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BALLOTINI OCCLUSION OF RETINAL ARTERIES*

COLLATERAL VESSELS

BY

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IN a recent communication (Ashton and Henkind, 1965), the details of a method for embolizing retinal arteries in experimental animals were described, and a brief survey of the findings was provided. A most striking effect of arterial occlusion was the subsequent appearance of collateral vascular channels; these were predominantly arteriolar in nature, but in several instances anastomoses between adjacent retinal veins were noted. While such collateral arteriolar channels have occasionally been described in man, particularly following embolic blockage of branch retinal arteries, they have not been reported experimentally. The purpose of this communication is to describe the collateral vessels seen in the retinae of cats, and to compare them with similar channels noted in human eyes. The relationship between collateral channels in the retina and those noted in other organs will also be discussed.

Domestic cats (*Felis domestica*) were used in this study because their retinal vascular pattern closely resembles that of man.

Material and Methods

More than forty adult cats were studied; all were injected *via* the external carotid artery with a solution of gum-arabic containing small glass balls, or ballotini, ranging from 15 to 40 μ in diameter (Ashton and Henkind, 1965). The animals that survived the procedure were observed frequently and fundus photographs or drawings were made at appropriate intervals. Fluorescein dye studies (Dollery's method, to be published) were performed on several occasions in order to ascertain the circulatory status following successful embolization; both still and cine photographs were taken.

Post mortem studies were performed on either ink-injected or pepsin–trypsin digested retinal tissue. Injected specimens were prepared in the following manner. The animal was terminally anaesthetized with sodium pentobarbitone (Nembutal), the chest was opened, and the descending aorta was clamped. Heparinized saline, or preferably sodium nitrate (0·2 per cent.) was injected into the left ventricle, and the right auricle was incised; injection of the flushing media continued until the fluid flowing from the right auricle was free of blood, and then either Indian ink or Berlin blue (5 per cent.) was injected. The ink or dye was perfused until direct ophthalmoscopic observation revealed the retinal vessels to be fully injected; the globes were then enucleated and placed in 10 per cent. formol saline. After 24 hours' fixation the retinae were removed *in toto* and mounted in glycerine jelly. Several retinae with evident collateral vessels were treated by pepsin–trypsin digestion (Ashton, 1963) and the isolated vascular tree was stained with periodic-acid–Schiff reagent (PAS) and haematoxylin.

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Observations

(1) *In Vivo* Study

The arterial portion of the retinal vascular tree was successfully embolized in 21 adult cats, which survived operation and were then followed up for at least 24 hours. In twelve of these animals collateral arteriolar channels became visible by direct ophthalmoscopy 2½ hours to 23 days* after embolization, generally appearing on the second to fifth day after operation (Table I). Similar vessels were never seen in untreated cats, or in those where the carotid artery was simply ligated, or in animals injected with a gum-arabic solution that did not contain ballotini. One, to more than one dozen, collateral channels were seen in the retinae of affected animals.

TABLE I

EXPERIMENTAL ARTERIOLAR ANASTOMOSES IN THE RETINA

Cat No.	Clinical Findings					*Post mortem* Study
	Eye	Survival (days)	First Appearance of Arteriolar Anastomosis (days)	Location of Anastomosis	Associated Findings	
1	L	56	23	Disc and equator	—	Digest
16	L	16	4	Disc and equator	—	Digest
18*	L R	23 16	Not seen clinic 9	(Disc and equator) Equator	Venous anastomosis	Indian ink Indian ink
19	R	6	2	Posterior pole	—	Flat No injection
20	R	19	5	Posterior pole	—	Indian ink
28	R	21	8	"All over"	Venous anastomosis day 5	Indian ink
36	R	13	2	Posterior pole	—	Berlin blue and digest
37	R	29 *hours*	2½ *hours*	Superior artery and posterior pole	—	Flat retina
38	R	13	2	Superior temporal and posterior pole	—	Berlin blue
44	R	7	2	Posterior pole	—	Indian ink
47	L	6	4	Posterior pole	—	Not done (for electron microscopy)
48	R	6	3	Posterior pole	—	Indian ink

* Injection into both carotids at separate times.

Appearing initially as little more than dilated and tortuous capillaries, the collateral channels broadened and became less tortuous over a period of several days to weeks, and then they seemed to stabilize. In several instances, however, a number of the smaller collateral channels regressed in size and disappeared. In two cats

* In the animal where collaterals were first noted on the 23rd day there had been only weekly or bi-weekly examinations until the time anastomoses were seen; the other animals were examined daily after operation.

venous collaterals developed in the neighbourhood of embolized retinal arteries, and their appearance preceded that of arteriolar collaterals.

Two types of arteriolar collaterals were seen. The first and least frequent type was a small tortuous channel which seemed to by-pass a visible ballotini, and joined the distal, non-perfused segment with the patent portion of the artery. Examples of this type of collateral were clinically visible mainly near the disc and posterior pole (Fig. 1).

