

A good understanding of the structure of the optic nerve and topographic localization of the nerve fibers in it from the various parts of the retina is essential for comprehension of various aspects of ischemic optic neuropathy.

The length of the optic nerve varies widely, even between the two eyes of the same person and is 35–55 mm from the eyeball to the chiasma (intraocular part 1 mm, intraorbital part 25 mm, intracanalicular part 4–10 mm and intracranial part 10 mm [1]). For descriptive purposes, the optic nerve can be divided into the following four parts:

1. Optic nerve head
2. Intraorbital part
3. Intracanalicular part
4. Intracranial part

The Optic Nerve Head

In the literature, the ophthalmoscopic term “optic disc” has been applied interchangeably either to the whole or a part of the anterior-most part of the optic nerve head (i.e., the surface nerve fiber layer and the prelaminar region) or to the entire optic nerve head. Similarly the term “papilla” has been used as a synonym for the optic disc or optic nerve head. The term “papilla” was coined by Briggs in 1676 [2] based on an erroneous impression that the normal optic nerve head was elevated like a papilla. Since the structure usually is not elevated above the level of the adjacent retina, lies in the same plane as retina and has in fact a central depression (i.e., the physiological cup) or may even be flat, the term “papilla” is a misnomer. It must, however, be conceded that the appearance of the optic nerve head

shows considerable variations, all of which may be “within physiological limits” (see Chap. 7). I prefer to use the term “optic nerve head”; however, I have retained the term “optic disc”, for two main areas of usage: firstly, in reviews of work by other authors where I am not sure how much of the optic nerve head has been included by them under this term, and secondly, in ophthalmoscopic descriptions of optic nerve head lesions, where it is not possible to be definite as to how much of the nerve head is involved.

The optic nerve head is about 1 mm long and about 1.5 mm (1.18–1.75 mm [3, 4]) in diameter, the vertical diameter being slightly greater than the horizontal – Ishii [5] described the average horizontal diameter as 1.618 mm and the vertical diameter as 1.796 mm. The diameter of the optic disc depends upon the diameter of the choriocleral canal at the level of Bruch’s membrane. The canal is usually conical in shape – the posterior part wider than the anterior part; but it may be cylindrical, and very rarely it may either be of a truncated (or triangular) type with its central part narrowest [6] or an elbow extension type with the central part widest [7]. The ophthalmoscopic configuration of the optic disc and of the physiological cup depends upon the size, shape and direction of the canal, as well as the diameter of the opening in the Bruch’s membrane and scleral canal. The shorter the canal diameter, the smaller is the cup and vice versa. This is because the total optic nerve tissue volume (i.e., the nerve fibers, glial tissue and blood vessels) in all probability does not vary significantly in normal eyes; if the canal is narrow the available space may be just enough to accommodate the tissue, with no physiological cup, but, on the other hand, with a wide canal the extra space may manifest as a physiological cup – the wider the canal, the larger the cup. The shape of the canal and mode of insertion of the optic nerve into the eyeball

may determine the shape of the cup. For example, oblique insertion of the optic nerve results in a different shape of the optic disc and size of the optic disc cup (see Fig. 7.8).

We [8] did histological studies on 12 eyes and optic nerves of adult rhesus monkeys which provided useful information. Most of the histological description in this chapter is based on our study [8], combined with that provided by other studies. For descriptive purposes, the structure of the optic nerve head can be further subdivided into the following three regions from front to back (Figs. 2.1–2.4); however, there is no sharp line of demarcation between these zones of the optic nerve head.

1. The surface nerve fiber layer
2. The prelaminar region
3. The lamina cribrosa region

The Surface Nerve Fiber Layer

This is the most anterior layer of the optic nerve head, containing the compact optic nerve fibers as they converge here from all over the retina and bend to run into the optic nerve (Figs. 2.1–2.6). It is separated from the vitreous by the inner limiting membrane of Elschnig [3, 4] which is composed of astrocytes [8–10] (Fig. 2.7). In the region of the physiological cup, this membrane is often thick and is called the central meniscus of Kuhnt, but is very thin when the cup is large. In addition to these tissues, this layer of the optic nerve head has a large number of blood vessels, consisting of not only a dense capillary network on its surface but also the large retinal vessels and venous tributaries (Fig. 2.8). A conspicuous remnant of the hyaloid artery (“Bergmeister’s papilla”) is very rare on the human disc (Fig. 2.9); however, in my study of rhesus monkeys, I have found it in almost all the eyes, examined both histologically as well as ophthalmoscopically (Figs. 2.4 and 2.10); it has a well-developed muscular coat, with, of course, a superficial coating of the glial tissue.

The region posterior to the surface nerve fiber layer is subdivided into three parts from front backward [8]: (1) pure glial part (prelaminar region), (2) mixed part – a transition zone between the prelaminar and the lamina cribrosa regions, and (3) connective tissue part (lamina cribrosa).

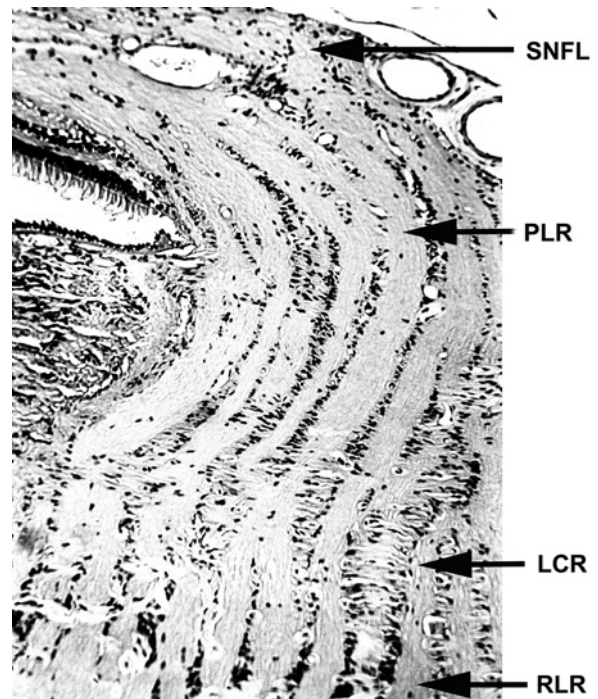


Fig. 2.1 Longitudinal section of a half of the normal human optic nerve showing the region of the optic nerve head and the retrolaminar optic nerve. *LCR* Lamina cribrosa region, *PLR* Prelaminar region, *RLR* Retrolaminar region, *SNFL* Surface nerve fiber layer

The Prelaminar Region

This part of the optic nerve head has been called the glial, choroidal or more commonly anterior part of the lamina cribrosa [8, 11–17] which has created a certain amount of confusion in communication. Sometimes even the very existence of this glial region as a distinct entity has been ignored [11, 12]. In any discussion on pathologic changes in anterior ischemic optic neuropathy, optic disc edema and glaucoma, this is perhaps one of the most important regions of the optic nerve.

This is almost entirely built up by glial tissue and the connective tissue fibers are seen only in connection with the vessels [8]. Glial fibers are much finer than the connective tissue fibers and they still retain a direction perpendicular to the nerve fiber bundles. Centrally, they remain attached to the connective tissue surrounding the central retinal vessels (Fig. 2.11), and peripherally they are attached to the choroid as well as to the elastic membrane (Fig. 2.12). The number of glial cells in this part is enormous; they are markedly flattened in the antero-posterior direction and are packed in dense transverse

Fig. 2.2 Longitudinal section of a normal rhesus monkey optic nerve showing the region of the optic nerve head and the retrolaminar optic nerve. *LCR* Lamina cribrosa region, *PLR* Prelaminar region, *RLR* Retrolaminar region, *SNFL* Surface nerve fiber layer

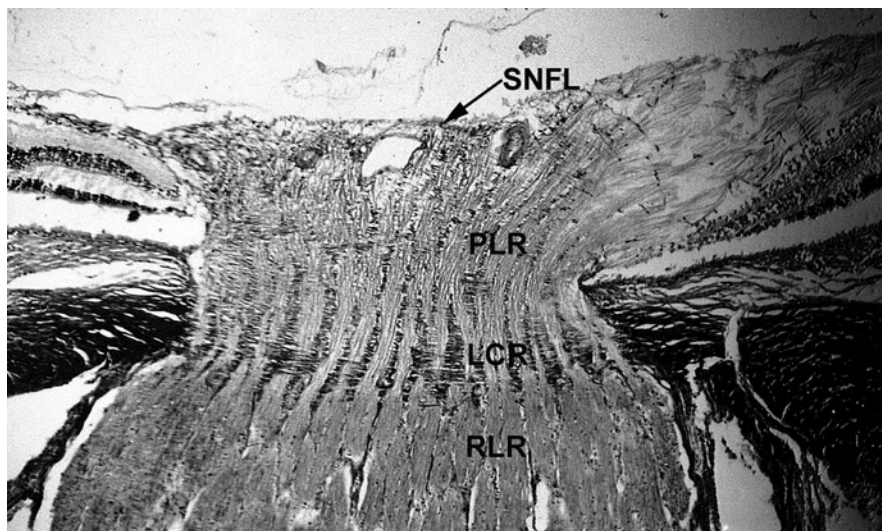


Fig. 2.3 Longitudinal section of a normal rhesus monkey optic nerve showing the region of the optic nerve head and the retrolaminar optic nerve and central retinal artery (A) and vein (V). *LCR* Lamina cribrosa region, *PLR* Prelaminar region, *RLR* Retrolaminar region, *SNFL* Surface nerve fiber layer

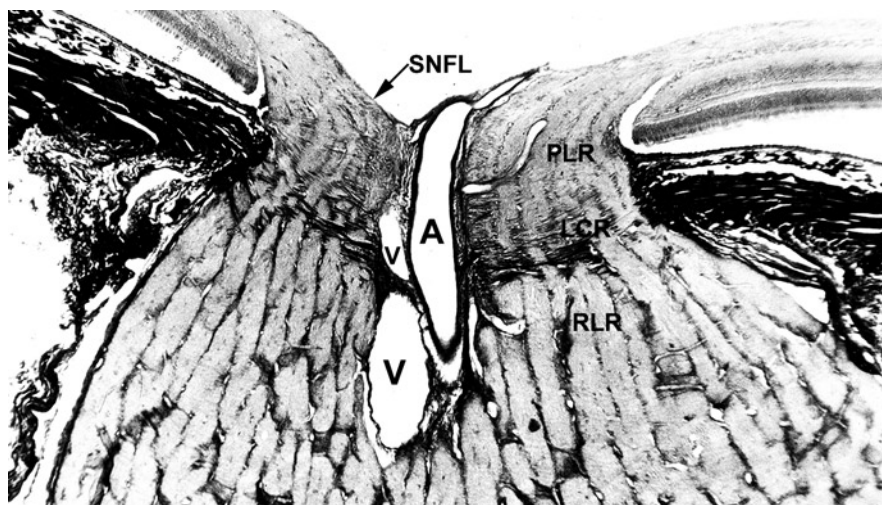


Fig. 2.4 Longitudinal section of a normal rhesus monkey optic nerve showing the region of the optic nerve head and the retrolaminar optic nerve and Bergmeister's papilla (BP). *LCR* Lamina cribrosa region, *PLR* Prelaminar region, *RLR* Retrolaminar region, *SNFL* Surface nerve fiber layer

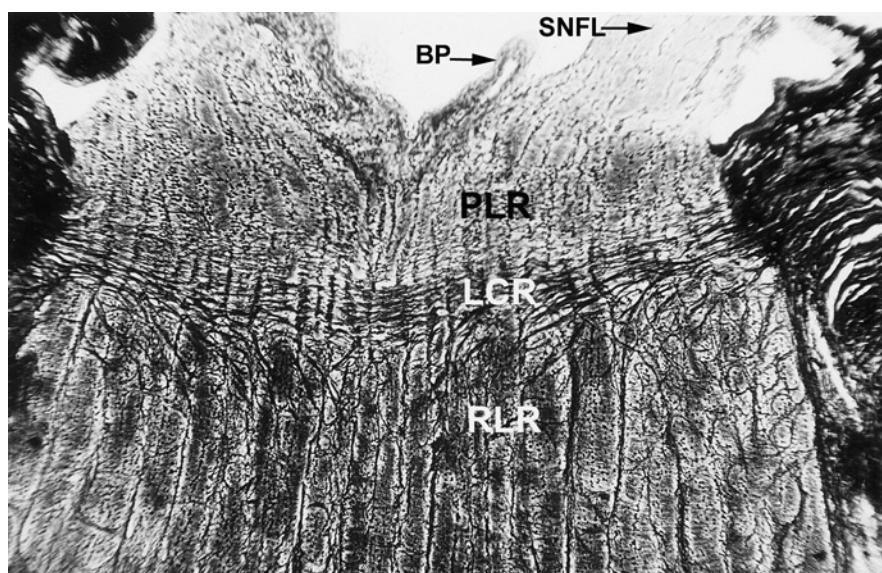


Fig. 2.5 Bundles of the optic-nerve fibers running from the retina to the lamina cribrosa in normal rhesus monkey. (Golgi's stain) *LCR* Lamina cribrosa, *PLR* Prelaminar region, *SNFL* Surface nerve fiber layer

