GENERAL DISCUSSION ON THE TREATMENT OF CHRONIC BERYLLIUM POISONING WITH ACTH AND CORTISONE

DR. HARRIET L. HARDY, Boston: The problem of correct diagnosis has to be thrashed out, as Dr. Dobson has said. How many of the fluorescent lamp-manufacturing series have ultimately succumbed to an acid-fast or have an acid-fast bacillus infection secondary to their chronic disease?

DR. GEORGE WRIGHT, Trudeau, N. Y.: Two of our 17 died, with acid-fast bacillus infection demonstrated.

DR. R. L. DOBSON, Berkeley, Calif.: I would like to speak of some points that have been raised and are pertinent to the case in which the patient was treated with ACTH, in Berkeley. Dr. Wright raised the question whether or not all the patients who have been treated really had beryllium poisoning, and I think he especially had in mind the case which we described, which was complicated with tuberculosis. He intimated that perhaps the patient had tuberculosis at the start. I think this is a well chosen question. I can say that during a little more than four years after the patient was first found to have a diffuse pulmonary disease, his tuberculin tests were repeatedly negative. His sputum was repeatedly negative for tuberculosis on culture, on smear and on guinea pig inoculation. Biopsy of a cervical lymph node done early in his disease, in the beginning of 1946 a few months after the first abnormal roentgenogram, showed a typical granuloma, which presumably backed up the diagnosis of granulomatous disease. In this granuloma no acid-fast bacteria were found. The second point I think is Dr. Frawley's point of the hazard of treating a tuberculous patient with ACTH. This, of course, entered our minds, and we thought many times before we instituted the ACTH therapy. We rationalized our intent on the ground that since this patient was moribund, no harm could be done. I think there is little question that his life was prolonged nine or 10 months by the ACTH therapy.

The subjective changes following ACTH I mentioned this morning. The patient felt very much better. The objective changes were an increase in vital capacity from 1.7 l. to 2.3 l., not very much of a change, and the moisture in his lungs cleared considerably; in fact, in some periods during his eight months of ACTH therapy his lungs were completely dry to auscultation whereas there were many coarse and crepitant rales when treatment was started.

DR. JOSEPH C. AUB, Boston: In all of our current discussions on ACTH and cortisone, one always wonders how their effects are produced. The laboratory work which is assembled has, so far, complicated the problem and given us no answer. All we know is that they are potent drugs, and their mechanism of action is obscure.

I should like to recall that just about 100 years ago, Trousseau said, "Let's hurry, hurry, use the new drug before it stops curing!" These drugs produce great effects. So far their curative effects are extremely limited. Now why should we treat a disease we don't understand, like chronic beryllium poisoning, with drugs whose mechanism we equally don't understand? I have been unable to hear all the discussion this morning, but it seems clear that ACTH and cortisone do something that seems to improve the x-ray picture and the physiological reactions of people suffering from chronic beryllium poisoning. What possible explanation can there be for this?

Adrenal glands apparently have an antagonistic action on the lymphocytes and the eosinophils. If I can refer to history again, I might mention that Marine in 1918 or 1919 showed that after the removal of the adrenal glands the thymus and the lymph nodes of animals became tremendously hypertrophied. It is now known that eosinophils fall after cortisone has been given. Weintrobe showed recently that the number of circulating lymphocytes also goes down under these circumstances. May I refer also to Florey's work? Some years ago he showed that the life of the lymphocyte is only a matter of hours. This may be a little too short, because in preserved blood the lymphocytes still remain after 48 hours, but, at any rate, their life in the blood stream is short.

What I am getting at is, in granulomatous lesions there are an enormous number of lymphocytes and eosinophils. You then give a drug which reduces the number of such cells. If the numbers of such cells are reduced around these granulomatous lesions, then one would expect to find a change in the roentgenogram, and indeed one ought to find obvious changes in the physiological reactions which are dependent on elasticity of the lungs.