As it is now accepted that these disorders are but phases of the same disease, it would be an advantage to have a single name to embrace the important features of all three. To avoid confusion in terminology Thannhauser (1947) suggested the name of "eosinophilic xanthomatous granuloma" as being descriptive of the main histological features. Until further knowledge is forthcoming on the aetiology of the disease this name should be adopted for the type of case described in this paper. The present case shows evidence of pulmonary, pituitary, and bony disease, and it is to be assumed that all three organs are affected by the same pathological process. The biopsy material from the bone showed granulation tissue and eosinophilic infiltration, and although lipophages were absent from this section it is probable, by analogy with other reported cases, that they may exist elsewhere.

That pulmonary infiltration occurs in eosinophilic xanthomatous granuloma has been recognized since Rowland (1928) described the case of a child aged 2 years who died from pulmonary fibrosis secondary to xanthomatosis. Since then many cases have been reported, and the recorded cases have been reviewed by Thannhauser (1940), Versiani *et al.* (1944), Weinstein *et al.* (1947), Ponseti (1948), Oswald and Parkinson (1949), and Schafer (1949). Oswald and Parkinson reported a case in which the granuloma gave rise to diffuse small cysts throughout both lungs, and they were able to find three similar cases in the literature. A similar case was reported by Schafer (1949). The case reported here shows the characteristic radiological changes of honeycomb lungs and is a further example of cystic pulmonary changes occurring in a more chronic phase of the disorder.

To clarify the protean manifestations of this disease it is suggested that eosinophilic xanthomatous granuloma should be regarded as a generalized disease of unknown aetiology, occurring in an acute or chronic form. In the acute variety, which occurs in infancy and early childhood, there is progressive infiltration of the skin, bones, lymph nodes, and viscera, leading to early death. The chronic variety, occurring in older children and adults, may present in a complete or an incomplete form. In the complete form there is pituitary, bony, and pulmonary disease, with possibly other visceral manifestations. In the incomplete forms, which are not uncommon, pulmonary, pituitary, and bony lesions occur either singly or in any combination. Thus, when the bony symptoms predominate the disease will be regarded as "eosinophilic granuloma of bone," and when the pituitary alone is affected it presents as diabetes insipidus.

It is the relation of the chronic form of this disease to pulmonary disorders that is particularly emphasized, for the possibility that lung fibrosis and cyst formation may be the sole manifestation of eosinophilic xanthomatous granuloma must be considered. It seems likely that such cases will arise, and confirmation of this concept is to be found in the association of pituitary disorders, transient or permanent, with honeycomb lungs (Oswald and Parkinson, 1949). Pathological evidence on this point is difficult to obtain, as in the chronic phase of the disease fibrosis obscures the histological picture. Further histological studies on this subject will be published elsewhere (Cunningham and Parkinson, in the press).

The response to irradiation therapy in eosinophilic xanthomatous granuloma is variable. In most instances the bony lesions respond symptomatically, and sometimes there is radiological improvement. The effect of irradiation on the pituitary and pulmonary disease is occasionally beneficial but usually without effect (Currens and Popp, 1943; Weinstein *et al.*, 1947; Ponseti, 1948). The present case had complete relief of pain in the femur, but the diabetes insipidus and the respiratory symptoms were unaffected; there were no radiological changes following treatment.

A final point of interest in this case is the age of the patient. The oldest case previously reported was that of a man aged 50 (Versiani *et al.*, 1944).

Summary

A case of eosinophilic granuloma of bone in a man aged 56 is described. The patient also had diabetes insipidus and honeycomb lungs.

Irradiation therapy relieved the pain of the bony lesion but did not affect the pituitary or pulmonary disease.

The name "eosinophilic xanthomatous granuloma" should be used to include the three diseases commonly known as the Hand–Schüller–Christian disease, Letterer–Siwe disease, and eosinophilic granuloma of bone.

The occurrence of pulmonary manifestations in this disease is discussed.

I wish to thank Dr. Neville Oswald for permission to publish this case, and Mr. Norman K. Harrison, of the Department of Medical Photography, St. Bartholomew's Hospital, for the photographs.

