcuate field defects in one eye and homonymous hemianopsia to the opposite side (Figure 6), a fourth had slightly incongruous right homonymous hemianopic scotomas (Figure 7), and a fifth had left homonymous hemianopsia which could not be plotted.

VISUAL DEFECTS

The visual defects encountered among these patients were of three

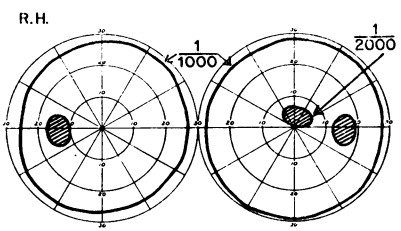

FIGURE 5. RIGHT EYE: SCOTOMA ABOVE FIXATION POINT; LEFT EYE: NORMAL

Other defects include retinopathy and amaurosis fugax, right eye. Result of insufficiency of internal carotid artery, right side.

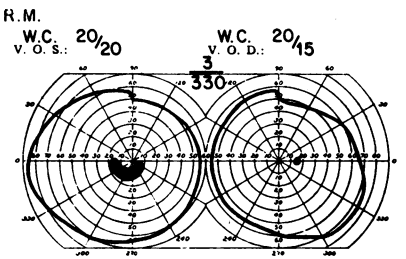

FIGURE 6. RIGHT HOMONYMOUS HEMIANOPSIA AND ARCUATE DEFECTS IN VISUAL FIELD OF LEFT EYE AS RESULT OF INSUFFICIENCY OF THE INTERNAL CAROTID ARTERY, LEFT SIDE

Other defects include cotton-wool patches in the retina and amaurosis fugax, left eye.

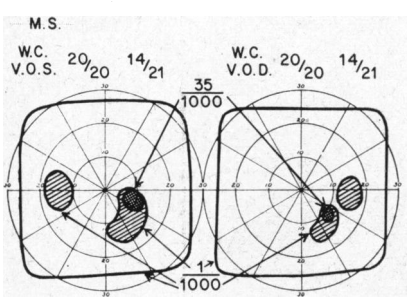

FIGURE 7. INCONGRUOUS RIGHT HOMONYMOUS LOWER QUADRANTANOPIC SCOTOMAS DUE TO INFARCTION IN LEFT TEMPOROPARIETAL REGION IN BRAIN

Result of insufficiency of internal carotid artery, left side. Other defects include cotton-wool patches in the retina, left eye.

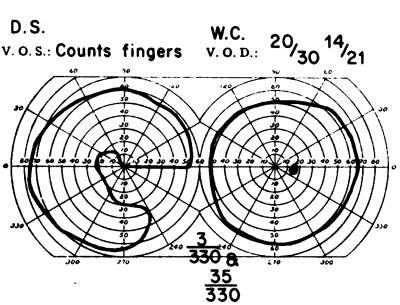

FIGURE 8. LEFT EYE: ARCUATE DEFECTS IN VISUAL FIELD, CAUSED BY OCCLUSION OF SUPERIOR TEMPORAL ARTERIOLE IN RETINA, LEFT EYE.

Result of thrombosis of internal carotid artery, left side.

kinds: (i) visual loss in the eye on the side of the affected carotid artery only; (ii) occlusion of a retinal artery or branch artery on the side of the affected carotid artery and homonymous hemianopsia to the opposite side; (iii) slightly incongruous homonymous hemianopsia.

Of the 86 patients who had intermittent insufficiency, 8 had occlusions of the central artery or a branch artery, and 6 of the 38 patients in whom the carotid artery had thrombosed had such occlusions. Measurements were made of the retinal artery pressure among only 8 of the 14 patients; all 8 had an appreciably lower

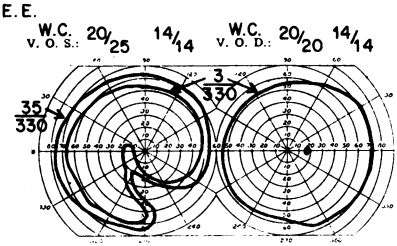

FIGURE 9. LEFT EYE: ARCUATE DEFECT IN VISUAL FIELD, CAUSED BY OCCLUSION OF SUPERIOR TEMPORAL ARTERIOLE IN RETINA, LEFT EYE.

Result of insufficiency of internal carotid artery, left side.

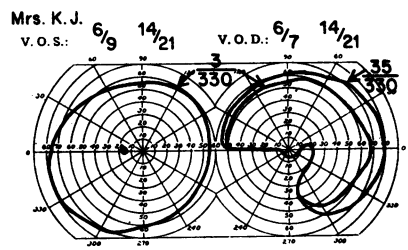

FIGURE 10. RIGHT EYE: ARCUATE DEFECT IN VISUAL FIELD, CAUSED BY OCCLUSION OF SUPERIOR TEMPORAL RETINAL ARTERIOLE, RIGHT EYE.

Result of insufficiency of internal carotid artery, right side. The patient had had 15 prior attacks of amaurosis fugax in right eye.

