S. S. Hayreh

Anterior Ischemic Optic Neuropathy

With 139 Figures and
16 Stereoscopic Illustrations

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Dedicated to my parents
as a small token
of my gratitude to them

Preface

"No attainment is ever final"

Vascular disorders of the optic disc and nerve are important not only to the ophthalmologist but also to the neurologist and the internist. To the first specialty group they represent one cause of blindness or severe visual impairment; to the second group the optic disc edema and optic atrophy seen in these disorders can pose serious problems of diagnosis, or give indications of the involvement of the cerebral circulation; while to the last group they are frequently indicative of systemic disease, particularly of the cardiovascular system. Recent advances in our knowledge of the blood supply of the optic nerve head have shed a significant new light on the subject. With the recent advent of fluorescein fundus angiography, an extra dimension has been added to the study of the ocular and optic disc circulations, and we have entered into a new era in the understanding of ocular vascular disorders *"in vivo"*. In the pre-angiography era, postmortem injection studies, although very valuable, did not completely reveal the vascular pattern of the optic disc in the living, in health, and disease. The ophthalmoscope, without doubt, has been valuable in assessing optic disc lesions, but could not give us information on the circulation of the eye and optic disc *"in vivo"*. This lack of information on the ocular and optic nerve head circulations has in the past resulted in confusion, ignorance, and misconceptions about the ischemic disorders of the optic nerve head, as is evident from the numerous names used to describe anterior ischemic optic neuropathy and the controversy about its pathogenesis.

One common and dangerous misconception is that anterior ischemic optic neuropathy is a rare condition. This lack of awareness has resulted from insufficient information on the subject, and unfortunately, leads to many patients with anterior ischemic optic neuropathy being misdiagnosed, particularly when they present for the first time with optic atrophy. Even when these patients are correctly diagnosed during early stages of the disease, the condition is almost always considered to be untreatable, and the patients are sent away with the advice that they should accept the visual loss as a natural calamity or "act of God". Recent studies, however, have indicated that a significant number of patients can be helped to regain fairly useful visual function, provided they are diagnosed early enough and adequate therapy instituted immediately. Recent studies have also suggested that anterior ischemic optic neuropathy, glaucoma, and low-tension glaucoma represent ischemic disorders of the anterior part of the optic nerve—the ischemia being of an acute and sudden onset in anterior ischemic optic neuropathy and of a chronic nature in the other two.

In this book, I have not only tried to describe fully the clinical picture, diagnosis, and management of anterior ischemic optic neuropathy, but also have laid out in some detail, the basic background information which has led us to a better understanding of this by no means uncommon disorder. The subjects discussed include the vascular pattern and histology of the optic nerve head in health and ischemia, and the pathogenesis of anterior ischemic optic neuropathy—information which has shed a significant light on the pathogenesis of a variety of visual field defects and of the optic disc cupping seen not only in anterior ischemic optic neuropathy but also in glaucoma and low-tension glaucoma. As anterior ischemic optic neuropathy, like optic disc edema, is not a disease in itself but a manifestation of a large number of systemic cardiovascular diseases and some ocular disorder (a fact not generally appreciated up to now), a brief account of these disorders has been considered desirable for a better understanding of their association with anterior ischemic optic neuropathy. Even though it is impossible to cover the entire literature, an attempt has also been made to review relevant literature on the various topics discussed in this book, to provide historic background information, and to place the present studies in their true perspective. I hope that the information provided in this book may help clinical ophthalmologists, neurologists, and internists to become more aware of anterior ischemic optic neuropathy and to assist them not only in its early diagnosis and better management, but also the other vascular disorders of the optic nerve head. I also hope that it will be of assistance to all those interested in the study of vascular disorders of the optic disc and nerve from a purely scientific viewpoint.

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Acknowledgements

It is a pleasure to acknowledge my indebtedness to many ophthalmologists for referring patients to me and to a host of colleagues for their invaluable help in this study—it would be invidious to make special mention of any one of them. I also wish to thank my wife, SHELAGH, for her help in the preparation of this manuscript, to Mrs. MARIA WARBASSE and Miss ELIZABETH CONKLIN for their secretarial help, to the British Journal of Ophthalmology, the American Academy of Ophthalmology and Otolaryngology, and to Butterworths and Company Publishers Ltd., for permission to reproduce illustrations from my various publications and to the American Journal of Ophthalmology for Figure 13c. I am grateful to the Medical Research Council of Great Britain and the National Institutes of Health of the United States (Program Project Grant No. NS-03354) for their research grants under which this study was carried out.

Contents

Introduction

In anterior ischemic optic neuropathy there is a comparatively sudden loss of vision in the entire eye or in one sector of the field of vision, initially associated with edema of the optic disc, which resolves to optic atrophy within a month or two, leaving a permanent visual defect. A large number of such cases have been reported in the literature, but, although this clinical entity is well-known under different names, its pathogenesis and management have, until recently, been ill-understood. An attempt is made to give a comprehensive clinical description of the condition, its management, and its pathogenesis, based on my own as well as on studies previously reported in the literature.

Terminology

This condition has been given different eponyms by various authors because its pathogenesis is controversial:

1. Optic neuritis [81, 454],
2. Acute optic neuritis of hypertension or arteriosclerosis [58, 59, 124, 125],
3. Arteriosclerotic papillitis [124, 125, 329, 339, 342, 473],
4. Papillary apoplexy [458],
5. Senile papillitis or senile papillopathy [35],
6. Pseudo-papillitis [342],
7. Vascular pseudo-papillitis [173, 182, 183, 185, 186, 201, 398],
8. Optico-malacia [325],
9. Infarction of the optic nerve [151],
10. Ischemic retrobulbar neuritis [70, 71],
11. Ischemic neuritis of Papilla [548],
12. Ischemic papillopathy [471],
13. Acute ischemia of the disc [498],
14. Ischemic edema of the disc [40, 309],
15. Ischemic optic neuritis [44, 285],
16. Ischemic optic neuropathy [88, 388].

