Graefe's Arch Clin Exp Ophthalmol (1999)
237:642–647

CLINICAL INVESTIGATION

Chiaki D. Gauntt
Tom H. Williamson
Michael D. Sanders

Relationship of the distal optic nerve sheath to the circle of Zinn

Received: 12 August 1998
Revised version received:
14 December 1998
Accepted: 15 December 1998

C. D. Gauntt · T. H. Williamson
M. D. Sanders
St. Thomas' Hospital,
Lambeth Palace Road,
London SE1 7EH, UK

M. D. Sanders (✉)
National Hospital for Neurology
and Neurosurgery,
Queen Square, London WC1 N 3BG, UK
Tel. +44-171-837-3611 ext. 3382
Fax +44-171-209-0751

Abstract ● Background: This study was designed to determine the relationship of the vascular circle of Zinn (CZ) and its branches to the termination of the subarachnoid space surrounding the optic nerve sheath, with particular reference to optic disc size. ● Methods: Serial sections of 29 normal human optic nerves were performed at 6-μm intervals. The position of the CZ and subarachnoid space were measured with WILD Heerbrugg objective graticules. The results were analysed with reference to the optic disc size. ● Results: The position of the CZ was variable but two major types were recognised. In type 1 the circle was located anterior to the distal sheath, and in type 2 posterior to the sheath. There were more small optic discs observed in type 2. ● Conclusion: In this study the CZ was more posteriorly located in small optic discs. This location may induce risk factors contributing to the development of ischaemic optic neuropathy. The combination of small discs, posterior placement of the CZ, and anatomical variations in the vascular pattern may predispose to ischaemic events.

Introduction

The microvascular structure of the anterior optic nerve, the peripapillary choroid and the sheath has attracted scientists over many years to correlate this change with the pathogenesis of clinical conditions, including papilloedema and ischaemic optic neuropathy (ION) [1, 5, 9, 10, 14, 15]. Many authors have described the circle of Zinn (CZ) in almost every specimen and suggested that the CZ contributes the main blood supply to the anterior optic nerve, through its pial branches and/ or recurrent choroidal branches [12–14]. On the other hand, some authors have reported that this arteriolar circle is totally lacking or incomplete in a significant number of cases [19].

In recent years, there have been morphological studies of the microvascular structure of the anterior optic nerve employing methylmethacrylate corrosion casting, an excellent way of demonstrating these fine vascular networks in three dimensions [11–14]. However, a disadvantage of this technique is that the soft tissue is completely removed, and the vascular structure is not always easy to relate to the surrounding structures. For this reason, we employed the classic histological serial sectioning in this study.

Statistically there is evidence that small optic discs have a greater incidence of anterior ION (AION) [2]. Suggestions have been made that there might be a morphological difference between small and normal-sized discs involving the microcirculation.

In this study, we have investigated the relationship between the CZ and the subarachnoid space with particular reference to the optic disc size in order to comprehend the pathogenesis of ION.

Materials and methods

Thirty-two human eye bank eyes from 32 individuals were harvested by the lid-sparing method. These eyes had no previous disease according to the referral forms for eye banking. They were immersion-fixed with glutaraldehyde solution (range of time to fixation

