Problem 1: The swollen and sunken optic disc

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The eye is firm to the touch as it is pumped up, like a football, by the ciliary body that secretes a fluid (the aqueous) from behind the iris. If the pressure rises too high then this leads to selective death of the axons that exit the eye. These axons exit as the optic nerve and leave the eye at a particular spot called the optic nerve head. At this point, the firm outer layer of the eye, the sclera, is perforated to let the axons pass through, but as a consequence of these perforations, the sclera is weak and will accordingly deform (the scleral sieve through which the axons pass is called the lamina cribrosa). Not only do the axons go from an area of one pressure to another, but they also undertake a sharp right angle change in direction. In glaucoma, the lamina cribrosa deforms backwards. Haemorrhages can occur at the optic nerve head and, as a consequence of both cell death and this backward deformation, the nerve head will appear "cupped".

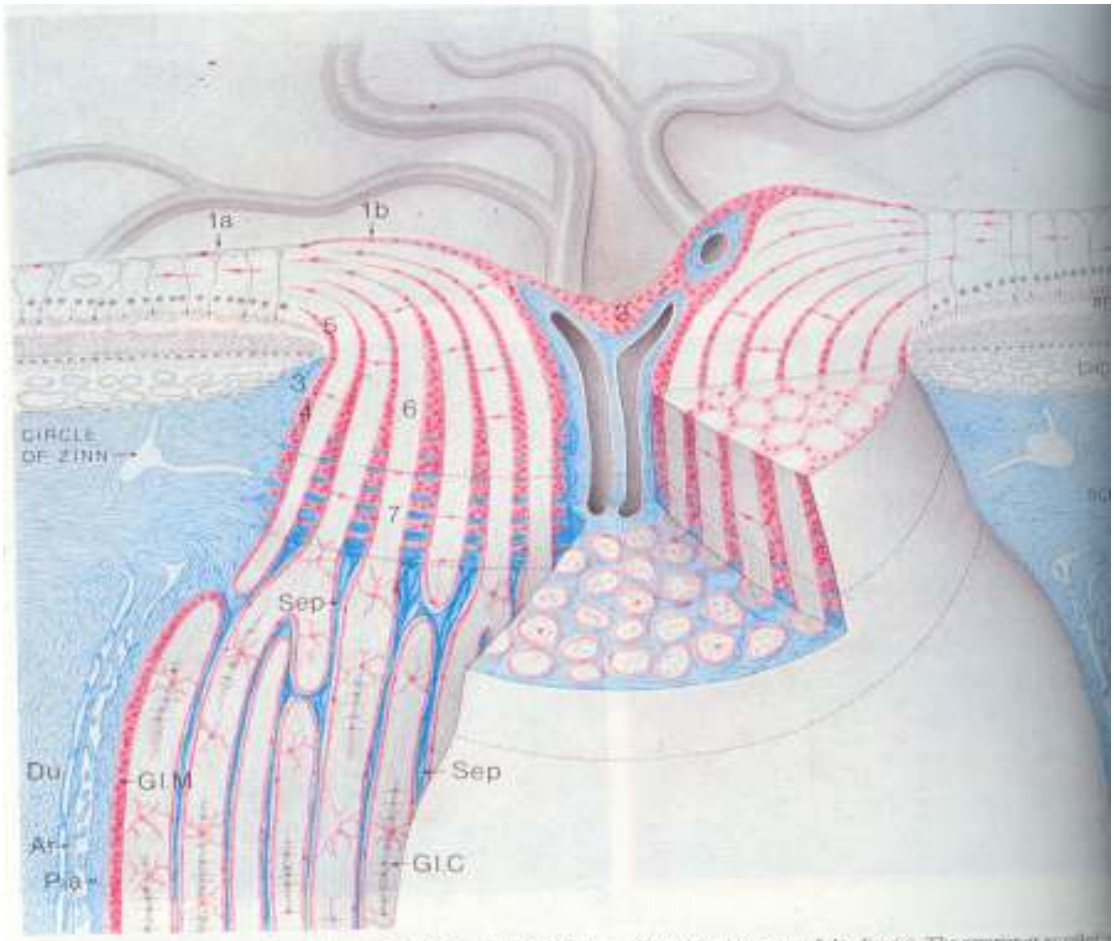
There is a second condition called papilloedema. This is caused by raised pressure of cerebrospinal fluid in the optic sheath in the sub-arachnoid space surrounding the optic nerve beneath the lamina cribrosa. Raised pressure here causes the lamina cribrosa to bow forward, the optic nerve head to appear swollen and again haemorrhages occur in a similar location. Over time the axons die in a similar manner.