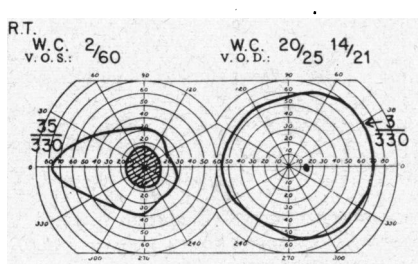

FIGURE 11. LEFT EYE: DEFECTS IN THE VISUAL FIELD, CAUSED BY ARTERIAL OCCLUSION IN LEFT OPTIC NERVE

Result of insufficiency of both internal carotid arteries.

pressure on the side of the affected carotid artery. The field defects are shown in Figures 4, 5, and 8 to 14 inclusive.

Four patients among the group of eighty-six having intermittent insufficiencies and two among the group of thirty-eight having thromboses had occlusion of a central or branch artery associated with homonymous hemianopsia to the opposite side. One of the four had lower pressure in the retinal artery on the affected side. One patient who had bilateral carotid occlusive disease had a higher pressure on

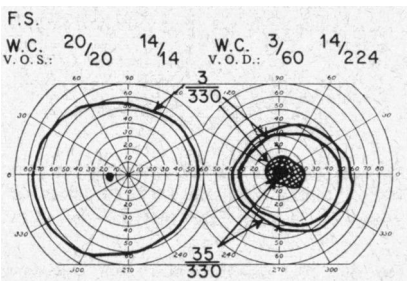

FIGURE 12. RIGHT EYE: DEFECTS IN THE VISUAL FIELD, CAUSED BY ARTERIAL OCCLUSION IN RIGHT OPTIC NERVE

Result of thrombosis of internal carotid artery, right side.

the side from which the symptoms arose, two had equal pressures on the two sides, and the remainder were not measured. The field defects are shown in Figures 6 and 15.

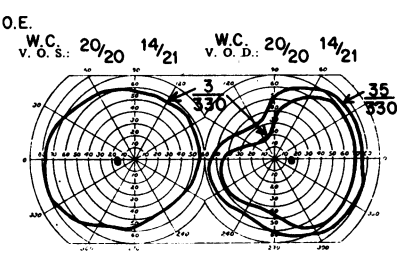

FIGURE 13. RIGHT EYE: DEFECTS IN THE VISUAL FIELD, CAUSED BY ARTERIAL OCCLUSION IN RIGHT OPTIC NERVE

Result of insufficiency of internal carotid artery, right side. Thirty prior attacks of amaurosis fugax, right eye.

Two of the eighty-six patients having intermittent insufficiencies of the carotid artery experienced transient homonymous hemianopsia. One of the two patients had a higher pressure in the retinal artery on

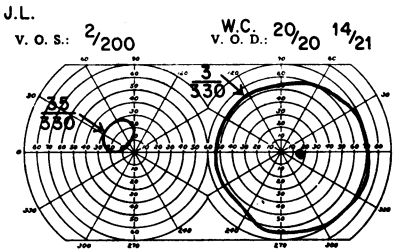

FIGURE 14. LEFT EYE: DEFECTS IN THE VISUAL FIELD, CAUSED BY OCCLUSION OF CENTRAL ARTERY OF RETINA OF LEFT EYE

Result of insufficiency of internal carotid artery, left side.

the side of the affected carotid, while the other had equal pressures on the two sides. Two of the group with intermittent attacks had permanent homonymous hemianopsia and both had lower pressures in the retinal artery on the affected side. Among the patients having thrombosis of the carotid artery, two had grossly demonstrable homonymous hemianopsia from which they recovered and both had lowered pressures in the retinal artery on the affected side. Six patients, however, had permanent homonymous hemianopsia. All six had lower pressures in the retinal artery on the side of the thrombosed internal carotid artery. Angiography had been used in two cases; one of the two patients died later. Some of the field defects are shown in Figures 7 and 16 to 19 inclusive.

ASYMMETRICAL HYPERTENSIVE RETINAL VASCULAR CHANGES

Eight patients among the group with intermittent insufficiency of the carotid artery, and two patients among the group with thrombosis of the carotid artery, had lesser retinal arterial hypertensive changes on the side of the affected carotid artery and all of these patients had lowered pressure in the retinal artery on that side (Figure 20).

