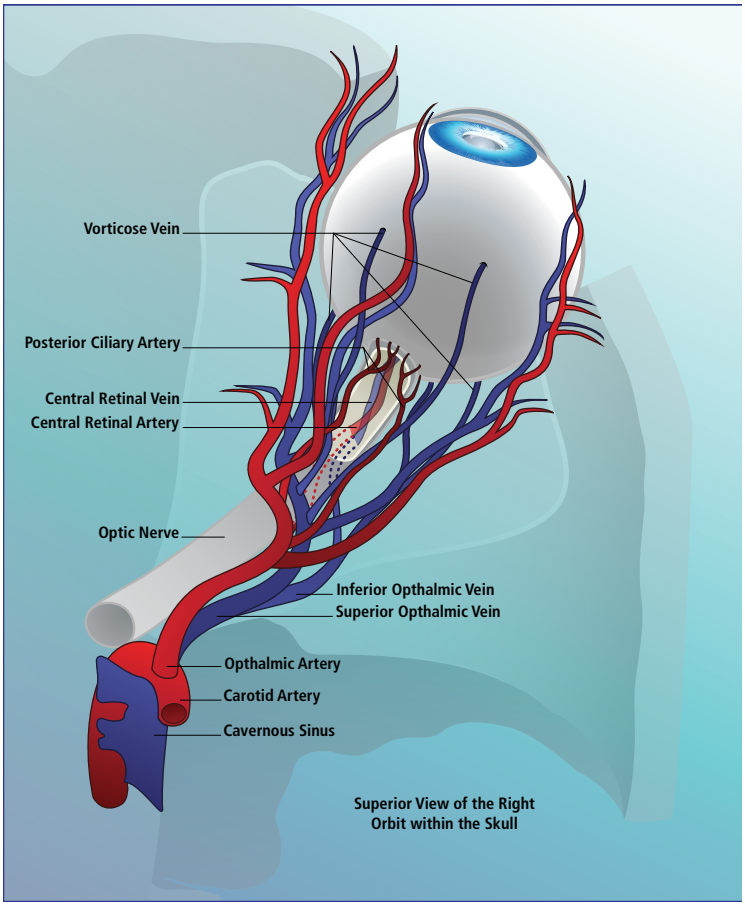
MODULE 5.2
Retinal Vasculature

The retina is among the most metabolically active tissues in the body, and, therefore, its oxygen demand is quite high.[1] A constant supply of oxygen must be available to the cells of the retina; however, a dense vascular network anterior to the photoreceptors would interfere with light transmission to these cells. To circumvent this potential interference, the outer portion of the retina receives almost all of its oxygen via the choroidal microcirculation, which is situated just behind the retinal tissue.

The choroidal circulation branches from the posterior ciliary arteries, which originate from the ophthalmic artery. The inner portion of the retina receives its oxygen from the retinal circulation, which is a separate branch (from the central retinal artery) of the ophthalmic circulation.

Oxygen profiles have helped to identify the sites of oxygen usage in the retina, with three dominant layers of consumption identified: (1) the inner segment of the photoreceptors; (2) the outer plexiform layer; (3) and the deeper region of the inner plexiform layer (IPL).[2] Retinal hypoxia, leading to the uncontrolled growth of new retinal blood vessels, is hypothesized to play a role in the development of diabetic retinopathy (DR).[3]