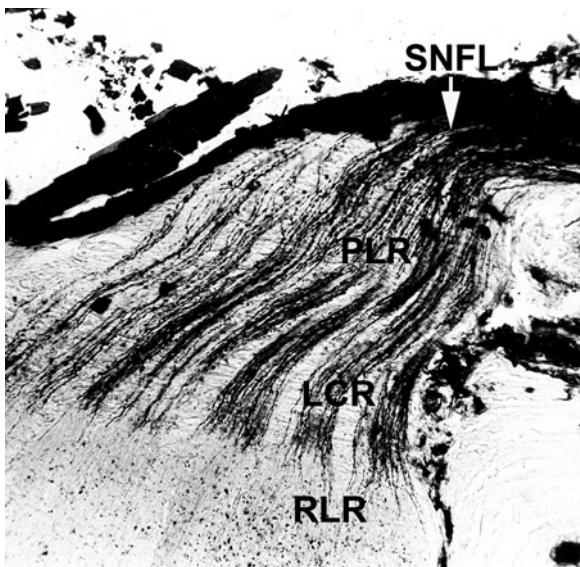
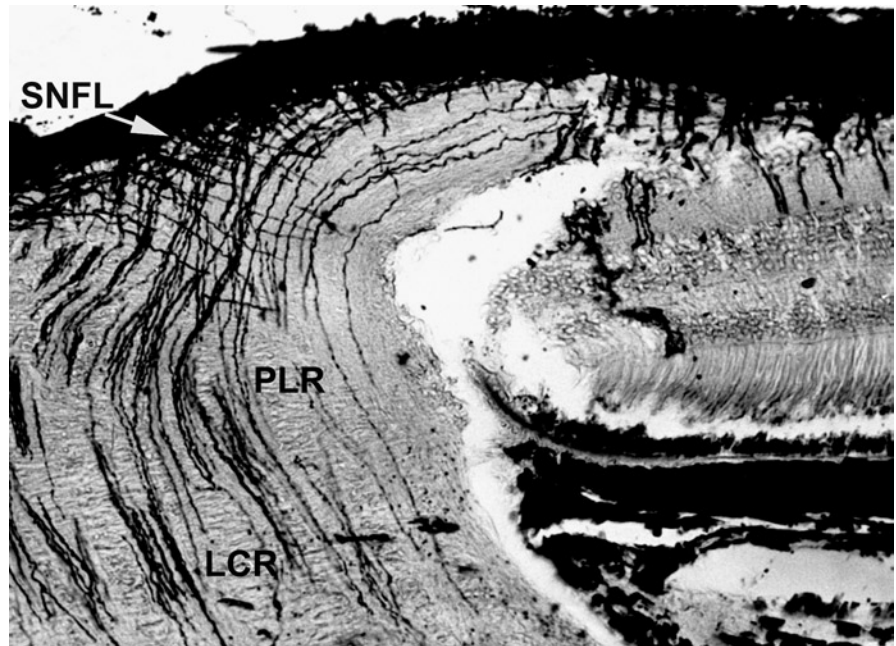


Fig. 2.6 Bundles of the optic-nerve fibers running from the retina to the lamina cribrosa in normal rhesus monkey (Golgi's stain). The nerve fibers are non-myelinated in the retina and prelaminar and lamina cribrosa regions but myelinated in the retrolaminar region. *LCR* Lamina cribrosa, *PLR* Prelaminar region, *RLR* Retrolaminar region, *SNFL* Surface nerve fiber layer (Reproduced from Hayreh and Vrabec [8])

sheets (Figs. 2.11 and 2.13). There may be many capillaries, surrounded by a glial limiting membrane, built up from the footplates of the glial cells (Fig. 2.14).

The prelaminar region consists of optic nerve fibers arranged in bundles (Figs. 2.1–2.6), surrounded by tube-like glial channels formed by specialized astrocytes, “spider cells” [11, 12, 15]. The glial tissue between the nerve fiber bundles forms trabeculae (Figs. 2.15–2.17), and capillaries are located within the glial septa. A narrow, perivascular, connective tissue space accompanies most of the capillaries [15]. Wolter [11, 12] described the presence of a shallow, cap-like “wicker basket”, composed of the “spider cells” lying in this part of the optic nerve head, closely connected to the lamina cribrosa at its base, and with its rounded convexity toward the vitreal surface of the optic nerve head. According to him, the basket acts as an important supporting, protective and nutritive organ to the nerve fibers. In our histological study [8] on the optic nerve head of rhesus monkeys, we did not observe an anterior limit of this basket. The only connective tissue seen in this part of the optic nerve head is that accompanying the capillaries [8, 15]. Wolter [11, 12] described glial fibers surrounding both the nerve fiber bundles and the individual nerve fibers in the bundle. Electron microscopic studies have shown that while the bundles are surrounded by the astrocytes, their long processes extend into the fascicles at right angles to the nerve fibers [18]; Anderson [15], however, found only an occasional astrocyte process going to the nerve

Fig. 2.7 Glial elements at the bottom of the physiological excavation in rhesus monkey (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])

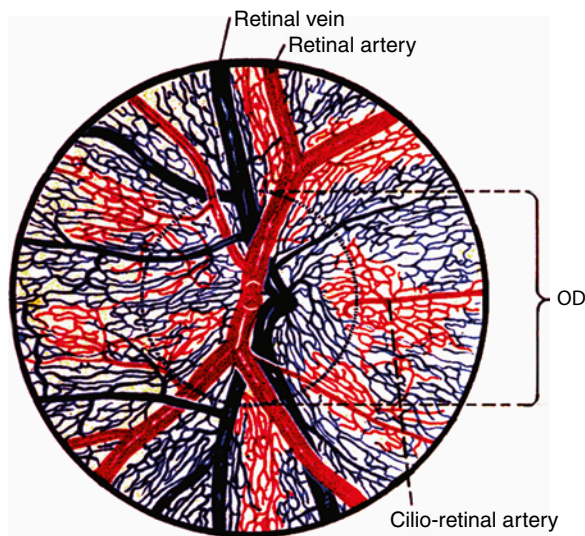
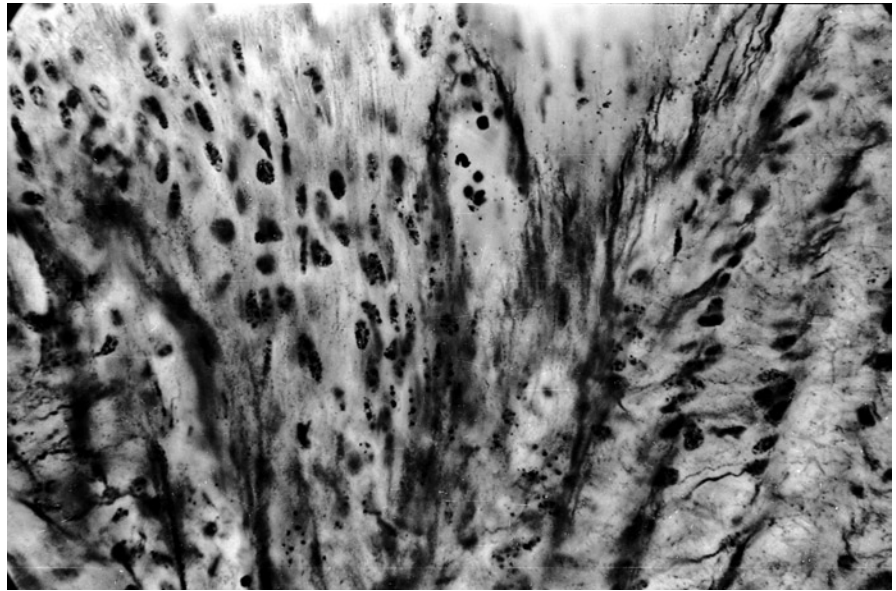


Fig. 2.8 Diagrammatic representation of blood vessels in the surface nerve fiber layer. OD Optic disc

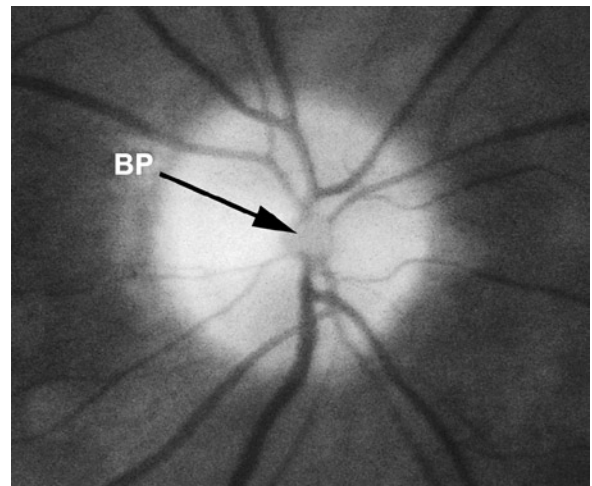


Fig. 2.9 Fundus photograph of a human eye showing obliterated remnant of the hyaloid artery (Bergmeister's papilla BP) at the center of the optic disc

fibers. The glial cells in the prelaminar portion are loose and the arrangement of the glial sheets is lost [8]. It would seem probable that this loose arrangement of the glial framework in the prelaminar portion might play a role in the pathologic swelling of the optic disc (Figs. 2.18 and 2.19).

In the central part exists a central depression of varying degree corresponding to the physiological cup (Figs. 2.12, 2.20 and 2.21). The bottom of this

depression is separated from the vitreous by the inner limiting membrane of Elschnig (Figs. 2.7, 2.20 and 2.21). When the depression does not reach the level of the lamina cribrosa, the central connective tissue sends some anchoring fibers distally to the bottom of the excavation [8] (Fig. 2.20). In other cases the central excavation may reach the lamina cribrosa (Fig. 2.21). In all these instances, the central connective tissue reaches the internal limiting membrane of Elschnig [8].

Fig. 2.10 Obliterated remnant of the hyaloid artery (Bergmeister's papilla – *BP*) at the optic nerve head in a rhesus monkey. (Hortega's stain) *LCR* Lamina cribrosa, *PLR* Prelaminar region, *RLR* Retrolaminar region (Reproduced from Hayreh and Vrabec [8])

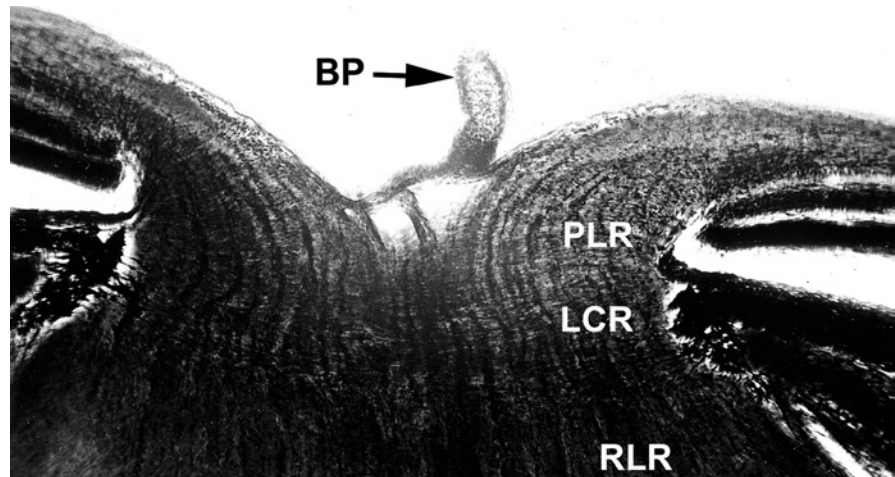


Fig. 2.11 Glial portion of the lamina cribrosa, showing its central attachment to the connective-tissue sheath of the central retinal vessels and the arrangement of glial fibers. (Hortega's stain) (*A*) Artery (Reproduced from Hayreh and Vrabec [8])

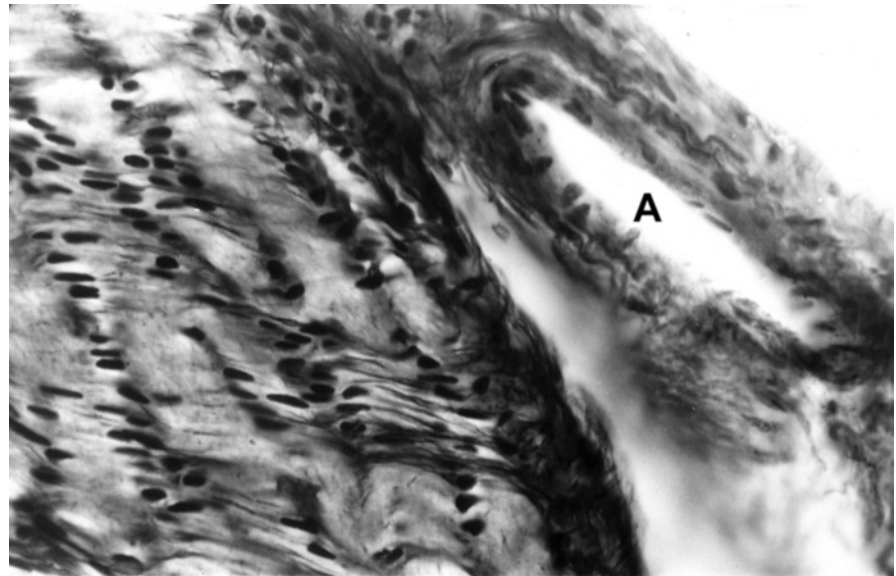


Fig. 2.12 Longitudinal section of a half of the optic nerve head, showing peripheral anchorage of the connective-tissue part of the lamina cribrosa to the sclera, and of the glial part to the choroid and elastic lamina (Bruch's membrane) (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])

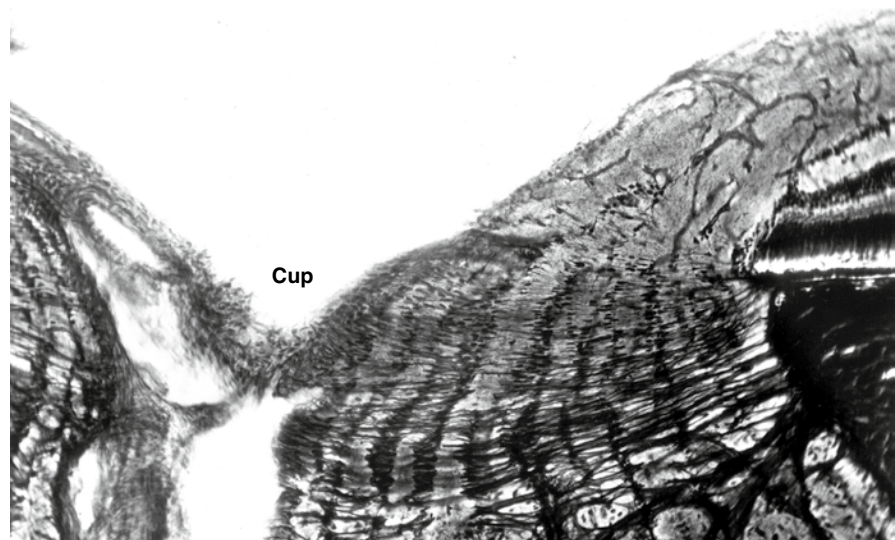


Fig. 2.13 Prelaminar region of the optic nerve head with very fine fibers and a large number of glial cells, markedly flattened in the anteroposterior direction and packed in dense transverse sheets (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])