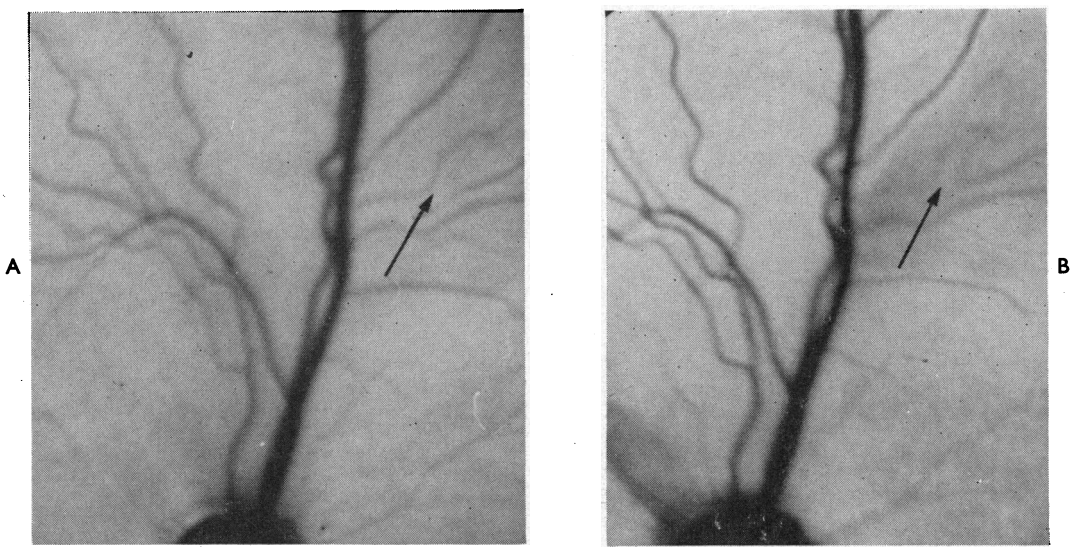


FIG. 1.—Cat 37. A, Fundus photograph taken 3 hours after a ballotini had lodged in an arteriole (*arrow*), showing the tortuous collateral channel by-passing the blocked vessel. B, 22 hours after occlusion. The collateral vessel is well formed and shows through the surrounding grey oedema of the retina.

Collaterals of the second type appeared larger and more prominent, and linked the blocked vessel with an adjacent patent artery; they were noted most often near the equator, usually at some distance from the visible emboli (Fig. 2, opposite). The instances of venous collateral formation were similar to the second arteriolar type, i.e., branches of one major vein trunk which had shown sluggish or diminished blood flow, demonstrable as sludging, joined with branches of adjacent veins of normal appearance (Fig. 3, opposite).

The clinical sequence from the time of operation to the appearance of collateral vessels is worth reviewing. Immediately following injection one or more ballotini were seen to lodge in the arterial tree, either at a bifurcation or where the vessel narrowed. The trapped ball often appeared to pulsate in time with the heart-beat and occasionally moved slowly down the arterial tree until it was firmly wedged. Usually a retrograde flow of sludged blood was evident in the artery distal to the ball; the packets of blood cells flowed slowly in a centripetal direction towards the optic disc, then entered the first bifurcation of the vessel distal to the ballotini, and proceeded centrifugally away from the disc. The veins adjacent to an occluded artery often showed sludged or sluggish flow, but the direction was always towards the nerve head. Within several minutes to hours after operation the retina in the region of the ballotini and along the path of the blocked artery became hazy, and occasionally

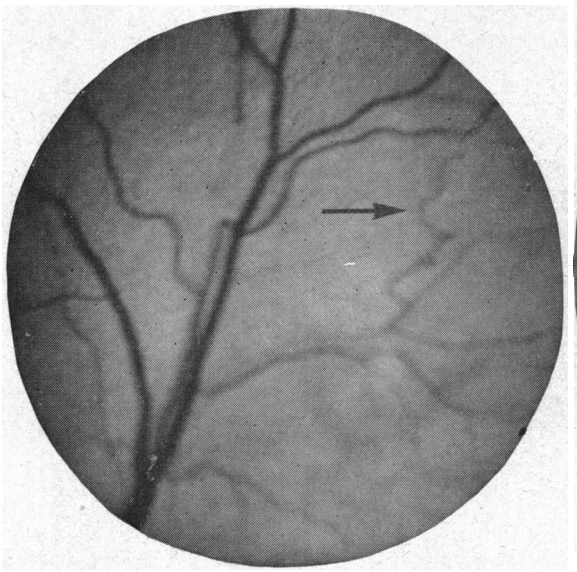


FIG. 2.—Cat 28. Fundus photograph of an arteriolar collateral (*arrow*) 21 days after embolization. (See Fig. 6 A for Indian ink study of this eye.)

