ANTIOXIDANTS & REDOX SIGNALING
Volume 3, Number 1, 2001
Mary Ann Liebert, Inc.

Tribute

In Memory of Daniel L. Gilbert— A Radical Spirit

CAROL A. COLTON, Ph.D.

THE DUAL NATURE OF oxygen as both life-giver and mediator of cell death has taken at least 100 years to be fully appreciated. The very characteristics of oxygen that allow it to be useful also allow it to impair and kill living organisms. In 1953, a highly interactive group of scientists at the University of Rochester began a series of experiments that explored the yin and yang of oxygen. Daniel L. Gilbert was among these scientists and was in the type of environment he loved best . . . where long hours could pass at the lab bench in the blink of an eye and where controversial topics were hotly debated. From this mix emerged the birth of a scientific career and the birth of a new and now dominant view of the toxicity of oxygen. Dan and his colleague, Rebbeca Gerschman hypothesized that oxygen-induced poisoning and x-irradiation–mediated toxicity had a common mechanism (Gerschman, R., D.L. Gilbert, S. Nye, P. Swyer and W.O. Fenn. *Science* **119:**623–626, 1954). In this seminal publication, they introduced the idea that reactive oxygen intermediates, that is, free radicals, could be damaging to biological systems. The toxic nature of reactive oxygen intermediates and free radicals was further examined by exposing mice to varying pressures of oxygen. In a 1958 paper, they demonstrated that survival time of mice was inversely related to the pressure of oxygen and that agents which prevented radiation-mediated toxicity also prolonged the survival of mice exposed to high levels of oxygen (Gerschman, R., D.L. Gilbert and D. Caccamise. *Am. J. Physiol.* **192:**563–571, 1958). Although the exact radical species was unknown, Dan and his colleagues predicted that one of the principal toxic substances produced under these circumstances was hydrogen peroxide (Gilbert, D.L., R. Gerschman, K.B. Ruhm and W. Price. *J. Gen Physiol.* **41:**989–1003, 1957).

Dr. Daniel L. Gilbert
1925–2000

To Dan, all of these "radical" ideas were perfectly logical and could be easily understood by looking at cell evolution. One of Dan's favorite publications was his treatise on the "Evolutionary Aspects of Atmospheric Oxygen and Organisms" which he prepared for the Handbook of Physiology in 1996 (*Handbook of Physiology*, Section 4. Adaptation to the Environment. Vol. 2; M.J. Fregly and C.M. Blatteis, eds., pp. 1059–1094). In this chapter, Dan described the changes in evolutionary pressures on organisms caused by the presence of blue-green algae. Photosynthesis and the production of oxygen by these organisms were responsible for a relatively abrupt change in the earth's atmosphere. The

shift from a reducing to an oxidizing environment resulted in the utilization of oxidation reactions to supply energy for cellular functions. However, as Dan delineated, the cost to the organism was high, and at least 7 distinct ways to protect against oxidation also evolved. Hours were frequently spent at the National Archives and the National Library of Medicine as Dan traced the history of the discovery of oxygen. Phlogiston was a word that Raymond, his son, could pronounce as soon as he could talk.

Dan devoted a large part of his career at the Lab of Biophysics at the National Institutes of Health in Bethesda to the study of oxygen and its effects on living organisms. Two outstanding books which he edited serve as evidence of his influence on the field of oxyradical research. The first book in 1981, entitled *Oxygen and Living Processes: An Interdisciplinary Approach* (Springer-Verlag, Berlin) predates the large increase in interest in reactive oxygen species which began in the late 1980's. In this edition, topics were introduced which demonstrated the diverse potential role of free radicals in biological functions. Typical of any new scientific concept, the emphasis of many of the contributing authors was on the existence of radical species and their reactions. The second edition published this past year (1999; *Oxygen and Living Processes: An Interdisciplinary Approach;* Kluwer Academic Publishers, New York) clearly shows the growth and maturation of this field. Topics ranging from the mechanisms of action to genetic regulation of free radical production were covered. Dan was always very proud to have contributed to the birth and continued development of the oxyradical field. He deserves our heartfelt thanks.

Address correspondence to:
Carol A. Colton, Ph.D.
Division of Neurology
Duke University School of Medicine
Durham, NC 27710

E-mail: Glia01@aol.com