The most popular term in the European literature has been "Vascular pseudo-papillitis". As will be evident from the pathogenesis of this condition, perhaps the most suitable term is "Anterior Ischemic Optic Neuropathy" because the condition is ischemic, involves both the optic nerve head and retrolaminar optic nerve (hence terms defining it as a disease only of the optic disc are not correct), is noninflammatory (therefore all terms with the suffix -itis are incorrect), and there is nothing "pseudo-" about it.

Part I Pathogenesis

A proper understanding of the pathogenesis of anterior ischemic optic neuropathy would make its clinical pattern and management easier to follow. A brief account of the anatomy and blood supply of the anterior part of the optic nerve, which consists of the optic nerve head and retrolaminar optic nerve, is an essential prerequisite. As far as the arterial blood supply of the optic nerve is concerned, the optic nerve head and retrolaminar region form a single unit. Hence, it is appropriate to study their structure and blood supply together.

A. Structure of the Anterior Part of the Optic Nerve

This has been discussed in detail elsewhere [254, 265]. Most authors divide the optic nerve head into the retinal, choroidal, and scleral parts, from the front backwards. For descriptive purposes, I have divided the optic nerve head into the following three parts (Figs. 1, 34) [250].

a) Surface Nerve Fiber Layer

This is the most superficial layer, containing the compact optic nerve fibers as they converge here from all parts of the retina and bend backward. The surface nerve fiber layer is covered by the inner limiting membrane of Elschnig, which is composed of astrocytes and which separates the nerve fiber layer from the vitreous [7, 465].

b) Prelaminar Region

This region has been called glial, choroidal, or, more commonly, the anterior part of the lamina cribrosa [6, 61, 144, 265, 354, 573, 575], resulting in a certain amount of confusion. Sometimes even the very existence of this glial region, as a distinct entity, has been ignored [575].

The prelaminar region consists of nerve fibers arranged in bundles surrounded by tube-like glial channels, formed by specialized astrocytes ("spider cells" [6, 575]). The loose glial tissue between the nerve fiber bundles forms trabeculae. Capillaries are located within the glial septa. A narrow, perivascular, connective tissue space accompanies most of the capillaries [6]. The capillaries are surrounded by a glial limiting membrane, built up from the foot-plates of the glial cells [265].

WOLTER [575] described the presence of a shallow, cap-like "wicker basket" (composed of the "spider cells" lying in this part of the optic nerve head) which is closely connected to the lamina cribrosa at its base, with its rounded convexity towards the vitreal surface of the optic nerve head. According to WOLTER, the basket acts as an important supporting, protective, and nutritive organ to the nerve fibers. In our studies we did not observe an anterior limit of this basket [265]. The only connective tissue seen in this part is that accompanying the capillaries [6, 265]. WOLTER [575] described glial fibers surrounding both the nerve fiber bundles and the individual nerve fibers in the bundle; ANDERSON [6], in studies with an electron-microscope, found that while the bundles are surrounded by glial cells, only an occasional astrocyte crosses through the bundle at right angles to the nerve fibers.

At its edge the prelaminar region is separated by a layer of glial tissue from the adjacent deeper layer of the retina ("Intermediary tissue of Kuhnt" [326]) and from the adjacent choroid ("Border tissue of Jacoby" [303]).

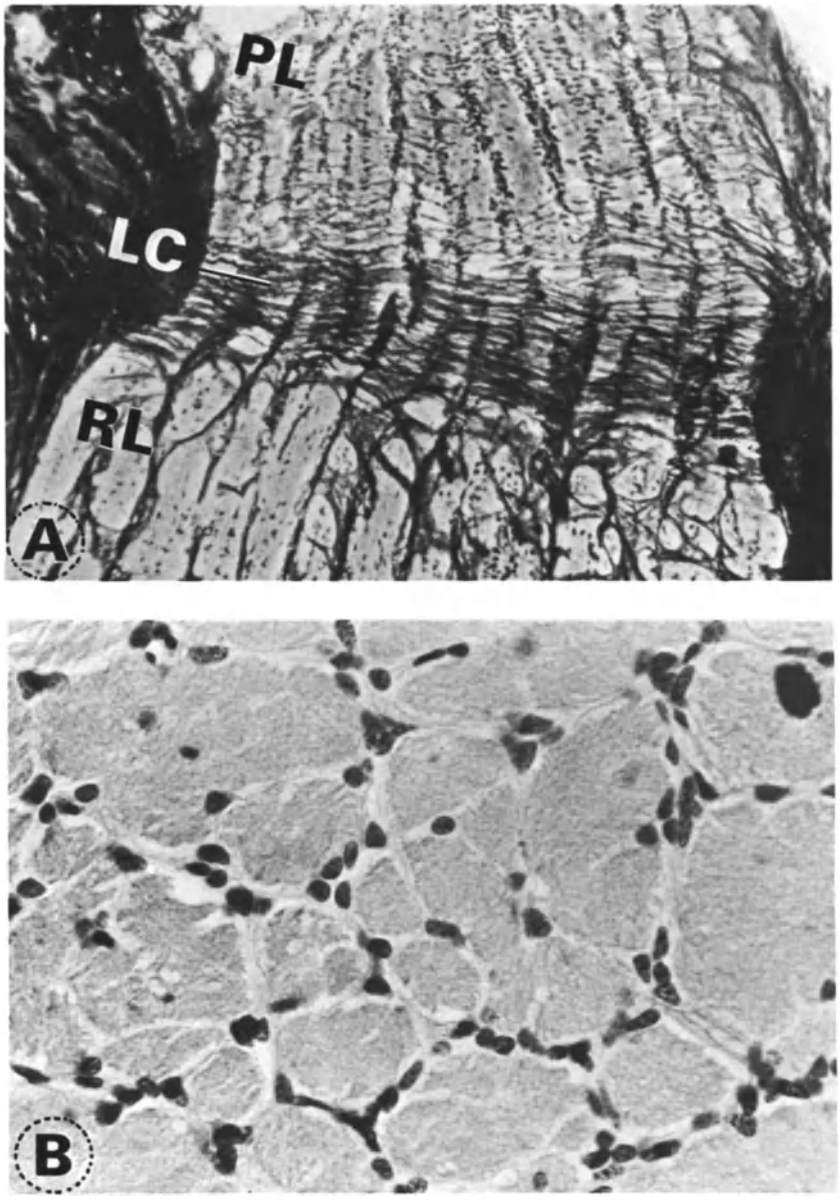

Fig. 1 A–D. Histological section of the optic nerve head and adjacent retrolaminar optic nerve in rhesus monkeys. A) Longitudinal section (*LC* Lamina cribrosa, *PL* Prelaminar region, *RL* Retrolaminar region). B, C, D) Transverse sections in (B) prelaminar, (C) lamina cribrosa, and (D) retrolaminar regions

