Macrophage Microbicidal Mechanism

TO THE EDITOR:

Jolly and Mahadevan have attempted to study the role of reactive oxygen intermediates in the intracellular killing of *Mycobacterium leprae* in human macrophages ([3]). The authors have reported 89 nmol of H_2O_2 and 0.3 nmol of superoxide (O_2^-) in the macrophages of lepromatous leprosy patients.

During phagocytosis, macrophages produce substantial quantities of O_2^- and H_2O_2 as shown by the following reactions: Superoxide is formed by the one electron reduction of oxygen: $2O_2 + NADPH \rightarrow O_2^- + NADP^+ + H^+$. Superoxide is converted to H_2O_2 by the reaction $2O_2 + 2H^+ \rightarrow O_2^- + H_2O_2$. This reaction is catalyzed by the enzyme superoxide dismutase.

Considering the fact that all of the oxygen taken up during the respiratory burst is converted to O_2^-, and that 80% of this O_2^- is converted to H_2O_2 by dismutation ([1]), it is difficult to understand from the paper ([3]) how 89 nmol H_2O_2 could be accounted for when only 0.3 nmol O_2^- was produced (Table 1).

However, there is a report which claims a direct conversion of molecular oxygen to H_2O_2 ([2]), as shown by the reaction: $NADH + O_2 + H^+ \rightarrow H_2O_2 + NAD^+$. This has been reported in guinea-pig neutrophils *in vitro*. It has also been argued that the rather high Km (0.4 mM) for NADH observed *in vitro* for this enzyme militates against significant activity during phagocytosis ([2]).

Under these circumstances, more confirmation is needed regarding the role of superoxide and H_2O_2 in the killing of *M. leprae* by human macrophages.

—Raji Swamy, M.D., Ph.D.

Department of Immunology
Tuberculosis Research Centre
Spur Tank Road
Chetput, Madras 600031, India

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