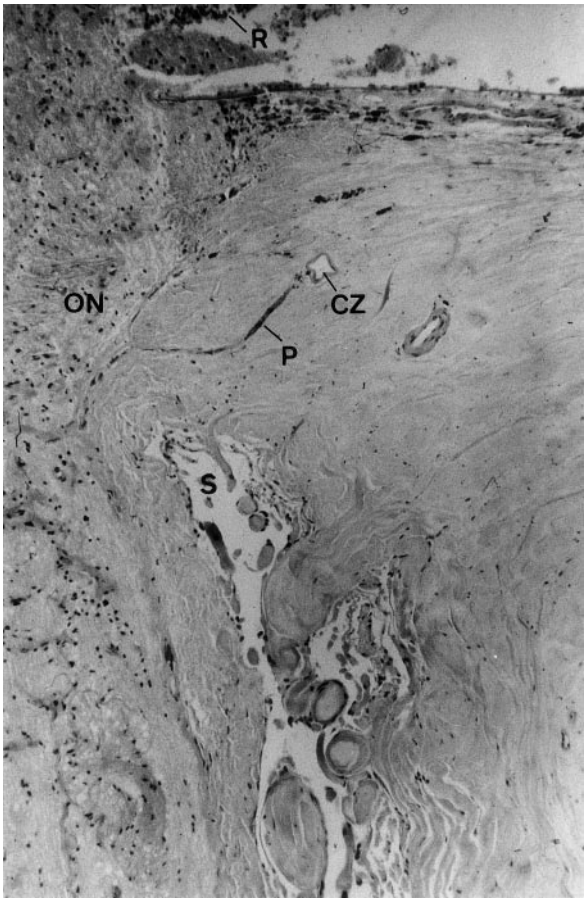

Fig. 1 The appearance of the circle of Zinn (*CZ*) and the surrounding structure in a longitudinal section of the optic nerve (*S* subarachnoid space, *P* pial branch of CZ, *R* retina, *ON* optic nerve)

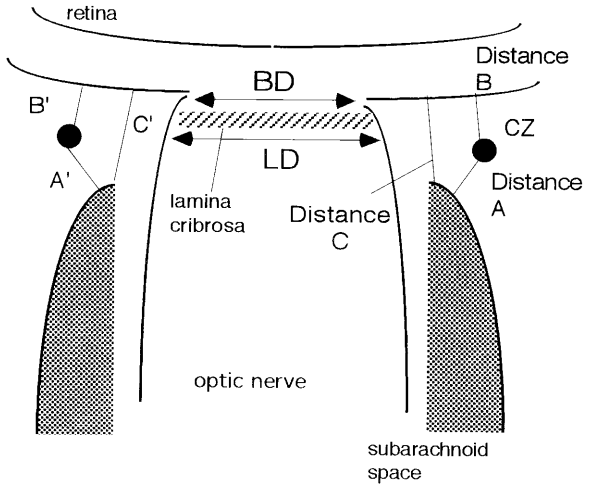

Fig. 2 The definitions used in this study. *Distance A* Minimum distance between surface of vascular lumen of CZ and internal surface of dural sheath of subarachnoid space. *Distance B* Minimum distance between surface of vascular lumen of CZ and scleral surface adjacent to choroid. *Distance C* Minimum distance between internal surface of dural sheath of subarachnoid space and scleral surface adjacent to choroid. *A′*, *B′*, *C′* Corresponding distances on other side of optic nerve. *BD* Diameter of optic nerve at level of Bruch's membrane, *LD* Diameter of optic nerve at posterior end of lamina cribrosa

40 min to 24 h 10 min, mean 10 h 6 min), and subsequently paraffin-embedded by a single experienced anatomist, using the same procedures and under the same conditions. Serial sections 6 μm thick were made from the blocks, prepared with haematoxylin and eosin (HE) stain in standard methods and observed with light microscopy (Fig. 1). The whole procedure was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

At first, the CZ was identified by tracing it through serial sections, its completeness being determined whenever possible. In each sample section, we identified and traced the CZ, the size of a typical arteriole (mean 43 μm in our study), that encircled the optic nerve. If a questionable branching was encountered, we traced both vessels until it became clear which one was the CZ.

Secondly, in order to estimate the precise position and typical size of the CZ, 20 central serial sections were chosen from each nerve for evaluation. To determine the centre of the optic nerve, we used the central retinal vessels and the maximum diameter of the optic nerve as a guide.