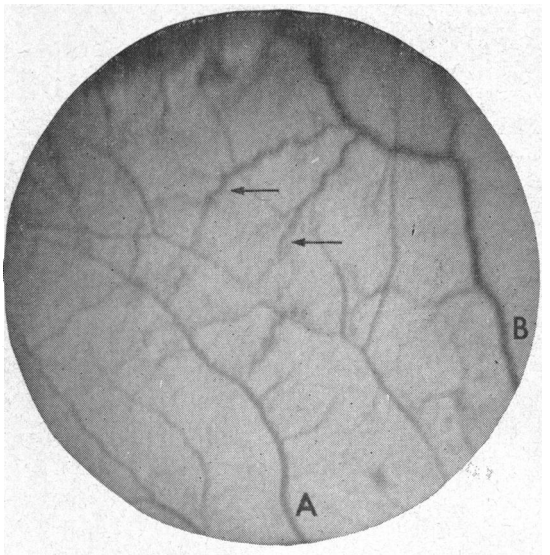


FIG. 3.—Cat 18, Right eye. Fundus photograph showing venous collaterals (*arrows*) two weeks after arteriolar embolization. The collaterals are present between adjacent veins A and B, the latter being in the area of a blocked arteriole. Note the dark and dilated appearance of vein B.

the nerve fibres looked as if they were swollen and spread apart. Often within these hazy patches dilated and tortuous capillary channels appeared. At first there seemed to be no connexion between these "newly appearing" vessels and the blocked artery, but over a period of several hours or days well-formed collateral communications became evident.

A fluorescein dye study performed at the time of embolization showed the vascular bed distal to the block to be closed at least to the dye; however, within minutes retrograde flow took place in the distal portion of the blocked artery and partially supplied this area. This back-flow of blood appeared to be derived from the surrounding capillaries supplied by adjacent, non-embolized vessels. Though initially extremely sluggish the retrograde flow increased in time.

Late fluorescein studies performed in one animal, both three and six days after operation, demonstrated the remarkably tortuous pathway of a collateral channel which had developed between a patent and an embolized artery near the disc.

(2) *Post mortem* Study

Seven retinae were injected, five with Indian ink, and two with Berlin blue. In the former, the entire retinal vascular pattern, including the capillary bed, was visible; Berlin blue gave a rather patchy filling of the vascular bed. Two types of arteriolar collaterals were noted. There were the short, broad, and tortuous pathways interconnecting the occluded distal portion of the vessel with its patent end, and which

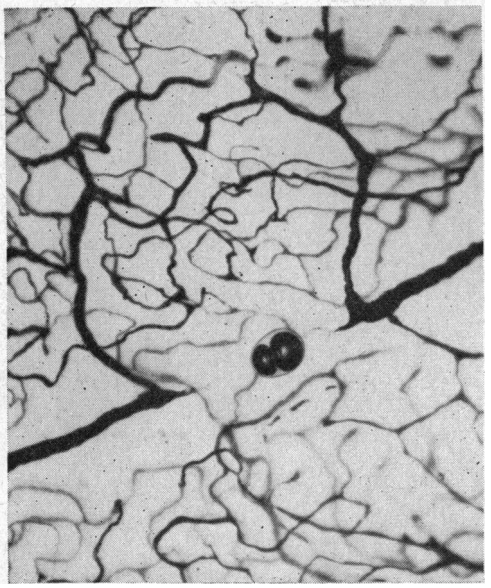


FIG. 4.—Cat 18, Left eye. Indian-inked specimen showing short tortuous collateral pathways circumventing the glass embolus, 16 days after embolization. ×125.

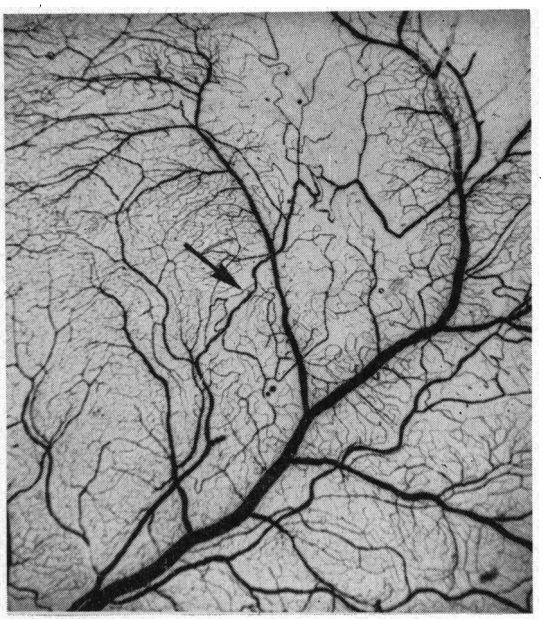
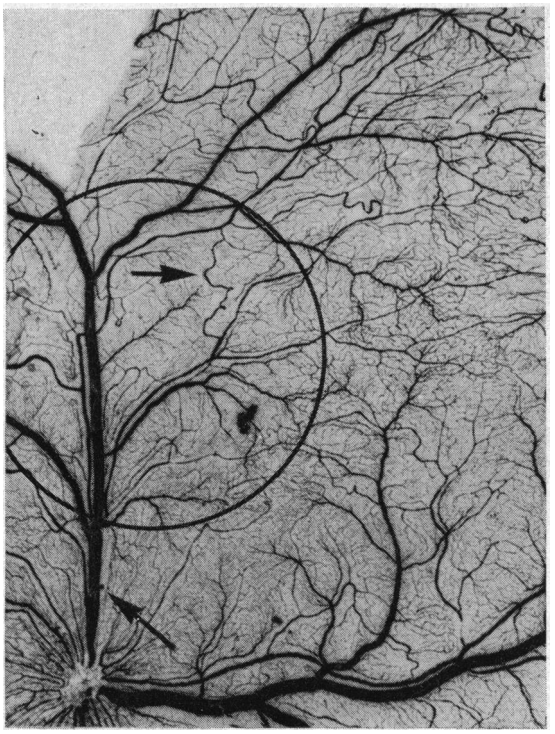


