MODULE 6.4
Oxidative Stress

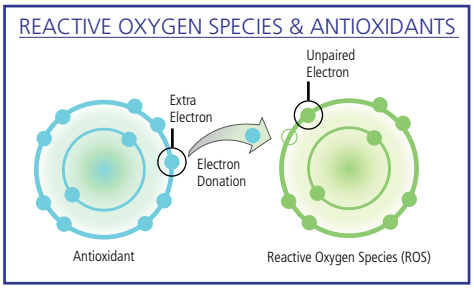
Oxidative stress can be defined as an imbalance between oxygen free radicals, or reactive oxygen species (ROS), and the antioxidant defenses of a biologic system.[1,2] Mounting evidence suggests that localized oxidative stress due to diabetes-induced metabolic abnormalities is an important mechanism associated with the pathogenesis of diabetic retinopathy (DR).[1,2] Increases in concentrations of ROS within ganglion cells lead to the activation of several pathologic mechanisms involved in DR. Notably, the damage or dysfunction caused by oxidative stress persists even after glycemia has been normalized.[2]

The retina is especially susceptible to oxidative stress because of its high energy demands and exposure to light. A number of the biochemical mechanisms that contribute to the pathogenesis of DR appear to be associated with overproduction of ROS by mitochondria. These mechanisms, discussed separately in other submodules in this series, include inflammation, increased flux in the polyol pathway, increased production of advanced glycation end products (AGEs), activation of protein kinase C (PKC), and overactivation of the hexosamine pathway.[2]

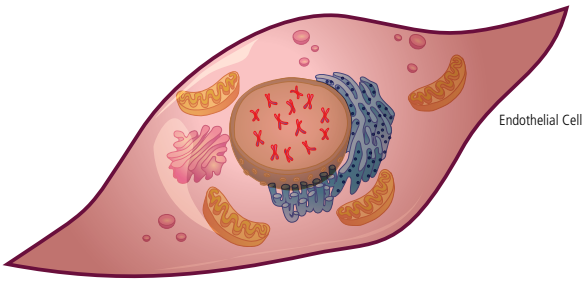
It has been suggested that oxidative stress constitutes a unifying mechanism that links all of the damaging mechanisms in DR induced by hyperglycemia. In this scenario, ROS produced by mitochondria cause DNA single-strand breaks, which in turn activates poly-(ADP-ribose)-polymerase (PARP). Activation of PARP inhibits the activity of glyceraldehyde phosphate dehydrogenase (GAPDH), causing the accumulation of glycolytic metabolites.[1-3]

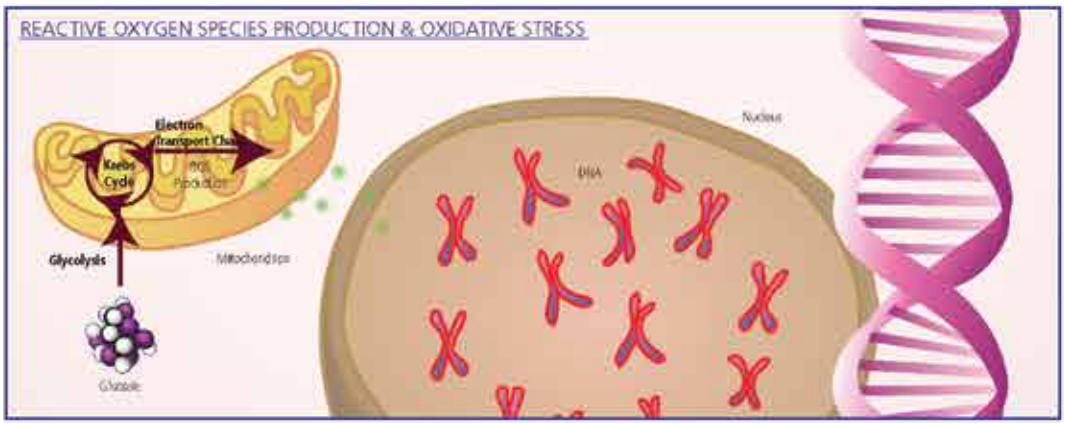
Although experimental work with antioxidants in animal models has shown some benefit, this has not been borne out in human clinical trials.[1]

Oxidative Stress



Since the eye is highly exposed to ultraviolet (UV) rays from light, it is especially susceptible to oxidative stress.





References

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

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. Brownlee M. The pathobiology of diabetic complications: a unifying mechanism. *Diabetes.* 2005;54(6):1615-1625.