These 20 sections were measured directly using a Leitz Laborlux S light microscope (Leitz Wetzlar, Germany) with a ×25 objective lens (Leitz Wetzlar, Germany) and WILD Heerbrugg objective graticules (Heerbrugg, Switzerland). For the purpose of numerical analysis, different distances were defined (Fig. 2). Distance A corresponds to the minimum distance between the surface of the vascular lumen of CZ and the internal surface of the dural sheath of the subarachnoid space. Distance B is the minimum distance between the surface of the vascular lumen of the CZ and the scleral surface adjacent to the choroid. Distance C is the minimum distance between the internal surface of the dural sheath of the subarachnoid space and the scleral surface adjacent to the choroid. BD corresponds with the diameter of the optic nerve at the level of the Bruch's membrane, and LD is the diameter of the optic nerve at the distal end of the lamina cribrosa.

Measurements from both the medial and lateral borders of the optic nerve were obtained where possible, and mean values of measurements from the 20 sections were obtained for each eye.

Subsequently the samples were categorized into two groups according to their ratio of distance B/distance C (B/C ratio). The group with B/C ratio less than 1 was classified as type 1, in which the CZ was located anterior to the plane of the distal end of the subarachnoid space. The other group, with B/C ratio 1 or more, was type 2, in which the CZ was at the same depth or posterior to the distal end of the subarachnoid space (Fig. 3).

After classification, the rest of the sections were examined to confirm the above patterns in each eye, since significant variation of each CZ's depth in the sclera was a major concern.

Thirdly, disc size was measured using the definition shown in Fig. 2.

The section giving the maximum BD and LD (the central section) was selected from each eye to determine maxBD and maxLD, respectively. Assuming that the optic nerve maintains a regular round contour, maxBD and maxLD were used to indicate its size, i.e. diameter.

Analysis was performed using Spearman rank correlation and the Mann-Whitney *U*-test to investigate correlation between distances A, B and C, the B/C ratio and the two measurements describing the disc size.

