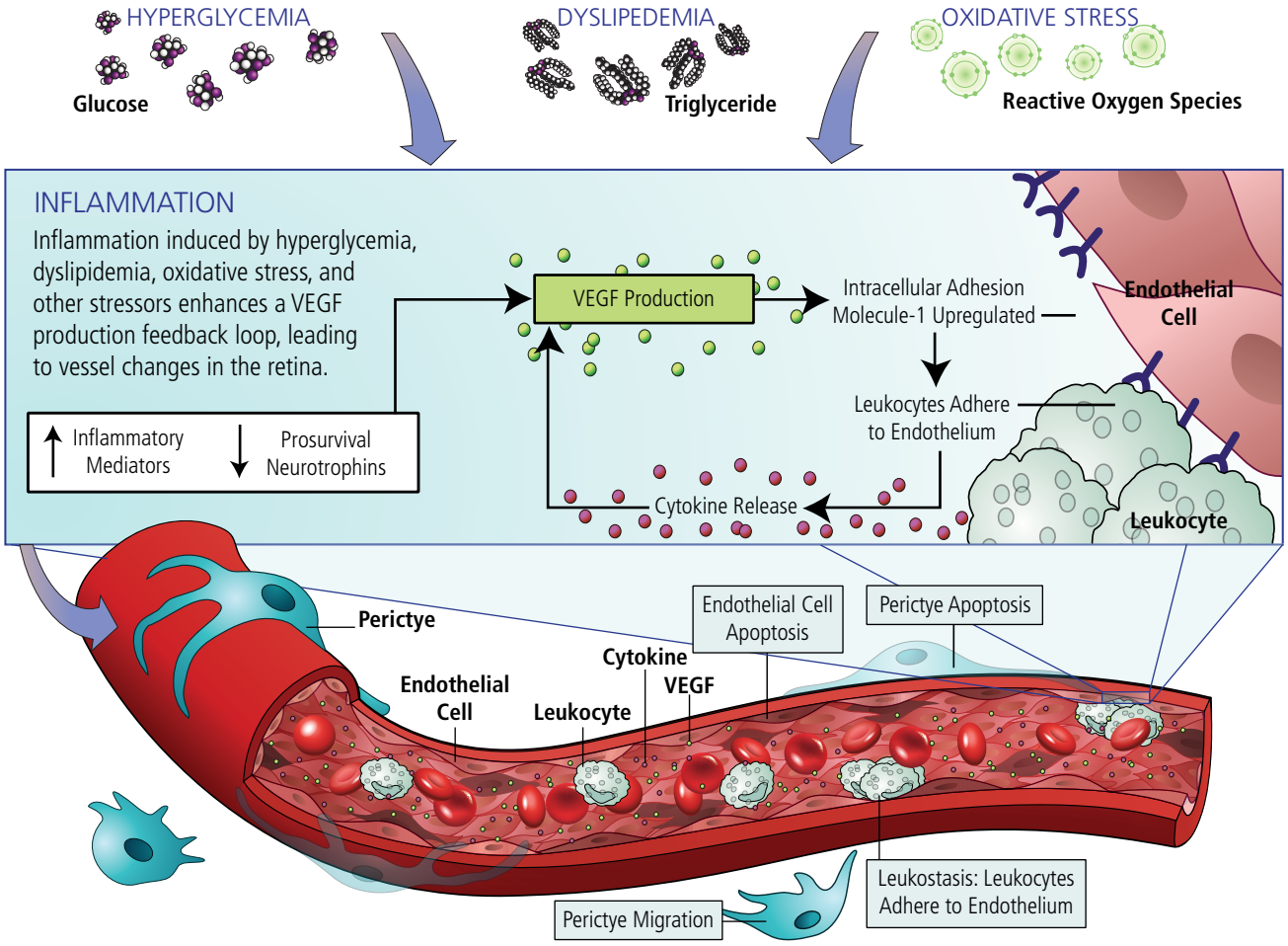
MODULE 6.9
Inflamation

Inflammation is increasingly recognized as playing a prominent role in the pathogenesis of diabetic retinopathy (DR).[1-3] An array of inflammatory mediators are upregulated in diabetes, in response to hyperglycemia, dyslipidemia, and other stresses. These mediators trigger parainflammatory responses that may cause abnormal reactions between leukocytes and endothelial cells (ECs), ultimately leading to damage to retinal microvasculature. This effect is thought to be local because there is little evidence of association between systemic inflammation and risk of DR.[2]

Disruption of the balance between inflammatory mediators and prosurvival neurotrophins leads to chronic inflammatory response in both neural and retinal ECs. This results in production of vascular endothelial growth factor (VEGF) and recruitment of inflammatory mediators, with several ensuing effects: increased vascular permeability, capillary nonperfusion due to apoptosis of ECs, neurodegeneration due to apoptosis of neural cells, and neovascularization.[2]

High vitreous levels of the proinflammatory molecule VEGF are highly correlated with retinal neovascularization and edema.[3] VEGF has been shown to form an inflammatory loop, promoting expression of intracellular adhesion molecule-1 from ECs, which leads to leukocyte activation and cytokine release, causing further expression of VEGF and amplification of the inflammatory response. Intravitreal administration of VEGF-inhibiting therapies is currently widely used clinically in the treatment of DME.[3]

Inflammation in DME



References

1. Antonetti DA, Barber AJ, Bronson SK, et al; JDRF Diabetic Retinopathy Center Group. Diabetic retinopathy: seeing beyond glucose-induced microvascular disease. *Diabetes*. 2006;55:2401-2411.

2. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet.* 2010;376:124-136.

3. Tang J, Kern TS. Inflammation in diabetic retinopathy. *Prog Retin Eye Res*. 2011;30:343-358.