The optic nerve fibers make a 90° bend and their main support is the glial tissue of the prelaminar region.

c) Lamina Cribrosa Region

This region has been described as the scleral or posterior part of the lamina cribrosa, which, as mentioned previously, is confusing terminology. I have restricted the term *lamina cribrosa* to only this part of the optic nerve head.

The lamina cribrosa region forms a band of dense, compact connective tissue that bridges across the scleral canal. In addition to an opening in the center for the central retinal vessels, this band contains many oval or rounded open-

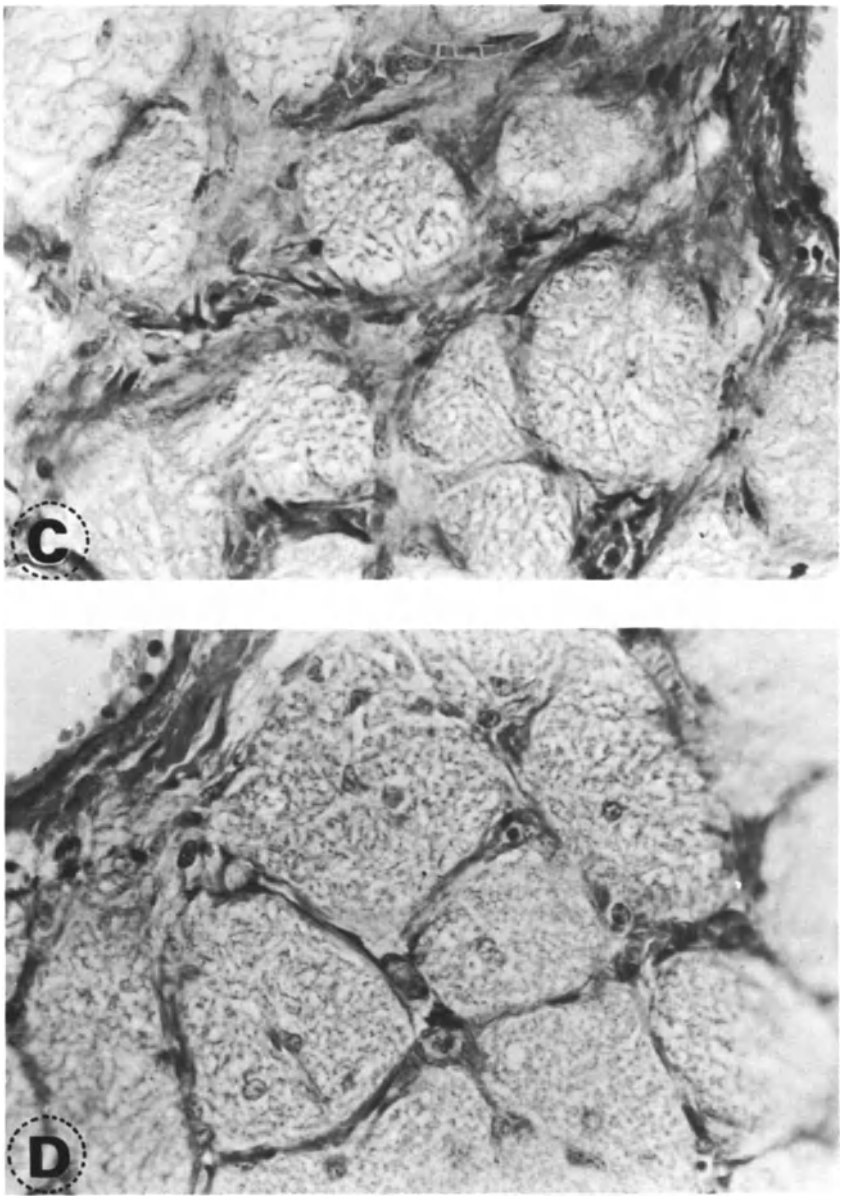

Fig. 1 (continued)

ings for the transmission of nerve fiber bundles. The lamina cribrosa shows a lamellar nature, with connective tissue alternating with glial sheets [6, 573]. Posteriorly the connective tissue sheets become more and more prominent. Connective tissue septa of the retrolaminar part of the optic nerve are attached to the posterior surface of the lamina cribrosa. WOLFF [573] and HOGAN *et al.* [282] found a large amount of elastic tissue in the lamina cribrosa, but ANDERSON [6] found it varied greatly from one eye to another. The openings in the lamina cribrosa are lined by astrocytes, which form a continuous glial membrane that surrounds each nerve fiber bundle, as in the prelaminar region. Thus nerve fiber bundles are separated from adjacent con-

nective tissue. Each trabecula has a capillary in its center. Most authors include the prelaminar region in their description of the lamina cribrosa.

The border tissue of Elschnig, which is more strongly developed on the temporal as compared to the nasal side, separates the sclera from the nerve fibers and is composed of dense collagenous tissue, with many glial and elastic fibers and some pigment [470]. It continues forward to separate the choroid from nervous tissue.

The lamina cribrosa and the prelaminar regions, throughout their entire thickness, are pierced centrally by the central retinal vessels with their accompanying connective tissue. The latter forms a cylindrical sheath surrounding the vessels.