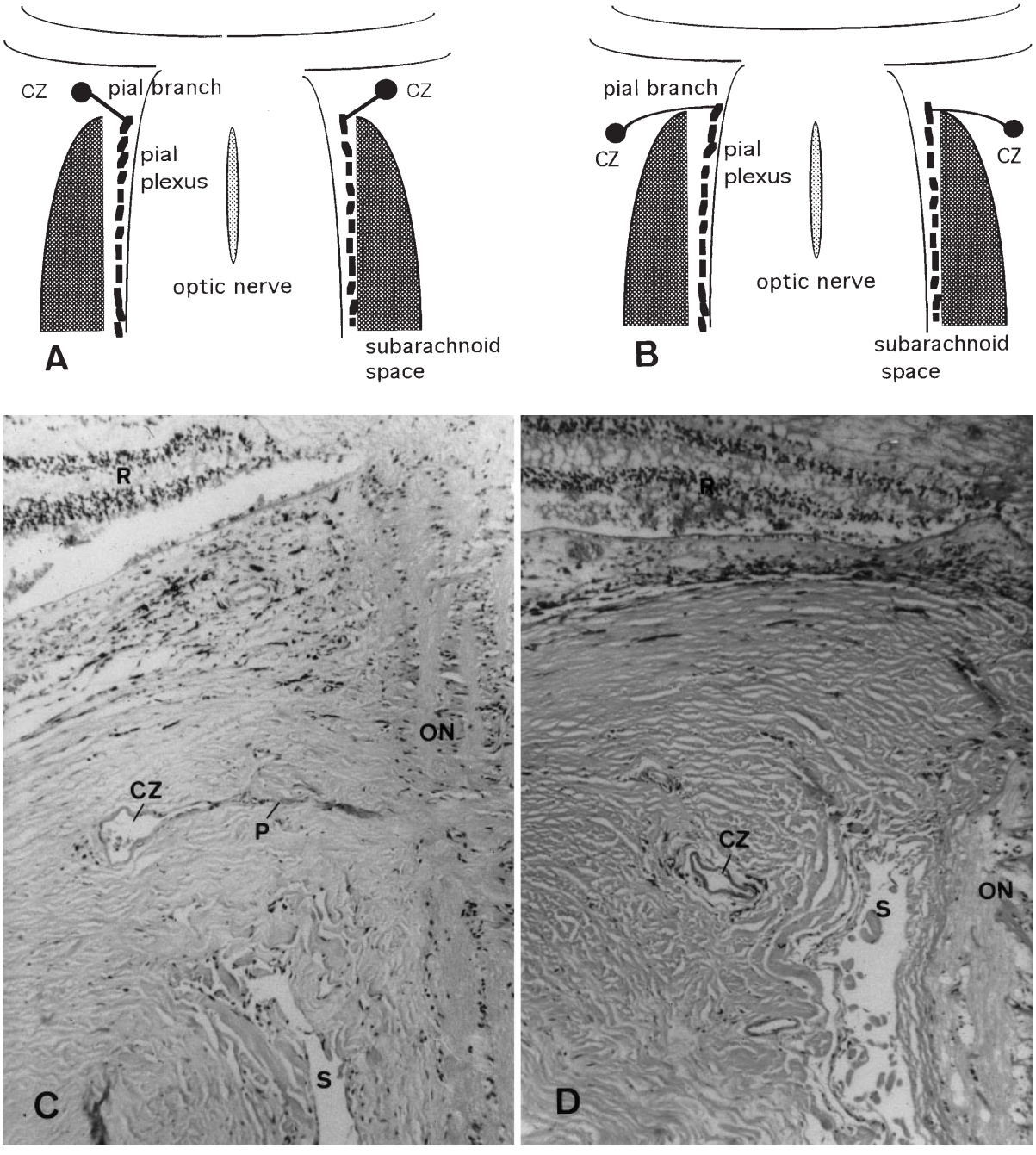

Fig. 3 **A** Type 1. B/C ratio less than 1.0: CZ positioned anterior to termination of subarachnoid space. **B** Type 2. B/C ratio 1.0 or greater: CZ positioned posterior to termination of subarachnoid space. **C** Typical example of anterior CZ location (Type 1). **D**: Typical example of posterior CZ location (Type 2). Abbreviations as in Fig. 1

Results

Mean values of the series of measurements from 20 central sections of the eyes are shown in Table 1. When the measurements were obtained at both borders of the optic nerve, the corresponding values (A and A', B and B', and C and C') were statistically close, giving further evidence that the CZ tends to encircle the optic nerve at a regular depth in the sclera. However, nine eyes yielded only one measurement at one side of the optic nerve; therefore, A', B' and C' were not included in the analysis.

In two specimens of type 2, pial branches of the CZ were seen extending closely around the end of the subarachnoid space by tracing through the sections. No similar observation was found in any specimens of type 1.