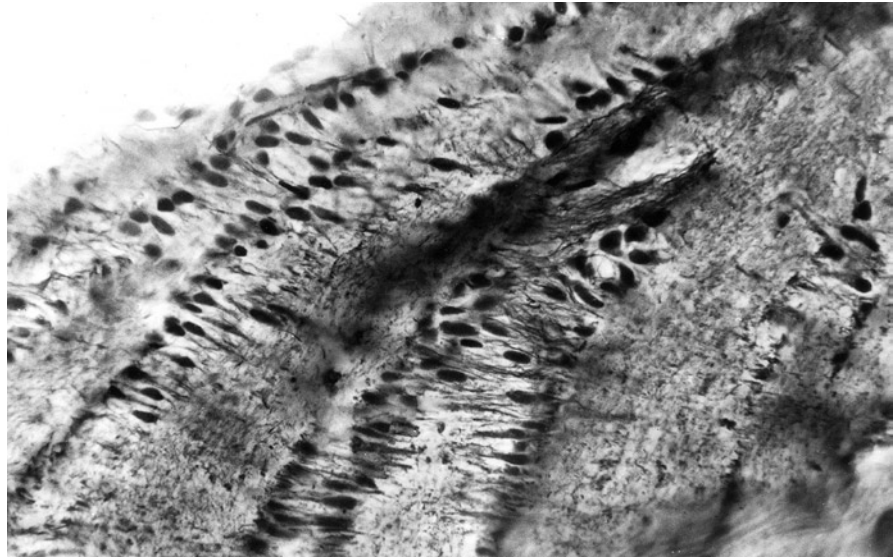
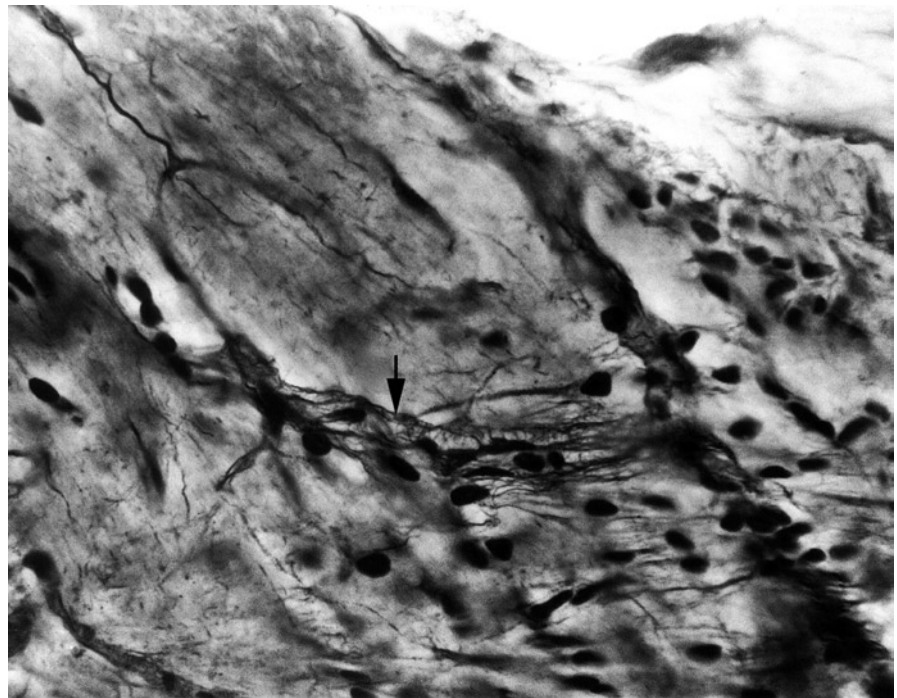


Fig. 2.14 Glial membrane surrounding the capillaries (arrow) in the prelaminar region of the optic nerve head (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])



The prelaminar region at its edge is separated by several layers of astrocytes from the adjacent deeper layers of the retina ("Intermediate tissue of Kuhnt" [6]) and from the adjacent choroid ("Border tissue of Jacoby" [19]). These astrocytes not only form a column around the circumference of the chorioretinal canal and send processes internally among the nerve bundles but also invest the connective tissue of all vessels entering this portion of the optic nerve head [18].

The optic nerve fibers coming from the retina make a 90° bend in the surface layer of the optic nerve head to run back in the optic nerve (Figs. 2.1–2.6); and as they make the bend their main support is the glial tissue of the prelaminar region. The nerve fibers are arranged in bundles. Within the bundles, the axons are separated either from each other by an intercellular space measuring 150 Å, or from an astrocyte process by a similar space [18]. Cohen [20] found the

Fig. 2.15 Transverse section of the glial part of the prelaminar regions of the optic nerve head showing the arrangement of the septa

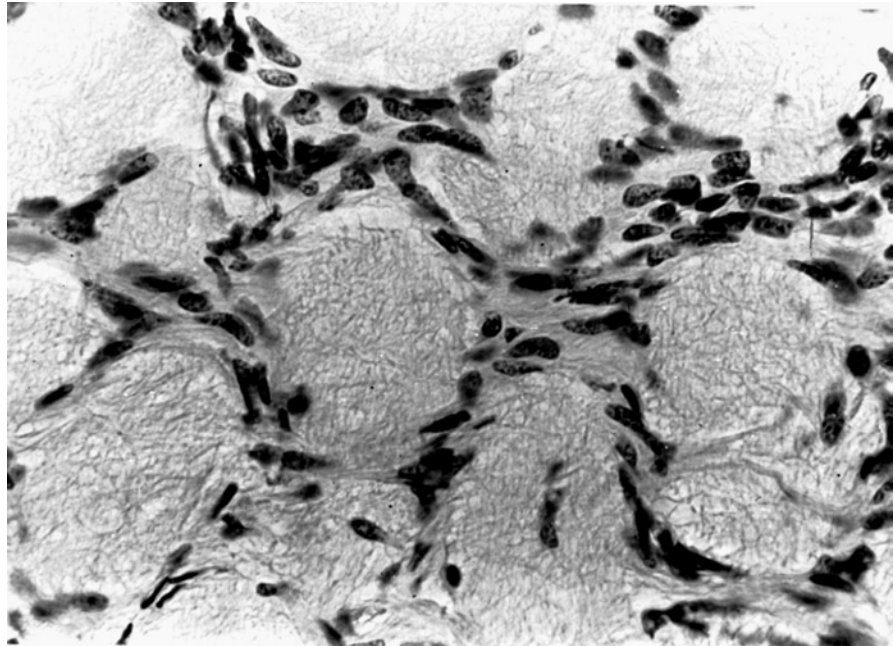
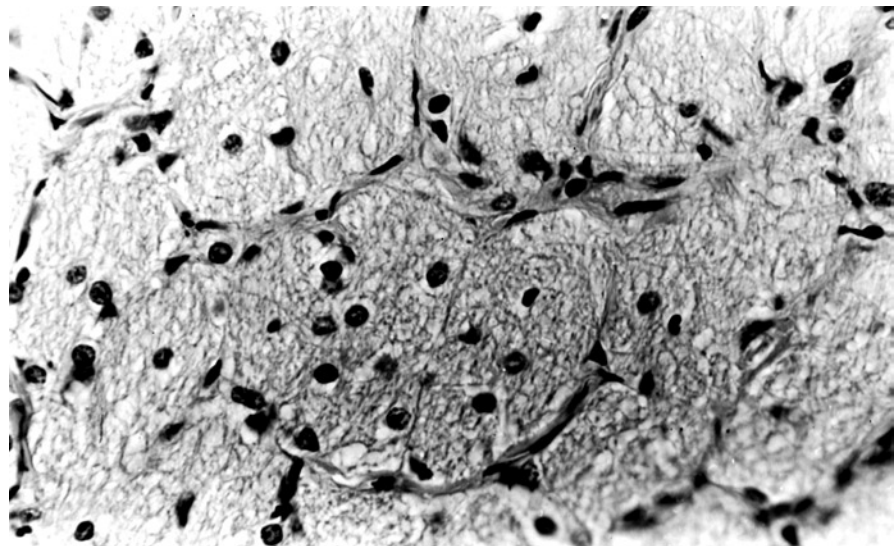


Fig. 2.16 Transverse section of the glial part of the prelaminar regions of the optic nerve head showing the arrangement of the septa



axons in this region to have no organized glial separation, often being contiguous with one another for up to 200 μm . The nerve fibers in this part, as in the surface nerve fiber layer and the retina, are unmyelinated and vary in diameter, and are arranged in bundles; toward the retina the bundles become closely packed (Figs. 2.5 and 2.6).

The Lamina Cribrosa Region

This region of the optic nerve head has been described as the scleral or posterior part of the lamina cribrosa. I have restricted the term lamina cribrosa to this part of the optic nerve head in order to avoid unnecessary confusion.

Fig. 2.17 Transverse section of the mixed part of the prelaminar region of the optic nerve head showing the arrangement of the septa (Reproduced from Hayreh and Vrabec [8])

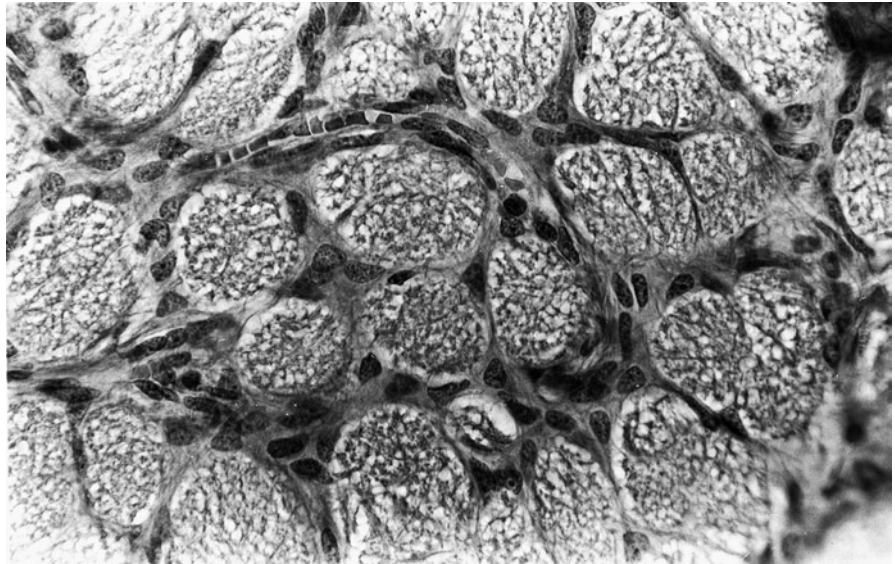


Fig. 2.18 Edema of the optic nerve head in a rhesus monkey due to the raised intracranial pressure (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])



The lamina cribrosa is usually convex posteriorly and concave anteriorly (Figs. 2.1–2.4 and 2.10). There is no sharp transition between the anterior prelaminar glial and posterior connective tissue parts, resulting in the transitional zone (mixed part) of varying size between the two.

The Connective Tissue Part

This extends transversely across the entire thickness of the optic nerve head, bridging the scleral canal (Figs. 2.2–2.4, 2.12 and 2.20–2.24). At the periphery, the connective tissue part of the lamina cribrosa is

Fig. 2.19 High-power view of Fig. 2.18 in the region of the glial part of the prelaminar region (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])

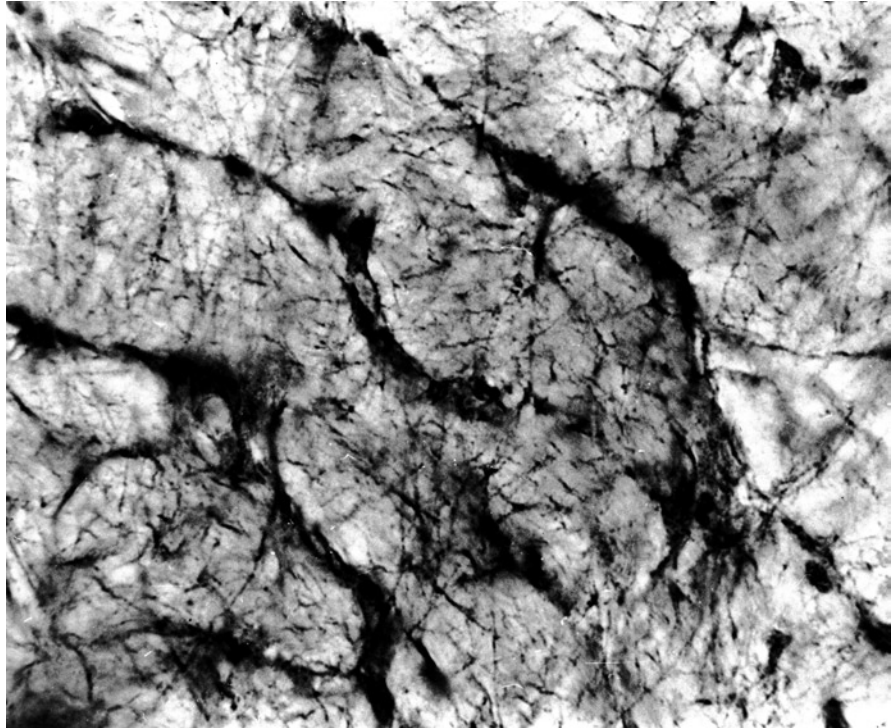
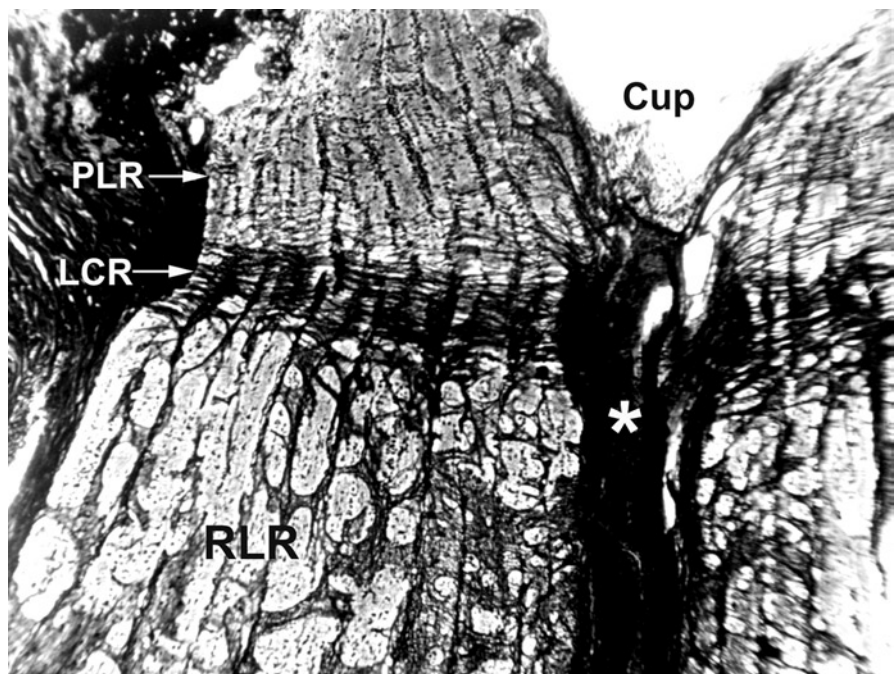


Fig. 2.20 Longitudinal section of the anterior part of the optic nerve in rhesus monkey showing a thick horizontal fibrous band of lamina cribrosa (*LCR*) and the connective tissue sheath of the central retinal vessels centrally (*), which reaches the bottom of the optic disc cup. (Hortega's stain) *LCR* Lamina cribrosa, *PLR* Prelaminar region, *RLR* Retrolaminar region



anchored to the surrounding sclera by thick columns of the connective tissue with enlarged bases (Figs. 2.25 and 2.26); the same kind of anchorage is present

centrally (Figs. 2.20, 2.21 and 2.24–2.26), binding the lamina cribrosa firmly to the connective tissue envelope of the central retinal vessels.