The glial framework occupies virtually the entire optic nerve head and seems to account for more than half its volume [6].

The capillaries in the optic nerve head, as in the retina [110, 301, 340, 341, 493], other parts of the optic nerve [5, 10], and in the central nervous system [21, 401, 456, 514, 574] have tight junctions between the adjacent endothelial cells, without fenestration [6]. These tight junctions may be responsible for the retinal-blood and blood-brain [456] barrier.

d) Retrolaminar Part of the Optic Nerve

This part of the optic nerve is enclosed in a thick sheath composed of the dura, arachnoid, and pia mater. The nerve fiber bundles lie in polygonal spaces formed by the connective tissue septa. The septa are attached to the pia on the surface, to the envelope around the central retinal vessels centrally, and to the lamina cribrosa in front. They contain blood vessels. As in the rest of the central nervous system, at the neuroectodermal-mesodermal junction the nerve fibers are always separated from collagenous tissue and blood vessels by an astroglial layer throughout the course of the optic nerve. Within the nerve fiber bundles lie astrocytes (which form the supporting glial framework), rows of oligodendroglia (responsible for the formation of myelin sheaths), and scattered microglial cells (reticuloendothelial cells); the latter are also seen in other parts of the optic nerve. The nerve fibers in this part are myelinated, whereas in the optic nerve head and retina, they are unmyelinated. The myelin sheaths stop shortly behind the lamina cribrosa. The absence of myelin sheath may be responsible for the smaller diameter of the optic nerve head compared to the retrolaminar optic nerve.

B. The Blood Supply of the Anterior Part of the Optic Nerve

I have discussed this subject fully elsewhere [245]. The pattern presented here is based on my studies in human eyes (neoprene latex injection in 100 eyes, serial histologic sections of 10 optic nerves and eyeballs, and fluorescein fundus angiography in about 500 eyes), and my experimental studies in rhesus monkey eyes (fluorescein fundus angiography and latex injection studies in over 200 eyes).

I would like to stress that *the pattern of blood supply varies greatly between individuals*. The following pattern usually is seen in most individuals. The blood supply in different parts of the optic nerve head is discussed using the divisions described for structure.

1. Arterial Supply

a) Lamina Cribrosa Region

Centripetal branches from the short posterior ciliary arteries and, in a few cases, by the so-called circle of Zinn and Haller supply this region in its entirety. I want to emphasize that a typical circle of Zinn-Haller is an uncommon finding and, when present, is quite often an incomplete circle; this finding also has been confirmed by others [354]. ANDERSON [8] never found this circle. It is unfortunate that the circle of Zinn and Haller is usually the only structure mentioned when the blood supply of the optic nerve head is discussed, attaching tremendous significance

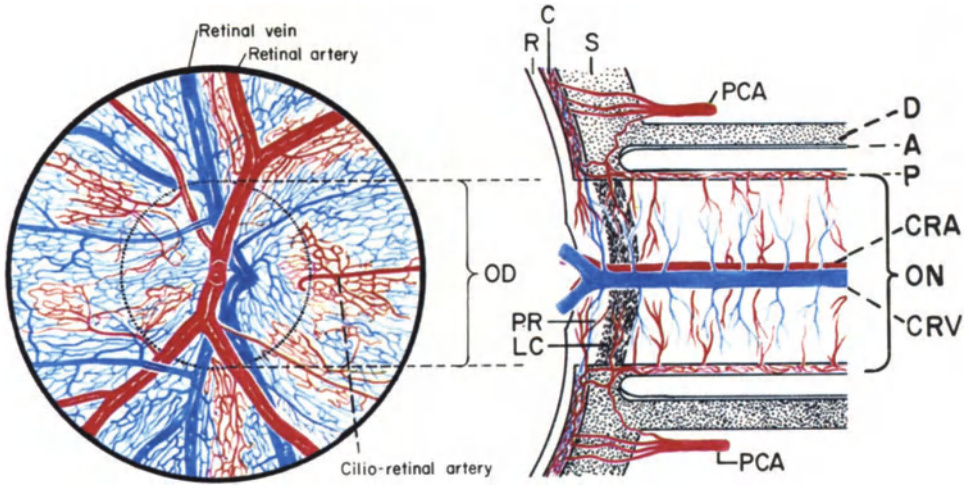

Fig. 2. Diagrammatic representation of blood supply of the optic nerve head:

A	Arachnoid	*D*	Dura	*P*	Pia
C	Choroid	*LC*	Lamina cribrosa	*PCA*	Posterior ciliary artery
CRA	Central retinal artery	*OD*	Optic disc	*PR*	Prelaminar region
CRV	Central retinal vein	*ON*	Optic nerve	*R*	Retina
				S	Sclera

to this uncommon structure. This reflects the widely-prevailing ignorance about the vasculature of this part of the optic nerve.

The blood vessels lie in the fibrous septa and form a dense capillary plexus. The central retinal artery gives no branch in this region.

b) Prelaminar Region

This region is supplied mainly by centripetal branches from the peripapillary pre-choriocapillaris choroidal vessels with no communication between the capillaries in the optic nerve head and peripapillary choriocapillaris. This choroidal supply to this region has been further confirmed by other workes [8, 273, 354, 532]. The distribution of these vessels, as revealed by fluorescein angiography, is sectoral (Fig. 3). Vessels in the region of the lamina cribrosa may also contribute to the blood supply in this region. Angiographic studies strongly suggest that the temporal part of this region is the most vascular and receives maximum contribution from the adjacent peripapillary choroid (Figs. 4–6). ERNEST and ARCHER [158], based on fluorescein angiography in one patient with a subtotal loss of peripapillary choroid and on a few questionable experiments on monkey eyes, concluded that the peripapillary choroid does not significantly contribute to the vasculature of the optic nerve head in man. My results, based on studies of many hundreds of eyes, completely refute their conclusions. Their finding represents one of the rare variations seen in the pattern of the blood supply of this region; however, a rare occurrence does not constitute a classic pattern. I have observed more than one similar instance in my studies. The central retinal artery does not contribute branches to this region.