Table 1 **1** The mean values of the measurement from each sample

Sample no.	MaxBD (μm)	MaxLD (μm)	BD/LD	Distance (μm)						B/C	B'/C'	Type	Others
				A	B	C	A'	B'	C'				
1022-94	1522.5	2160.5	0.70	361.5	322.8	424.6				0.76		1	CZ incomplete
1053-94	1566.0	2305.5	0.68	218.4	261.0	5428.8	202.2	374.7	447.2	0.49	0.84	1	
1054-94	1435.5	2247.5	0.64										CZ(−)
1061-94	1537.0	2102.5	0.73	205.6	330.9	502.7				0.66		1	
1063-94	1421.0	2015.5	0.71	268.3	323.4	545.9	250.9	337.9	539.4	0.59	0.63	1	
1067-94	1261.5	2131.5	0.59	229.1	595.3	606.4				0.98		2	
1073-94	1479.0	2291.0	0.65	111.5	496.6	601.8	54.4	547.4	536.5	0.83		1	CZ incomplete
1089-94	1624.0	2305.5	0.70										CZ(−)
1091-94	1537.0	2102.5	0.73	104.4	330.4	420.5	105.1	297.7	370.2	0.79	0.80	1	CZ narrow
1092-94	1537.0	1957.5	0.79	99.9	379.1	449.5	129.1	546.4	456.8	0.84	1.20	2	
1093-94	1348.5	1957.5	0.69	142.1	478.5	508.6	201.6	473.4	569.9	0.94	0.83	1	
1094-94	1885.0	2392.5	0.79	219.8	233.5	438.8				0.53		1	CZ incomplete
1095-94	1740.0	2320.0	0.75	356.4	338.1	598.3	390.0	202.2	574.7	0.57	0.35	1	CZ narrow
1097-94	1609.5	2030.0	0.79										CZ(−)
1099-94	1450.0	2030.0	0.71										CZ(−)
236.95	1450.0	1943.0	0.75	185.3	306.1	377.9	143.4	236.8	265.8	0.81	0.89	1	CZ narrow
237-95	1537.0	2465.0	0.62	111.7	183.4	336.4	203.7	226.2	435.7	0.55	0.52	1	CZ narrow
241.95	1421.0	1957.5	0.73	269.7	302.3	411.1	227.2	328.4	505.8	0.74	0.65	1	CZ narrow
243.95	1435.5	1957.5	0.73	192.9	420.9	424.5	148.8	383.9	375.5	0.99	1.02	1	
246-95	1754.5	2204.0	0.80	154.2	399.9	569.3	140.2	485.8	539.4	0.70	0.90	1	
248.95	1885.0	2233.0	0.84	164.9	258.4	364.4	188.5	382.8	393.0	0.71	097	1	
249.95	1377.5	1841.5	0.75	168.9	271.9	342.9	149.4	319.7	330.6	0.79	0.97	1	
250-95	1566.0	2320.0	0.68	146.6	247.3	270.9	157.7	327.2	406.9	0.91	0.80	1	CZ narrow
251.95	1667.5	1812.5	0.92	200.9	563.4	448.0	209.7	530.9	431.9	1.26	1.23	2	
252.95	1566.0	1856.0	0.84	249.9	286.6	506.0	281.3	229.8	498.1	0.57	0.46	1	CZ narrow
253.95	1493.5	2001.0	0.75	193.2	346.6	485.8	254.9	525.1	537.3	0.71	0.98	1	
254.95	1450.0	2117.0	0.68	168.8	473.1	584.5	219.0	580.0	677.2	0.81	0.86	1	CZ narrow
255-95	1595.0	2044.5	0.78	81.4	478.5	460.0	90.3	467.3	449.5	1.04	1.04	2	
256.95	1479.0	1957.5	0.76										CZ(−)
Mean	1487.7	2035.3	0.7	177.1	345.1	644.3	178.4	371.6	444.8	0.7	0.8		

Table 2 The occurrence of various location and morphology of the circle of Zinn

	Number of specimens	Percentage
Type 1	20	69.0
Type 2	4	13.8
CZ(−)	5	17.2

In five eyes, no CZ was detected by our regular tracing method through the serial sections [CZ(–)]. Direct supply of the pial system by the short posterior ciliary arteries was noticed in these eyes.

Table 2 shows the numbers of the eyes that belong to type 1 and type 2. Twenty eyes (69.0%) had an anteriorly positioned CZ (Type 1) and 4 eyes (13.8%) had the CZ posteriorly located (Type 2).

A statistically significant correlation between small disc size and posterior location of the CZ relative to the subarachnoid space was suggested by the analysis (LD vs B/C ratio r=–0.45, Spearman rank correlation P=0.03). We found no specific correlation between BD and B/C ratio. Distances A, B and C alone showed no association with disc size. We observed no particular correlation between lack of the CZ and small disc size.

This study found no choroidal branch or direct branch of the central retinal artery supplying the retrolaminar area and thus supports the current view that the retrolaminar region is mainly supplied by the ciliary-CZ-pial system [10].

Three eyes were not preserved in suitable condition for acquiring measurements.