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ACUTE PNEUMONITIS IN A BERYLLIUM-WORKER

BY

G. RIDDELL ROYSTON, M.D., M.R.C.P., D.C.H.

[WITH PHOTOGRAVURE PLATE]

The following case of acute bronchiolo-alveolitis is thought to be due to working in an atmosphere containing beryllium dust. It is believed to be the first acute case to be reported in this country.

Beryllium was discovered in 1797 by Vauquelin, who called it glucinum, owing to the sweet taste of its salts. It is a brittle steel-grey metal that is soluble in acids, and occurs chiefly as beryl, the double silicate of beryllium and aluminium ($Be_3Al_2(SiO_3)_6$). Phenacite (Be_2SiO_4) and chrysoberyl ($Be_2Si_2O_4$) also occur.

During the 1939–45 war beryllium was used in increasing quantities as an important component of certain alloys and for the production of phosphors for fluorescent lighting and gas mantles. The exact compositions of fluorescent mixtures for the manufacture of strip lighting are trade secrets, but they usually contain varying proportions of beryllium, zinc, manganese, and silica.

G. RIDDELL ROYSTON: ACUTE PNEUMONITIS IN A BERYLLIUM-WORKER

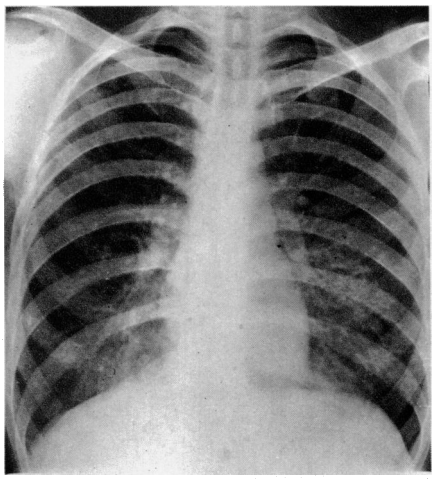

FIG. 1.—Soft mottling. (June 27, 1947.)

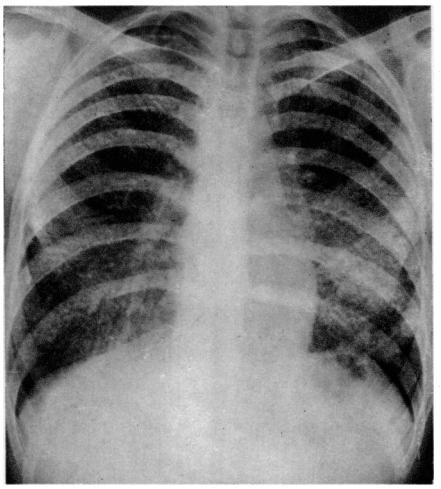

FIG. 2.—Apparently typical miliary tuberculosis. (July 11, 1947.)

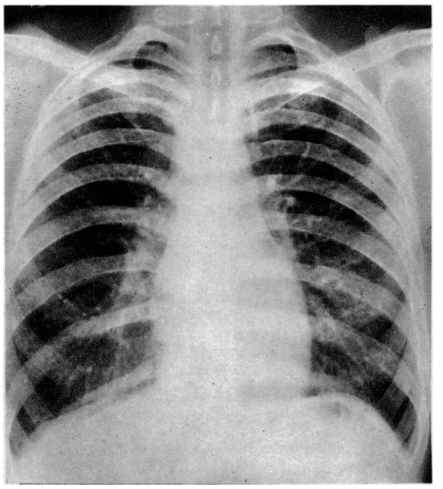

FIG. 3.—Considerable resolution. (Aug. 7, 1947.)

F. D. BEDDARD: ARTERIOVENOUS FISTULA OF THE LUNG

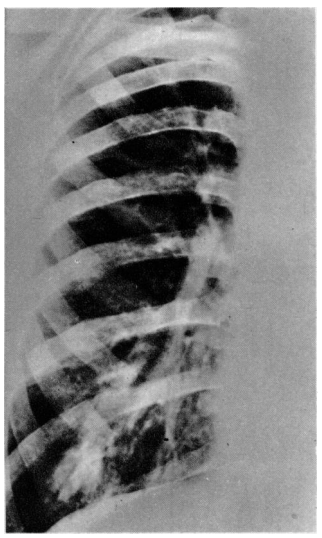

FIG. 1.—Postero-anterior view.