c) Surface Nerve Fiber Layer

Blood to this area is supplied mainly by branches of the retinal arterioles. These branches commonly arise from the main retinal arterioles in the circumpapillary region and less often on the disc. Capillaries on the surface of the disc are continuous with capillaries of the peripapillary retina and with the long radial peripapillary capillary network described by MICHAELSON and CAMPBELL [387], TOUSSAINT *et al.* [539] and HENKIND [271]. On the disc the capillaries usually

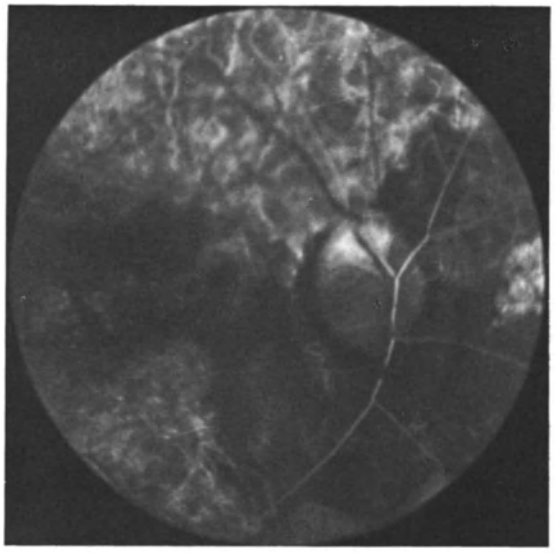

Fig. 3. Fluorescein fundus angiogram of a normal human right eye, showing sectoral filling of the choroid and the adjacent prelaminar region of the optic nerve head

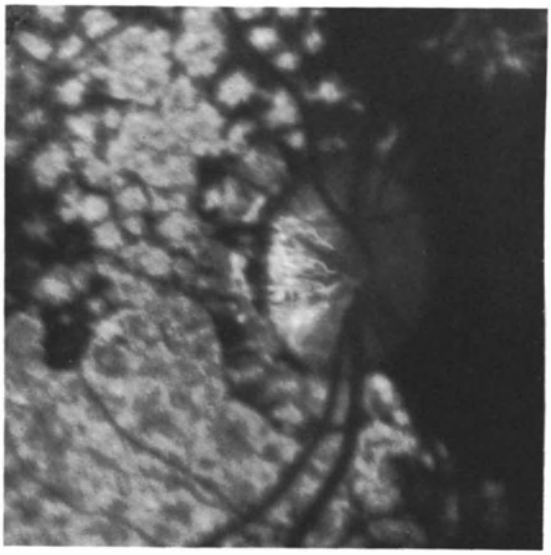

Fig. 4. Fluorescein fundus angiogram of right eye of a monkey during the preretinal-arterial phase, showing filling of temporal half of the choroid and prelaminar vessels in temporal part of the optic disc

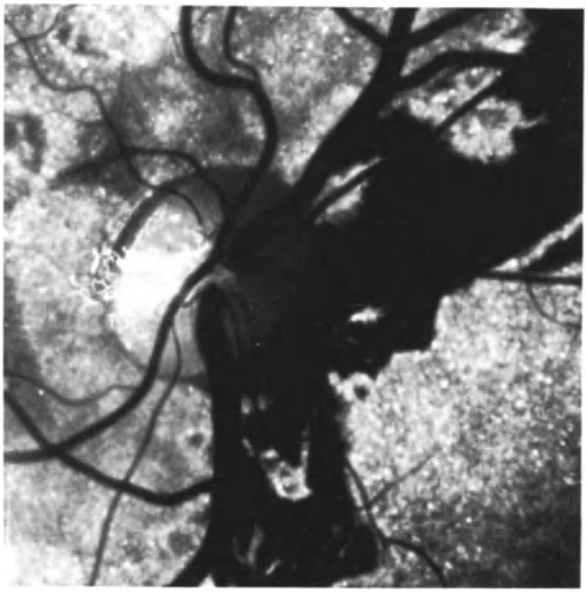

Fig. 5. Fluorescein fundus angiogram of right eye of a monkey after experimental occlusion of the central retinal artery in the orbit. The lateral posterior ciliary artery supplies the temporal half and the superior nasal part of the choroid. Filling of the medial posterior ciliary artery is seen in the inferior nasal sector of the choroid. The border zone between the two and the nasal peripapillary region is still not filled. Part of the optic disc supplied by the lateral posterior ciliary artery is filled

are venous in nature and drain into the central retinal vein or its tributaries. The capillaries in this region are continuous with those in the prelaminar region.

It is not uncommon to find vessels of choroidal origin, derived from the adjacent prelaminar part of the disc, in the surface nerve fiber layer. These vessels are seen most often in the temporal sector of the disc, and one may enlarge to form the cilioretinal artery.

d) Retrolaminar Region of the Optic Nerve

On the basis of blood supply, this region forms an integral part of the optic nerve head. It is

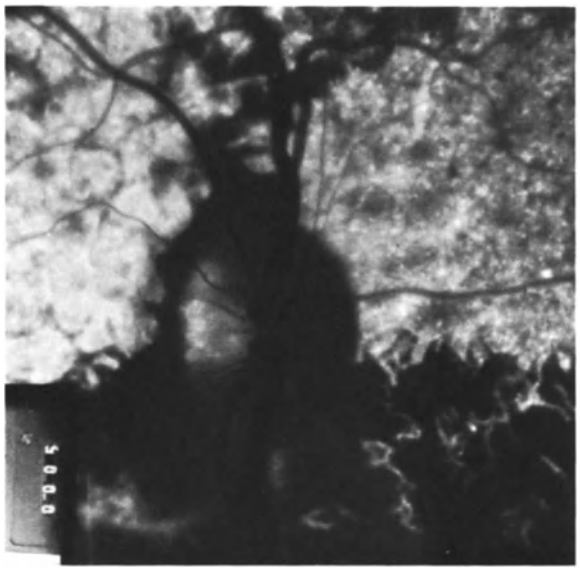

Fig. 6. Fluorescein fundus angiogram of right eye of a monkey after experimental occlusion of the central retinal artery in the orbit, showing filling of the upper half of the choroid and optic disc, with a well demarcated horizontal border