The Retinal Vasculature



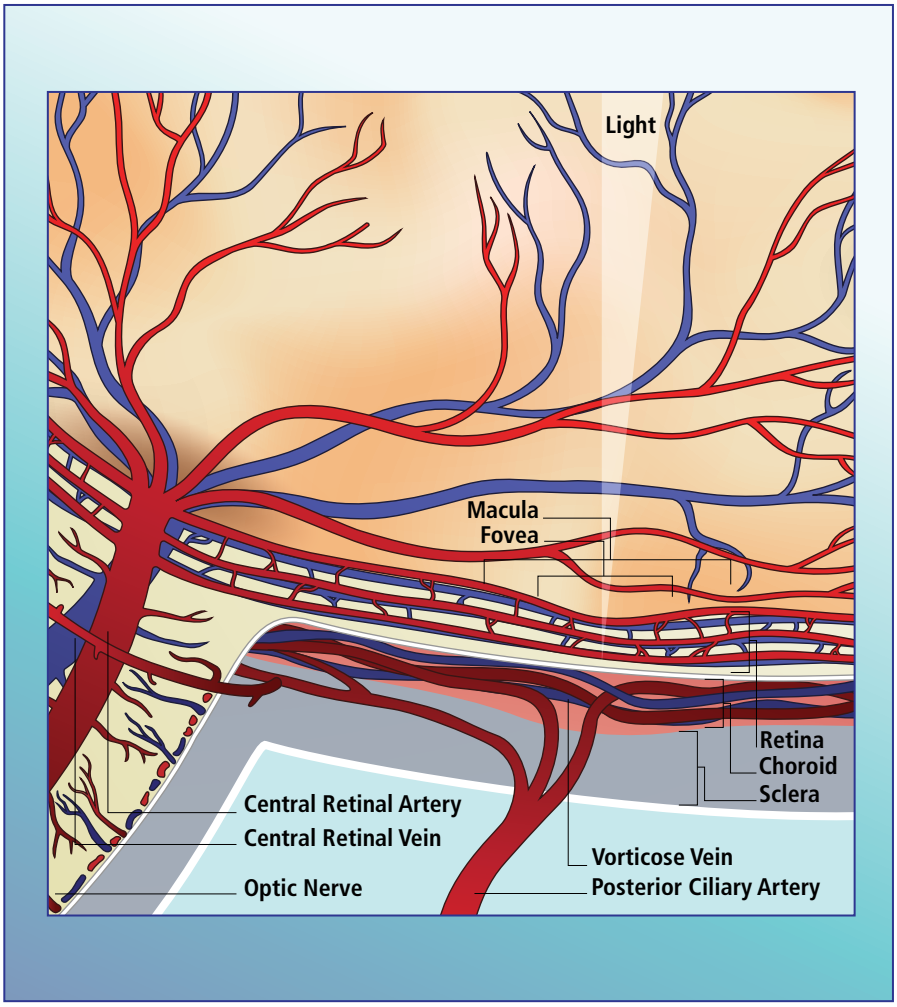
Interestingly, investigators using animal models have not been able to detect signs of retinal hypoxia within the first year of experimentally induced diabetes in cats and dogs. However, retinal hypoxia has been demonstrated in a longer-term animal model of diabetes (>6 years of diabetes).[4] This study reported a decrease in retinal oxygen tension of >50% in diabetic animals compared with controls.

The pathogenesis of diabetic macular edema (DME) involves the breakdown of the blood-retinal barrier (BRB), which comprises an inner BRB and an outer BRB. The inner BRB is made up of tight junctions (TJs) between retinal vascular endothelial cells (ECs) as well as retinal glial cells (astrocytes and Müller cells).[5,6] Under normal conditions, these TJs constitute a barrier that is impermeable to proteins. TJs between retinal pigment epithelial (RPE) cells form the outer BRB. DME is hypothesized to be caused primarily by the breakdown of the inner BRB.[7] Breakdown of the BRB permits the extravasation of proteins and other solutes from capillaries into the extracellular space. This produces a shift in the balance of hydrostatic and oncotic pressure, resulting in the accumulation of fluid within the extracellular space and the development of macular edema.[5]

In the retina of an individual with diabetes, some of the earliest changes seen histologically are adhesion of leukocytes to capillaries and the accumulation of advanced glycation end products (AGEs).[8] These deleterious changes contribute to activation of inflammatory mediators and eventual EC death. The death of these cells contributes to the breakdown of the BRB and can lead to a state of ischemia. Breakdown of EC TJs also occurs.[7,9] DR progression is also associated with the loss of pericytes. These cells are located outside of the BRB and function to stabilize blood vessels. The loss of pericytes may be related to the accumulation of AGEs and to the effects of inflammatory mediators.[10,11] Pericyte loss is also associated with the formation of microaneurysms (MAs) and the breakdown of the BRB. Interestingly, the animal model study of long-term diabetes found that retinal hypoxia was correlated with EC death, MAs, and leukocyte plugging of vessels.[4]

The Retina's High Oxygen Profile

The retina is among the most metabolically active tissues in the body, and, therefore its oxygen demand is quite high. A constant supply of oxygen must be available to the cells of the retina; however, a dense vascular network anterior to the photoreceptors would interfere with light transmission to these cells. To circumvent this potential interference, the outer portion of the retina receives almost all of its oxygen via the choroidal microcirculation, which is situated just behind the retinal tissue. The choroidal circulation branches from the posterior ciliary arteries, which originate from the ophthalmic artery. The inner portion of the retina receives its oxygen from the retinal circulation, which is a separate branch (from the central retinal artery) of the ophthalmic circulation.



References

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