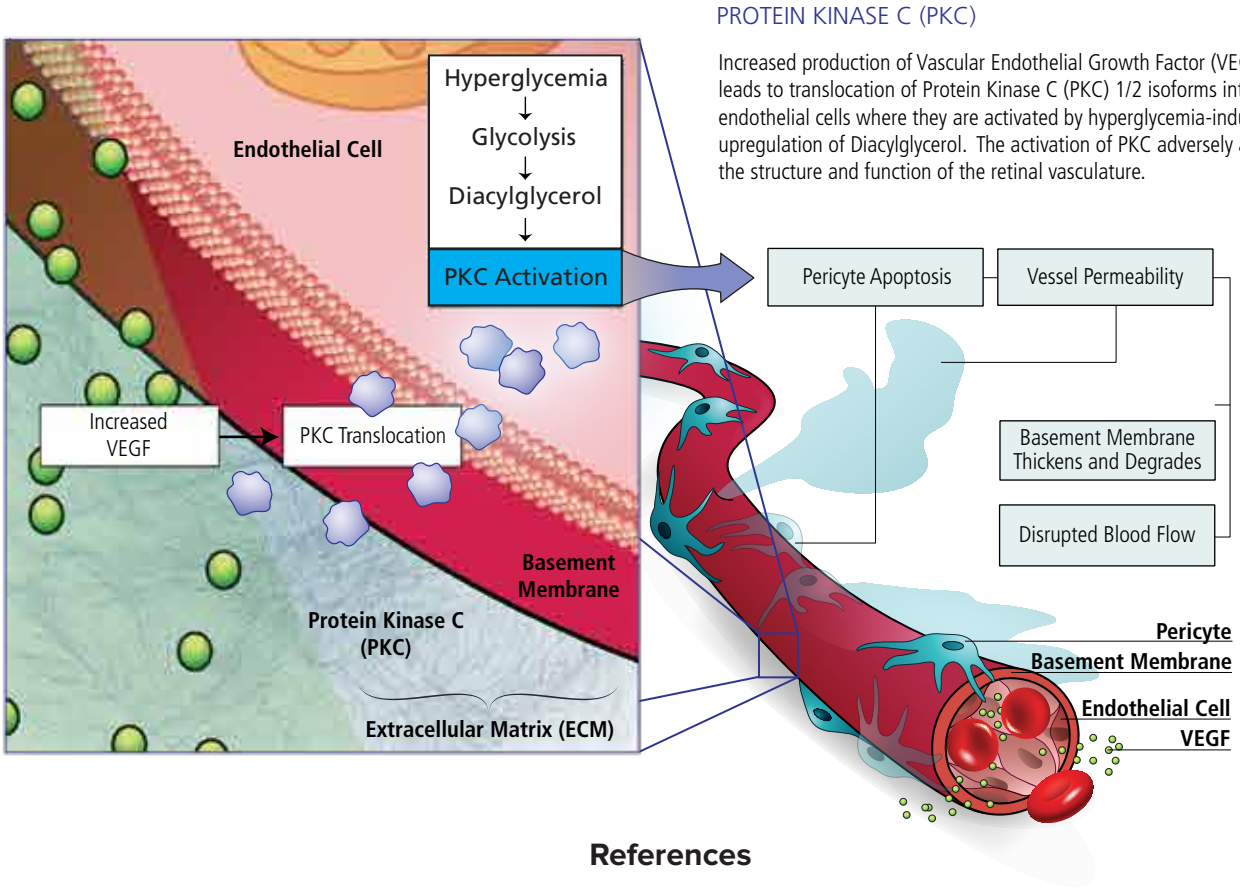
MODULE 6.3
Protein Kinase C

Activation of the enzyme protein kinase C (PKC) is one of the interconnecting biochemical mechanisms implicated in the pathogenesis of diabetic retinopathy (DR). PKC is a family of enzymes; expression of its beta-1/2 isoforms (PKCβ 1/2) is enhanced in individuals with diabetes, and these isoforms appear to be closely associated with the development of DR.[1]

Oxidative stress caused by hyperglycemia increases activation of PKC in retinal cells, leading to increased expression of matrix proteins and vasoactive mediators. These changes have adverse effects on both structure and function in the retinal vasculature. Structural consequences include pericyte apoptosis and thickening of the basement membrane. Functional effects include increases in retinal vascular permeability and disruption of retinal blood flow.[2]

PKC is involved in the regulation of numerous physiologic pathways. Its activation leads to a cascade of effects on other pathways, which in turn cause changes in the retina. The synthesis and remodeling of extracellular matrix are affected, angiogenic factors (including vascular endothelial growth factor [VEGF]) are released, and endothelial and leukocyte dysfunction lead to capillary blockage and leukostasis.[1] The PKC pathway therefore influences other pathways including inflammation and neovascularization, which contribute to the pathogenesis of DR.[1]

Protein Kinase C (PKC) Activation in DME



References

1. Tarr JM, Kaul K, Chopra M, Kohner EM, Chibber R. Pathophysiology of diabetic retinopathy. *ISRN Ophthalmol.* 2013;2013:343560.

2. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet.* 2010;376(9735):124-136.