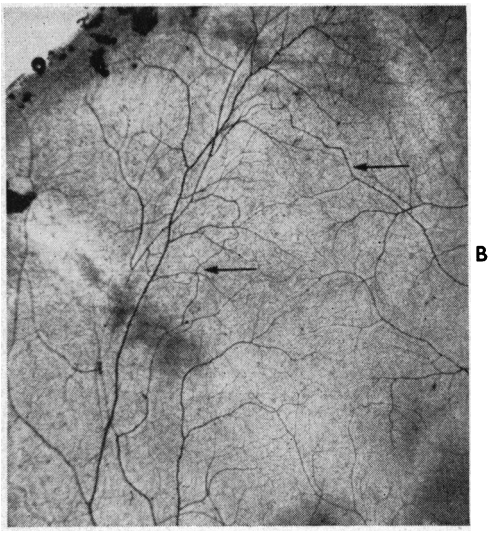
FIG. 5.—Cat 28. Indian-inked specimen showing a large tortuous collateral arteriolar pathway (*arrow*) linking the segments of a multi-embolized arteriole, 21 days after operation. Note also the filling in of a smaller central portion of the vessel by collaterals. ×15.

seemed to re-establish the circulation (Fig. 4). Occasionally, longer pathways of this type connected a vessel that was embolized in several places (Fig. 5). At the equator, or more peripherally, it was noticeable that these collateral channels often ran through a vascular bed seemingly devoid of many of its capillaries (Figs 5 and 6A). Longer anastomoses of a second type were also noted, and they linked the occluded with adjacent patent arteries (Fig. 6A, B, opposite). These channels were quite broad and tortuous and apparently derived from the existing capillary bed; the area immediately surrounding them contained relatively few, ink-filled, capillary-size vessels. In several instances a combination of both types of arterial anastomoses was seen supplying one embolized vessel (Fig. 7, opposite). Venous collaterals resembled the second type of arteriolar collateral; adjacent veins were joined by their peripheral branches via dilated pre-existing capillaries. In these cases the adjoining capillaries were well filled with ink (Fig. 8, overleaf). There were no examples of anteriovenous intercommunications in any specimen.

Three retinae with clinically visible collateral arteriolar channels were subjected to pepsin–trypsin digestion, and while there was some distortion (which is inevitable owing to the collapse of unsupported vessels), the details of the cellular structure and the basic pattern of the microcirculation were quite clear. In the case of a 53-day specimen numerous collateral channels between arterioles were quite evident, and they did not have the characteristics of capillaries from which they obviously arose, but rather of arterioles with a fairly well-defined coat of muscular elements



A



B

B, Cat 36. Low-power photomicrograph showing collateral arterioles (*arrrows*) which developed between an embolized and adjacent patent vessel, 13 days after embolization.

FIG. 6.—A, Cat 28. Low-power photomicrograph of an Indian ink specimen, 21 days after operation. The circle corresponds to the fundus photograph shown in Fig. 2, and the *arrow within* it points to the arteriolar collateral between the blocked artery (*lower arrow* points to the embolus) and an adjacent patent arteriole. Other arteriolar collaterals are present as well. Note that there are few capillaries around the collaterals.

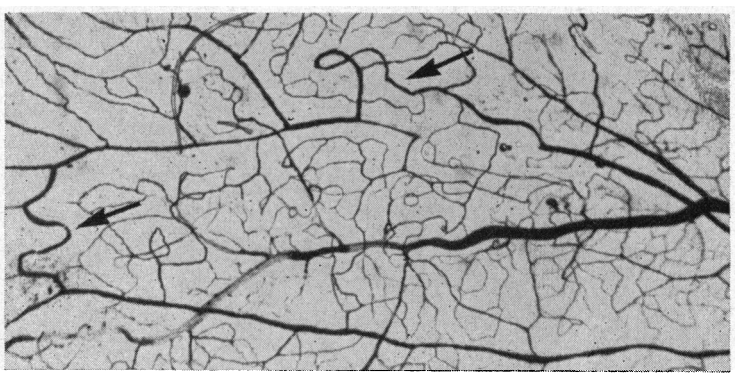


FIG. 7.—Cat 28. Indian-inked specimen showing a tortuous anastomosis (*upper arrow*) circumventing the blocked arteriolar segment, while a small collateral (*lower arrow*) joins the patent to the occluded vessel, 21 days after operation. ×51.

(Fig. 9, overleaf). The two types of collaterals previously described were seen (Fig. 10A, B, overleaf).

In the 16-day specimen the collateral channels were broader than capillaries, but had not taken on the appearance of arterioles. In both instances the capillary bed adjacent to the collateral channels contained many collapsed acellular strands representing capillary remnants.