supplied mainly by centripetal branches from the pial vessels, which most often are recurrent pial branches from the peripapillary choroid, although some are from the circle of Zinn (or usually its substitute, i.e., direct branches from the short posterior ciliary arteries [241]). Although in 75 percent of optic nerves the central retinal artery gives out centrifugal branches during its intraneural course in the optic nerve [240–244, 503], in many instances there may be no branch from the artery in the region immediately behind the lamina cribrosa. In such cases the pial supply from the posterior ciliary arteries may be the only or the major source of blood to the retrolaminar region.

From this description of the blood supply of the optic nerve head and retrolaminar region, it is evident that the *posterior ciliary arteries are the only source to 'a' and 'b' and the main (if not the only) source of 'd', and they may supply the temporal part of 'c'*. Other workers also have described the choroid and posterior ciliary arteries as the major source of blood to the optic nerve head [34, 159, 273, 354]. The posterior ciliary arteries have a segmental distribution, the main artery supplying the nasal or temporal half or the superior or inferior half of the choroid and optic nerve head [247, 249, 259]. The short posterior ciliary arteries may supply smaller sectors. All capillaries in the optic nerve head are interconnected, being continuous posteriorly with those of the retrolaminar region and anteriorly with the adjoining retina but no connection is seen with the choriocapillaris.

I have never seen the so-called "central artery of the optic nerve" [174–177, 180, 571] in any of my specimens [238, 239, 503]. This experience has been confirmed by others [26, 513].

Usually there are two to three posterior ciliary arteries, arising from the ophthalmic artery [239], that supply the choroid and optic nerve head (Fig. 7). These are designated medial and lateral posterior ciliary arteries, depending on their relationship to the optic nerve near their site of entry into the sclera. The main lateral or medial posterior ciliary artery usually supplies half of the choroid and optic nerve head, the distribution being either vertical (Figs. 4, 5, 24n, 27b) or horizontal (Fig. 6) [247]. If there are three posterior ciliary arteries, a smaller sector may be supplied by each artery (Fig. 3). Smaller divisions of the main posterior ciliary arteries would supply smaller sectors.

Venous Drainage. The optic nerve head and retrolaminar region are drained by the central

retinal vein. The prelaminar region also drains into the choroidal veins and, via these channels, the central retinal vein communicates with the choroidal veins.

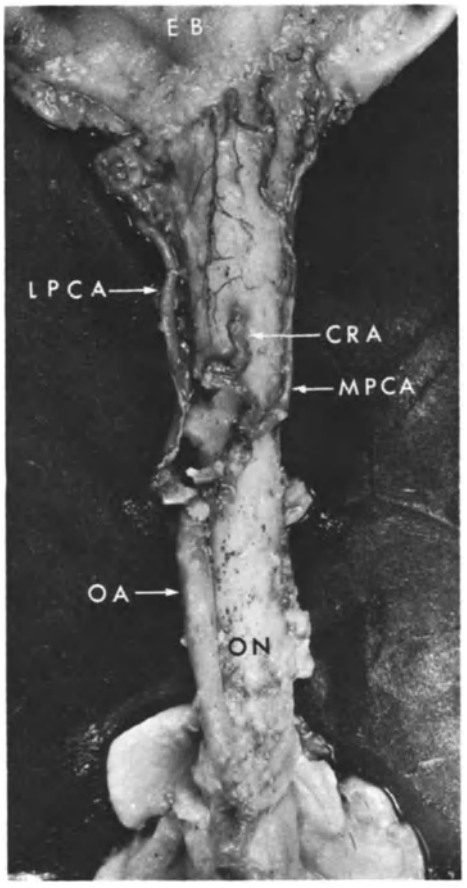

Fig. 7. Photograph of inferior surface of human right eyeball (*EB*) and optic nerve (*ON*), showing ophthalmic (*OA*), central retinal (*CRA*), lateral posterior ciliary (*LPCA*) and medial posterior ciliary (*MPCA*) arteries

C. Fluorescein Angiography Pattern of Normal Optic Disc

Fluorescein angiography plays an important role in studies of the blood supply of the optic nerve head in health and disease. It is therefore essential to know the normal pattern of fluorescence of the optic disc. The subject has been discussed fully elsewhere [245, 251, 262].

Usually, the optic disc starts to show fluorescence before the retinal arteries show any filling, because the posterior ciliary artery (and choroidal) circulation is slightly faster than the retinal arterial circulation (Figs. 3, 4). However, the reverse is also common. Frequently, a large number of vessels in the prelaminar region fill from the adjacent choroid. In the disc this initial filling usually is prominent in the temporal sector.

Preretinal-arterial or initial filling of the optic disc represents the posterior ciliary artery's contribution to the optic nerve head; it is due most often to prelaminar filling, but also is frequently due to the filling of vessels in the lamina cribrosa, which is a very vascular structure. ERNEST and ARCHER [158] attributed preretinal-arterial fluorescence of the optic disc to fluorescein in the retrobulbar vessels and theorized that "the greater the atrophy (of the optic disc) the more the fluorescence will be transmitted. This is because the decrease in the plexus of small vessels—and thus the amount of blood in the optic nerve—may offer less impediment to the light from the extraocular vasculature which does contain fluorescein." The interpretation and assumption of ERNEST and ARCHER seem to be wrong, because a) the connective tissue of the lamina cribrosa is opaque like sclera, and one does not expect to see immediate and significant fluorescence from retrobulbar tissue; b) fluorescence of the optic disc always is reduced in optic atrophy and frequently is nonexistent [61, 245, 262, 263, 412].

