Circulating Antibodies in Pulmonary Tuberculosis

Although much has been written on the subject of cell-mediated immune responses in pulmonary tuberculosis, relatively little is understood about the role of circulating antibodies in tuberculous infection.\(^1\)

Recently there has been much interest in the measurement of serum IgE levels in a variety of pulmonary diseases with immunologic aspects, since allergic reactions in the lung are largely mediated by antibodies belonging to the IgE class of immunoglobulins. In an investigation of adult asthmatic patients, it was found that 60 percent of patients with allergic asthma had IgE concentrations exceeding the normal upper limit of 800 ng/ml (333 IU/ml), whereas only 5 percent of patients with nonallergic asthma had significantly elevated levels.\(^2\) Approximately 30 to 40 percent of the total serum IgE content of patients allergic to ragweed or grass pollens is due to the presence of specific IgE antibodies directed against pollen allergens.\(^3\)

Elevated serum IgE levels, often reaching extremely high values of 5,000-20,000 ng/ml are found in over 90 percent of patients with the clinical findings of allergic bronchopulmonary aspergillosis, but not in patients with aspergillomas or farmer’s lung. In one investigation it was found that most of the IgE in the sera of patients with bronchopulmonary aspergillosis was not directed against the A fumigatus antigen employed for skin testing purposes.\(^4\)

From these results it might be concluded that the major portion of the IgE in the sera of patients with allergic bronchopulmonary aspergillosis is the result of nonspecific stimulation by Aspergillus organisms, in some yet undefined manner, of IgE producing plasma cells in the respiratory tract.

Most parasitic infections involving the lung or gastrointestinal tract are associated with major elevations of serum IgE, particularly during the acute phases of the illness. Examples of parasitic infestations that result in increased serum IgE levels include: ascariasis, visceral larva migrans due to Toxoca canis, intestinal capillariasis caused by the roundworm Capillaria philippinensis, schistosomiasis, ankylostomiasis, echinococcosis, trichinosis and tropical eosinophilia, currently considered to be due to parasitic infection.

The findings in patients with allergic asthma, bronchopulmonary aspergillosis and parasitic infestations suggest that the production of IgE antibodies by individuals exposed to certain types of invading microorganisms, or noxious stimuli such as pollens, may have distinct survival advantages. In rats, for example, it has been shown that IgE antibodies help to combat parasitic infections, and it is possible that they may act similarly in man. In allergic individuals, reactions mediated by IgE immunoglobulins certainly contribute to the elimination of undesired allergenic irritants from the respiratory and gastrointestinal tracts through coughing, expectoration, vomiting and diarrhea.

In the rat, infection with helminthic parasites can have the remarkable effect of causing a sustained increase in an IgE antibody (reagin) production against antigens unrelated to those of the invading parasite. This phenomenon, which has been called the potentiated reagin response, is best explained by postulating a parasite-derived potentiating factor that activates a population of T cells to produce a substance capable of selectively stimulating IgE producing B cells regardless of their antigenic specificity.\(^5\) Conversely, it has been observed in rats that the experimental depletion of T cells will result in the overproduction of specific IgE antibodies, presumably by diminishing the inhibitory effect of suppressor T cells.\(^6\) A number of external and immunologic influences may thus serve to amplify the IgE response to parasites.

In this issue of Chest, Casterline, Evans and Ward (see page 21) report normal serum levels of IgE in patients with moderate to far-advanced pulmonary tuberculosis. Invasion of the lung parenchyma with M tuberculosis apparently does not result in the production of specific IgE antibodies, or the release of nonspecific IgE potentiating factors similar to those postulated for helminthic and some fungal infections. The authors did, however, find that the mean IgG level in the group of patients studied was
significantly higher than in control patients. This observation is consistent with the previously reported finding of circulating IgG hemagglutinating antibodies to PPD in 60 percent of patients with moderate and 80 percent of patients with far-advanced pulmonary tuberculosis of more than one year's duration. It is thus more than likely that the increase in serum IgG levels in pulmonary tuberculosis reported in this issue is a reflection of the presence of antibodies directed against allergenic constituents of M tuberculosis rather than a non-specific response.

The humoral IgG antibodies to M tuberculosis probably do not protect the human host against either active or recurrent infection because they appear at the height of the disease and disappear with clinical improvement. They seem to be produced as a direct consequence of the presence of large numbers of actively multiplying tubercle bacilli in the human lung parenchyma over a prolonged period of time—an epiphenomenon that has no apparent influence on the course of the disease.

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REFERENCES


Nontransmural Myocardial Infarction

Myocardial infarction unassociated with acute development of ST-segment elevation and Q waves has been thought until recently to be a relatively benign syndrome. Indeed, the incidence of power failure and other serious complications has been considered to be low, and chest pain is intermediate between the discomfort of angina pectoris and the severe precordial pain of transmural myocardial infarction.

Recently accumulated clinical experience, however, paints a less optimistic picture for myocardial infarction accompanied only by changes of the ST segment and T wave on the electrocardiogram. In a recent issue of Chest, Kossowsky et al added further evidence that nontransmural infarction is not always a benign disorder. They described a group of 35 patients with enzymatically verified myocardial infarction and ECGs showing symmetrically inverted T waves, who had a high incidence of progression to transmural myocardial infarction. Furthermore, two (15 percent) of the 13 patients who developed transmural infarction died of pump failure, while none of the 22 patients without this complication did so.

Current experience regarding the outcome of nontransmural myocardial infarction has varied somewhat in the hands of different investigators. In two recent reports, the incidence of arrhythmias and shock and the in-hospital mortality were similar in patients with nontransmural and transmural myocardial infarction, when the former had enzymatic curves suggestive of myocardial necrosis. Furthermore, electrical instability has been noted in a high percentage of patients with ST-segment and T-wave changes, even in the presence of equivocal enzymatic alterations, whereas power failure has been found only in patients with significant enzymatic changes. These results suggest that patients with severe but transient coronary ischemia are at risk for fatal arrhythmias, but that myocardial necrosis may be required for power failure to ensue.

Another consideration is whether patients with predominant ST-segment depression on the ECG are separable on clinical grounds from those showing only symmetric T-wave inversions. Both patterns are classified as nontransmural myocardial infarction. The electrocardiographic pattern of ST-segment depression has been associated in some reports with a mortality similar to that encountered in patients with transmural myocardial infarction, while patients with only T-wave inversion were found to have a benign in-hospital course. The experience of Kossowsky et al, which deals with a group of patients described as showing only T-wave inversion, corroborates this clinical observation only for the group of patients who did not suffer an extension to transmural infarction. These reports and the variable outcome that they describe emphasize the need for more careful clinical subcategoriza-

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