The axons themselves are like little tubes and there is flow down them (from the nucleus, where new proteins are made and which is located in the retina, to the synapses in the brain; the flow of axoplasm is required for "maintenance"). These tubes are highly deformable and go from an area of one pressure to another.

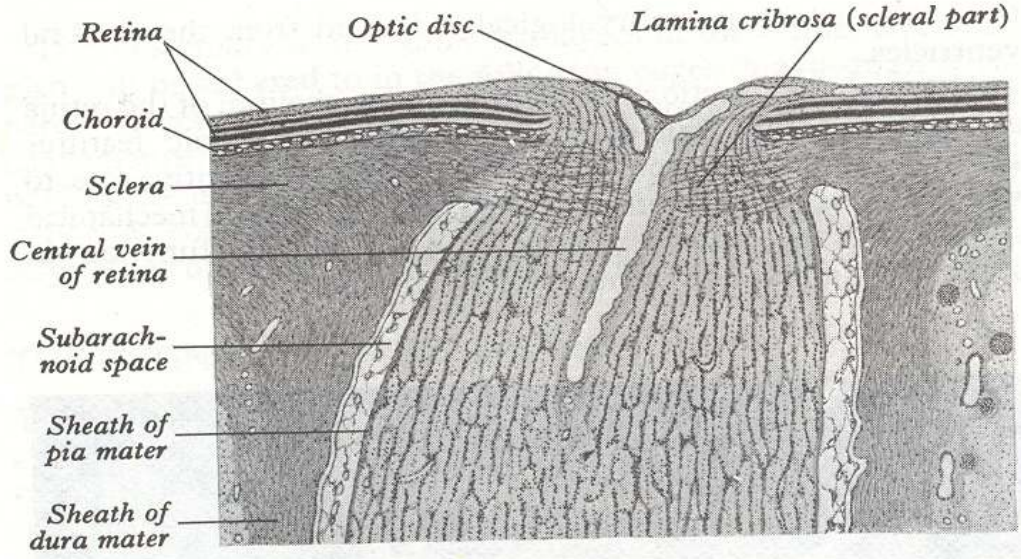
There is a fourth pressure system to be considered. The blood supply has to enter both the optic nerve and the retina and it has its own pressure supply and the blood vessels themselves are potentially collapsible.

This problem is to assemble a model of the back of the eye that has four compartments: the intraocular space; the optic nerve; the vascular space; and the outside. The Study Group is asked to look at flow of blood and of axoplasm as they traverse these compartments and to look for potential blocks in the flow. The aim is to see if there are spots where either the blood vessels or the axons experience high internal pressure that could, in turn, lead to rupture. Rupture of capillaries would be a convincing explanation for the observed haemorrhages at the optic nerve head and would be a novel and plausible explanation for the observed optic nerve fibre death observed in these conditions.

A second layer of complexity to the problem can be added by considering eye movements. The eye rotates on a vertical axis (most scanning eye movements are horizontal) and these movements cause the optic nerve to bend; the analogy is that the weakest part of a cable is the join with the plug. The initial axon loss is not random but preferentially affects the 6 and 12 o'clock positions and eye movements would be a plausible explanation for this distribution.



7.258B Schematic representation of the exit of the human optic nerve from the eyeball, showing the distribution of collagenous (blue) and neuroglial (magenta) tissues. Sep—septa of collagenous connective tissue carried into the nerve from the pia mater and dividing the nerve fibres into numerous fascicles. Gl.M—astroglial membrane separating nerve fibres from connective tissue. Gl.C—astrocytes and oligodendrocytes among the fibres in their fascicles. Du, Ar, Pia—dura, arachnoid and pia maters respectively. 1a is the internal limiting lamina of the retina, which is continuous with an astroglial membrane (of Elschnig) covering the optic disc (1b). An accumulation of astrocytes forms a central meniscus (of Kuhnt) in the centre of the disc (2). The anterior or so-called 'retinal part' of the lamina cribrosa (6) is separated from the choroid by collagenous tissue (3). The 'border tissue of Jacoby' (4), which astroglia, frequently extends beyond the choroid (5) to separate the retina from the 'retinal part' of the optic nerve head. The post of the lamina cribrosa (7) contains collagenous tissue derived optic nerve septa and fenestrated sheets of collagen fibres contin those of the sclera. (Reproduced by kind permission of Dr. D Anderson and Dr. W. F. Hoyt, *Arch. Ophthal.*, 82(4), 506– Copyright 1969, American Medical Association.)



7.258A A horizontal section through the optic nerve at its point of exit from the human eyeball.