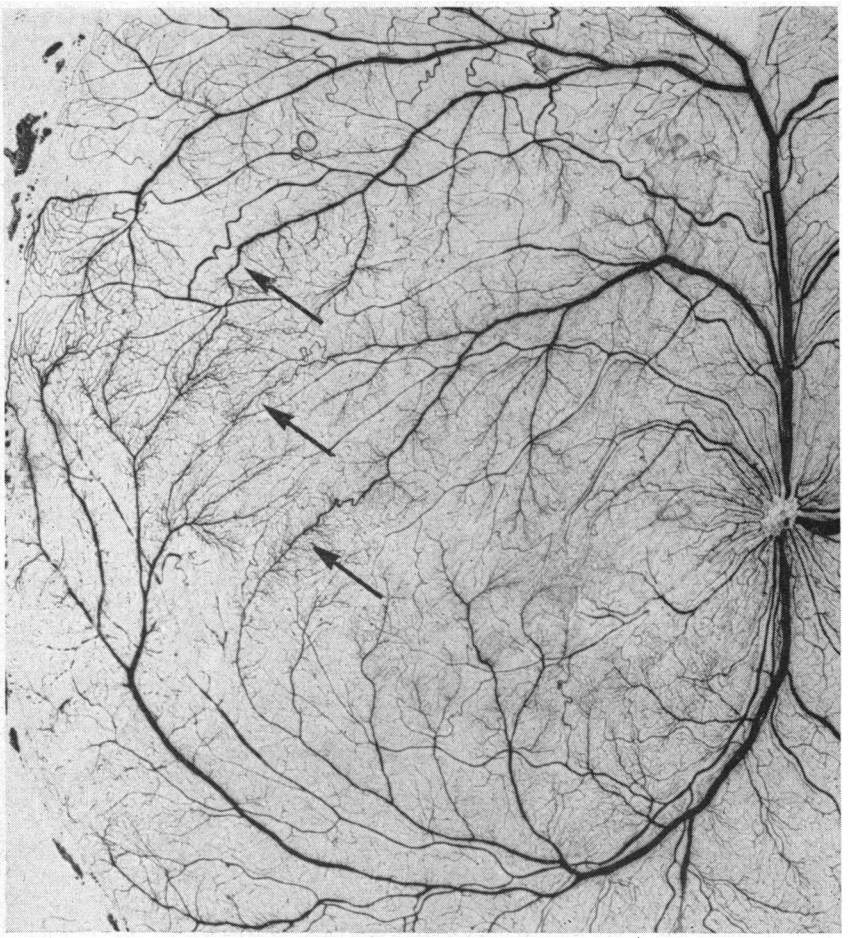
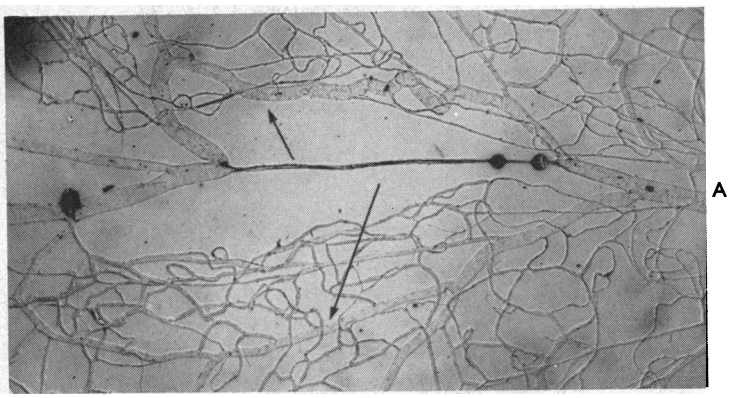
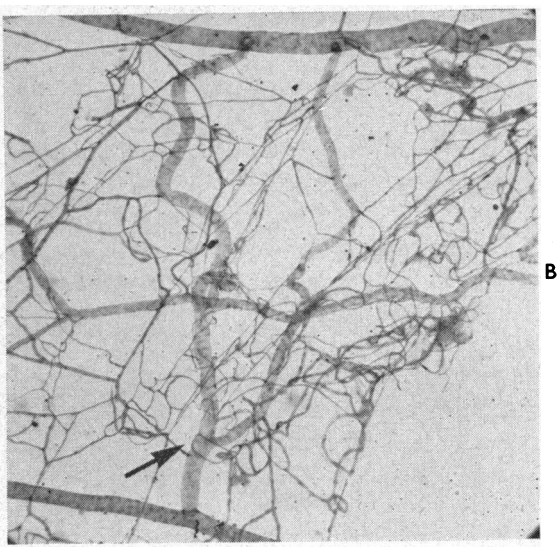


FIG. 8.—Cat 28. Low-power photomicrograph of an Indian-inked specimen showing large tortuous venous collateral channels (*arrows*) with well-filled adjacent capillaries. There are many arteriolar collaterals visible in this picture.

FIG. 9.—Cat 1. Digest preparation. The collateral channel (*arrow*) has dilated almost to the size of the blocked arteriole and its wall appears to have muscular elements, 56 days after operation. P.A.S. and haematoxylin. ×49.



