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Replenishing the Starved Patient
When Do Lung Immune Cells Recover?

Starvation and malnutrition remain prevalent problems in clinical practice. The World Health Organization reports that more than one third of the world population suffer from malnutrition. Even in industrialized societies, no hospital ward lacks undernourished patients. Such patients are more susceptible to pneumonia, and in the critically ill malnourished patient, pulmonary sepsis and respiratory failure are among the major causes of death. Prolonged protein and calorie restrictions produce abnormalities in pulmonary defense mechanisms, pulmonary structure and function, control of breathing and respiratory muscular contractility. Such changes have recently been reviewed in this journal by Rochester and Esau. At present, our understanding of why malnourished patients are more vulnerable to pulmonary infections remains incomplete.

Immunologically, nutritional deficiencies have been shown to be associated with impairments of T-lymphocytes, complement system, polymorphonuclear leukocyte bacterial killing, B-lymphocyte function and antibody production. On the other hand, no change was detected in the chemotactic and bactericidal functions of peritoneal macrophages obtained from rats subjected to protein calorie malnutrition. In another study, peripheral monocytes of children suffering from severe malnutrition were also found to have unaltered bactericidal and phagocytic capabilities. The latter two studies suggest that the mononuclear phagocytic system (MNP) maintain its normal immune functions and are unaffected by protein calorie malnutrition. However, the pulmonary alveolar macrophage, which plays an important role in lung host defense, is a different breed of MNP since its metabolic and cell surface characteristics are different from those of peritoneal, liver or other resident tissue macrophages. Thus, the findings of normal MNP function in malnourished patients should not be extrapolated directly to the alveolar macrophage without further investigation. Our recent study in rats in fact shows that starvation can reduce alveolar macrophage phagocytic activity to less than half of the normal, using an in vitro assay technique against radioactively tagged microorganisms. Interestingly, on refeeding the animals, a delay of up to three weeks in the recovery of alveolar macrophage phagocytic activity was noted, even though the clinical appearance and the absolute lymphocyte counts of these animals had returned to normal within a week of refeeding. This is in contrast to experiments by other investigators which showed that a number of systemic immune functional parameters recovered in less than three weeks on refeeding malnourished animals. In rats, the mean turnover rate of alveolar macrophage is about three weeks, which seems to suggest that the effect of starvation on the resident alveolar macrophages may be irreversible, and that only when the whole macrophage cell population in the lungs has been replaced would the complete recovery of its phagocytic activity become apparent.
further imply that various indices of immune function currently used to recognize the susceptibility of malnourished patients to infection may have important limitations. It will be valuable to find out whether simple clinical tests such as changes in lymphocyte counts, skin tests for delayed hypersensitivity, and peripheral polymorphonuclear leukocyte functions may in fact correlate with changes in alveolar macrophage functions.

The development of suitable clinical tests to assess the adequacy of pulmonary immune competence would further advance our understanding and improve the management of our patients who are vulnerable to pulmonary infections.

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Current Treatment Modes for Tuberculosis
Public Policy and Implementation

The treatment of tuberculosis always has been a public issue of great complexity. Galvanized by fear and superstition,1 immortalized in literature and the arts,1 and finally, politicized as the responsibility of the public domain, the treatment of tuberculosis has become an institution unto itself. Prior to the advent of chemotherapy, tuberculosis was a unique disease—infec
tious, epidemic, and requiring those afflicted to be isolated for sustained periods. With the advent of antituberculosis chemotherapy, that specialized single disease hospital, the tuberculosis sanitarium, has disappeared. The disease has retreated in large part to the socially disadvantaged segments of our population where it remains a public health problem. Tuberculosis control is a concept referring not only to control of the patient’s disease, but to preventing its spread to succeeding generations. As treatment for tuberculosis becomes progressively more decentralized and returns to the mainstream of medicine, the means by which public policy for treatment of tuberculosis is formulated becomes ever more important—and potentially fragmented.5

Since 1978, we have monitored tuberculosis treatment and prevention practices to determine the standards of practice in the major metropolitan health departments in the United States.3,4 We found a high degree of uniformity in chemoprophylaxis and infection surveillance practices. In some respects, the standard of practice seems to reflect the complexity of the issue involved. Chemoprophylaxis is a relatively simple issue. Clear policy guidelines,4 which are easily implemented, exist, and virtually all health departments follow the combined recommendations of the American Thoracic Society/Centers for Disease Control/American College of Chest Physicians (ATS/CDC/ACCP). The 28 health departments surveyed formulated these surprisingly uniform policies despite controversies regarding other potential approaches. All rejected the use of bacillus Calmette-Guérin (BCG) vaccination, even though the World Health Organization and some American experts contend that the vaccine is a useful preventive tool. All health departments rejected routine biochemical monitoring of hepatic enzymes, despite scientific (and emotional) concern regarding the hepatotoxicity of isoniazid.5,6

Despite uniform chemoprophylaxis practices, the departments surveyed were less likely to adopt uniform treatment policies. The departments all tended to adopt shorter course rifampin-containing regimens in the initial treatment of pulmonary tuberculosis, but diverged in other aspects of treatment. Health departments differed on the question of monitoring patients for drug side effects during chemotherapy. They disagreed on the number of sputum samples required for exclusion of bacteriologically positive disease, upon the need for monitoring sputum samples during chemotherapy, and upon the value of following patients routinely after chemotherapy has been completed. All health departments regarded their treatment programs to be “ambulatory,” but the percentage of patients hospitalized for initial treatment in our current survey was found to vary from 0 to 95 percent. Although ATS/CDC/ACCP guidelines leave some discretionary options, clear policy choices exist, but are not followed. Documentation exists in the literature demonstrating: 1) the useless routine of followup after successful completion of treatment;2 2) the need to monitor patients receiving hepatotoxic and nephrotoxic drugs;4 3) the efficacy of total ambulatory treatment of tuberculosis even in patients with substantial symptoms,5,6 and 4) the absence of “back conversion” of sputum in patients receiving adequate chemother-