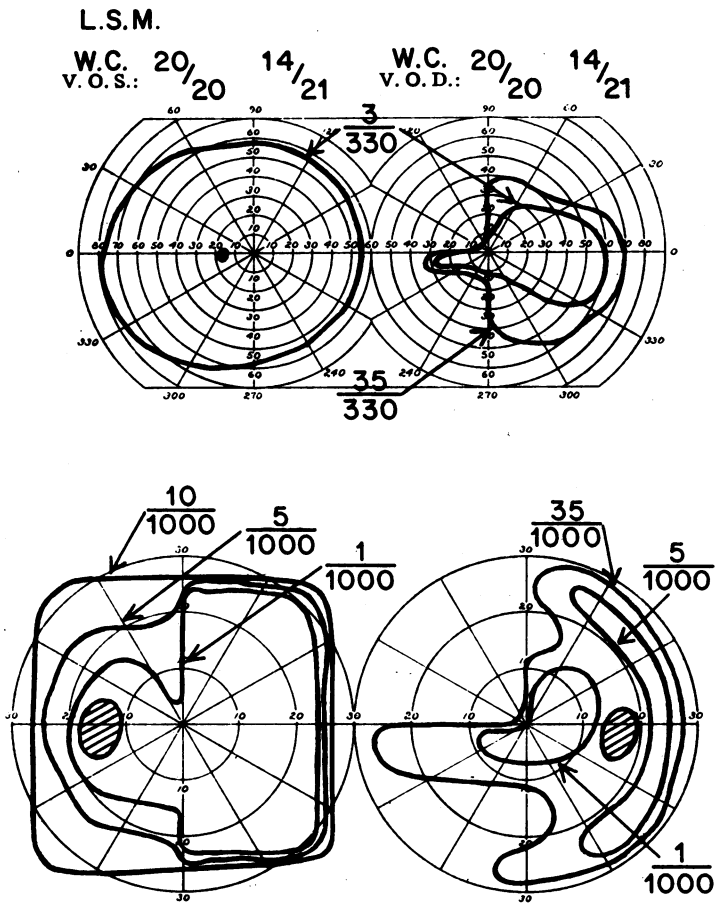

FIGURE 15. DEFECTS IN VISUAL FIELD OF RIGHT EYE, CAUSED BY PARTIAL OCCLUSION OF CENTRAL ARTERY OF RIGHT EYE, AND RELATIVE LEFT HOMONYMOUS HEMIANOPSIA, DUE TO ISCHEMIA IN RIGHT TEMPORAL LOBE
Result of thrombosis of internal carotid artery, right side.

Papilledema or retinal hemorrhages were not found in any patient. Intraocular pressure was measured in only two patients and was found to be normal in both.

TREATMENT

Five of the six patients who had amaurosis fugax as their only

symptom were placed on anticoagulant therapy and this immediately stopped their attacks. In two the attacks recurred when the therapy was discontinued. Of the remaining 80 patients who were having attacks of intermittent insufficiency of the internal carotid artery 19

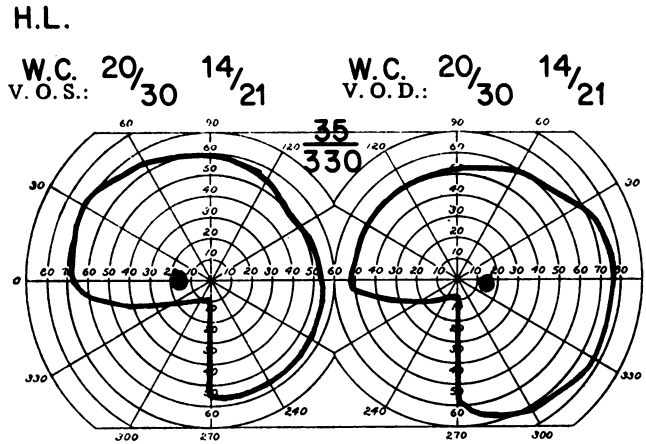

FIGURE 16. SLIGHTLY INCONGRUOUS LEFT HOMONYMOUS LOWER QUADRANTANOPSIA, CAUSED BY AN INFARCT IN TEMPORAL LOBE, RIGHT SIDE

Result of thrombosis of internal carotid artery, right side, proved by angiography.

were not treated. Only one of the 19 was traced, and his attacks had stopped. Of the 18 who were advised to have anticoagulant therapy administered by their home physicians none could be traced. In 37 of the 80 patients there was an immediate cessation of the attacks after the administration of anticoagulants was started. Hemiplegia developed in another patient while on this therapy. Three had good results from anticoagulants, but hemiplegia developed when use of the drug was stopped. One patient showed improvement when treated with priscoline. The attacks experienced by one patient who had hypotension stopped when ephedrine was used for treatment.

Among the 38 patients who had thrombosis of the internal carotid artery, 25 were not treated, 2 received anticoagulants, but no follow-up study could be made, and 6 received anticoagulants and had a satisfactory recovery. Of the patients who were treated with anticoagulants 5 had poor results and 3 of this group died.

