THE CORTICOSTEROIDS AND TUBERCULOSIS

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The manufacturer's pamphlet and the medical press [1, 2, 3] warn the users of the corticosteroid drugs of the risk that re-activation of latent or quiescent tuberculosis may occur as a sequel to the therapy. The Committee on Therapy of the American Trudeau Society[4] in 1952 correlated information available at that time, and recommended certain precautions to be taken before, during and after treatment with cortisone or corticotropin. The committee recommended, *inter alia*, frequent X-ray examination of the chest and microscopic examination of the sputum in the presence of old, apparently inactive, tuberculosis, and also pointed out that there may be exacerbation of unsuspected tuberculosis lesions.

The first flood of therapy with corticosteroids is receding and the association with tuberculosis has been little in the news, but the recent admission to this sanatorium of 2 patients in whom active pulmonary tuberculosis occurred after therapy with corticosteroids has shown the need to sound the warning again.

The case reports of these 2 patients and of 2 other patients in our records are published below. The reports are incomplete in that information is not available of all the details of the dosage of cortisone or adrenocorticotropic hormone, but in the case of cortisone the scheme of treatment was the usual one, namely, an initial 'loading dose' with progressive decrease to the 'maintenance dose'.

Considering that our admission rate is low (448 patients admitted during 1955) and that our admissions are restricted mostly to one group of the population, namely, European employees of the gold-mining industry, it is probable that the incidence of this sequel to therapy with corticosteroid drugs is higher than may be thought.

CASE RECORDS

Case 1. A male miner, aged 55, was admitted to another hospital in January 1955 for broncho-pneumonia, hepatic insufficiency, splenomegaly and neutropenia. At that time radiological examination showed normal lung-fields and microscopic examination of several specimens of sputum showed no *Mycobacterium tuberculosis*. He was given cortisone and ACTH continuously from 10 February to 24 August. No other X-ray examination of the chest or examination of the sputum was made until these were prompted by another episode of pneumonia in early September. Then extensive bilateral fibro-caseous pulmonary tuberculosis with tubercle bacilli in the sputum was found. The patient was admitted to Springkell Sanatorium on 13 September 1955, and his prognosis is poor.

Case 2. A male miner, aged 45, is a sufferer with rheumatoid arthritis, which first showed its effects in 1953. He was admitted to another hospital in August 1954 and remained there until October 1954. Whilst in hospital, cortisone and ACTH were given together for a period of 10 weeks. The dosage of ACTH was 40 mg. on alternate days. Towards the end of this course of treatment a mild pyrexial episode occurred, associated with a productive cough, which subsided quickly, although a slight cough persisted. No chest X-ray or sputum examination was done before or during this treatment but, as it happened, he had been examined by routine once or twice a year from March 1949 by the authority set up to examine all gold-miners. A survey of the series of routine radiographs of the chest of this patient, dating from March 1949 to July 1954, showed a round dense shadow, 1 cm. in diameter, situated in the right first anterior intercostal space, which remained unchanged throughout the series of films. This shadow still remains unchanged, but, the routine radiograph taken in January 1955 showed a new shadow, which indicated tuberculous disease in the apex of the right upper lobe. At that time, several sputum tests were negative, but in March 1955 *M. tuberculosis* was found. The patient was admitted to Springkell Sanatorium on 1 April 1955 and, following the use of tuberculostatic drugs and sanatorium regime, the shadow in the right apex has regressed and prolonged search has failed to find the tubercle bacillus.

Case 3. A male miner, aged 45, was seen elsewhere in November 1952, presenting with the butterfly rash of lupus erythematosus, malaise, pain in the chest, and haemoptysis. Radiological examination of the chest showed two thin-walled cavities with minimal infiltration about them in the right upper zone. Many sputum tests were negative for tubercle bacilli and 'LE cells' were found in the patient's blood. The radiological changes in the lung field were thought to be those seen in disseminated lupus erythematosus and this diagnosis was made. During the 12 months of the year 1953 cortisone was administered, the maintenance dose being 100 mg. daily. Then, in January 1954, another haemoptysis occurred and radiological examination of the lung fields showed that the two cavities previously seen were markedly distended and an infiltration was present in the right lower zone. The sputum contained many tubercle bacilli. He was admitted to Springkell Sanatorium on 30 January 1954. With the sanatorium regime and tuberculostatic drugs the disease rapidly regressed. In June 1954 tomography failed to reveal any cavitation and all subsequent examinations of the sputum have been negative. The patient remains well and is working.

Case 4. A woman, aged 38, was suffering with rheumatioid arthritis and in 1949 had a course of cortisone for 1 month. There is no record of the dosage of the drug. Radiological examination of her lung fields before this treatment showed no abnormality. In August 1951 she was given cortisone again to relieve the symptoms of rheumatoid arthritis and, at this time, radiological examination of the chest and many sputum tests showed no evidence of pulmonary tuberculosis. Three weeks after the commencement of this therapy with cortisone there was an episode of pyrexia of sudden onset associated with cough. Another radiological examination of the chest and microscopic examination of the sputum gave positive evidence of pulmonary tuberculosis. She was admitted to Springkell Sanatorium on 3 September 1951 and died of pulmonary tuberculosis on 27 January 1954. Her brother had died of pulmonary tuberculosis in 1941.

COMMENT

One must emphasize that whilst a patient is having corticosteroid therapy, the recrudescence of latent or quiescent tuberculosis is always possible. It is not enough to look for pulmonary tuberculosis at the beginning of therapy, but frequent—I suggest monthly—investigations should be made during and after the therapy. Tuberculosis of organs other than the lungs may also become manifest. It is difficult to eradicate tuberculosis, particularly when it has been overlooked

and allowed to progress. It is easy to have the lungs examined radiologically and the sputum examined microscopically.

I have pleasure in acknowledging the permission to publish these cases, granted by Dr. M. A. Pringle, Medical Superintendent of Springkell Sanatorium.

REFERENCES

1. Bayliss, R. I. S. (1955): Lancet, 2, 1078.
2. Editorial (1955): *Ibid.*, **2**, 1071.
3. Johnson, J. R. and Davey, W. N. (1954): Amer. Rev.Tuberc., **70**, 623.
4. The Committee on Therapy of the American Trudeau Society (1952) *Ibid.*, **66**, 254.