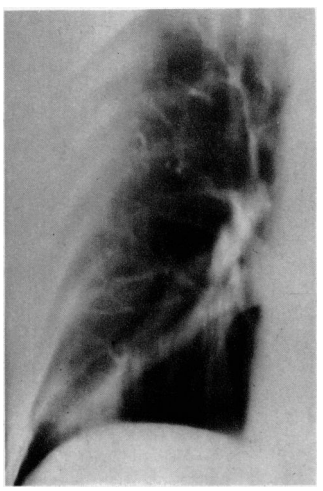

FIG. 2.—Tomogram.

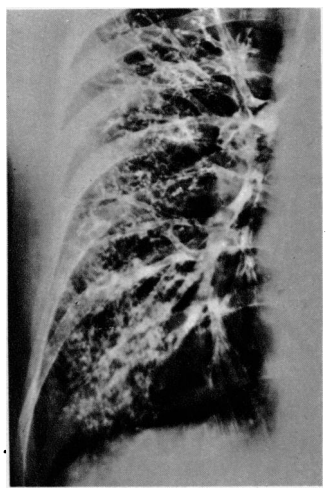

FIG. 3.—Bronchogram.

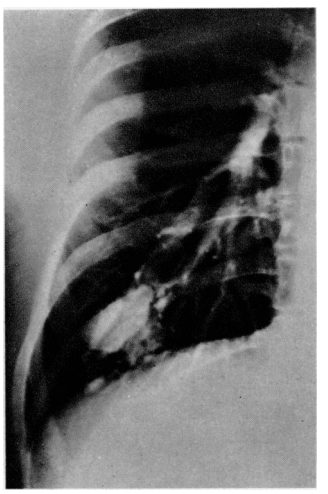

FIG. 4.—Angiogram.

K. DAMODARAN: INFECTIVE HEPATITIS AND PORTAL CIRRHOSIS

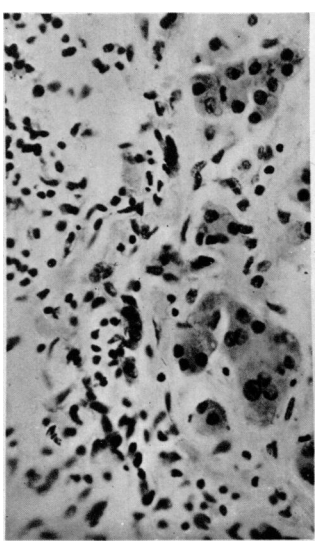

FIG. 1.—Liver × 300. Marked cellular infiltration. Second week.

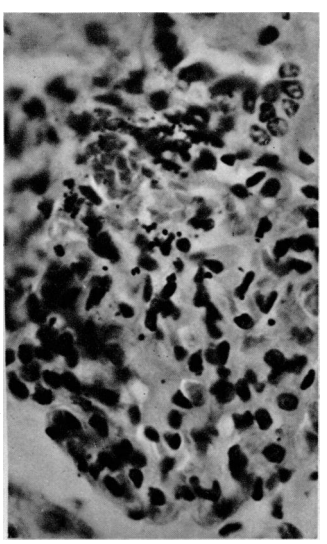

FIG. 2.—Glomerulus × 400. Showing pigment granules. Second week.

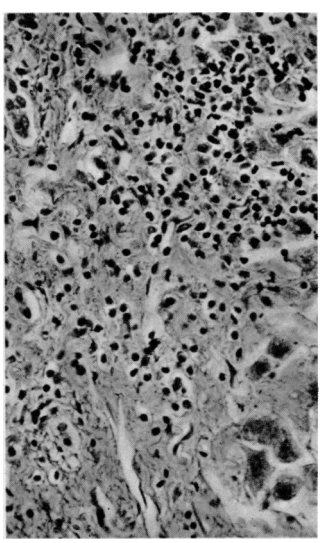

FIG. 3.—Liver × 250. Post-arsenical hepatitis. Cirrhosis and round-cell infiltration.