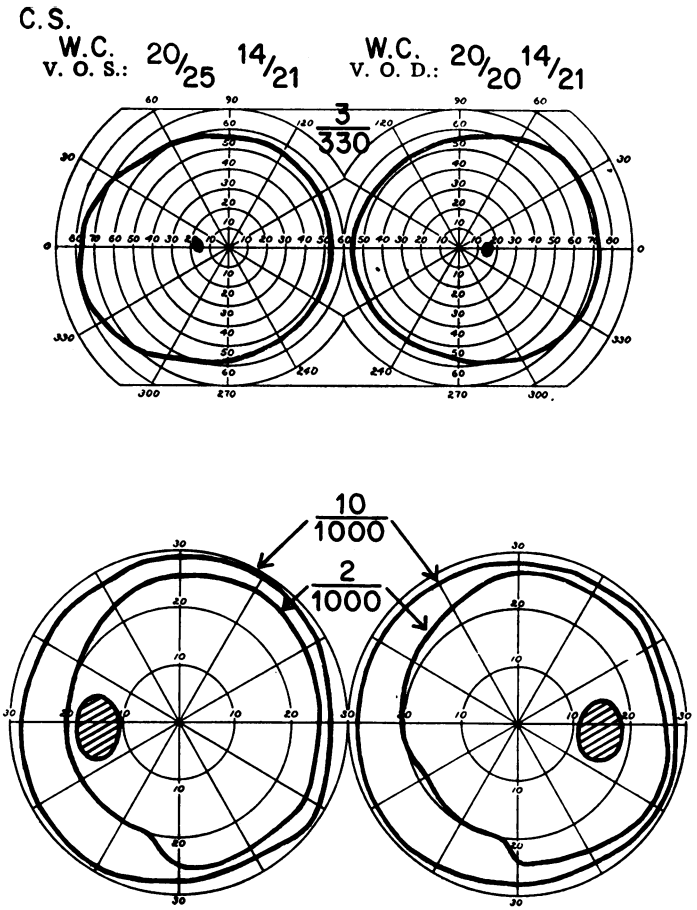

FIGURE 17. RELATIVE LEFT HOMONYMOUS HEMIANOPSIA CAUSED BY ISCHEMIA CF TEMPORAL LOBE, RIGHT SIDE

Result of thrombosis of internal carotid artery, right side.

ETIOLOGIC AND PATHOGENIC FACTORS RELATED TO THE SYNDROME OF OCCLUSIVE DISEASE OF THE CAROTID ARTERY

Millikan, Siekert and Shick (16), discussing this subject, stated:

Our present concept of the pathogenesis of attacks is as follows: A thrombus begins to form on an area of diseased endothelium. This soft material may

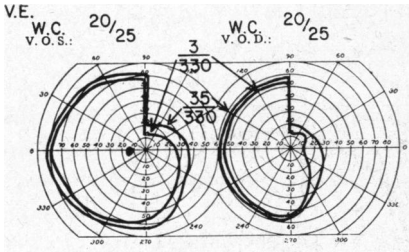

FIGURE 18. SLIGHTLY INCONGRUOUS RIGHT HOMONYMOUS HEMIANOPSIA, CAUSED BY TEMPORO-OCCIPITAL INFARCTION, LEFT SIDE OF BRAIN

Result of thrombosis of internal carotid artery, left side, proved by angiography and at necropsy.

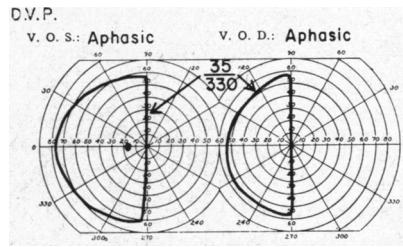

FIGURE 19. COMPLETE RIGHT HOMONYMOUS HEMIANOPSIA, CAUSED BY INFARCTION OF LEFT SIDE OF BRAIN

Result of thrombosis of internal carotid artery, left side, verified by angiography.

reach a size sufficient to produce enough alteration in blood flow to cause symptoms, break from its source, fragment and be carried away. More likely, however, appears the possibility that the newly formed clot becomes dislodged before symptoms occur, travels to a place where the vessels branch, lodges for a few minutes (symptoms produced) and then fragments and is carried away. [This concept may explain] the rapid onset and short duration of the attacks, the remarkable constancy of the attacks, the absence of residual neurologic signs, and the cessation of attacks during adequate anticoagulant action.

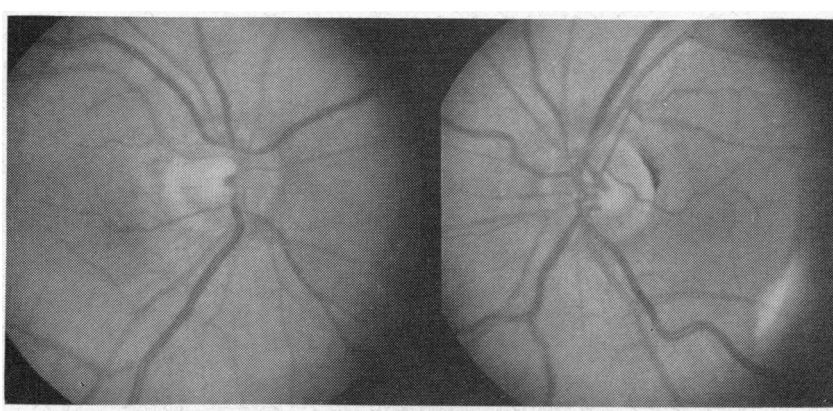

FIGURE 20. RIGHT EYE: ARTERIOLES OF RETINA NARROWED, MILDLY SCLEROTIC, AND IRREGULAR; LEFT EYE: ARTERIOLES LARGER THAN NORMAL AND REGULAR IN CALIBER

Result of insufficiency of internal carotid artery, left side.

