

## MODULE 6.0

## Introduction: DR/DME Etiology

The retina has a high metabolic demand, making it vulnerable to metabolic stress from diabetes. This metabolic stress leads to molecular and tissue level changes in the eye that lead to diabetic retinopathy (DR) and diabetic macular edema (DME). In this Module, you will learn about:

- Metabolic Pathway to DME
- Hyperglycemia
- Protein Kinase C (PKC)
- Oxidative Stress
- Advanced Glycation End Products (AGEs)
- Polyol Pathway
- Hexosamine Pathway
- Renin-Angiotensin System (RAS)
- Inflammation
- Retinal Vessel Changes
- Retinal Changes and Edema

**Introduction**

The biological path to decreased vision due to DR and DME begins with chronically elevated blood glucose levels. Over time, poor glycemic control damages the vascular tissue, in particular the endothelial cells (ECs) and the pericytes of

retinal blood vessels, resulting in vascular dysfunction, inflammation, and hypoxia that characterizes DR.<sup>1</sup>

Continued elevated blood glucose causes retinal blood vessels to swell and microaneurysms (MAs) to form. Because of the vascular dysfunction, retinal hypoxia develops, which stimulates production of vascular endothelial growth factor (VEGF). Increased VEGF levels in retinal tissue lead to increased vascular permeability and an accumulation of fluid. As the vessels leak in the retina, the macula develops edema.<sup>1</sup> Swelling and thickening of the macula reduces visual acuity.<sup>2</sup>

All people with diabetes are at risk of developing DR and DME. The onset of DME is usually insidious and asymptomatic, so patients have no warning signs that DME is occurring until they notice a blurring of their central vision. The severity of the condition can range from mild - a loss of just one line of vision on a standardized eye chart - to blindness.<sup>1</sup>

**References**

1. National Eye Institute. Facts about diabetic retinopathy. <http://www.nei.nih.gov/health/diabetic/retinopathy.asp>. Last reviewed September 2015. Accessed October 20, 2015.
2. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy: IV. Diabetic macular edema. *Ophthalmology*. 1984;91:1464-1474.
3. American Diabetes Association. Living with diabetes: eye complications. <http://www.diabetes.org/living-with-diabetes/complications/eye-complications/>. Last edited November 1, 2013. Accessed October 20, 2015