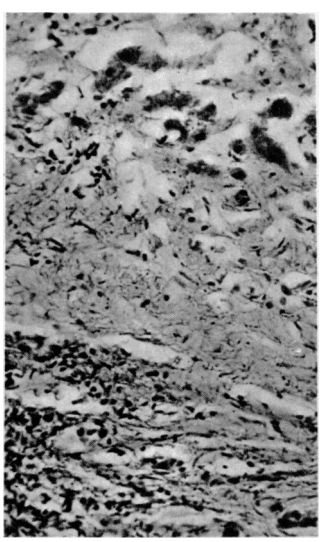

FIG. 4.—Liver × 240. Portal cirrhosis, showing round-cell infiltration.

Illustrations printed in Collogravure by HARRISON & SONS, LTD., Printers to His Majesty The King, London, Hayes (Middx.) and High Wycombe.

Case Record

A man aged 30 had been working in the laboratory of a radio factory for five weeks, when he developed shortness of breath on exertion and a slight unproductive cough. Dyspnoea became progressively worse, and three weeks later, on June 27, 1947, he attended hospital as an out-patient. There was no history of a haemoptysis or any symptoms of nasopharyngitis. His appetite was good, his bowels normal, and there had been no night sweats or unusual taste in the mouth. He felt perfectly fit and well except for his dyspnoea, though he thought he might have lost a little weight. His main disability was his dyspnoea on effort that interfered with his hurrying for a bus.

His occupational history revealed that from 1936 to 1939 he worked in a rolling mills, rolling zinc sheeting. There were no fumes. From 1939 to 1946 he was in the Army and served in North Africa and Italy, having what sounded like an attack of infective hepatitis on returning to this country in 1946 and two attacks of malaria. He then worked for a year on a guillotine machine in a rolling mills, after which he started work in a laboratory of the radio factory. There he spent about two hours of each working day mixing the powders used for coating the insides of the tubes used for strip lighting. I was unable to determine the exact composition of this powder, as it was a trade secret, but beryllium and zinc were definite constituents. The actual mixing was done by hand by stirring the dry powders in a large bowl without a lid and without the aid of extractor fans or the wearing of masks. The atmosphere was heavily laden with dust during the mixing process. The dust settled in the laboratory, and during the day was no doubt often disturbed, becoming air-borne.

On examination on June 27 he looked well built and was without any cyanosis or finger-clubbing. He had an unproductive cough and became markedly dyspnoeic with the effort of undressing. Respiratory movements were good, and abnormal physical signs were confined to the lungs, where rhonchi and medium rales could be heard scattered throughout. These added sounds were not more pronounced at the bases. The heart appeared normal, and the blood pressure was 110/65.

As his dyspnoea was out of all proportion to the physical findings he was admitted on July 4 as a suspected case of tuberculosis. His subsequent progress was as follows. From July 4 until his discharge on Aug. 16 he remained afebrile with a normal pulse rate. By July 12 his symptoms had practically disappeared and added sounds could no longer be heard in the lungs. The erythrocyte sedimentation rate (Wintrobe), which on admission was 22 mm. in one hour, remained unchanged. Three specimens of fasting-stomach contents and one specimen of lung juice were all negative for tubercle bacilli both on direct examination and on culture. Seven specimens of sputum were similarly negative. A blood count on July 7 showed 104% haemoglobin (Haldane) and 8,300 white cells (4,814 polymorphonuclears, 2,656 lymphocytes, 332 monocytes, and 498 eosinophils). Cold agglutinins were present up to a dilution of 1 in 16 on July 10.

The *x*-ray appearances were of particular interest. The first picture (Plate, Fig. 1), taken on June 27, showed an indeterminate soft mottling, which in some areas was almost millet-seed. It was distributed all over the lungs, being especially marked in the lower zones and the axillary part of the right upper zone. It suggested an early miliary tuberculosis or possibly a sarcoid. The second picture (Fig. 2), taken a fortnight later, seemed to be typical of miliary tuberculosis. The appearance was unchanged on July 22, but a further picture on Aug. 7 (Fig. 3) showed considerable resolution. On Sept. 10 almost complete resolution had occurred without any evidence of fibrosis, and it became difficult to imagine that the condition was tuberculous. A final radiograph on March 5, 1948, was perfectly normal and showed no trace of the original changes.