These authors expressed the opinion that "cerebral infarction may occur as a result of interplay between a number of variable factors which include the degree and extent of arteriosclerosis, local and systemic blood pressure, cardiac disease, vasospasm, blood viscosity, and the degree of tendency to clot and to form a thrombus." They stated, "We have not found adequate evidence to support the contention that any single factor is the primary one in all cases of cerebral infarction."

They called attention to the various sites at which symptoms seem to be produced. Apparently, the site of an atheromatous narrowing of the affected internal carotid artery is not the only factor which determines the character of the attack of insufficiency or the extent of damage if cerebral infarction occurs. The first branch of the internal carotid artery is the ophthalmic artery. Then the internal carotid artery gives off in order the posterior communicating artery and the anterior choroidal artery, and finally divides into the anterior and middle cerebral arteries. Damage may be produced in any of these major vessels or in their most minute branches. Fisher (13) found the commonest site of atherosclerotic occlusion to be within the carotid sinus. Berry and Alpers (14) stated that the gross pathologic alterations seemed to be located predominantly in the distribution of the middle cerebral artery. Three theories as to the origin of the attacks (16) of intermittent insufficiency in the carotid system are as follows: (i) vasospasm, (ii) fluctuations in blood pressure, and (iii) embolism.

VASOSPASM

Ecker (17) described four patients who had relatively severe dysfunction of the brain brought about by mild trauma of the internal carotid artery resulting in spasm of this vessel. Later, Ecker and Riemenschneider (18) arteriographically demonstrated spastic changes occurring in the internal carotid, anterior and middle cerebral arteries and their branches. The common element in all their cases seemed to be that of traction exerted on the arterial wall. Yates (19) wrote:

> A feature of the lesions of atherosclerosis is the presence of thin-walled capillaries and sinusoids in the atheromatous plaques and in the wall of the artery beneath the plaques. Occasionally these rupture, allowing hemorrhage into the muscular wall of the vessel. I believe such a naturally occurring injury may produce arterial spasm, which, if shortlived, will give rise to fleeting neurological signs and, if prolonged, offers an explanation of infarcted cerebral tissues which at autopsy are seen to be supplied by arteries not thrombosed and only slightly occluded by atheroma.

Kinmonth (20) found that direct mechanical trauma applied to the vessel wall produced a lasting spasm which could not be relieved by sympathectomy or by the use of heparin or any other agents except papaverine. He found that electric stimulation of large arteries did not produce contraction of these vessels, but that arterial contraction by shrinkage was brought about by a fall in the systemic blood pressures.

FLUCTUATIONS IN BLOOD PRESSURE

Meyer and Denny-Brown (21) analyzed the adjustments made in the collateral circulation between cerebral arteries after occlusion and decided that the most important factor in controlling such adjustments was the intraluminal blood pressure. They stated that a localized reduction in intraluminal pressure results in a dilatation of the vessel and an increased flow from neighboring collaterals having a higher head of pressure. "Such local changes in blood flow are rapid and occur within 30 seconds after occlusion. Delayed circulatory adjustments appear to be mediated by a combination of factors, including reduction in oxygen tension and the localized accumulation of acid metabolites." Denny-Brown and Meyer (22) produced cerebral infarction by ischemic anoxia through lowering the blood pressure briefly and found the changes to be reversible in the early stages. Alman and Fazekas (23) found that some patients appear to tolerate reduction of cerebral blood flow much better than others.

EMBOLISM

A large proportion of patients who have occlusive disease of the cerebral vessels have had previous coronary-artery infarctions. Embolism is an important mechanism in the production of ischemic infarction of the brain. Villaret and Cachera (24) noted the lodgment of solid emboli in vessels of the pia-arachnoid and brisk contractions not only of the occluded vessels but also of neighboring arteries. Fisher (13) found emboli in some patients with internal carotid artery occlusion. Among 21 necropsy specimens reported by Berry and Alpers (14), 5 were occluded by emboli.

Turner (25) showed pathologically discrete foci of ischemic necrosis in the brain, some of which he thought were embolic in origin. Hill and associates (26) described the production of cerebral infarcts by injecting homologous clots into the carotid artery of the dog. It is perhaps of some interest that of the 86 patients who had intermittent insufficiency of the carotid artery 4 had plaques at the bifurcation of some of

the arterioles in the retina. It could not be decided ophthalmoscopically whether these were small atheromas or the remains of emboli which had lodged at the site at some earlier time. Three of the four patients had plaques only in the eye on the side of the affected carotid artery, and the fourth patient had them in both eyes. The latter patient was re-examined six months later and the plaque in one eye had disappeared, indicating the probable embolic nature of this particular lesion. No such plaques were found among the 38 patients who had sustained thrombosis of the carotid artery.