A



B

FIG. 10.—A, Cat 1. Digest preparation. The collaterals (*arrows*) circumvent the blocked portion of the arteriole and have undoubtedly developed from the capillary bed. Many surrounding capillaries appear as acellular strands. P.A.S. and haematoxylin. ×49. B, Arteriolar collaterals (*arrow*) linking a patent arteriole (*above*) with the blocked vessel (*below*). P.A.S. and haematoxylin. ×49.

Discussion

(1) Some Points concerning Retinal Circulation

Before embarking on a discussion about collateral vessels, there is a point concerning the normal vascular tree of the retina which is relevant. It is generally stressed that the circulation of the retina is an "end artery" circulation, that is, a vascular bed with no alternative blood supply from adjacent vessels. It is true that the arteries of the retina, once they leave the region of the optic disc, do not communicate with any extra-retinal vessels. Within the retina, however, the vessels are so arranged (in man, monkey, and cat) that alternative pathways are potentially present (Henkind, 1966). In the first place the retinal arterioles are arranged in arcuate fashion somewhat in the manner of the microcirculation described for the bat wing (Webb and Nicoll, 1954; Nicoll and Webb, 1955), and this provides for collateral pathways and ensures a uniform distribution of blood to the capillary bed; secondly, the rich intercommunications between capillaries link adjacent arterioles or venules.

In essence, if the blood supply to the retina is cut off, at or behind the optic disc, no alternative blood supply will be present; on the other hand, if a vessel that lies

within the retina is obstructed, alternative pathways *may* overcome the obstruction, and such pathways are already present, in a potential form, in normal retinae.

(2) Collateral Circulation in General

A brief account of the general knowledge concerning collateral circulation will help place our findings in proper perspective. Liebow (1963) gives an excellent summary of work in this field.

Collateral circulation is blood flow that pursues a channel or system of vessels which is alternative to, or develops in substitution for, a major vascular pathway. The vessels may be pre-formed or arise *de novo*, and it may be difficult to determine their origin. Learmonth (1950) has described two types of collaterals. In the first, after a short course in alternative channels arterial blood is returned to the main artery, and there is little loss of flow or blood pressure. In the second, blood reaches the occluded vessel via terminal vascular branches of adjacent vessels and both the volume flow and the blood pressure are decreased in the main channel. It should be borne in mind that Learmonth based his discussion on a consideration of large arteries.

The development of collateral circulation depends to a large extent on the anatomical configuration of the vascular bed involved; and upon this may be engrafted mechanical, chemical, or neural factors. John and Warren (1961) list the following as potential stimuli for the growth of collaterals: (1) Increase in pressure gradient around the block. (2) Increase in blood flow around the block. (3) Release of vasoconstrictor tone in collateral vessels. (4) Accumulation of metabolites in tissue distal to the block. In accord with other authors they feel that the initial stimulus for collateral development is the pressure gradient alone, but that the later growth of collaterals may depend upon tissue activity among other factors.

Chemical substances may affect the development of alternative vascular channels in at least four ways (Liebow, 1963): (1) by regulating vasodilation; (2) by controlling the proliferation of new vessels; (3) by stimulating and inhibiting the growth of vessels; and (4) by guiding vessels to specific destinations. The work of Ashton (1954), Michaelson (1954), and Wise (1956) suggests that some substance or substances formed in hypoxic retinal tissue can induce vasoproliferation and vascular dilatation; Williams (1959), in his study of connective tissue autografts, concluded that hypoxia was a stimulus for the growth of vascular endothelium. Liebow (1963) reviewed the evidence that the nervous system can influence both the immediate and the late development of collaterals; North and Sanders (1958), however, felt that in the mouse ear nervous innervation played no role in the development of collateral vessels.

A number of workers (Longland, 1953; Winblad, Reemtsma, Vernhet, Laville, and Creech, 1959; John and Warren, 1961) who have studied the rate of development of collateral channels by means of angiography, have demonstrated the almost immediate expansion of pre-existing arterial collaterals, and in certain situations a progressive increase in the size of these channels may continue for months. On the other hand, collateral pathways tend to regress after an interrupted vascular channel has regained its continuity (Jacobson and McAllister, 1957; Winblad and others, 1959).

Still to be explained is the observation that though collateral arteries join with other arteries, and veins join veins, arteriovenous collaterals do not appear except

under certain circumstances, for example, in beds where arteriovenous shunts are normally found. When both an artery and a vein are compromised there may be separate expansion of the arterial and venous collateral systems, and in this situation the venous collaterals appear more rapidly and attain larger size than adjacent arterial collaterals (North and Sanders, 1958; North, Sanders, and Florey, 1960).

The structure of collateral vessels appears to reflect the mechanical conditions to which they are subjected, and such vessels that develop from capillaries may acquire the structure of arteries or veins, depending upon their function. The exact factors responsible for these alterations are not known, but it has been suggested that they are similar to those causing differentiation of arteries and veins from the capillary rete of the embryo.

Much of the above material deals with vessels of higher order (larger size arteries and veins) than those found in the retina, but the general principles are probably equally applicable.