Fluorescence of the optic disc peaks at the early retinal arteriovenous phase. The peak is due in part to the contribution by the posterior ciliary artery to the optic disc, but is due most often to filling of the dense capillary plexus in the surface nerve fiber layer, which represents a retinal arterial contribution (Fig. 8) [251].

Fluorescence of the disc then fades rapidly, but a certain amount of well-defined staining of the optic disc is seen in the late phases (10–15 minutes after the dye is injected), usually more marked near the margin of the disc, and prob-

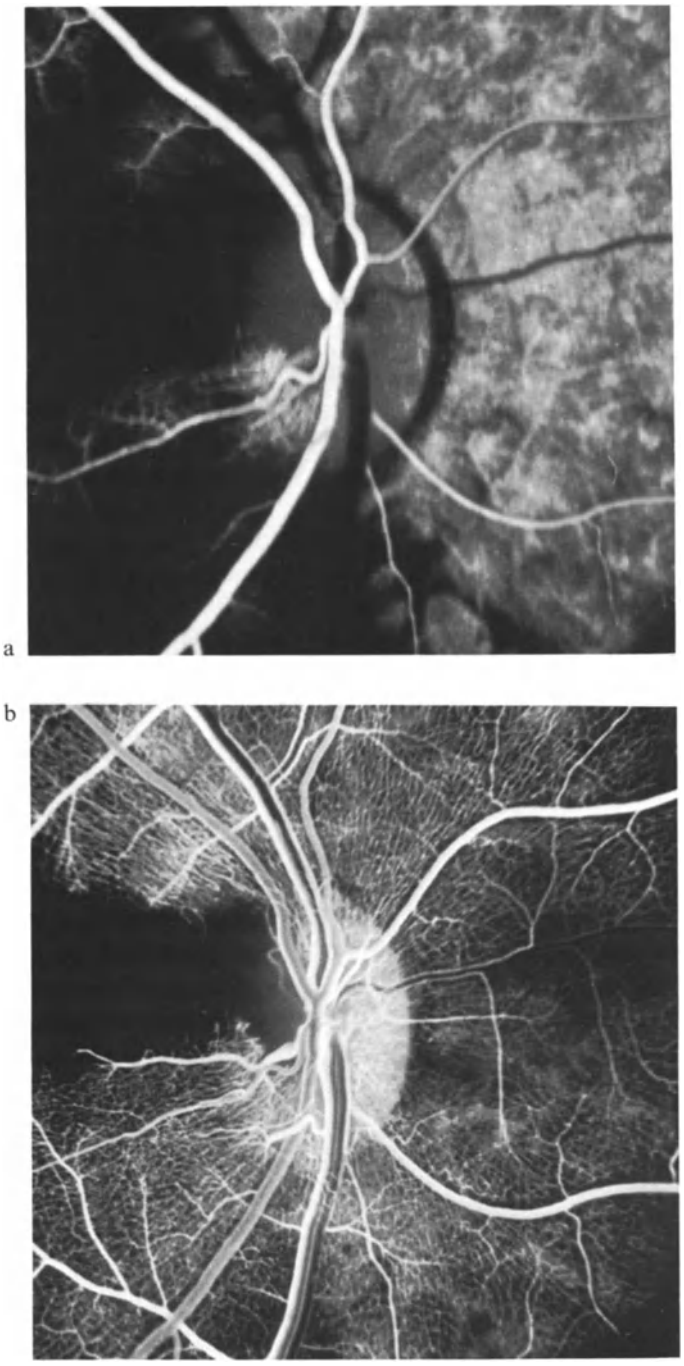

Fig. 8a and b. Fluorescein fundus angiograms of a rhesus monkey after experimental occlusion of the lateral posterior ciliary artery: Note the complete absence of filling of the temporal part of choroid and optic disc (a) as well as of the retinal vasculature in a sector of the retinal capillary bed supplied by a cilioretinal artery on the temporal side (b)

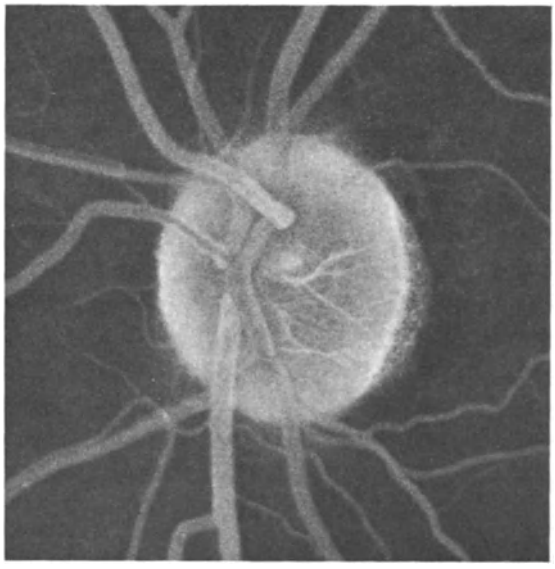

Fig. 9. Fluorescein fundus angiogram of a human eye showing normal late fluorescence pattern of the optic disc

ably because of a diffusion from the choroid of the dye which stains the connective tissue of the lamina cribrosa in a manner similar to that seen in the sclera (Fig. 9).

Fluorescein angiographic studies of the optic disc have shown that the temporal part of the optic disc, in spite of its paler appearance, usually is more vascular than the nasal part. This indicates that redness is not a true index of the vascularity of the normal disc [245, 251, 262]. Possible explanations for this phenomenon are discussed elsewhere [245, 251].

D. Pathogenesis of Anterior Ischemic Optic Neuropathy

Many theories have been proposed to explain the pathogenesis of anterior ischemic optic neuropathy.

Review of the Literature

The site of the lesion in anterior ischemic optic neuropathy is thought to lie in the optic nerve, although some authors considered it to be due to involvement of the retina. It is almost universally agreed that it is due to interference with the circulation of either of these structures. SKILLERN and LOCKHART [505], however, thought that anterior ischemic optic neuropathy in diabetes is due to the toxic effect of prolonged hyperglycemia and failure of glucose utilization, and did not consider arterial circulatory disorders a significant factor.