Fig. 2.21 Optic nerve head with a deep excavation (*Cup*). (Hortega's stain) *LCR* Lamina cribrosa, *PLR* Prelaminar region, *RLR* Retrolaminar region. *Connective tissue around central retinal vessels (Reproduced from Hayreh and Vrabec [8])

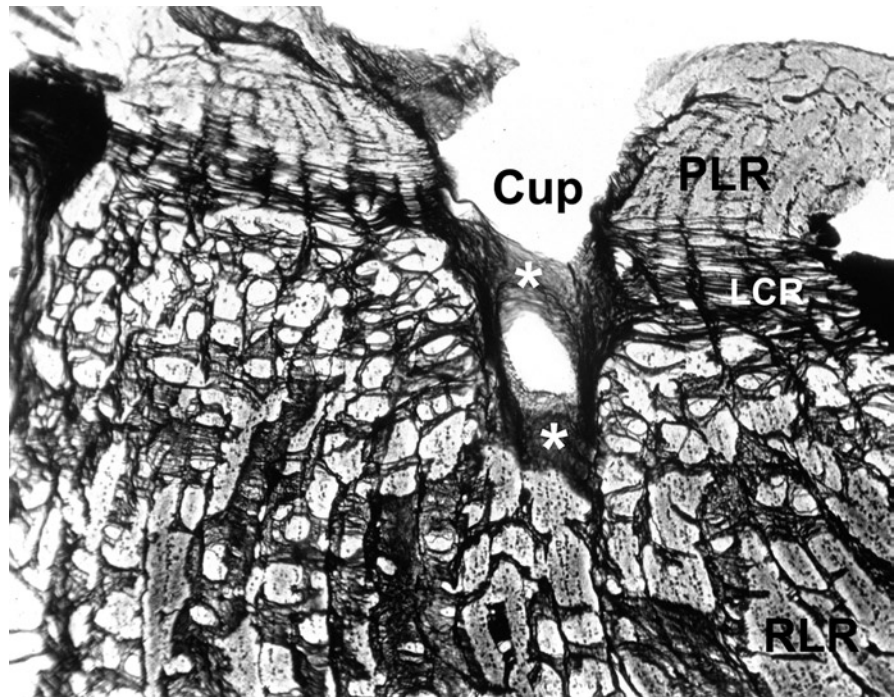
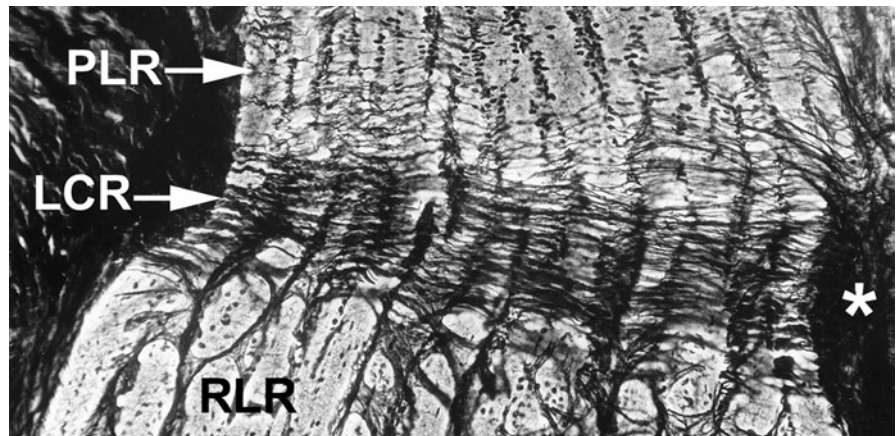


Fig. 2.22 Longitudinal section of the anterior part of the optic nerve in rhesus monkey, specifically showing anchorage of the connective tissue strands of the lamina cribrosa to the sclera at the periphery and to the connective tissue sheath of the central retinal vessels centrally (*). (Hortega's stain) *LCR* Lamina cribrosa region, *PLR* Prelaminar region, *RPR* Retrolaminar region. (Reproduced from Hayreh and Vrabec [8])



The connective tissue fibers of the lamina cribrosa are tightly packed together so that, in a longitudinal section through this region, it is seen as a dense compact band of the connective tissue bridging the scleral canal (Figs. 2.2, 2.4 and 2.20–2.24). In cross sections of the lamina cribrosa, this compact connective tissue reveals many openings for the transmission of the optic nerve fiber bundles (Figs. 2.25–2.29). The lamina cribrosa is of a lamellar nature with collagen bundles alternating with glial sheets [15, 17]; posteriorly the collagen tissue sheets become increasingly prominent.

Wolff [17] and Hogan et al. [18] found a large amount of elastic tissue in the lamina cribrosa, but Anderson [15] found it to vary greatly from one eye to another. The posterior part of this is not sharply delimited from the septal system of the retrolaminar optic nerve, so that the connective tissue septa of the latter are attached to the posterior surface of the lamina cribrosa (Figs. 2.4, and 2.20–2.24). Numerous vessels arising from the circle of Haller and Zinn or paraoptic short posterior ciliary arteries (see Chap. 3) penetrate into the optic nerve and large capillaries are seen within the

Fig. 2.23 Longitudinal section of the anterior part of the optic nerve in rhesus monkey showing transitional strands between the connective-tissue part of the lamina cribrosa and the retrolaminar connective tissue. *LCR* Lamina cribrosa region, *PLR* Prelaminar region, *RPR* Retrolaminar region (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])



Fig. 2.24 Longitudinal section of the anterior part of the optic nerve in rhesus monkey showing anchoring connective-tissue fibers running from the central connective-tissue strand (surrounding the central retinal vessels *) to the bottom of the optic disc cup (Hortega's stain)



connective tissue trabeculae. A continuous glial membrane, similar to that seen in the retrolaminar part, separates the nerve fibers from the connective tissue in the region of the lamina cribrosa.

It has been shown that there are regional differences in the fine structure of the lamina cribrosa, with superior and inferior parts containing larger pores and thinner connective tissue septa than in the nasal and temporal parts of the lamina cribrosa [21]. Another histological study showed that the

connective tissue and glial cell structural elements were greater in the nasal-temporal region compared with the inferior and superior quadrants [22]. The openings are mostly oval or round and their diameter varies greatly (Figs. 2.25–2.29). Some of the larger openings of the lamina cribrosa are subdivided by the connective tissue. All the openings in the lamina cribrosa are not only lined by astrocytes but are further subdivided by glial trabeculae so that a large number of the glial fibers are seen crossing the opening. The

Fig. 2.25 Transverse section of the lamina cribrosa, showing coarse connective-tissue septa, rounded openings for the nerve bundles and, in the periphery, glial fibers expanded across the openings. (A) Central retinal artery, (V) Central retinal vein (Hortega's stain) (Reproduced from Hayreh and Vrabec [8])

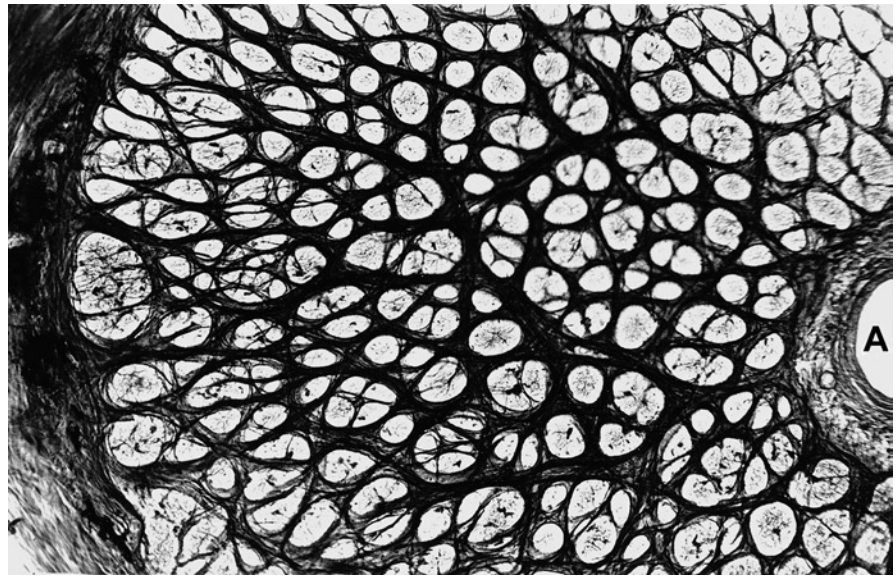


Fig. 2.26 Transverse section of the lamina cribrosa, showing coarse connective-tissue septa, rounded openings for the nerve bundles and, in the periphery, glial fibers expanded across the openings. (A) Central retinal artery, (V) Central retinal vein. (Hortega's stain.) (Reproduced from Hayreh and Vrabec [8])



glial tissue forms a continuous glial membrane surrounding each nerve fiber bundle, as in the prelaminar region; thus it separates the nerve fiber bundles from the adjacent connective tissue. In the middle of the opening many typical fibrous astrocytes can be seen (Figs. 2.28 and 2.29). As the myelin sheath is lacking here (Figs. 2.5 and 2.6), the openings of the lamina cribrosa are considerably smaller than the interseptal space in the retrolaminar part. The coarse connective tissue trabeculae (Figs. 2.25–2.29), show mostly oval or round openings of very variable diameter as compared with the polygonal large spaces of the retrolaminar septal system.

Hernandez et al. [23], on immunofluorescent staining, found that the lamina cribrosa consists of elastin fiber and collagen III and IV and laminin; at the insertion of the lamina cribrosa in the sclera there are concentric circumferential elastin fibers surrounding the lamina cribrosa and astrocytic processes extend into the bundles of elastin fibers. They [24] found that there was an age-related increase in apparent density of collagen types I and III and elastin and increase in density of collagen type IV.

The lamina cribrosa, throughout its entire thickness, is pierced centrally by the central retinal vessels with their accompanying connective tissue (Figs. 2.3, 2.12, 2.20–2.22 and 2.24–2.26). The latter tissue forms

Fig. 2.27 Transverse section of the lamina cribrosa region of the optic nerve head showing the arrangement of the septa (Reproduced from Hayreh and Vrabec [8])

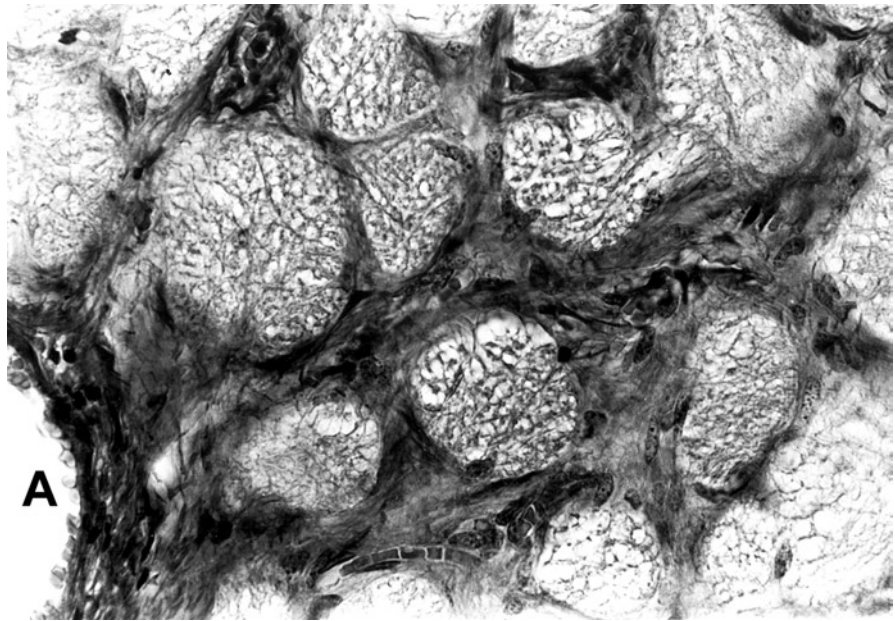
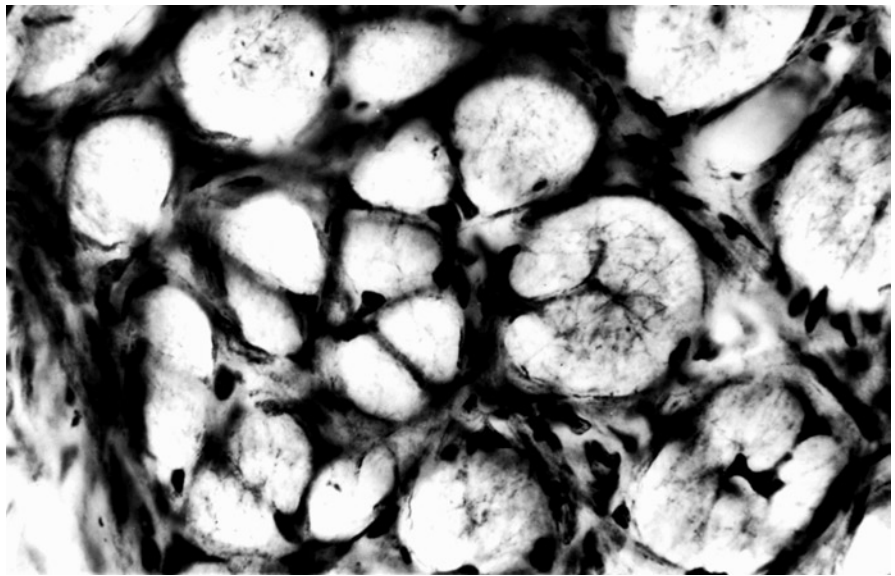


Fig. 2.28 Transverse section of the lamina cribrosa, showing fibrous astrocytes in the openings of the lamina cribrosa (Hortega's stain)



a cylindrical sheath surrounding the vessels, within which numerous fine nerve fibers (autonomic) are seen running along the central vessels to the optic disc [8]. Some of these are closely attached to the vessel wall. In our study [8], in some sections we were able to follow larger trunks of such nerve fibers, representing the so-called nerve of Tiedemann (Fig. 2.30).