Discussion

The retrolaminar portion of the human optic nerve has a confluent internal anastomosis of capillaries derived from the superficial pial system and small numbers of branches from the central retinal artery and those from laminar and prelaminar portions interconnecting longitudinally [10, 14]. The pial system is a fine network of capillaries that surrounds the optic nerve in the manner of a cuff. This system is supplied by the CZ at the laminar/retrolaminar portion of the optic nerve through pial branches of the CZ. Though branches arising from the central retinal artery contribute, the pial system is the main vasculature

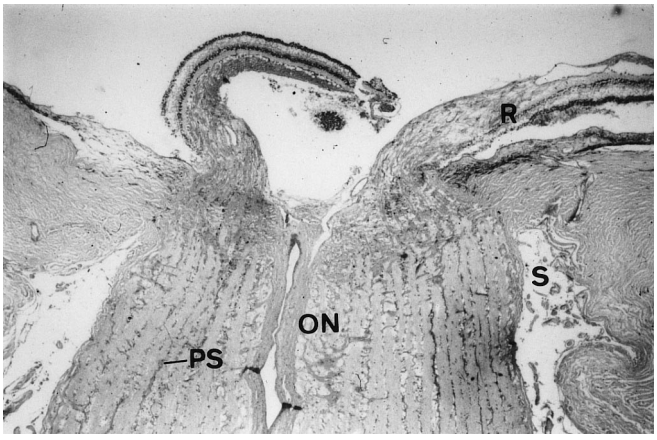

Fig. 4 Light micrograph of longitudinal optic nerve section (HE stain). Note the pial septum (PS), composed of prominent collagen fibres. Other abbreviations as in Fig. 1

that supplies the optic nerve posterior to the lamina cribrosa [10].

The location of the CZ in relation to the optic nerve sheath varies significantly. The varieties were grouped into two types. In type 1, which consists of about 70% of the eyes in this study, the blood supply to the pial system through pial branches of the anteriorly located CZ appeared to be relatively direct, since the branches travelled only a short distance by a relatively straight route to enter the pial system. However, in type 2 (seven eyes), pial branches of the CZ were occasionally observed to extend around the distal end of the subarachnoid space to supply the pial system. Posterior location of the CZ may result in a circuitous and/or more complicated course of the blood vessel in closer relation to the subarachnoid space.

Studies have shown that AION is due to interference with the blood supply from short posterior ciliary arteries to the anterior optic nerve [6–8, 10]. Histology has shown a ischaemic lesion in the core of the optic nerve just posterior to the lamina cribrosa [16]. As described above, pial branches play the most important role in supplying the pial plexus, which supplies the optic nerve posterior to the laminar cribrosa as a main source. The pial branches are small precapillaries and have a mean radius of 18.9 μm in this study. We presume that the pial branches in type 2, extending for a greater distance closely around the distal end of the subarachnoid space, are relatively vulnerable to fluctuation in cerebrospinal fluid (CSF) pressure or any other predisposing factor to closure, which may lead to ischaemic events.

In the five eyes with no CZ, all the optic nerves were supplied by direct branches of short posterior ciliary arteries to the pial system. We unfortunately did not have enough specimens to interpret either the most common route or the size of these branches in the current study. We do not know whether these cases without CZ show higher or lower predisposition towards ION.

The mechanism of the development of papilloedema has been explained by stasis of axoplasmic flow of the optic nerve [3, 4, 17, 18]. The anatomical substructure of the optic nerve consists of bundles of axons enclosed by collagen septa, which provide a firm mechanical support from the retrolaminar portion to the intraorbital portion against distortion (Fig. 4). It may be conceivable that the earliest stages of papilloedema start from ischaemia, since the main blood supply from the pial branches of CZ appears to be cut off long before the well-supported optic nerve itself is strangled by raised CSF pressure in the sheath. Axoplasmic flow may be blocked when the encased axons swell because of the ischaemia.

Visual obscurations which last seconds are precipitated by movement, stressing or Valsalva manoeuvre and occur in patients with papilloedema. This phenomenon probably results from transient closure of the pial branches of the CZ or compression of the pial plexus itself by the raised CSF pressure.

The morphological relationship between the optic nerve sheath and the CZ was investigated by serial sectioning of 29 human eye bank eyes with reference to optic disc size. Two types were observed, type 1 with anteriorly positioned CZ, and type 2 with CZ location posterior to the distal end of the optic nerve sheath.