Most authors, while describing a circulatory lesion in the optic nerve, have made nonspecific, vague statements as to the exact lesion. It was considered to be a circulatory disturbance in the optic nerve [309, 433] due to pathologic changes [193, 296, 297, 457, 515] or occlusive disease [40, 81, 329, 473] of the small vessels of the nerve. Occlusion of the small nutrient vessels of the optic nerve was generally considered to be due to arteriosclerosis [39, 76, 119, 183, 193, 274, 296, 297, 352, 359, 433, 457, 515, 543]; others thought the change mainly affected the central retinal artery [1, 43, 227, 466] although IGERSHEIMER [297] and RINTELEN [457] were of the opinion that arteriosclerosis of the central retinal artery has little effect on the optic nerve. The possibility that arteritis of vessels of the optic nerve and retina is responsible for this has also been mentioned [506]. Some authors have stated that these small vessel changes are located in the anterior retrobulbar part of the optic nerve [39, 68, 300, 462]; while according to others these are in the vessels of the optic disc [103, 170, 382, 471]. MEADOWS [384] mentioned that there is ischemic damage to the papilla and anterior portion of the optic nerve.

FRANÇOIS and co-workers [173, 180, 183, 185, 186] and others [441, 442, 473] postulated that anterior ischemic optic neuropathy was due to occlusion of a "central artery of the optic nerve", an artery whose existence they assumed. According to them, this artery arises directly from the ophthalmic artery, proximal to the origin of the central retinal artery [174], enters the optic nerve behind the central retinal artery, and divides into anterior and posterior branches on reaching the center of the optic nerve; the anterior and posterior branches run to the lamina cribrosa and

optic foramen respectively in the center of the optic nerve. The anterior branch anastomoses with the circle of Zinn and Haller. They state that it is "impossible to explain the symptoms without the presence of an individualized axial arterial system in the optic nerve" and concluded that "a central optic nerve vascular system always exists" [180]. My anatomic studies on the blood supply of the optic nerve and branches of the ophthalmic artery in about 100 human specimens [238, 239, 241, 243, 502, 503] and those of BEAUVIEUX and RISTITCH [26] and STEELE and BLUNT [408] failed to reveal a "central artery of the optic nerve" corresponding to the description mentioned by FRANÇOIS *et al.* [174, 175, 176, 177, 180]. Hence, occlusion of the "central artery of the optic nerve" cannot be significant in the etiology of anterior ischemic optic neuropathy.

Interference with the blood supply to the retina as the cause of anterior ischemic optic neuropathy has been considered by some workers [44, 416, 506] because central retinal artery pressure fell, as judged by ophthalmodynamometry. UHTHOFF [543] and SMITH and GREEN [506] thought it was due to the involvement of vessels in both the optic nerve and retina.

There are many histopathologic studies on patients with anterior ischemic optic neuropathy [79, 88, 94, 103, 105, 221, 272, 275, 322, 325, 363, 364, 369, 382, 462, 490, 511, 576]. The area of greatest involvement in the optic nerve is at the retrolaminar and optic nerve head (mentioned as lamina cribrosa in reports pertinent to the lamina cribrosa and prelaminar regions) [88, 103, 272, 322, 325, 363, 364, 462, 511]. The lesion begins with infarction and evolves through liquefaction necrosis (in four weeks, Fig. 13a) [364], a reactive increase in astrocytes and lymphocytes in eight weeks [103], and finally to retrolaminar fibrosis in four months (Fig. 13c) [272]. The involved part of the optic nerve usually is well-defined and circumscribed. All but two of these reports are of patients with temporal arteritis; the remaining two are of anterior ischemic optic neuropathy due to arteriosclerosis [88, 322]. In 16 reports of temporal arteritis [79, 94, 103, 105, 221, 272, 275, 325, 363, 364, 369, 382, 462, 490, 511, 576], the central retinal artery was involved in 11 [88, 94, 103, 105, 221, 325, 363, 369, 462, 511, 576], the posterior ciliary artery in 10 [88, 103, 105, 221, 325, 363, 364, 462, 511, 576], and the ophthalmic artery in 7 [88, 103, 105, 275, 325, 363, 511]. There is only one case in which none of these arteries was involved [272], and this finding was explained as due either to the long-term use of corticosteroids before the patient died, or to the self-limiting nature of the disease. RODENHAUSER [462] is the only investigator to report arteritis in the choroidal arteries and retinal arterioles. KNOX and DUKE [322] reported focal necrosis of the temporal half of the optic nerve head and retrolaminar optic nerve, with some distension of the lamina cribrosa in that region, in a patient with occlusion of the left common carotid artery and generalized arteriosclerosis, two weeks after the onset of visual disturbance. COGAN [88] also reported a case of anterior ischemic optic neuropathy with well-defined infarction of the retrolaminar optic nerve in the entire temporal half (Fig. 13b).

It is interesting to note that ELLENBERGER *et al.* [151] examined 40 optic nerves of people older than 45 years for atherosclerosis and arteriosclerosis and found that changes in the optic nerve vessels were similar to those seen elsewhere in the body, suggesting that the optic nerve vessels were constantly involved in systemic atherosclerosis and arteriosclerosis. In anterior ischemic optic neuropathy, vascular changes in the optic nerve correlated slightly or not at all with those in the retina [296, 433]. WOLTER *et al.* [576] and MACFAUL [363] reported that temporal arteritis involves only the extraocular parts of the short posterior ciliary arteries and not the choroid, which is contrary to the opinion expressed by RODENHAUSER [462].

Various mechanisms for the production of ischemic necrosis in the anterior part of the optic nerve have been postulated. KREIBIG [325] considered it to be due to combined involvement of the axial and peripheral (from short posterior ciliary arteries) vascular system due to occlusion of the ophthalmic artery and short posterior ciliary arteries. SPENCER *et al.* [511] agreed with