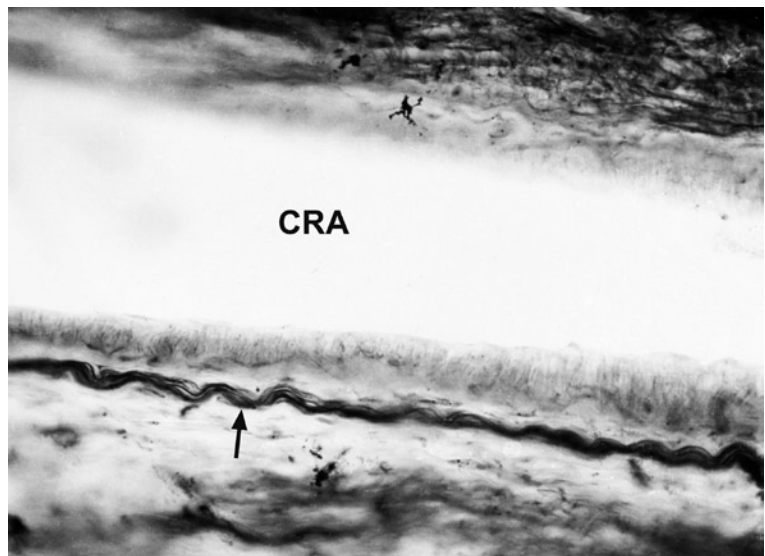
The nerve fibers in this region are similar to those seen in the prelaminar region. The border tissue of

Elschnig, much more strongly developed on the temporal than on 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 [8, 25]. It continues forward to separate the choroid from the prelaminar region. The glial framework, formed by the astrocytes, extends throughout the entire optic nerve head and seems to account for more than half of the volume of the optic nerve head [15].

Fig. 2.29 Transverse section of the lamina cribrosa, showing fibrous astrocytes in the openings of the lamina cribrosa (Hortega's stain)



Fig. 2.30 Longitudinal section of the optic nerve in rhesus monkey showing nerve of Tiedemann (*arrow*) running parallel with the wall of the central retinal artery (CRA) in the optic nerve. (Gros-Schultze's stain) (Reproduced from Hayreh and Vrabec [8])



Intraorbital Part of the Optic Nerve

This extends from the eyeball to the optic canal. The diameter of the optic nerve in the retrolaminar region is about twice that of the optic disc (i.e., 3–4 mm); this is because the nerve fibers are myelinated in the orbital part and rest of optic nerve, but they are unmyelinated in the lamina cribrosa and anterior to that (Figs. 2.5 and 2.6). This part of the optic nerve is surrounded by the meningeal sheath which consists of the dura mater, arachnoid mater and pia mater, and cerebrospinal fluid

in the subarachnoid space (Figs. 2.31 and 2.32). The pia mater is closely related to the optic nerve.

This part of the optic nerve has coarse connective-tissue septa (Figs. 2.33 and 2.34), containing blood vessels. They run in all directions – longitudinal and transverse septa in the optic nerve are all attached to one another (Figs. 2.3, 2.4, 2.20–2.24, 2.35 and 2.36). In the central part of the optic nerve, near the central vessels, the main direction of the connective-tissue fibers is longitudinal (Fig. 2.37). These can easily be differentiated from the glial fibers because of their

Fig. 2.31 A diagrammatic copy of a longitudinal section of a normal human optic nerve, showing the optic nerve sheath in its different parts. *A* arachnoid, *C* choroid, *D* dura, *OC* Optic canal, *ON* optic nerve, *P* Pia, *R* retina, *S* sclera (Reproduced from Hayreh [26])

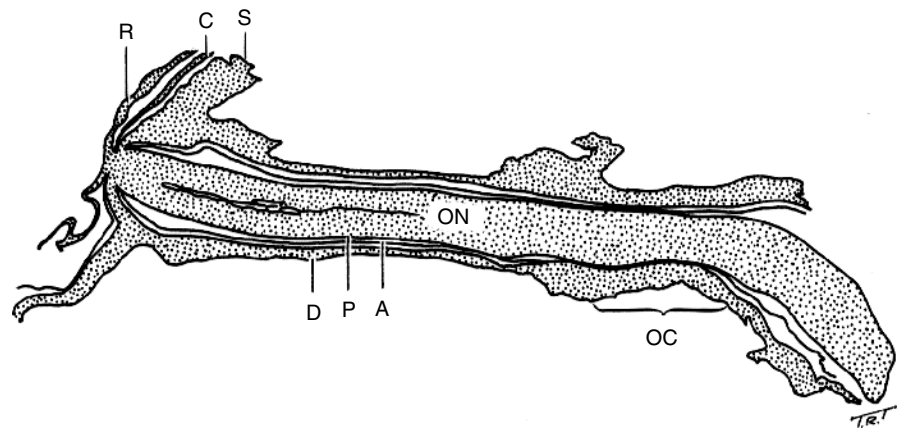
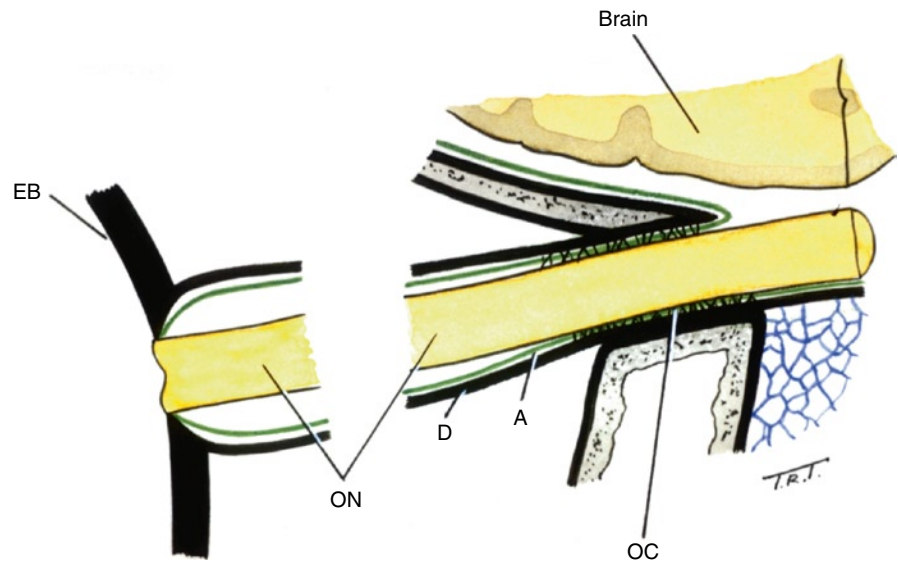


Fig. 2.32 Schematic diagram, showing various regions of the optic nerve sheath. *A* arachnoid, *D* dura, *EB* Eyeball, *OC* Optic canal, *ON* optic nerve (Reproduced from Hayreh [26])



coarse and sinuous character. The longitudinal fibrous septa of the retrolaminar part of the optic nerve are firmly anchored to the posterior surface of the lamina cribrosa (Figs. 2.4 and 2.20–2.24). The transverse septa at the periphery are attached to the pia on the surface, and to the fibrous envelope around the central retinal vessels centrally (Figs. 2.33 and 2.34). The septa form a rather complicated intercommunicating polygonal tubular framework, and enclose within them the nerve fiber bundles with the accompanying glia (Fig. 2.34). The large connective tissue tubes are often bridged by fine fibrous tissue bands (Fig. 2.36).

As in the rest of the central nervous system, at the neuroectodermal-mesodermal junction the nerve fibers are always separated from the collagenous tissue and

blood vessels by an astroglial layer, throughout the course of the optic nerve. The supporting glial framework is built up by fibrous astrocytes lying within the nerve fiber bundles. The astrocytes are connected to the connective tissue septa (Fig. 2.38), and their capillaries by well-marked footplates. The course of all their fibers is best seen in specimens stained by Golgi's methods (Fig. 2.39).

Within the nerve fiber bundles are situated longitudinal rows of angular elements of the oligodendroglia, with densely impregnated cytoplasm and short protoplasmic processes (Figs. 2.40–2.42). Scattered among the nerve fibers are the thin, branched microglial cells, with typical nuclei and processes (Figs. 2.41 and 2.42) – they constitute a part of the reticuloendothelial

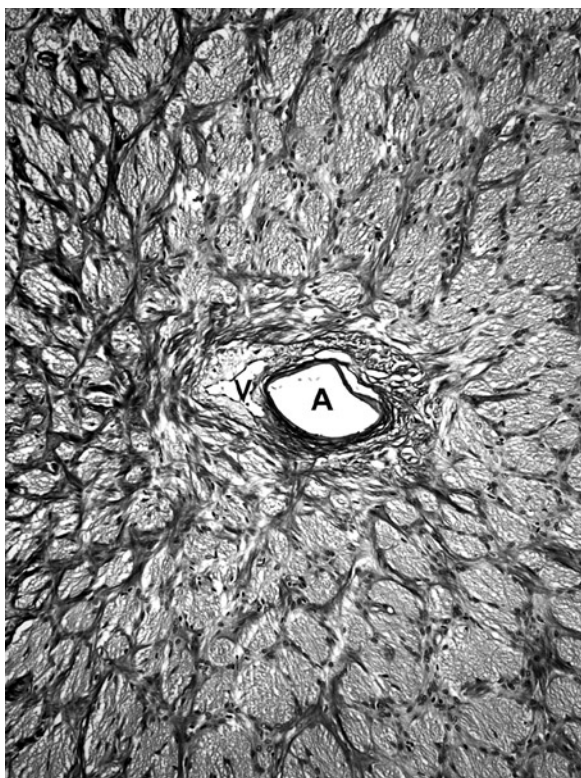


Fig. 2.33 Transverse section of a human retrolaminar optic nerve, showing the arrangement of the septa. A Central retinal artery, V Central retinal vein

system. Impregnation of oligodendroglia, however, is very difficult and requires practically intravital fixation of the material. That is perhaps the reason why in the normal human material most of the authors were not able to stain these cells successfully [11, 12]. In our study [8] of rhesus monkeys, we did the intravital fixation of the tissues. The rows of oligodendrocytes (Fig. 2.43), as well as the myelin sheaths, stopped shortly behind the lamina cribrosa. We did not find any typical oligodendroglia anterior to the retrolaminar region. Oligodendroglia are responsible for the formation of the myelin sheaths.

The nerve fibers are arranged in bundles (Figs. 2.1–2.4 and 2.20–2.24), with frequent interchanging of some fibers between the neighboring bundles, thus forming a sort of network. The myelin sheaths reach almost to the posterior part of the lamina cribrosa. Within the nerve fiber bundles are situated longitudinal rows of angular elements of the oligodendroglia, with densely impregnated cytoplasm and short protoplasmic processes (Fig. 2.43).

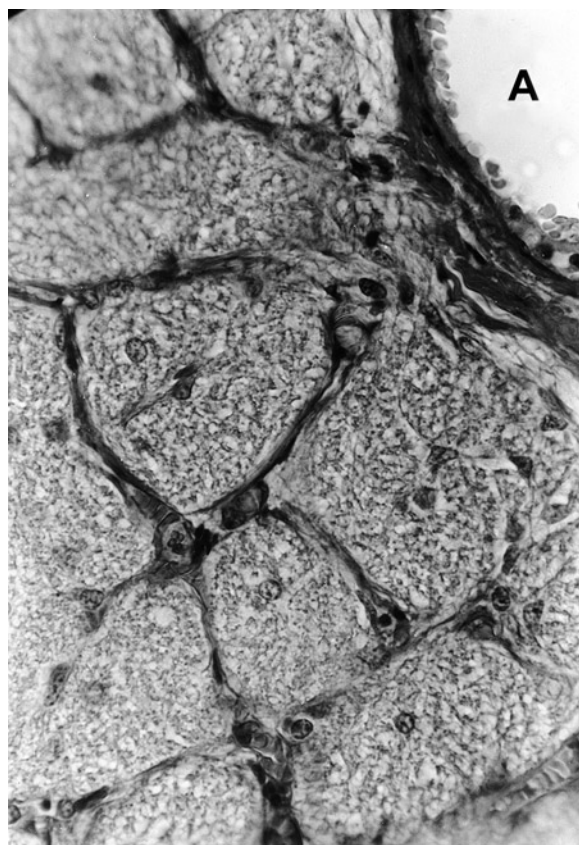


Fig. 2.34 Transverse section of the retrolaminar optic nerve in rhesus monkey, showing the arrangement of the septa. A Central retinal artery (Reproduced from Hayreh and Vrabec [8])

In the center of the anterior intraorbital part of the optic nerve lie the central retinal vessels enclosed in their envelope (Figs. 2.33, 2.34, 2.44 and 2.45). In the center of the posterior part lie some inconstant vessels (see Chap. 3). The pia mater has a dense vascular plexus on the surface of the orbital optic nerve, formed by branches from the various branches of the ophthalmic artery (Fig. 2.46); this plexus forms the centripetal vascular system of blood supply to the optic nerve (see Chap. 3). The dura mater also has vessels on it but much less than on the pia mater. Most of the dural vessels penetrate the dura to supply the pial plexus (Fig. 2.44).

The ophthalmic artery lies in close relationship to this part of the optic nerve – the first part of the ophthalmic artery is almost adherent to the inferolateral part of the optic nerve (Fig. 2.47), its second part crosses over (in 83%) or under (17%) the optic nerve in close relationship to the sheath, but the third part runs in a superior and medial direction away from the



Fig. 2.35 Longitudinal section of the retrolaminar part of the optic nerve in rhesus monkey, showing coarse connective-tissue septa. (Hortega's silver carbonate) *LCR* Lamina cribrosa, *PLR* Prelaminar region, *RLR* Retrolaminar region (Reproduced from Hayreh and Vrabec [8])

optic nerve [30] (Fig. 2.48). The central retinal artery and vein, after their entry/exit from the optic nerve (5–15 mm, median 10 mm behind the eyeball [31]) lie in close relationship or adherent to the inferior aspect of the sheath (Fig. 2.49). Near the eyeball, the nerve is surrounded by multiple short posterior ciliary arteries and ciliary nerves (see Chap. 3).

