

CURRENT RESEARCH PROBLEMS CONCERNING PULMONARY GRANULOMATOSIS IN BERYLLIUM WORKERS

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IT IS TRUE that probably none of us wants to make positive statements, and, first, I had decided to say only that we are dealing with the effect of a drug about which we know nothing, on a disease of unknown pathogenesis. In other words, all one could reasonably say about the theoretical implications of the effect of cortisone on granulomatosis is that we cannot draw any conclusions. Yet, that would leave you rather unsatisfied. I believe you want to hear about the thoughts which one might have when one sees that a pathological process like this can be at least partly reversed by a drug.

The first question, of course, is what does adrenal hormone do to tissues? I am not really qualified to discuss this question because of lack of firsthand experience. Nevertheless, looking through the literature one comes to the conclusion that one can say only that the hormones in question modify the responses of mesenchymal tissue to a variety of very nonspecific causes. There is experimental evidence that reactions of sensitivity as well as reactions to certain straight chemical and mechanical causes are influenced by cortisone. Therefore, observations of the effect of cortisone on a pathological state do not permit any conclusions about the cause or the pathogenesis of the disease. While the exact etiologic factor of the granulomatosis is still uncertain, I think it is generally agreed that beryllium is an outstanding factor. The problems with which we are confronted at present are those of the metabolism of beryllium compounds, the question of their presence and possible state in tissues, and the exact mechanism of their toxic action.

For the purpose of the investigation of the pathogenesis, at least, it appears advantageous to differentiate between the acute pneumonitis which is seen in persons who have been exposed to relatively high concentrations of the more soluble beryllium compounds, and the chronic granulomatosis which has been observed following the inhalation of insoluble beryllium compounds, at times in astonishingly low concentrations. While in the first instance it might be assumed that damage of tissue occurs because, as is known, beryllium interferes with certain enzymes,¹ such an explanation cannot possibly hold in most cases of pulmonary granulomatosis. The reason for this is that the amount of soluble beryllium found in tissues is entirely inadequate to account for any of the effects which have been observed in

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1. Klemperer, F. W.; Miller, J. M., and Hill, C. J.: The Inhibition of Alkaline Phosphatase by Beryllium, *J. Biol. Chem.* **180**:281, 1949. Grier, R. S.; Hood, M. B., and Hoagland, M. B.: Observations on the Effects of Beryllium on Alkaline Phosphatase, *ibid.* **180**:289, 1949.