An Unusual Case of Joint Pains and Fever
Berylliosis and Pulmonary Hypertension Mistaken for Rheumatic Fever

By Howard B. Sprague, M.D., and Harriet L. Hardy, M.D.

DR. SPRAGUE: Dr. Hardy, we are going to discuss this morning the case of our patient, Mrs. George C, whom I first saw in September, 1953 and later referred to you for observation and treatment.

She was a 32 year old married woman who had never been ill prior to February of 1953. Her first baby had been born in September of 1952. In February, for the first time, she began to have redness and swelling of the ankles with considerable pain. This arthralgia migrated to the elbows and to the hands, and she also had pain in the back and shoulders. Her temperature rose to 100.4 F., and she was laid up for about seven weeks. During this time she had some small, red, desquamating nodules over her body, but particularly the arms and legs. She suffered also from shortness of breath, cough, and a tachycardia at a rate of 120 beats per minute. X-ray films of the spine were said to show arthritis. She was treated with bed-rest, oil of wintergreen locally, and sodium salicylate by mouth.

Her cough and dyspnea continued after she got out of bed, and she found herself unable to care for her house and the new baby. There was also extreme fatigue and some sore throat, and she lost 15 to 20 pounds. For a time she was given penicillin by mouth and by inhalation.

When I examined her, she was a thin, ill-appearing, young woman, obviously dyspneic on slight exertion and even at rest, with slight cyanosis. She coughed vigorously on lying down, and it was necessary to examine her in the sitting position. There was no increase in the venous or arterial pulsations in the neck. The heart was not enlarged to percussion. The sounds were of good quality. The pulmonic second sound was louder than the aortic. There were no murmurs. The rhythm was regular at a rate of 100, and her blood pressure was 105/65. I could not make out any dullness of her lungs to percussion, and there were no rales. The liver was not enlarged, and there was no edema of the ankles. There were numerous red, slightly scaly spots over the arms and legs, three or four millimeters in diameter.

Electrocardiogram showed prominent P waves in leads II and III and inverted T wave in lead III and in lead aVF. There was an RR\(^1\) complex in the precordial lead V\(_1\) with low T waves across the precordium, and inverted in V\(_1\) and V\(_2\) (Fig. 1).

Fluoroscopic examination showed a striking abnormality in the lung fields with an extremely dense motting throughout both sides. There was no abnormality in the size or the shape of the heart.

With this clue, I investigated her history of industrial exposure more thoroughly. She first said that she had worked as a stenographer, but it appeared on further questioning that in 1943 and 1944, she had worked for a company making fluorescent lamp bulbs and had been exposed to beryllium dust. Radiologic study of the chest (fig. 2) showed the following: "Fluoroscopic examination and films of the chest show diffuse linear nodular densities scattered throughout both lungs from apex to base. The heart is normal in size and shape, and
FIG. 1. Electrocardiogram. Top line, leads 1, 2, 3, aV\textsubscript{R}, aV\textsubscript{L}, aV\textsubscript{F}. Bottom line, leads V\textsubscript{1} to V\textsubscript{6}.

FIG. 2. X-ray, Oct. 6, 1953. Fluoroscopy revealed some limitation of diaphragmatic motion although both leaves moved synchronously. Both lung fields are diffusely studded with small nodular densities. There is increased prominence of both lung roots probably representing some adenopathy. The heart is not enlarged grossly.

The esophagus is normal in position and appearance. No gross enlargement of the mediastinal nodes is present. Conclusion: The diffuse reticulation in both lungs suggests berylliosis. Without the history, Boeck's sarcoid would also be a good possibility, despite the lack of gross hilar adenopathy."

Dr. Hardy, would you be good enough to let us know what investigations you undertook when this patient was hospitalized?

DR. HARDY: Because of this particular patient's apprehension about her prognosis, she did not have preliminary pulmonary function studies, as we intend all our cases should. We studied the liver function with the conventional tests and did a variety of biochemical determinations which have been of interest to us, such as blood calcium and phosphorus, and alkaline phosphatase. We also were careful to do tuberculin testing, sedimentation time, and sputum studies, because it is likely we shall one day mistake miliary tuberculosis for beryllium disease.

DR. SPRAGUE: I was particularly interested in bringing out the point here that this woman was considered to have rheumatic fever, and her dyspnea was attributed to rheumatic heart disease. Would you please tell us, Dr. Hardy, about the relationship between the pregnancy and the activation of her beryllium reaction, and also about your experience with joint and skin manifestations of this disease?

DR. HARDY: In our study of cases of chronic beryllium poisoning, we have been impressed and stimulated by the observation that women who have been exposed to beryllium compounds may show no evidence of disease by sign or symptom until a successful pregnancy has been completed. I want to emphasize that the pregnancy, itself, appears, if anything, to be a helpful process, but when the child is 4 to 6 months old the patient may notice inability to gain weight, shortness of breath, and cough, as did Mrs. C.