Sheath of the Optic Nerve

I investigated the anatomy of the sheath of the optic nerve and its communication with the cranial cavity in 80 human and 20 rhesus monkey optic nerves, and in

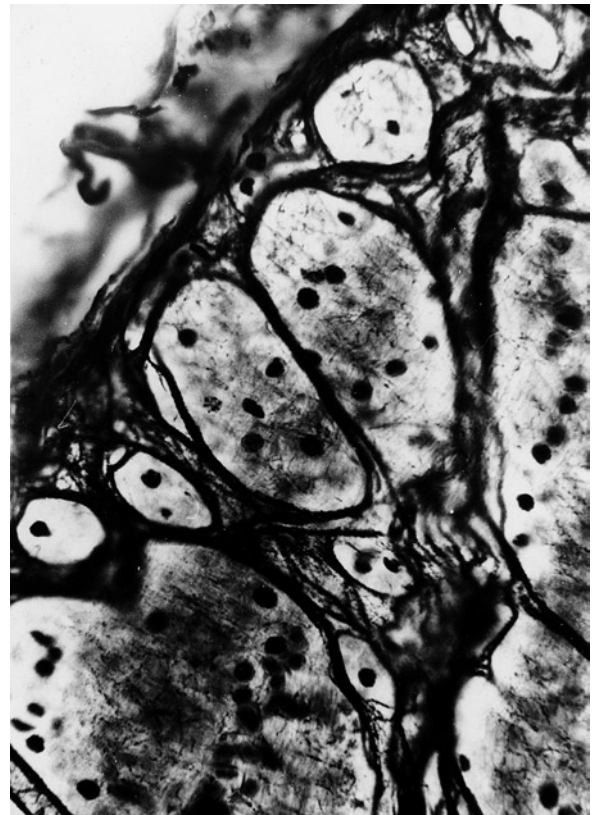


Fig. 2.36 A high-power view of a part of Fig. 2.35, showing fine connective-tissue strands bridging over a large connective-tissue tube (Reproduced from Hayreh and Vrabec [8])

rabbits [32]. The pattern was similar in the human and monkeys. The sheath (i.e. dura mater and arachnoid mater) normally is loose near the eyeball, with a much bigger subarachnoid space between the optic nerve and the sheath than elsewhere in its course, consequently presenting a bulbous appearance just behind the eyeball [32] (Figs. 2.31 and 2.32). The space ends blindly at the junction of the sheath and the eyeball. The subarachnoid space between the optic nerve and the sheath is narrowest in the region of the optic canal. In the optic canal, the optic nerve is attached to the surrounding dura by thick fibrous bands (Figs. 2.32 and 2.50), which stretch from the dura to the pia, with the arachnoid interrupted at the sites of the bands but continuous in-between. The amount of these fibrous adhesions shows marked interindividual variation. The characteristics of the optic nerve sheath in rabbits differed from the human and monkeys in that there were neither similar adhesions in the optic canal nor looseness of the sheath behind the eyeball.

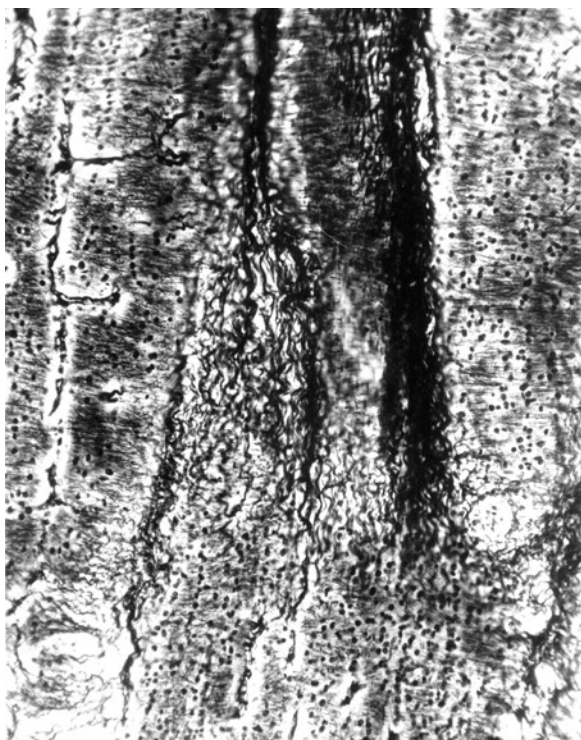


Fig. 2.37 Longitudinal connective-tissue fibers near the central retinal vessels. Fine glial fibers are seen running perpendicular to the connective-tissue septa (Hortega's silver carbonate) (Reproduced from Hayreh and Vrabec [8])

At the apex of the orbit, at the orbital opening of the optic canal, the optic nerve sheath is attached and surrounded by the annular tendon to which are attached the various recti muscles. In the optic canal region, the two layers of the dura mater are joined together but at the orbital end of the canal they split – the outer layer forms the periosteum of the orbital bones while the inner layer forms the dural sheath of the optic nerve (Fig. 2.32). In the optic canal, the ophthalmic artery is closely related to the optic nerve, and lies partly in the subdural space and partly between the two layers of the dura mater, usually the inferior and lateral aspect of the optic nerve [33] (Fig. 2.47).

The anatomy of the sheath of the optic nerve in the region of the optic canal deserves special consideration because it seems to have great importance in more than one way. The length of the bony optic canal is smaller than the canal *in situ* in the normal body in

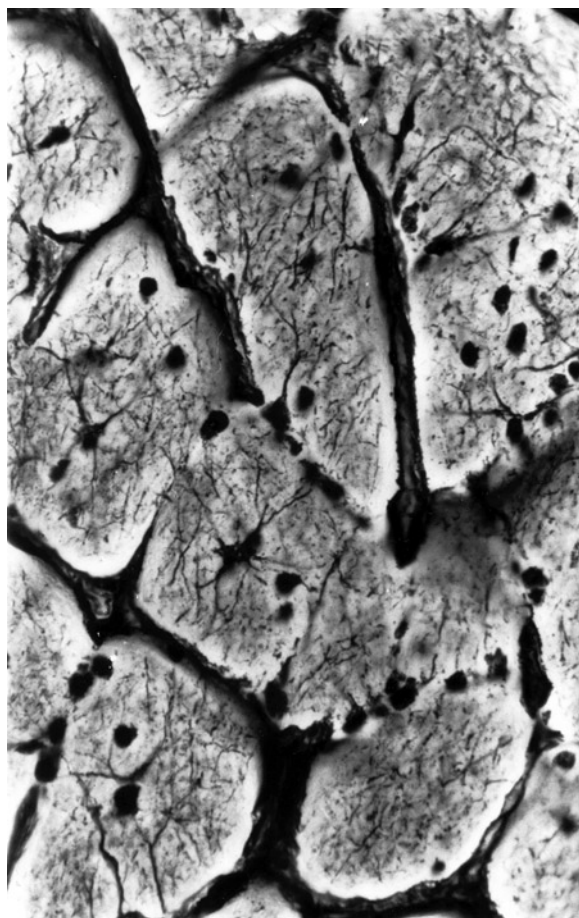


Fig. 2.38 Transverse section of the optic nerve, showing fibrous astrocytes and their processes within the nerve-fiber bundles (Hortega's silver carbonate) (Reproduced from Hayreh and Vrabec [8])

man, because the upper bony margin of its cranial cavity is prolonged by 0.5–0.6 mm into the cranial by a falciform fold of dura [33] (Fig. 2.51). Unlike the orbital part of the sheath, the optic nerve in the optic canal, as discussed above, is firmly bound down to the dura by numerous thick fibrous bands which connect the dura to the pia (Figs. 2.32 and 2.50). These bands not only firmly hold the optic nerve in position in this region but also hold the dura and the optic nerve close to one another. In this region, the subarachnoid space is reduced to almost a capillary size (Fig. 2.50 – SAS), which is interrupted by these bands. Therefore, the space assumes the character of a trabecular meshwork of closely knit fibers in the

Fig. 2.39 Fibrous astrocytes and their processes in the optic nerve (Golgi's stain) (Reproduced from Hayreh and Vrabec [8])

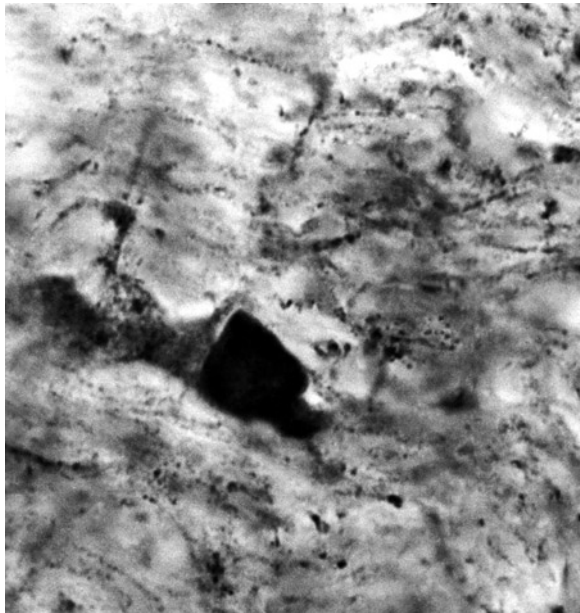
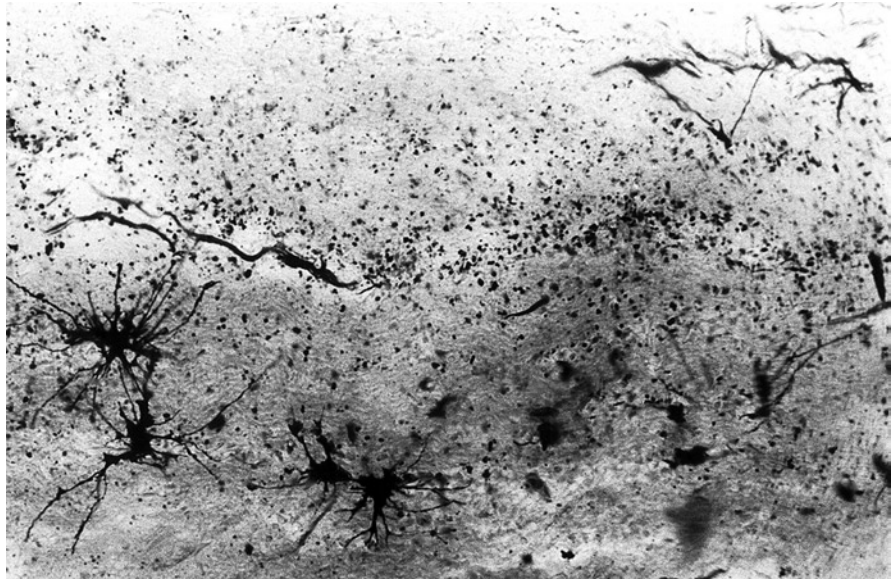


Fig. 2.40 An oligodendrocyte (Penfield's stain) (Reproduced from Hayreh and Vrabec [8])

canal. It must, however, be added that in some cases only scanty adhesions were seen all round the optic nerve in this region.

The normal bulbous appearance of the sheath has often erroneously been assumed to be caused by

stretching and distension of the sheath due to raised cerebrospinal fluid pressure in it; however that is not possible because the dura, being firm collagen fibers (not elastic fibers), is incapable of distension with any amount of raised cerebrospinal fluid seen in patients. In my studies of orbital surgery in about 400 monkeys for experimental occlusion of various ocular vessels, distension of the sheath of the optic nerve, filled with cerebrospinal fluid, was always present normally. The anatomy of the sheath in the region of the optic canal plays a crucial role in the dynamics of conveying the cerebrospinal fluid pressure of the cranial cavity into the sheath of the optic nerve. Communication between the subarachnoid spaces of the cranial cavity and the optic nerve sheath is almost always seen; however, the extent of communication in the optic canal shows wide interindividual variation [32]. To reach the orbital part of the sheath, the cerebrospinal fluid has to percolate through the capillary meshed trabecular network formed by the adhesions in the optic canal. The extent of those adhesions determines the speed with which the cerebrospinal fluid pressure can be transmitted from the cranial cavity to the orbital part of the sheath. It is well-established now that it is the raised cerebrospinal fluid pressure in the orbital part of the sheath that plays a role in the development of optic disc edema in raised intracranial pressure [26, 34, 35].

Fig. 2.41 A group of oligodendrocytes together with a microglial element (*arrow*) (Penfield's stain) (Reproduced from Hayreh and Vrabec [8])

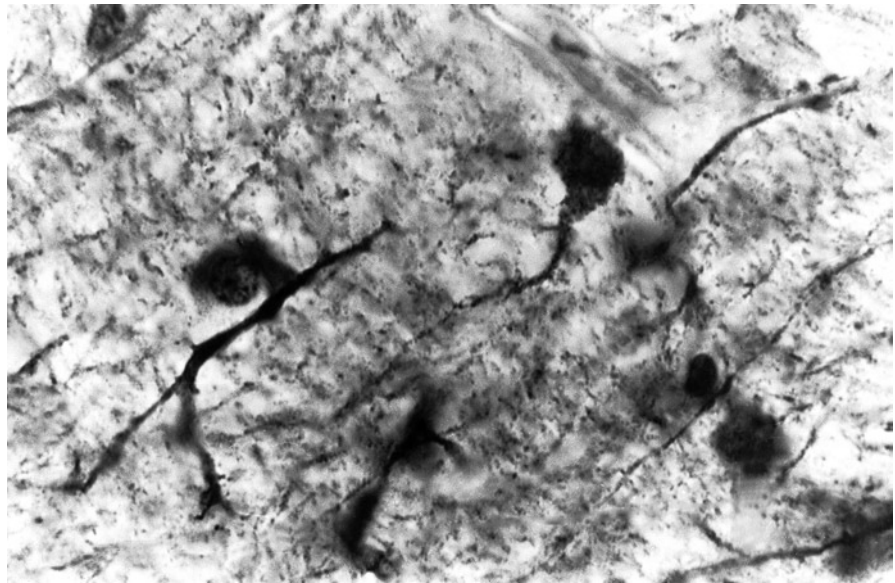
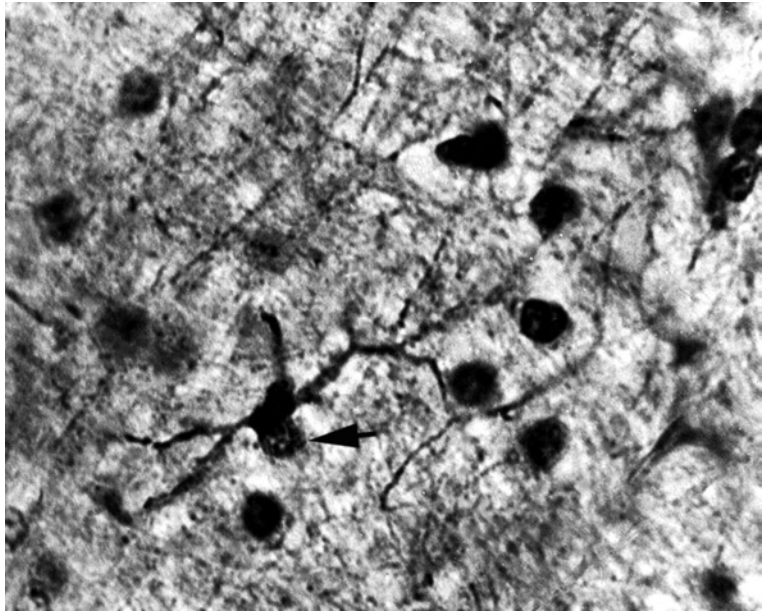


Fig. 2.42 Oligodendrocytes and microglia (Penfield's stain) (Reproduced from Hayreh and Vrabec [8])

Intracanalicular Part of the Optic Nerve

This part lies in the bony optic canal (Fig. 2.32), surrounded by the meningeal sheath (see above). The basic structure of this part of the optic nerve is almost the same as that of the adjacent intraorbital part.