COLLATERAL CIRCULATION

An important factor in the variability of the clinical picture which is encountered among patients with insufficiency or thrombosis of the internal carotid artery is undoubtedly the extent of the collateral circulation available to the affected vessel. Elschnig (6) in 1893 demonstrated on cadavers that injection of dye into the external carotid artery would be followed by a filling of the peripheral branches of an occluded internal carotid artery. Walsh and King (27) showed that a free anastomosis exists in the orbit between branches of the internal and external carotid arteries. Marx (28) was said by Lin and Scott (29) to have been the first to demonstrate arteriographically that such collaterals existed. In both his cases the collateral circulation between the external and internal carotid arteries was accomplished through the ophthalmic artery. Lin and Scott reported five similar cases. Sachs (30) reported cases of two such patients neither of whom sustained visual impairment from the thrombosed internal carotid artery. In one, the branches of the internal carotid artery filled through this route. Vaernet's (31) four cases demonstrated the same interesting phenomenon.

Bossi and Pisani (32) discussed the possible anastomoses between the external carotid system and the ophthalmic artery, which has nasal, lachrymal, and supraorbital branches. Such collateral circulation arises from the external carotid artery, passes through the internal maxillary artery, and from here takes one of the following pathways: (i) to the anterior branch of the middle meningeal artery and to the recurrent meningeal branch of the lachrymal artery, or (ii) to the deep anterior temporal artery and thence to the zygomatic and temporal branches of the lachrymal artery (the commonest variation). The circulation may go from the external carotid artery to the external maxillary artery and thence, via angular and posterior nasal arteries, to the nasal branch of

the ophthalmic artery. Or it may go from the external carotid artery to the superficial temporal artery and to supraorbital branches of the ophthalmic artery. They called attention to three ways in which compensatory circulation is established after thrombosis of a cerebral vessel occurs: (i) through the basilar collateral circulation via the circle of Willis, (ii) by means of collateral circulation through anastomoses joining the territory of the external carotid artery with that of the internal carotid artery and of the vertebral artery, and (iii) by means of peripheral collateral vessels through meningeal arterial anastomoses joining the three vascular areas of the brain.

These anastomoses probably spare the visual apparatus in large numbers of patients who have sustained thrombosis of the large vessel supplying the ophthalmic artery.

DIAGNOSTIC CONSIDERATIONS

Besides observing the rather characteristic symptoms and signs described herein, various authors have pointed to the value of palpating the affected internal carotid artery, in which pulsations may be absent or diminished. Palpation through the oral pharynx is more reliable than is palpation over the neck. Fisher (33) noted in some patients a cranial bruit on the side of the patent artery, which was heard best over the eye. Parkinson (34) and also Webster and Gurdjian (35) pointed out the diagnostic value of employing digital compression of the normal carotid artery to produce signs of intracranial insufficiency, thereby proving that the contralateral carotid artery is occluded.

Arteriography will satisfactorily demonstrate the site and extent of the occlusion, but a number of authors have discussed the dangers inherent in the use of this procedure. Millikan, Siekert, and Shick (16) prefer not to use arteriography in patients suspected of vascular occlusive disease unless there is doubt of the diagnosis. Usually even then a trial of anticoagulant therapy may be given. Fisher (13) and Smyth (36) do not justify the use of carotid arteriography as a routine procedure in suspected cases, because statistically it has been associated with a rather high incidence of progression of the neurologic defect and an increased mortality rate. Yates (19) encountered a patient in whom angiographic needling caused a hematoma and even extensive dissection of the wall. Furthermore, arteriography may change carotid insufficiency into carotid thrombosis. At the meeting

at which Johnson and Walker's paper (10) was presented, four cases were reported in which the patients died after angiography of the non-occluded carotid arteries.

For the aforementioned reasons, the majority of patients in the series I am reporting were not subjected to arteriography. The neurologic and neurosurgical consultants who saw these patients were sufficiently convinced of the nature of the disease that they were reluctant to endanger the patients' lives by subjecting them to arteriography; therefore, most of them were started on treatment with anticoagulants. The wisdom of this decision is apparent from data presented.

COMMENT

The 107 cases collected and reported by Johnson and Walker (10) constitute the largest series on this condition in the literature. Only 42 of the 107 patients having thrombosis of the carotid artery had ocular manifestations: 5 had episodes of transient blindness, 11 had optic atrophy, 12 had homonymous hemianopsia, 6 had diplopia, 6 had ptosis, 2 had papilledema, and 14 had pupillary changes (10 of these had a smaller ipsilateral pupil, 3 had a larger ipsilateral pupil and 1 had a fixed ipsilateral pupil). Walsh (37), Walsh and Smith (38), and Walsh (39) found homonymous hemianopsia to be the commonest manifestation, but also reported that homolateral blindness often was preceded by transient attacks of visual loss in the same eye. They observed that retinal hemorrhages were reported in only one case in the literature; they did not encounter any cases of papilledema. They had two patients who suffered from homolateral blindness and contralateral loss of the temporal field. One patient had Horner's syndrome and one had ophthalmoplegia associated with concomitant thrombosis of the cavernous sinus. Several patients had transient attacks of homonymous hemianopsia. Of the series reported by Milletti (40), 28 (58.3 percent) of the 48 patients had ophthalmologic findings: 8 had homonymous hemianopsia, 2 had mild papilledema and 7 had miosis on the side of the affected carotid artery.