(3) Collateral Circulation of the Retina

(*a*) *Human Data*

While it is well known that collateral communications develop between retinal veins following branch vein occlusion both in man and animals, it is less widely appreciated that similar arteriolar anastomotic channels can occur after branch artery obstruction. In 1938 Jensen reviewed eighteen such cases, including two he had personally observed (and he had access to the records of a third case). To these can be added the more recent reports of Wise (1956), Ballantyne and Michaelson (1962), Larsen (1964), and Kornzweig, Eliasoph, and Feldstein (1964; a pathological report). (Table II.)

The cases may be divided into two groups: (*a*) those where the anastomotic or collateral arteriolar channels appeared upon, or adjoining, the optic disc, and which were apparently dilated communications between the blocked artery (obstruction occurring near to the disc) and branches from the circle of Zinn which are not ordinarily visible; and (*b*) those instances where the collateral vessels appeared in the retina away from the disc, either joining an occluded and an adjacent patent artery, or circumventing a block. The majority of reports deal with the former situation, but at least eight cases of definite communications within the retina have been recorded (Table II, overleaf). Kornzweig and others (1964) recently noted arteriolar collaterals in the digest preparation of a retina from a patient who had sustained a branch artery occlusion many years previously. In most instances the occlusion was caused by an embolus from a diseased heart valve, but carotid artery disease (Jensen, 1938) and thrombosis without embolism have also been implicated (Burnett, 1899).

The initial appearance of collateral arterioles has rarely been determined accurately, for as Jensen (1938) points out, most cases have been found on occasional ophthalmoscopy some time after an occlusive episode, and few patients have been subjected to careful and repeated examination. Barkan (1902) noted arterial collaterals in the retina seven days after occlusion, while Rados and Candian (1921) saw similar vessels eight days after arterial block. Most cases, however, were first seen months or years after arterial occlusion.

TABLE II

CLINICAL CASES WITH ARTERIAL COLLATERALS

Author and Year	Age	Sex	Eye	Location*	Time after Occlusion	General Condition
Hock, 1869	?	?	?	Temporal disc	1 mth	?
Story, 1883	"Young"	M	R	Between superior and inferior nasal artery	?	?
Nettleship, 1891	"Young"	M	?	Around disc	12 mth	?
Elschnig, 1893	56	F	L	Near disc	1 mth	?
Holden, 1893	34	F	R	Near disc	1 yr	Valvular heart disease
Königshöfer, 1899	29	M	R	Retina	Within 2 mth	
Burnett, 1899	85	M	R	Near disc	6 mth	?
Barkan, 1902	38	M	R	Nasal retina	7 dy	Mitral insufficiency
Gonin, 1905	64	F	L	Around disc	3 mth	?
Coats, 1914	27	M	R	Disc	Within 1 mth	Valvular heart disease
Harms, 1914	47 25 47	M F F	R L R	Temporal retina Near disc Around disc	? 2 wk 2 mth 11 mth	Endocarditis Mitral disease Heart disease
Leber, 1915	23	M	L	Retina	?	Congenital syphilis
Rados and Candian, 1921	22	F	R	Disc	8 dy	Rheumatic fever
Jensen, 1938	36 61 20	F M F	L L L	Disc Disc Disc	3 wk–2 mth 2 yr 3–5 wk	Rheumatic heart disease Heart murmur Carotid hemiplegia
Wise, 1956	32	M	L	Near disc	1 yr	Rheumatic heart disease
Ballantyne and Michaelson, 1962	?	?	?	Retina	?	?
Larsen, 1964	57 33	M M	L L	Disc and retina Retina	? ?	? ?

* *Disc or near disc* implies connexions with branches of circle of Zinn. *Retina* implies intraretinal collaterals.

In several instances small retinal haemorrhages have been noted in the area where collaterals developed (Burnett, 1899; Coats, 1914), and Burnett thought the bleeding had occurred from ruptured adjacent veins. He also mentioned marked venous changes, including loop formation and anastomoses, in his patient with arterial obstruction, but he was uncertain whether these were "newly formed vessels, or old vessels filled out". Regression of retinal arteriolar collateral channels has been noted both by Coats (1914) and Jensen (1938).

Arteriolar collaterals within the retina most likely arise from the pre-existing capillary bed, a point first mentioned by Story in 1883, and later by Coats (1914) and Jensen (1938). Story is worth quoting, for he provides an interesting explanation of the reason why arterial collaterals occur predominantly in young people, in spite

of the fact that 90 per cent. of arterial occlusive disease of the retina affects patients over 50 years of age (Minton, 1937): "There are, as we all know, no arterial anastomoses between retinal vessels, but capillary anastomoses must exist, which at the period of life at which embolus of the central [Story probably meant branch] retinal artery usually occurs are useless for the purpose of re-establishing the circulation, but there is no reason why in the young subject these capillary anastomoses may not be capable of developing sufficiently to effect good collateral circulation." We should not forget, however, that patients over the age of 50 years may develop arteriolar or venous collaterals in the retina; Kornzweig and others' (1964) histological observations were made in a patient who was 76 when she sustained a superior temporal artery occlusion, and Burnett's patient was 85 years old.

Histological examination of arteriolar collaterals in the human retina has been undertaken only in the case of Kornzweig and others (1964), but unfortunately these vessels were not described clinically. Retinal digestion by the technique of Kuwabara and Cogan (1960) revealed collateral channels with thick walls resembling arterioles, but "being originally capillaries, they were much more tortuous and irregular".