In answer to your question about experience with joint and skin manifestations of this disease, our observations include another case
with a similar history to Mrs. C. The original diagnosis was rheumatoid arthritis and later proved to be beryllium disease with the joint picture a part of the chemical intoxication. In addition, we have a definite group of patients with mild to moderately severe beryllium poisoning who have intermittent joint pain without x-ray evidence of joint changes or any increase in sedimentation time. These patients’ symptoms are relieved with aspirin. Skin manifestations of beryllium effect are divided roughly into three categories: first, the reaction of irritation following direct contact with acid salts of beryllium; second, a subcutaneous granuloma associated in some cases with introduction of beryllium compounds accidentally or, in animals, experimentally; and finally, as in the case of this patient, a small but definite group of cases in which spontaneous skin lesions of great variety simulating Boeck’s sarcoid appear as one manifestation of chronic beryllium poisoning (fig. 3).

Dr. Sprague: During the time that this patient was in the hospital, the question was again raised as to the significance of the evidence of some degree of right-sided heart strain. How much cor pulmonale have you seen in your patients with beryllium poisoning?

Dr. Hardy: Cor pulmonale is a complication in most cases of beryllium disease of any severity. Failure of the right heart is the usual cause of death.

Dr. Sprague: You have also explained, Dr. Hardy, that your concept of berylliosis is that it is a completely generalized process. In what other organs and tissues have you found beryllium granuloma or abnormal concentration of beryllium?

Dr. Hardy: Beryllium was found at autopsy and biopsy in the lung and also the liver, spleen, kidney; cervical, hilar, and abdominal lymph nodes; bone and skin. The so-called beryllium granuloma, which incidentally we believe is only one part of the pathologic reaction to certain beryllium compounds, has been described in lung, lymph nodes, liver, spleen, kidney and skin.

Dr. Sprague: Another point which I should like you to discuss is the relationship between this disease and Boeck’s sarcoid. It is my im-

pression that there has been an opinion that sarcoid is commoner in places in the world where the natural concentration of beryllium in the environment is relatively high. Is there anything to support this contention?

Dr. Hardy: Dr. Sprague, you are referring to a very interesting but as yet undeveloped observation that the incidence of Boeck’s sarcoid can be correlated with the patient’s residence in an area where certain soil is found. The original discovery brought out the fact that this particular soil is described as containing small amounts of beryl, the ore from which beryllium comes. However, studies of water, air, and vegetation in these so-called “sarcoid belts” has not borne out the idea that beryllium is present in a detectable concentration. It is
too soon, however, to know whether, with increased knowledge of detection of trace materials in soil, this may or may not be an important lead in the understanding of granulomatous diseases.

Dr. Sprague: I have, of course, been immensely pleased at the favorable reaction to cortisone in this case. What is your general experience about the effectiveness of this new therapy? I see that you have cautioned her local physician to have her urine tested once a week for sugar because of the possibility that cortisone might produce glycosuria.

Dr. Hardy: We are very much impressed with the effectiveness of cortisone in the management of chronic beryllium poisoning. We do not believe that we are curing the disease although it has been shown in one or two cases by biopsy that the drug has made some change in the granulomata. Klemperer has shown that there is no change in the excretion of beryllium after cortisone therapy. However, if we persist in this form of treatment, our patients are amazingly improved in their general health, an observation which has been checked objectively by pulmonary function studies, showing that there is actual improvement in the oxygen saturation of the blood. We have seen several transient glycosurias in cortisone-treated cases of beryllium poisoning. We have, however, never had to stop treatment for this reason. We have learned that the cortisone must be continued in most cases and medical supervision is required, especially in the presence of infection and when there is any evidence of irritation in the upper intestinal tract.

Dr. Sprague: Thank you very much, Dr. Hardy, for discussing these very interesting points. Here, then, is a patient in whose history appear fever, joint pains, and swelling, skin nodules, dyspnea, cough, orthopnea, tachycardia and fatigue. The electrocardiogram suggests some right ventricular strain, and the whole process was originally mistaken for rheumatic fever and rheumatic carditis. The differential diagnosis actually, however, was not difficult because of the negative findings in the heart on auscultation and the characteristic pulmonary pathology on x-ray examination. The delay of almost 10 years in the appearance of beryllium reaction to the level of clinical symptoms is a discouraging fact in the natural history of this disease. It certainly means that all persons thus exposed must continue under medical observation for many years, and the industrial compensation liability is one of indefinite duration. However, there is real hope of successful therapy by cortisone.
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