Chrást and Gottwald (41) reported twenty-eight cases of thrombosis of the internal carotid artery and two cases of thrombosis of the common carotid artery. Three patients had homonymous hemianopsia, and one of these had transient episodes prior to the onset of the permanent defect. Three had nystagmus and eight had homolateral miosis. In all, 10 percent had papilledema and 16.5 percent had homolateral

optic atrophy. Compression of the intact contralateral carotid artery caused retinal ischemia on the side of the thrombosis in three patients. Bregéat (42) mentioned reports of papilledema in this syndrome. Fisher (13) had three patients with a homolateral Horner's syndrome; Krayenbühl and Weber (43) had two patients with a larger homolateral pupil. Webster and collaborators (44) found blindness in only three of sixty patients and homonymous hemianopsia in only four. Sugar, Webster, and Gurdjian (45), and King and Langworthy (46) also discussed the ocular manifestations. Golowin (47) reported that ligation of the carotid artery caused a decrease in the intraocular pressure of 2 to 3.5 mm. of mercury, but Elschnig (7) stated he could not confirm this in his own cases. Chrást and Gottwald (41) mentioned that five of fifteen patients had a lower intraocular tension on the affected side.

OPHTHALMODYNAMOMETRY

Measurement of the pressure in the retinal arteries with the ophthalmodynamometer has received scant attention in the American literature until quite recently. Probably the first investigator to call attention to the lowering of pressure in the retinal artery on the side of an occluded internal carotid artery was Baurmann (48) in 1936. He also noted that the pressure in the contralateral retinal artery increased under the same circumstances. However, this phenomenon remained essentially unknown in the United States. Koch (49–51) wrote three excellent articles in which the ophthalmodynamometer was mentioned, but apparently he was unaware of the effects of carotid occlusion on the retinal artery pressure. In 1944 Trotot (52) reported the case of a patient who had internal carotid thrombosis, right homonymous hemianopsia and lower pressure in the retinal artery of the left eye. Krayenbühl (53) measured pressures in the two retinal arteries in only two of his twenty-five patients and found them to be equal. Milletti (40, 54) alone and later with Di Luca (55) wrote several articles on the subject of ophthalmodynamometry. Johnson and Walker (10) mentioned the retinal artery pressures in seven cases which they collected from the literature: in four the pressures were equal on the two sides, in two the pressure was lower on the side of the occluded carotid artery, and in one no comparison of the two sides was made. Since then, a large number of articles on this subject have appeared in the literature (56–69).

The data presented in my series of 124 patients validate these

measurements as a valuable tool for diagnosis. By means of intra-arterial pressure measurements Bakay and Sweet (70) showed that when the internal carotid artery is occluded the percentage drop is the same in all portions of the internal carotid artery distribution and its accessible branches. Some of the arteries they measured were only 0.4 mm. in diameter. They found that ligation of the cervical carotid artery usually lowered the arterial pressure by about 50 percent. These are approximately the same figures reported by means of ophthalmodynamometry in the papers of Hollenhorst, Wilbur, and Svien (66) and of Blodi and Van Allen (67). Controls numbering into the thousands have been measured by the author and by others, and a remarkably equal pressure level has been noted in the two retinal arteries of normal persons. Consequently, a variation of 5 mm. for pressures below 50 mm. of mercury and a variation of 10 mm. for pressures above 50 mm. has been used as a measure of significant difference in the diastolic pressures between the two sides. In practice, the differences are usually much greater than this. Usually the pressure on the occluded side is from 25 to 50 percent of the pressure recorded on the normal side. A lower pressure on one side therefore has considerable significance in indicating a disturbance of the carotid artery circulation on the side of the lower pressure. If the pressures are equal on the two sides, occlusion of the carotid artery is not ruled out, since collateral circulation may serve to maintain the pressure in the retinal artery on the side of the occluded carotid artery. In some patients the pressure has been found to be higher on the side of the suspected carotid occlusion. In this event the patient probably has bilateral occlusion of the carotid arteries, but with only unilateral symptoms. One such case was proved by angiography.

VISUAL DISTURBANCE

Loss or impairment of vision resulting from thrombosis of the internal carotid artery or of its branches may be of several types: (i) occlusion of a branch of the central artery of the retina will cause arcuate field defects; (ii) occlusion of the central artery or of the ophthalmic artery will cause total or almost total blindness in one eye; (iii) occlusion of the middle cerebral artery or one of its branches will produce homonymous hemianopsia of slightly incongruous type characteristic of lesions of the optic radiations in the temporal lobe; and (iv) occlusion of a branch of the central artery, of the central artery, or of the ophthalmic artery with simultaneous involvement of

the middle cerebral artery will produce blindness or partial blindness in the eye on the side of the abnormal internal carotid artery and a loss of vision in the temporal field of the opposite eye. Among patients who have intermittent insufficiency of one or several of these vessels, there may be transient attacks of loss of vision in one eye or transient homonymous hemianopsia lasting usually only a few minutes. The frequency may vary from 10 to 12 attacks daily to attacks several months apart.