Clinical Picture

Beryllium has on several occasions been blamed for causing illness. Two of the first accounts were by Zamakhovskaya (1934) and Martinskovsky and Syroechkovsky (1934), both of whom were quoted by Gelman (1936). They considered toxicity could be attributed to beryllium fluorides, of which the oxyfluoride was particularly toxic. Gelman, discussing poisoning due to the vapours arising from the foundry method of extracting beryllium, considered that their special physical condition (great dispersion) explained their characteristic toxic effect, and that the tissue damage was due to the fluorine being separated from the oxyfluoride at the level of the bronchioles and the alveoli.

Two main types of respiratory disease have been described—the acute and the delayed. In the acute form Van Ordstrand *et al.* (1943) described three cases which they called chemical pneumonia, occurring in workers exposed to beryllium. The exact compounds were not stated, but the fluorides were specifically excluded. They considered the aetiology unknown, having seen a similar case in a worker in a rayon factory where there had been no exposure to beryllium. These cases all presented insidiously, with increasing dyspnoea on exertion, a dry cough, low-grade fever with shallow respirations, some cyanosis, and fine rales throughout the lower halves of both lungs.

The onset of the symptoms preceded the *x*-ray changes by three weeks or more. The *x*-ray changes started with diffuse haziness of both lungs, progressing to soft irregular areas of infiltration accompanied by increase in the peribronchial markings. This was followed by absorption of the diffuse infiltration and the appearance of a small nodular infiltration which cleared completely within one to two months. Six additional patients from the same beryllium plant were all found to have identical radiological changes.

Van Ordstrand *et al.* (1945) had 128 cases with respiratory manifestations over a period of four years; 38 of these, including five fatalities, were described as chemical pneumonitis. The onset of symptoms was insidious, with cough and occasional blood-stained sputum, followed by dyspnoea, an abnormal taste in the mouth, anorexia, and some loss of weight and increasing fatigue. Of the signs, cyanosis was usual, with rapid pulse, reduced vital capacity, and fine rales scattered throughout the lungs. *X*-ray changes were not usually present until two to three weeks after the onset of the disease and were as already described (Van Ordstrand *et al.*, 1943). They cleared in from one to four months, and it is emphasized that as a rule this was before complete subsidence of the symptoms or disappearance of the physical signs, though in one case they persisted for a further two months. In these cases they considered the severity to be proportional to the degree of exposure to chemical irritation by dust and fumes. Ninety had chemical nasopharyngitis and/or tracheobronchitis. This latter type of illness developed predominantly among furnace-workers.

The laboratory investigations were unremarkable. The erythrocyte sedimentation rates were essentially normal, and blood counts and blood chemistry were also normal. Tubercle bacilli have not been found (Van Ordstrand *et al.*, 1945). Reports on the morbid anatomy consist of five cases described as a typical pneumonitis (Van Ordstrand *et al.*, 1945). The salient features appear to be grossly heavy lungs (1,100–1,380 g.) with diffuse pulmonary oedema and haemorrhagic extravasation, considerable plasma-cell infiltration with a relative absence of polymorphonuclear cells, and some evidence of organization.

Treatment is symptomatic, with both penicillin and the sulphonamides being useless (Van Ordstrand *et al.*, 1945). Complete bed rest is regarded as essential, and no work should be permitted until all signs and symptoms of the disease have disappeared and the *x*-ray appearance of the lungs has returned to normal.

In the delayed form of the disease 17 cases of delayed chemical pneumonia were reported by Hardy and Tabershaw (1946) and Hardy (1947). Four of these came on while the patients were still exposed to beryllium after periods of exposure varying from eight months to five years. Two of these died. The remaining 13, four of whom died, developed symptoms from three months to three years after cessation of exposure to beryllium. Of the survivors only one is regarded as cured. Pascucci (1948), in his follow-up of the 11 survivors, found 30% dead and the same proportion *in statu quo*. The interval between exposure and the onset of symptoms may be as great as six years (Wilson, 1948). Agate (1948) has described a case in which the chest radiograph at first suggested miliary tuberculosis.

