Alveolar Macrophages
Enhancers or Suppressors of Pulmonary Immune Reactivity?

Alveolar macrophages, the resident mononuclear phagocytes of the lung, are situated at the air-tissue interface, strategically located for initial contact with inhaled particulates. The critically important role of alveolar macrophages in defense of the host against inhaled microorganisms and environmental toxins has been clearly established. Elimination of respirable particles and microbial organisms from distal air-spaces of the lung depends most importantly upon the phagocytic and microbicidal activity of alveolar macrophages. These cellular functions provide effective, efficient and nonspecific defense of the lung.

Immunologically-specific mechanisms of host-defense are also operative in the lung. While such specificity is ultimately provided by lymphocytes, interactions of lymphocytes with alveolar macrophages appear necessary for initiation, modulation and expression of pulmonary immune reactivity. Potentially, alveolar macrophages participate in pulmonary immune reactions in several ways. First, they have been shown to serve as effectors for cell-mediated immune reactions: particulate antigens interact with specifically sensitized T-lymphocytes in the lung resulting in local elaboration of lymphokines which activate alveolar macrophages. Activation in this context equates with enhancement of phagocytosis and microbicidal activity, particularly with respect to viruses, fungi, and intracellular bacteria. Second, they may initiate the induction phase of humoral and cellular immune responses: alveolar macrophages ingest particulate antigens, "process" and present them on their surface membranes to specific antigen-reactive B- and T-lymphocytes, inducing them to proliferate and differentiate into effectors of humoral and cell-mediated immunity respectively. Third, alveolar macrophages may serve a regulatory role by modulating the induction or the expression of immune reactions. In this role, alveolar macrophages might enhance or suppress the proliferation, differentiation, or functional activity of antigen-stimulated lymphocytes. Recently, considerable investigative attention has focused on defining the role of alveolar macrophages in modulating immune responses.

The ability of alveolar macrophages to regulate lymphocyte reactivity has been examined experimentally in vitro using either antigens or mitogens to stimulate lymphocyte proliferation. The present discussion will be limited to studies involving stimulation by mitogens. Although mitogens are nonspecific stimuli, under controlled conditions they serve as reliable and convenient experimental models for investigating immune reactivity of lymphocytes. In these models, preparations of lymphocytes from blood or lymph nodes are depleted of macrophages and incubated with mitogens (eg, Con-A) in the absence or presence of various proportions of added alveolar macrophages. The enhancing or the suppressive influence of the added alveolar macrophages are then determined by measuring increases or decreases in lymphocyte proliferative responses.

In animal models, studies of the effect of alveolar macrophages on mitogen-induced lymphocyte proliferation have yielded conflicting results. Normal alveolar macrophages from guinea pigs and rabbits enhance, while those from rats and dogs suppress mitogen responses. Similar studies performed with human alveolar macrophages are fragmentary and have also produced conflicting results. Initial studies of Daniele et al suggested that human alveolar macrophages enhanced, while those of Barsoum et al indicated that human alveolar macrophages suppress mitogen-induced lymphocyte proliferation.

In the current issue of Chest, McCombs et al (see page 266) report the results of more extensive studies than previously available which examine the effect of human alveolar macrophages on mitogen-responses of blood lymphocytes. In carefully performed studies, utilizing cells obtained from 14 smokers and ex-smokers, they found that graded doses (0.1 to 20 percent) of alveolar macrophages...
consistently produced dose-dependent suppression of lymphocyte proliferation. They further showed
that the suppressive activity was present in soluble mediators released by adherent alveolar macro-
phages. It is of interest that two of the 14 macro-
phage preparations, when added in low propor-
tions, resulted in enhancement of lymphocyte proliferation.
This latter observation hints at a paradox which
has plagued and confused the issue regarding the
enhancing or suppressing activities of alveolar macro-
phages. Essentially, the paradox is that on the
one hand, small numbers (approximately 1 percent
or less) of macrophages are known to be an abso-
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