Almost 20 years ago, endothelium-derived relaxing factor was identified as nitric oxide,1,2 and since that time, the field has witnessed extraordinary growth and complexity. Biologists now recognize that nitric oxide is a multifunctional molecule with roles in neurotransmission, immune regulation, oxidative metabolism and oxygen delivery, inflammation, and control of cell growth, apoptosis, and necrosis, among others. The central importance of nitric oxide in human biology and pathobiology was recognized by the Nobel Committee in 1998 by their awarding the prize to Robert Furchgott, Louis Ignarro, and Ferid Murad for their seminal contributions to the field.

Among the many mechanisms by which nitric oxide exerts its effects are included its redox activities. In 1992, the year in which nitric oxide was named “molecule of the year” by Science, we summarized the complexity of these redox reactions highlighting the differences among nitrosonium, nitrogen monoxide, and nitroxy anion as redox-active species and their relevance to biological systems.3 The redox activity of nitric oxide was appreciated by chemists, of course, but gained little attention from biologists until its reaction with superoxide to form peroxynitrite was identified in cellular systems.4 Over the ensuing 15 years, abundant evidence supports the importance of redox biochemistry as the basis for multifaceted biological and pathobiological actions of nitric oxide.

Redox regulation is a general biochemical mechanism for governing cell function and phenotype,5 and its modulation offers a novel approach to pharmacotherapeutics.6 The role of nitric oxide in redox regulation is amply demonstrated in its ability to participate in posttranslational modification of the vascular thiol proteome, modulation of mitochondrial function and energetics in the vasculature, promotion of endoplasmic reticulum stress, actions in the pulmonary vasculature as they relate to normal pulmonary vascular responses and pulmonary hypertension, and regulation of oxygen delivery by hemoglobin. This series will, then, provide a state-of-the-art update on the redox-dependent actions of nitric oxide in cardiovascular biology and disease states. It is a topic well worth revisiting as the field continues to be enriched by new and very interesting observations.

**References**


4. Beckman JS, Beckman TW, Chen J, Marshall PA, Freeman BA. Apparent hydroxyl radical production by peroxynitrite: implications for endothelial injury from nitric oxide and superoxide. *Proc Natl Acad Sci U S A*. 1990;87:1620–1624.


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