Intracranial Part of the Optic Nerve

In this part, the optic nerve lies above the diaphragma sellae at first and then above the cavernous sinus, and is in close relationship to the ophthalmic artery infero-laterally, internal carotid artery laterally (Fig. 2.51) and

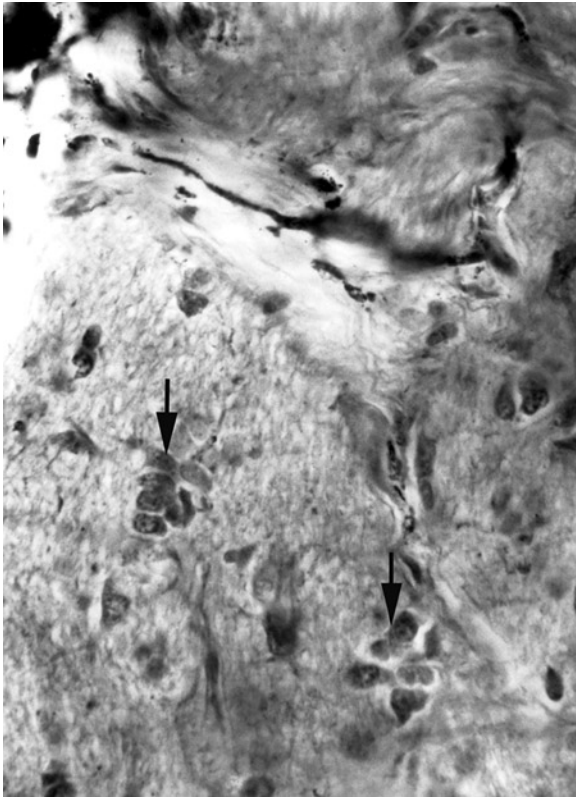


Fig. 2.43 Oligodendrocytes (arrow) in the retrolaminar portion of the optic nerve (Penfield's stain) (Reproduced from Hayreh and Vrabec [8])

anterior cerebral artery superiorly. The nerve is covered by the pia mater and there is no meningeal sheath comparable to that in the orbit and the optic

canal. The ophthalmic artery is always attached to the under surface of the optic nerve by a loose meshwork of vascular connective tissue [33]. Unfortunately, this part of the optic nerve being a no-man's land between neurologists and ophthalmologists, little information about its structure is available.

Optic Nerve Fibers

There are about one million optic nerve fibers. They are of 5 types: (1) visual afferent (serving visual function and going to the lateral geniculate body), (2) pupillary afferent (serving the pupillary reflex and going to the tectum), (3) efferent to the retina (unknown function), (4) photostatic (running to the superior colliculus) and (5) autonomic fibers [1].

The nerve fibers vary in diameter (between 0.7 and 10 μm , mostly 1 μm [18]). According to Polyak [36] – the smaller axons come from the midganglion cells of the central retina and the larger axons from the ganglion cells from the peripheral retina. In the prelaminar region, the nerve fibers are unmyelinated (Figs. 2.5 and 2.6) and arranged in bundles (Figs. 2.1–2.6). Toward the retina the bundles become closely packed. In the lamina cribrosa region the nerve fiber bundles lie in its pores and are unmyelinated (Figs. 2.5 and 2.6). In the retrolaminar and orbital parts of the optic nerve, the nerve fibers are arranged in bundles (800–1,200 bundles [18]). They lie in polygonal spaces formed by the fibrovascular septa in the orbital part of the optic nerve.

Fig. 2.44 Schematic representation of blood supply of the optic nerve. A arachnoid, C choroid, CRA central retinal artery, Col. Br. collateral branches, CRV central retinal vein, D dura, LC lamina cribrosa, ON optic nerve, PCA posterior ciliary arteries, PR prelaminar region, R retina, S sclera, SAS subarachnoid space

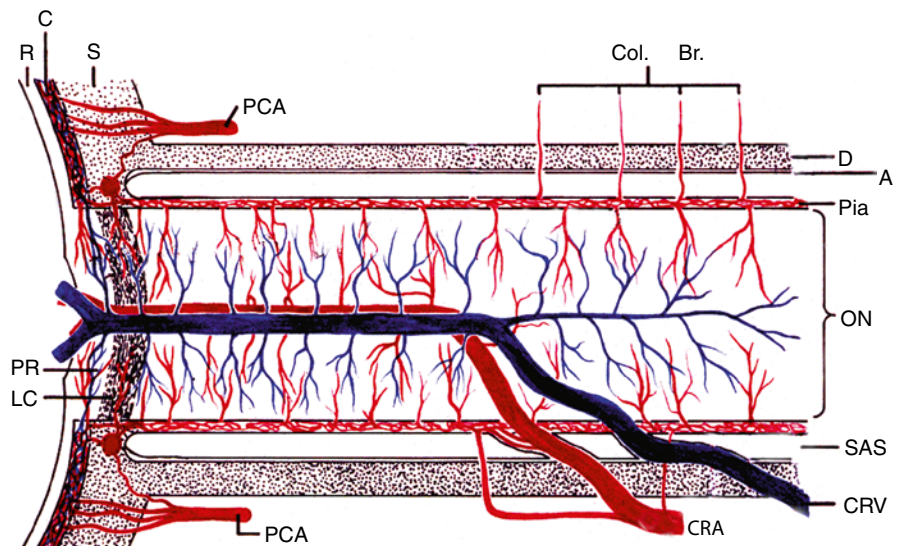


Fig. 2.45 Transverse section of the central part of the retrolaminar part of the optic nerve, showing central retinal artery (CRA) and vein (CRV) enclosed by a common fibrous tissue envelope (FTE) (Mason's trichrome staining) (Reproduced from Hayreh et al. [27])

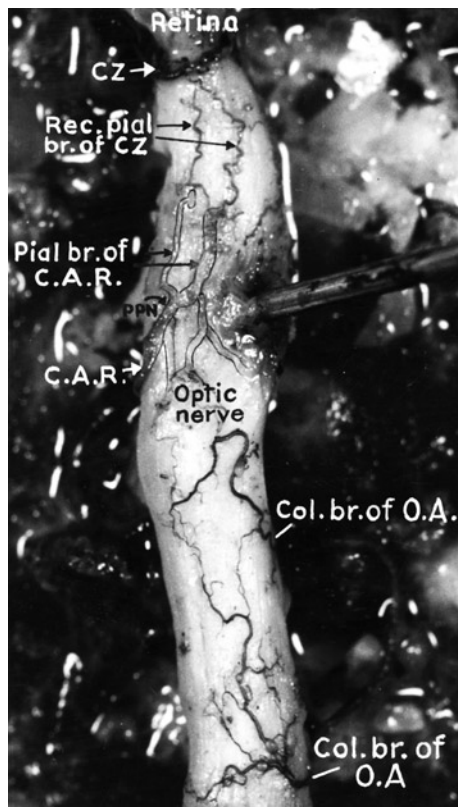
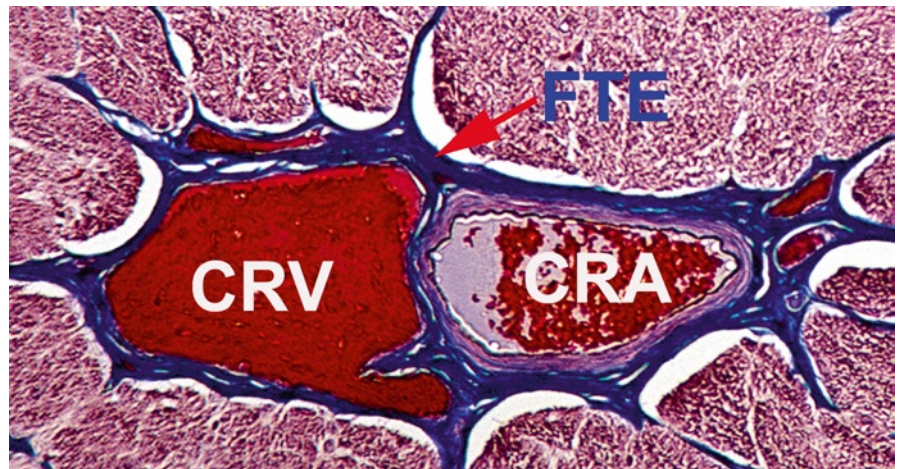


Fig. 2.46 Inferior surface of the human optic nerve (intraorbital part) after removal of the sheath, showing pial vessels arising from different sources. C.A.R. Central artery of the retina, Col. Br. Of O.A. Collateral branches of ophthalmic artery, CZ Circle of Zinn and Haller, Pial br. of C.A.R. Pial branches of central artery of the retina, Rec. pial br. of CZ Recurrent branches of Circle of Zinn and Haller (Reproduced from Singh (Hayreh) and Dass [28])

The nerve fiber bundles lie in the complicated intercommunicating tubular framework formed by the septa, accompanied by glia. There is a frequent interchange of fibers between the neighboring bundles, thus forming a sort of network. Within the bundles, the nerve fibers are insulated from their neighbors by neuroglia. The myelin sheaths reach almost to the posterior part of the lamina cribrosa. Within the nerve fiber bundles are rows of supporting astrocytes, oligodendrocytes and some microglial cells. A continuous glial membrane formed by the astrocytes separates the nerve fibers from the connective tissue in the lamina cribrosa and the retrolaminar region.

Topographic Localization of the Nerve Fibers from the Various Parts of the Retina in the Optic Nerve

This subject is of tremendous significance to any discussion and understanding of the type, location and pathogenesis of visual field defect in optic neuropathies.

In the retina there is no functional overlap between the superior and inferior temporal halves and the two meet at a sharp horizontal temporal raphe, situated between the temporal periphery and the macula (Fig. 2.52). One could compare that to unfolding a Japanese fan, with its central axis corresponding to the optic disc and the two free borders meeting in the temporal part. The nerve fibers diverge from the raphe

Fig. 2.47 Intraorbital course of the human ophthalmic artery, as seen from the lateral side of the optic nerve. OA Ophthalmic artery, OC Optic canal, ON Optic nerve, I, II and III Three parts of the intraorbital part of the ophthalmic artery (Reproduced from Hayreh [29])

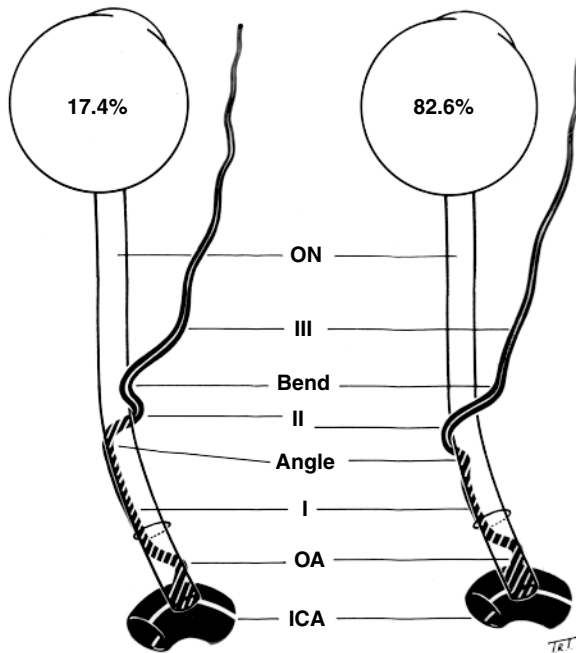
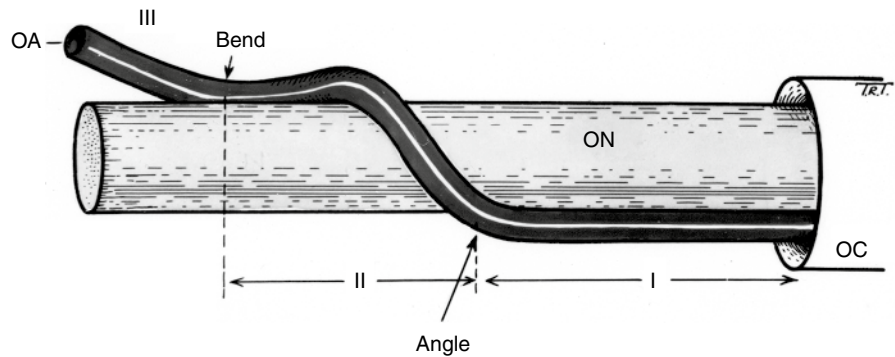


Fig. 2.48 Course of the human ophthalmic artery – left figure when it crosses under the optic nerve (in 17.4%) and right figure when it crosses over the optic nerve (in 82.6%). ICA Internal carotid artery, OA Ophthalmic artery, ON Optic nerve, I, II and III Three parts of the intraorbital part of the ophthalmic artery

to go to the optic disc. This arrangement is most easily understood if the raphe is looked upon as a fold in the temporal margin of the retina drawn in toward the macula with its edges falling into apposition [38]. This gave an erroneous impression to some authors that the optic nerve fibers in the optic nerve head had a maculocentric arrangement. In fact the fibers are centered at the optic disc.