Significant correlation between small disc size and the relative positions of the CZ and the sheath was observed. From the morphological aspect, the higher risk of AION among eyes with smaller discs may be explained by the relative vulnerability of pial branches of the CZ in this group.

We suggest that the microvascular structure described here may relate to the mechanism of papilloedema, since eyes with posteriorly located CZ appear to be more vulnerable when raised CSF pressure exists.

The opportunity to investigate eyes with known AION or papilloedema is so rare that we based our suggestions on studies of normal specimens. We hope that more studies will be performed in this field.

Acknowledgements The authors would like to thank Ann Patmore for her kind help in producing the photographs, Dr. George E. Marshall for harvesting and preparing the eyes, and Frances Biggins for the help in histological preparation. This study was supported by the Iris Fund, London, UK.

References

1. Anderson DR, Braverman S (1976) Re-evaluation of the optic disc vasculature. Am J Ophthalmol 82: 165–174
2. Beck RW, Servais GE, Hayreh SS (1987) Anterior ischaemic optic neuropathy. IX. Cup-to-disc ratio and its role in pathogenesis. Ophthalmology 94: 1503–1508
3. Hayreh SS (1977) Optic disc edema in raised intracranial pressure. V. Pathogenesis. Arch Ophthalmol 95: 1553–1565
4. Hayreh SS (1977) Optic disc edema in raised intracranial pressure. VI. Associated visual disturbances and their pathogenesis. Arch Ophthalmol 95: 1566–1577
5. Hayreh SS (1990) In vivo choroidal circulation and its watershed zones. (review) Eye 4: 273–289
6. Hayreh SS, Chopdar A (1982) Occlusion of the posterior ciliary artery. V. Protective influence of simultaneous vortex vein occlusion. Arch Ophthalmol 100: 1481–1491
7. Hayreh SS, Baines J (1972) Occlusion of the posterior ciliary artery. III. Effects on the optic nerve head. Br J Ophthalmol 56: 754–764
8. James CB, Smith SE (1991) The effect of posture on the intraocular pressure and pulsatile ocular blood flow in patients with non-arteritic anterior ischaemic optic neuropathy. Eye 5: 309–314
9. Lieberman MF, Maumenee AE, Green WR (1976) Histologic studies of the vasculature of the anterior optic nerve. Am J Ophthalmol 82: 405–423
10. Mcleod D, Marshall J, Kohner EM (1980) Role of axoplasmic transport in the pathophysiology of ischaemic disc swelling. Br J Ophthalmol 64: 247–261
11. Olver JM, McCartney AC (1989) Orbital and ocular micro-vascular corrosion casting in man. Eye 3: 588–596
12. Olver JM, Spalton DJ, McCartney AC (1990) Microvascular study of the retrolaminar optic nerve in man: the possible significance in anterior ischaemic optic neuropathy. Eye 4: 7–24
13. Olver JM, Spalton DJ, McCartney ACE (1994) Quantitative morphology of human retrolaminar optic nerve vasculature. Invest Ophthalmol Vis Sci 35: 3858–3866
14. Onda E, Cioffi GA, Bacon DR, Van Buskirk EM (1995) Microvasculature of the human optic nerve. Am J Ophthalmol 120: 92–102
15. Primrose J (1964) Mechanism of production of papilloedema. Br J Ophthalmol 48: 19
16. Sanders MD (1997) The Bowman lecture: Papilloedema: 'The Pendulum of Progress'. Eye 11: 267–294
17. Tso M, Hayreh SS (1977) Optic disc edema in raised intracranial pressure. III. A pathological study of experimental papilloedema. Arch Ophthalmol 95: 1448–1457
18. Tso M, Hayreh SS (1977) Optic disc edema in raised intracranial pressure. IV. Axoplasmic transport in experimental papilloedema. Arch Ophthalmol 95: 1458–1462
19. Zhao Y, Li F (1987) Microangioarchitecture of optic papilla. Jpn J Ophthalmol 1987: 147–159