The frequency with which arteriolar collaterals develop following branch occlusion of retinal arteries is not known; Jensen (1938), however, feels that a number of cases escape attention, initially because they may be obscured by retinal oedema, and later because regression of the collaterals may occur if the occluded circulation is re-established.

(*b*) *Experimental Data*

It has been possible to examine both clinical and histological material. The *in vivo* observations were made on the vessels of the retina within an intact normal eye, and the *in vitro* studies were conducted with either whole injected retinae, or with digest preparations of the retinal vascular tree.

Collateral arterial communications were noted as early as two and one-half hours after embolization, but were more frequently visible two to five days later. In some instances the collateral channels may have been hidden in the retinal haze that ensued after arterial occlusion. The rather rapid appearance of collaterals emphasizes the fact that the retinal vascular system of the cat possesses potential inter-arteriolar (and inter-venular) communications; that these develop primarily within the pre-existing capillary bed has been demonstrated by fluorescein dye studies not only in the cat, but more recently in the pig (Henkind and Dollery, 1966). These findings fit in well with data on the rapid appearance of collaterals in other organs. The two types of collateral pathways, those between adjacent vessels, and the variety circumventing a block of the artery are similar to those described by Learmonth (1950) for larger vessel systems than the arterial tree of the retina. However, the same basic principles seem to hold true, and the shorter pathways of the second type appear to be more efficient in re-establishing normal haemodynamics. It has not been possible to determine why one type of collateral pathway develops in preference to another, or even whether it pursues the most efficient possible route; however, it can be stated that the collateral develops in response to occlusion of a normally used vascular channel. In all likelihood pressure dynamics, and particularly the change in pressure gradient around the occlusion, play a large role in the initial development of these alternative pathways.

The ability of small vessels, in this case capillaries, to attain the size and cellular characteristics of larger vessels, the function of which they replace, was strikingly demonstrated in this study, and once again is in line with observations made upon other circulatory systems. A point of considerable interest was the absence of micro-aneurysms in any of the specimens, and this would tend to suggest that the collateral channels themselves, in spite of carrying blood under pressure probably in excess of that normally present in the capillary bed, are not prone to develop such lesions, at least under the circumstances of this experiment.

Noteworthy was the fact that collateral vessels were either arterio-arteriolar or veno-venous, but never arterio-venous in character. Arterio-venous collaterals seem to develop in organs that possess A-V anastomoses as part of their routine circulatory pattern, and such communications are absent in normal retinae (except if one considers as A-V shunts the broad capillary channels at the periphery of the retina which join the terminal artery and vein).

While it is possible to imagine that the development of arteriolar collaterals following embolization of an arteriole depends primarily on blood finding its way from an area of high pressure to one of low pressure within the existing vascular bed, it is more difficult to explain the development of venous collaterals following such occlusion. In our experiments the venous circulation was embarrassed secondarily to arterial blockage, and, indeed, the two eyes that showed venous collaterals in the retina were the most heavily embolized in the study. While differences in venous pressure most likely account for the appearance of collaterals, there is the possibility that retinal hypoxia is at the basis of this phenomenon, for in hypoxic conditions one may often see venous dilatation and neovascularization (Wise, 1956).

Not all vessels that were embolized were later served by collaterals, and in these instances the vascular bed distal to the block could not be injected with Indian ink or Berlin blue. Collaterals appeared most frequently at the posterior pole and equator, and less commonly at the retinal periphery. Whether this was due to the greater capillary network in the former areas, thus providing more possibilities for the development of collaterals, or possibly because of a higher arterial pressure gradient in these areas, is not known. It is conceivable that the greater nourishment of the retinal periphery from the choroid may limit the need for collateral pathways to develop in this area.

Even when collaterals developed the vascular pattern was not entirely restored to normal, for alternative arterial pathways often ran through a vascular bed in which the surrounding capillaries either did not fill with ink, or appeared narrow and acellular in digest preparations. Whether these capillaries became non-functioning and atrophied during the time of embolization, or later, is uncertain; however, one would have imagined that if the collaterals carried blood under pressure higher than that normally contained by surrounding capillaries, these capillaries, if patent, should be perfused. While it is conceivable that the arteriolar collaterals have induced the formation of a "capillary free" zone such as is seen around arterioles in the retina, there is no immediate way of confirming this. It is interesting that the capillaries surrounding venous collaterals perfused well with Indian ink, and no avascular zone was apparent.

On several occasions small collaterals disappeared after a few days, but more

usually these channels enlarged in size, their calibre often approaching that of the blocked vessel itself. No experiments were carried out for periods longer than two months, so it is impossible to state what the ultimate fate of the collaterals would be; however, if the occlusion persisted one would expect alternative pathways to remain. It would be quite interesting to follow the fate of collaterals if the retina atrophied appreciably.

It should be emphasized that the present work tells us little or nothing about the possible protective effect of collaterals in preserving retina function following localized vascular occlusion. Rather, it is concerned with the potential of the vascular system of the retina to react to a particular stress. The fact that the vascular system is capable of providing collaterals should, however, be encouraging to those studying ways of maintaining retinal viability following arterial occlusion.

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