In the retina the nerve fibers are arranged in layers, so that the fibers which arise from the ganglion cells in

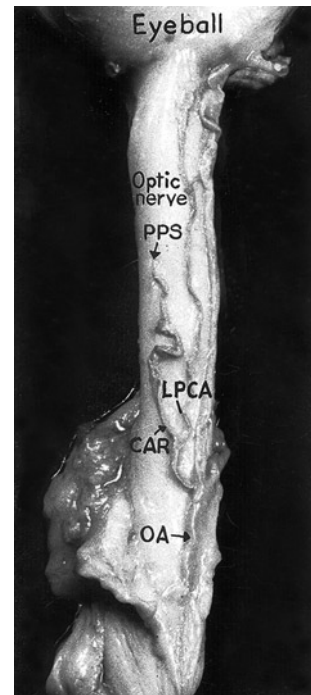


Fig. 2.49 Origin and intraorbital course of the human central retinal artery as seen from below. CAR Central artery of the retina, LPCA Lateral posterior ciliary artery, OA Ophthalmic artery, PPS Point of penetration of the sheath by the central artery of the retina (Reproduced from Hayreh and Dass [31])

the peripheral retina maintain a deep position in the nerve fiber layer, while those which arise closer to the optic disc course forward through the nerve fiber layer to lie more superficially in the nerve fiber layer (Fig. 2.53). Thus, the longer and more peripheral nerve fibers lie deeper in the nerve fiber layer in comparison with the shorter fibers, which arise nearer the disc [39–41]. When these fibers reach the optic nerve head, the more peripheral fibers come to lie in

Fig. 2.50 Longitudinal section of the optic nerve in the region of the optic canal, showing a capillary subarachnoid space (SAS) and fibrous bands connecting the optic nerve with the surrounding sheath (Mason's trichrome staining)

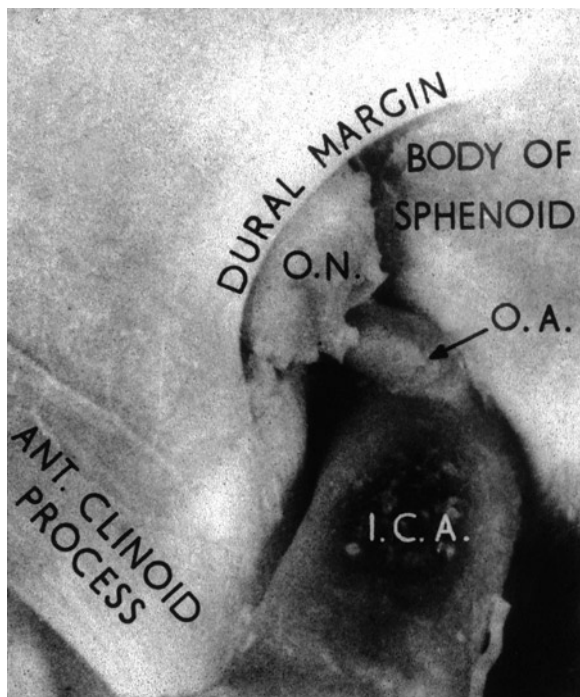
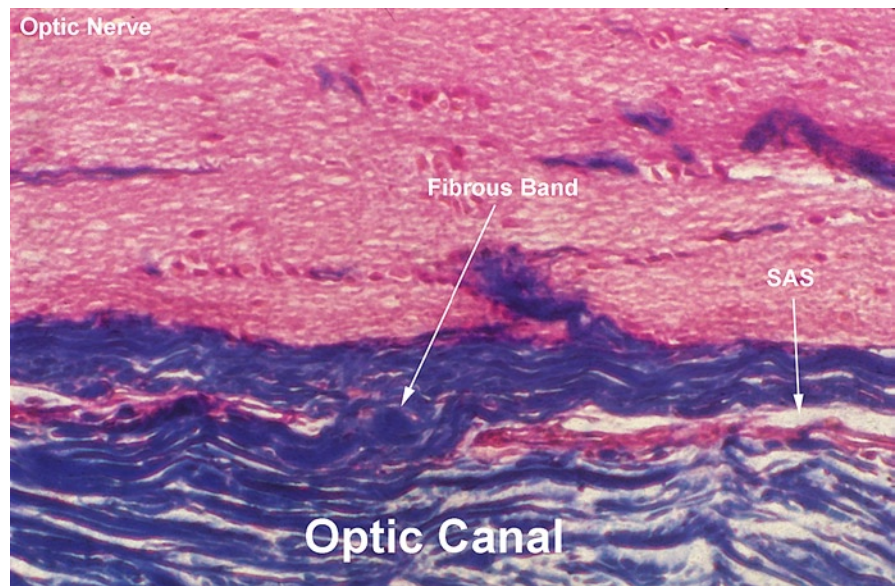


Fig. 2.51 Human ophthalmic (O.A.) and internal carotid (I.C.A.) arteries and optic nerve (O.N.), as seen intracranially, with the intracranial end of the optic canal and optic nerve in it (Reproduced from Hayreh [33])

peripheral part of the nerve head, while the fibers arising from the retinal ganglion cells near the optic nerve head pass across the surface of the optic disc to leave the eyeball near the center of the nerve head [36, 41–47]

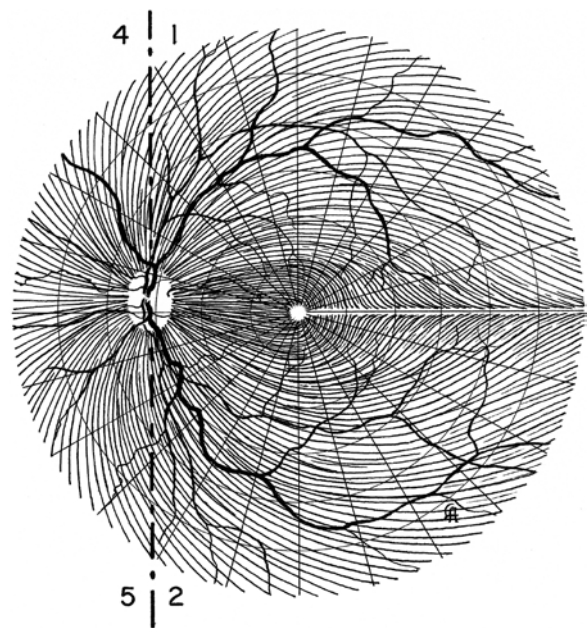
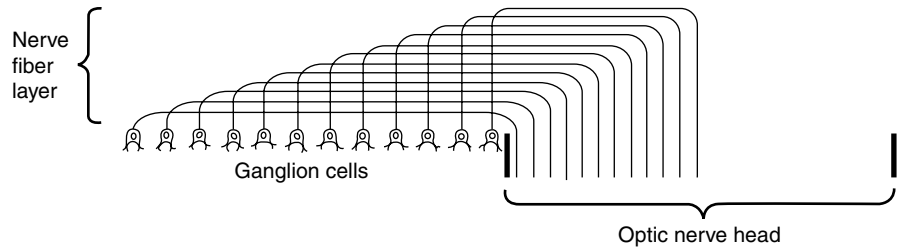


Fig. 2.52 Schematic representation of the optic nerve fibers in the nerve fiber layer of the retina: 1 and 2 from the superior and inferior temporal quadrants of the retina respectively, 4 and 5 from the superior and inferior nasal quadrants of the retina respectively (Reproduced from Hayreh [37])

(Fig. 2.53). However, autoradiographic studies of the arcuate fibers in the retina in rhesus monkeys revealed that the nerve fibers intermingle freely along their intraretinal course; the segregation of the nerve fibers

Fig. 2.53 Schematic representation of arrangement of optic nerve fibers in the nerve fiber layer of the retina and the optic nerve head (Reproduced from Hayreh [37])



takes place at or immediately after the fibers cross the edge of the disc, so the fibers from the far periphery of the retina come to lie in the outer part of the disc, while those from nearer the disc go to the center of the nerve head [48]. In the optic nerve the fibers rearrange themselves as they travel posteriorly in the nerve.

The studies by Hoyt and colleagues [49–52] have contributed significantly to our present concept of the topographic localization of the nerve fibers from the various parts of the retina in the anterior part of the optic nerve. They investigated the topographic localization of the optic nerve fibers in various parts of the optic nerve in monkeys by producing lesions in the retinal nerve fibers by photocoagulating different regions of the retina and histologically localizing the nerve fiber degeneration in different part of the optic nerve. They found the following.

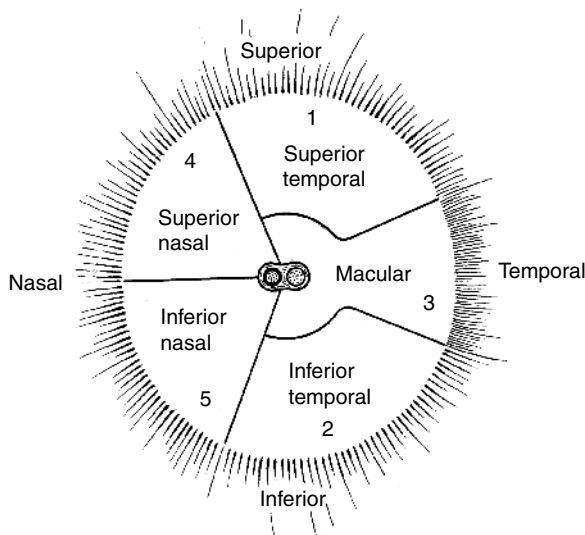


Fig. 2.54 Schematic representation of the arrangement of optic nerve fibers in the optic nerve head, based on the studies of Hoyt and Luis [50]: 1 and 2 from the superior and inferior temporal quadrants of the retina respectively, 4 and 5 from the superior and inferior nasal quadrants of the retina respectively, 3 from the macular region (Reproduced from Hayreh [37])

1. Lesions in the Upper and Lower Temporal Sectors of the Retina Temporal to the Fovea

This resulted in interruption of most of the peripheral and all paracentral axons (sparing the macula) from the upper and lower temporal retinal quadrants [50]. This caused degeneration of the optic nerve fibers in upper and lower temporal sectors of the optic nerve up to 2 to 3 mm behind the eyeball (Fig. 2.54) and these sectors were joined behind that. The two groups of fibers were separated by a temporal horizontal area and they maintained their relative position through the optic nerve. They extended to the central retinal vessels and became more crescentic in the middle and proximal thirds of the optic nerve. The apices of the two sectors did not reach as far as the center of the optic nerve (Fig. 2.54). There was incomplete sector-shaped degeneration in the superior and inferior temporal part of the optic nerve in the distal one third of the nerve. The sectors receded farther away from the center of the optic nerve, as the chiasma was approached. Both the upper and lower sectors extended slightly into the nasal half of the optic nerve.

In another study, Hoyt [49] produced photocoagulation lesions in monkeys, in the retina at or near the optic disc, to investigate the location of arcuate nerve fibers bundles in the optic nerve. This showed that arcuate bundles have a stable and predictable arrangement within the optic nerve. These fibers are located in the temporal half of the optic nerve, corresponding to their site in the retina. In the anterior part of the optic nerve, the apex of the sector extends to the central core of the nerve adjacent to the central retinal vessels. In the middle and posterior parts of the nerve, the apices of the sectors are blunted and compressed toward the outer portion of the nerve. The density of the sector varies directly with the nearness of retinal lesion to the optic disc and its width varies with the number of arcuate bundles cut. The closer the lesion to the optic disc, the closer the apex of the degenerating sector approaches the core of the nerve.

2. *Lesions in the Retina Nasal to the Optic Disc*

This resulted in very discrete sector degeneration of nerve fibers in the distal portions of the optic nerve [50]. Both upper and lower quadrant sectors extended to the central retinal vessels (Fig. 2.51) and laterally were adjacent to each other along the horizontal meridian. That sector location persisted throughout the optic nerve. Retinal lesions in the far nasal periphery produced degeneration only in the nasal periphery of the optic nerve.

3. *Lesion in the Macular Region*

Hoyt and Luis [50] found that following macular lesion, the macular fibers were scattered over a temporal sector occupying at least one third of the cross sectional area of the nerve in the most anterior part of the optic nerve. In the proximal part of the optic nerve, the macular fibers spread out rapidly toward the nasal side of the nerve, distributed diffusely throughout the nerve, and were found peripherally as well as centrally. Before reaching the middle third of the nerve, some macular fibers had already migrated nasally. Unlike the peripheral axons, which are closely packed and run directly posteriorly, the macular fibers constantly wandered throughout the nerve and seemed to be crossing through the bundles of the optic nerve. This resulted in widespread mixing of these fibers throughout the area, except in the most distal part of the nerve. But, according to others, they lie in the central part of the optic nerve posteriorly [53].

4. *Lesions in the Region between the Fovea and the Optic Disc*

The nerve fibers from this area are limited to an area of the optic nerve on the horizontal meridian temporal to the central retinal vessels, and the nerve fibers are of moderately large size.

5. *Lesions in the Region of the Arcuate Nerve Fibers*

In this study the lesions were placed in the retina temporal to the optic disc in the region occupied by the arcuate nerve fiber bundles. The result was well demarcated sector shaped areas of degeneration in the optic nerve just behind the lamina cribrosa, in the temporal half of the optic nerve. The apices of the sectors in the anterior part of the optic nerve extended to the central core of the nerve adjacent to the central retinal vessels. In the middle and posterior parts of the nerve the apices of the sectors were blunted and compressed toward the outer portion of the nerve.

A study by Hoyt and Kommerell [52] in patients with homonymous hemianopia showed that near the vertical poles of the optic disc, the retina has far more nerve fibers coming from the temporal peripheral retina than from the nasal proximal retina. This may be due to the fact that the fibers from the nasal retina have widespread access to the nasal part of the optic disc, but the fibers arising from the temporal peripheral retina have no similar access to the lateral aspects of the optic disc, which is already occupied by the macular fibers, so that the temporal peripheral fibers have to crowd near the poles to enter the optic nerve head (Fig. 2.49).

The information provided by these studies has tremendous practical implications. Lesions in different parts of the optic nerve are likely to produce very different types of visual field defects. This topographic localization of the optic nerve fibers may help in a better understanding of the visual field defects in various types of ischemic optic neuropathy.

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Ischemic Optic Neuropathies

Hayreh, S.S.

2011, XII, 456 p., Hardcover

ISBN: 978-3-642-11849-4