The term "amaurosis fugax" is applied to transient losses of vision which occur in one eye only. The obscuration of vision may be either partial or complete; it usually occurs without warning, reaches its maximum in a few seconds and is followed in the next five minutes or so by a gradual return to normal. Wagener (71) discussed this problem thoroughly. This symptom was present among 5 of the 107 cases collected by Johnson and Walker (10). Fisher (72) reported seven cases in which amaurosis fugax was associated with hemiplegia, all probably due to occlusion of the internal carotid artery. He considered this a vasospastic phenomenon, but admitted the inadequacy of this as the sole explanation. He also called attention to those patients who have amaurosis fugax and who get relief from this symptom without visual loss when hemiplegia occurs (12). There are a few descriptions in the literature in which the fundus was observed during the attack of transient visual loss. Lindenberg and Spatz (73) reported the case of a patient whose retinal vessels gradually became "snow-white" and then as redness reappeared the vision returned. In one branch of the retinal artery the blood flowed backwards. Foerster and Guttmann's (74) patient suffered repeated attacks of blindness in the right eye. One attack occurred under ophthalmoscopic examination, and vision was lost first in the lower field. The vessels running to the upper part of the retina became bloodless. Elschnig (7) did not observe any change in the appearance of the retina when the internal carotid artery was ligated. The three instances reported in this paper in which ophthalmoscopic examination was carried out during an attack show that various phenomena occur.

With regard to homonymous hemianopsia, Walsh (39) stated that often there was a relative sparing of the upper quadrants of the defective half fields, which he ascribed to the fact that the superior portion of the optic radiations is supplied by the middle cerebral artery and the lower portion by the posterior cerebral artery. The findings in the present series support this statement.

Two phenomena were observed in this series of patients which have not before been reported in the literature on spontaneous thrombosis or insufficiency of the internal carotid artery, although there are references to the phenomena having been observed among patients who had ligation of one internal carotid artery. The first of these manifestations is the appearance of cotton-wool patches in the retina of the eye homolateral to the lesion in the internal carotid artery. A search of the literature revealed two recent reports of this type of retinopathy. Swan and Raaf (75) described five patients whose common and external carotid arteries were ligated for treatment of a carotid-cavernous sinus communication and one patient who had ligation of the internal carotid artery only. Hypotonia occurred and lasted three to six weeks. The arterioles narrowed but the venules widened. In three of these patients cotton-wool patches developed after 80 to 90 hours, increased in size and number for 8 to 10 days, and cleared up 3 or 4 weeks later. Schenk (76) encountered two similar cases and found reports of four more in the literature. He called this "traumatic retinopathy of Purtscher" and ascribed it to stasis in the retinal veins and to serum transudation into the retina. The mechanism of production of the retinopathy is unknown. However, the finding in this series of a much lower retinal artery pressure in the eye containing the retinopathy among 14 of the 15 patients strongly suggests that the cotton-wool patches are in fact ischemic infarcts in the nerve fiber layer of the retina produced by hypotension.

The phenomenon of lessening of the hypertensive arteriolar narrowing and the disappearance of focal constrictions on the side of the occluded internal carotid artery was described by Kirby and Hollenhorst (77) in two patients who had ligation of these vessels for treatment of an intracranial aneurysm. This too appears to be a result of lowered retinal arterial pressure, as all ten of the patients who had this finding were shown to have lowered pressure on the affected side.

SUMMARY

The ocular manifestations of 124 patients who had insufficiency or thrombosis of the carotid artery system were investigated and reported. The diagnosis was made either clinically or by angiography.

The major symptom among the group of 86 patients who had intermittent insufficiency of the internal carotid artery was that of amaurosis fugax, which was present among 48, and which was cured in most instances by anticoagulant therapy.

Other ocular manifestations included retinopathy on the side of the affected carotid artery in 15 of the 124 patients, asymmetric hypertensive retinal vascular changes in 10 patients, and lowering of the pressure in the retinal artery on the side of the affected carotid artery among 83 patients. Occlusions of the retinal artery or branch artery were discovered among 14 patients and 6 more had an associated homonymous hemianopsia to the opposite side. Only 3 patients had hallucinations in the homonymous half fields; 3 others had transient homonymous hemianopsia, and 8 had permanent homonymous hemianopsia.

The importance of establishing the diagnosis of carotid occlusive disease during the period of intermittent insufficiency is stressed. Ocular symptoms which point to impending carotid occlusion include episodes of transient or permanent diminution of vision in one or both eyes. Such signs as a lowered pressure in the retinal artery of one eye, cotton-wool patches in one eye, or asymmetric hypertensive changes should alert the examiner to the possibility of carotid artery disease.

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