

# Increased incidence of pulmonary tuberculosis in chronic interstitial lung disease

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**ABSTRACT** Of 162 patients with chronic interstitial lung disease, eight (seven of them male) had active tuberculosis. This was 4.5 times higher than the incidence in the general population. The frequency of tuberculosis was similar in patients treated with and without corticosteroids.

## Introduction

With the decline of tuberculosis in Western countries, there has been a relative increase in patients in whom tuberculosis presents with an unusual radiographic appearance.<sup>1,2</sup> This factor, in conjunction with a decreasing awareness of tuberculosis by clinicians, increases the chance of misdiagnosis.<sup>1</sup> A patient with chronic interstitial lung disease in whom tuberculous granulomas were found at necropsy prompted a retrospective review of 162 patients with chronic interstitial lung disease for evidence of associated tuberculosis.

## Methods

The notes and chest radiograph reports of all patients admitted to the chest department from 1 January 1970 to 1 January 1984 were reviewed. One hundred and sixty two patients (93 male, 69 female; mean age 57, range 18-86 years) were found to have a bilateral reticular or a reticulonodular pattern on their chest radiograph.<sup>3</sup> These patients were investigated retrospectively and followed up until 1986, or until they were lost from follow up or had died. Patients thought to have bronchiectasis (productive cough and abundant sputum with compatible radiographic appearance) were excluded. All the chest radiographs were reviewed by two senior physicians. Lung function tests showed a restrictive pattern in 70% and a mild obstructive pattern in 3%; in 27% results were normal except for an impaired transfer factor for carbon

monoxide. Active tuberculosis was diagnosed if one or more sputum cultures were positive for *Mycobacterium tuberculosis* from an average of three consecutive sputum cultures. The colonies were counted by eye.

## Results

Of the 162 patients, 23 had pulmonary sarcoidosis, 122 idiopathic chronic interstitial lung disease, and the remaining 17 various conditions (collagen vascular disease 5 cases, histiocytosis X 4, pneumoconiosis 3, post-radiation fibrosis 2, pulmonary amyloidosis 1, haemosiderosis 1, and extramedullary haematopoiesis 1). The diagnosis was made by transbronchial biopsy, open lung biopsy, or mediastinal biopsy (or a combination of these) in 35 of the patients with idiopathic chronic interstitial lung disease (32 showing a fibrotic and three a desquamative pattern) and in all patients with sarcoidosis, histiocytosis, haemosiderosis, amyloidosis, and extramedullary haematopoiesis. In the five patients with collagen disease the diagnosis was confirmed by skin or muscle biopsy or by serology, or both. In the remaining 87 patients diagnosis was based on clinical and radiographic features only. Thirteen of the 23 patients with sarcoidosis and 40 of the remaining 139 patients had been treated with corticosteroids before being seen in hospital.

Active tuberculosis was diagnosed in eight patients, seven of whom were male. None had chronic alcoholism or was of low socioeconomic status. The main clinical and laboratory data are summarised in table 1. Seven of the patients had chronic interstitial lung disease and one systemic sclerosis. None had a history of tuberculosis. Sputum culture grew 83-> 100 colonies of *Mycobacterium tuberculosis* in repeated sputum cultures in three patients and 3-15 colonies in one or two cultures in four patients.

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Table 1 Characteristics of patients with tuberculosis and chronic interstitial lung disease

	Sex	Age (y)	Duration (y)	Aetiology	Lung function	Corticosteroids	No of colonies
1	F	67	6	Systemic sclerosis	Restrictive	28 y	83
2	M	66	5	Idiopathic*	Not tested	—	> 100
3	M	73	7	Idiopathic*	Not tested	—	15
4	M	60	7	Idiopathic*	Restrictive	3 mo	11
5	M	75	2	Idiopathic (necropsy)	Restrictive	7 mo	[Histology proved]
6	M	79	13	Idiopathic*	Restrictive	—	3
7	M	50	1	Idiopathic (open lung biopsy)	Restrictive	—	6
8	M	63	6	Idiopathic*	Restrictive	—	> 100
Mean		66	6				

\*On the basis of clinical and radiographic features.

In one patient pulmonary tuberculosis was diagnosed only at necropsy. The positive culture for tuberculosis was made 5.9 (range 1–13) years after the diagnosis of chronic interstitial lung disease. The presenting symptoms at the time that pulmonary tuberculosis was diagnosed were fever in two patients and increased dyspnoea and cough in six. The chest radiograph in all eight patients gave no indication of tuberculosis in any of the eight patients. In patient 8 tomography showed a cavity in the left upper lobe.

The ratio of corticosteroid to non-corticosteroid treated patients was similar in the two groups (table 2). Six patients survived their stay in hospital and were treated with isoniazid and rifampicin for nine months. Sputum cultures became negative after one to two months of treatment. No changes in the chest radiographs were observed after treatment. Two patients died of respiratory failure. Necropsy was performed only in one.

## Discussion

The incidence of pulmonary tuberculosis in Israel is now one of the lowest in the world,<sup>4,5</sup> the average annual incidence of new cases during 1970–85 being 3.4/10 000 persons over the age of 65 years<sup>4</sup> and less in younger people. Nevertheless, we found eight cases of newly discovered tuberculosis in 162 patients with chronic interstitial lung disease with a mean age of 57 years during a maximum follow up period of 16 years, giving an incidence of at least 30 per 10 000 person years (most of our patients had a shorter follow up

period, so this incidence is an underestimate). The incidence of tuberculosis in patients with chronic interstitial lung disease was at least 9.1 times that of the general population. It may be argued that a sputum culture with less than 20 colonies is not clinically significant, being due to relatively quiescent foci.<sup>6,7</sup> Exclusion of four of our eight patients with less than 83 colonies still gives an incidence 4.5 times greater than expected. The male predominance of tuberculosis in our patients with chronic interstitial lung disease was greater than the male:female ratio (1.8:1) of tuberculosis in the general population of Israel.<sup>4</sup>

Corticosteroid treatment was unlikely to be a causative factor in our patients, as the frequency of pulmonary tuberculosis was similar in treated and untreated patients. No study has yet shown an increased incidence of tuberculosis in patients treated with corticosteroids.<sup>8</sup>

Our study suggests that a diffusely damaged lung increases the susceptibility to dormant tuberculosis. A similar observation was made in patients with bronchogenic carcinoma,<sup>9</sup> and an increased incidence of atypical mycobacteria has been seen in patients with chronic lung diseases.<sup>10</sup>

Tuberculosis in our patients was not evident on the chest radiograph, presumably because of the increased interstitial markings. Our experience suggests that sputum culture should be performed in any patients with chronic interstitial lung disease with an unexplained deterioration in their respiratory symptoms.

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Table 2 Characteristics of patients with idiopathic chronic interstitial lung disease with and without cultures positive for *Mycobacterium tuberculosis*

Culture	Sex (M:F)	Age (y, mean (range))	Corticosteroids (No(%))		Total No of patients
			Treated	Not treated	
Positive	7:0	66 (50–79)	2 (29)	5 (71)	7
Negative	66:49	58 (18–86)	33 (29)	82 (71)	115

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