MODULE 6.1
The Metabolic Pathway to Diabetic Macular Edema

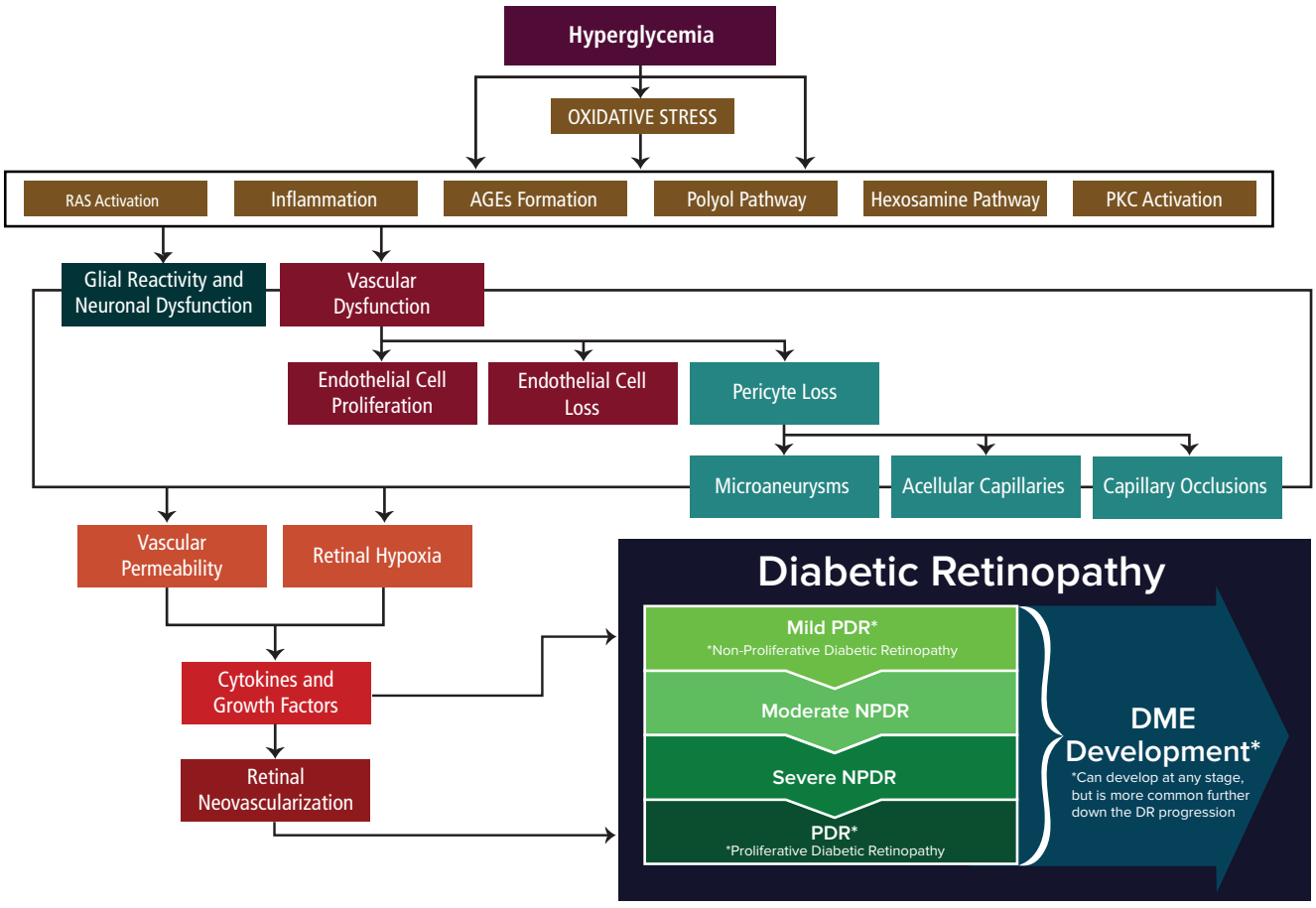
The scientific understanding of the pathophysiologic mechanisms underlying the development of diabetic retinopathy (DR) and diabetic macular edema (DME) is continually evolving. Currently, it is accepted that chronic hyperglycemia leads to a cascade of biochemical and physiologic changes that ultimately result in microvascular damage and retinal dysfunction that characterizes DR and DME.[1]

The sequelae of hyperglycemia, each addressed in more detail in subsequent units in this module, include increased oxidative stress, inflammation due to intraocular renin-angiotensin system (RAS) upregulation, activation of protein kinase C (PKC) isoforms, and upregulation of advanced glycation end-products (AGEs), polyol, and hexosamine pathways.[1,2] The metabolic sequelae of hyperglycemia affect not just the retinal vasculature, but the entire neurovascular unit, which includes pericytes, glial cells, and neurons, in addition to blood vessels.[3,4]

The disruption of the neurovascular unit contributes to the pathophysiology of DR, which includes DME.[4]

The upregulation of the above-mentioned metabolic pathways results in neuronal and vascular dysfunction in the retina, including endothelial cell (EC) proliferation and loss of ECs and pericytes, causing microaneurysms, accellular capillaries, and capillary occlusions. The vascular permeability and retinal hypoxia that result from this contributes to the release of cytokines and growth factors, a hallmark of DR.[1] Neovascularization in the retina may occur, defining a severe form of DR known as proliferative diabetic retinopathy. DME may develop at any stage of the DR severity scale, but is more common in the later stages. DME occurs when retinal capillaries become leaky and the central part of the retina, known as the macula, swells from an accumulation of blood, fluid, and hard exudates.

Metabolic Pathway to DME



References

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2. Wu Y, Tang L, Chen B. Oxidative stress: implications for the development of diabetic retinopathy and antioxidant therapeutic perspectives. *Oxid Med Cell Longev.* 2014;2014:752387.

3. Zhang X, Zeng H, Bao S, Wang N, Gillies MC. Diabetic macular edema: new concepts in patho-physiology and treatment. *Cell Biosci.* 2014 May;4:27.

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