T-lymphocytes and Pleural Tuberculosis

Development of monocyte-derived epithelioid cell granulomas in patients with pulmonary diseases such as tuberculosis, sarcoidosis and berylliosis provides direct evidence for the presence of heightened cellular immune response in these patients. However, patients with these diseases often exhibit anergy to common recall antigens, suggesting a state of depressed cellular immune response. Partial resolution of this apparent paradox was obtained from studies in which the response of peripheral lymphocytes was compared to that of cells obtained from bronchoalveolar lavage sample or pleural fluid. Cells obtained from these two sources presumably are representative of cells present at the site of inflammation.

These studies demonstrate several differences between the peripheral blood cells and those from the inflammatory sites. First, the cells from bronchoalveolar lavage or pleural fluid contained a significantly higher proportion of T-lymphocytes than comparable peripheral blood cells. Second, a greater proportion of the T-lymphocytes were helper T-lymphocytes in the bronchoalveolar lavage or pleural fluid cells, while the peripheral blood cells had an increased proportion of suppressor/cytotoxic T-lymphocytes. Third, the T-lymphocytes from bronchoalveolar lavage fluid spontaneously secreted significantly greater quantities of lymphokines (i.e., monocyte chemotactic factor, macrophage activating factor, interleukin-1 and gamma-interferon), which are crucial to the formation and maintenance of the granuloma, than the peripheral blood cells did. Finally, the cells from bronchoalveolar lavage or pleural fluid exhibited a significantly greater proliferative response when challenged by the appropriate antigen (BeSO, for berylliosis patients, PPD for tuberculosis patients) than was observed for the corresponding peripheral blood cells.

From these studies emerged the concept of "compartmentalization," which suggests that the responding T-lymphocytes have been partitioned from the peripheral blood to the site of inflammation. This concept provides a possible explanation for the observation that in vitro T-lymphocytes isolated from pleural fluid of patients with tuberculosis proliferate in response to PPD, while peripheral T-lymphocytes from the same patients do not. It is, however, clear that patients with advanced tuberculosis also have an increased number of suppressor cells in their peripheral blood. These suppressor cells could inhibit the proliferation of responding T-lymphocytes in the peripheral blood and thereby mask their presence.

Fujiiwara and Tsuyuguchi, in their article in this issue (page 530), have examined this possibility by using the technique of limiting dilution analysis to examine the frequency of PPD-responding T-lymphocytes in the peripheral blood and pleural fluid of tuberculosis patients, and compared them to the frequency of PPD-responding T-lymphocytes in the peripheral blood of healthy individuals with a positive tuberculin skin test result. This study clearly demonstrates that the frequency of PPD-responding T-lymphocytes in tuberculosis patients is significantly greater in the pleural fluid than in their peripheral blood. However, the frequency in their peripheral blood is the same as that observed in the normal, tuberculin-positive patients.

Although a limited number of patients were studied, the results obtained suggest that, at least for tuberculosis, the increased local cellular immune response is most likely due to clonal expansion of PPD-responding T-lymphocytes, and the decreased peripheral blood cellular immune response is most likely due to the action of suppressor cells rather than the migratory loss of PPD-responding T-lymphocytes from blood to the inflammation site.

The activity of suppressor cells on B-lymphocytes may also reduce the humoral immune response to mycobacterial antigens and, along with other factors, frustrate efforts to develop a reliable serologic test for tuberculosis. The search for useful serologic tests in the diagnosis of tuberculosis will and should continue. Nevertheless, as our understanding of useful events at the inflammatory site improves, perhaps in time these observations will also have diagnostic significance.

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Training in Resuscitation

Is It Worthwhile?

Ever since the American Heart Association and the American Red Cross began large-scale training in cardiopulmonary resuscitation (CPR), there have been arguments about the appropriate recipients and depth of training. When the American Heart Association developed the training program in advanced cardiac life support (ACLS) for physicians and nurses, the argument intensified as many critics contended that there was no evidence that training could influence survival. Critics stated that physicians had the basic knowledge, and making them take tests on the material was ritualistic and not of benefit. The article by Lowenstein et al on "The Benefits of Training Physicians in Advanced Cardiac Life Support," appearing in this issue (see page 512), appears to prove the critics wrong. In this article, the authors have pointed out that short-term survival following cardiac arrest was significantly improved (from 32 to 60 percent) in their hospital after training. Long-term survival showed a favorable trend (increasing from 13 to 23 percent after training), but this increase was not statistically significant due to the low number of patients. It is easy to throw stones at this type of research because it is not randomized; it is sequential, rather than simultaneous; and the patients' conditions may not be identical. However, it is virtually impossible to randomize training without seeing an influence on others in the same institution. If you utilize different institutions, there are likely to be greater differences in patients' conditions, staff response times, and other factors that might influence the results. There was a difference in patients' conditions between the two groups, but these differences loaded the after-training group with high risk patients and actually worked against the premise. Hence, this article is as convincing as any previous attempt to show that training does make a difference.

As physicians, we must begin to recognize the need for training in skills and the integration of skills into an organized approach to certain clinical problems. The need for physician training in various skills is great. Obviously, physicians who work in high risk areas such as emergency rooms, operating rooms, and intensive care units must have adequate training; every physician probably should have some training in CPR and ACLS. Thus, physicians must be willing to accept the challenge and submit themselves to the training and testing that is needed to improve skills.

It is very easy, however, to be over-zelalous and to feel that any training program would be beneficial. Training programs are beneficial when they can alter outcome. Some continuing education programs are extremely esoteric and contribute little or nothing to the physician's understanding or performance. As more and more programs are developed, we must evaluate these programs and see what their benefit might be. Due to the limited amount of time that a physician has to attend training programs, we must design these training programs so that their impact will be as beneficial as possible. This means that many programs must be of practical significance to the physician and not esoteric in nature. We therefore must continually evaluate our training programs, as has been done by Lowenstein et al, to determine their true benefit to the consumer, our patient.

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Mitral Valve Prolapse Diagnosed by Echocardiography?

Mitral valve prolapse is an anatomic entity which is clinically diagnosed in the presence of a mid-