Discussion

On admission and for the first few weeks of observation this case was considered to be miliary tuberculosis; and, though the patient was afebrile, felt remarkably fit and well, and had only a slightly raised erythrocyte sedimentation rate, the *x*-ray film of the lungs on July 7 certainly seemed to confirm the diagnosis. However, the subsequent course of the illness as shown by serial radiographs rendered the diagnosis of miliary tuberculosis unlikely. Not only had the lungs cleared radiologically in eight weeks without streptomycin treatment but they had cleared completely without any residual fibrosis.

Eosinophilic lung is unlikely with only 500 eosinophils per c.mm. in the white count and the absence of bronchial spasm.

Ascariasis remained a possibility, but stools were free from ova when examined one year later, at which time they might well have been expected to be positive had the original infection been due to roundworm larval migration.

Miliary changes of similar distribution to those of miliary tuberculosis can occur in sarcoidosis, but though they may clear completely they take three to ten years to do it. They also tend to fluctuate over a period of months or years and are often accompanied by changes in other structures.

Pneumoconiosis is ruled out by the occupational history, the mycoses by the examination of the sputum, and carcinomatosis by the recovery of the patient.

It is of interest that the *x*-ray changes simulating miliary tuberculosis have not previously been described in the acute form of the disease but have been seen in the delayed type. The symptoms antedated the *x*-ray changes by about three weeks, but they cleared completely after eight days, at which time the *x*-ray miliary appearance was at its maximum. The *x*-ray changes subsequently persisted for a further two months in spite of the apparent well-being of the patient.

It seems possible that this man's illness was due to his contact with beryllium.

Summary

A case presenting clinically as a bronchiolitis occurring in a man handling fluorescent powders containing beryllium is described.

The *x*-ray changes were miliary in character and completely cleared in eight weeks without residual fibrosis.

The patient made a complete recovery.

The literature is briefly reviewed.

I am indebted to Dr. H. Joules, at whose suggestion the diagnosis was made, to Dr. T. R. Riley for his reports on the earlier *x*-ray films, and to Dr. G. Doel for his reports on the later ones. I wish also to thank Dr. C. A. Birch for permission to publish this case.

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INFECTIVE HEPATITIS AND PORTAL CIRRHOSIS

BY

K. DAMODARAN, M.B., B.S.

Major, R.A.M.C.

[WITH PHOTOGRAVURE PLATE]

This paper is based on the clinical findings in 550 cases of infective hepatitis and necropsy findings in 22 fatal cases in different stages of hepatitis occurring in various theatres of war. The clinical types, signs, symptoms, pathology, and complications were discussed in two previous articles (Damodaran and Hartfall, 1944; Damodaran, 1948). The present paper is mainly concerned with the course of infective hepatitis and its sequelae.

Infective hepatitis, as already shown, causes a diffuse inflammation of the hepatic cells, varying from mild cloudy swelling to frank necrosis. Complete resolution takes place in a few weeks in the majority of cases. In a small proportion, however, fibrous-tissue reaction occurs in the portal spaces, producing various degrees of cirrhosis. The hepatic cells show different stages of necrosis, which is more advanced in the central zones of the lobules. This centrilobular zonal necrosis becomes apparent only at the later stage of the disease, approximately at the end of the second week. Round-cell infiltration is pronounced in the early stages, especially in the portal tracts. In later stages cellular infiltration diminishes and is almost confined to the periphery of the lobules, unless there has been an acute exacerbation or relapse.

Fig. 1 (Plate) shows the picture of the liver in the second week of the disease. The section was taken from the liver of an Indian soldier who died of fulminating infective hepatitis. Note the intense infiltration by round cells, most marked at the periphery of the lobules. The hepatic cells are in the early stage of necrosis. These changes were seen diffusely throughout the liver. The only other organ affected as seen at necropsy was the kidney. Fig. 2 (Plate) shows the swollen glomerulus with a few bile-pigment granules.