SAMJ
ARTICLES

The lungs in rheumatoid arthritis — a clinical, radiographic and pulmonary function study

Stephen C. Morrison, Girish M. Mody, Solly R. Benatar, Orlando L. Meyers

Objective. To determine the prevalence and spectrum of pulmonary abnormalities in patients with rheumatoid arthritis (RA) in a developing country.

Design. This was a prospective hospital-based survey of a randomly selected group of patients with RA who were seen in a rheumatic diseases unit.

Setting. Groote Schuur Hospital and Princess Alice Orthopaedic Hospital, Cape Town.

Patients. A group of 104 patients with RA were randomly selected from a total of 330 patients with RA who were seen in the rheumatic diseases unit. All the patients were interviewed and a clinical assessment, chest radiographs and pulmonary function tests were performed.

Results. Fifty-six patients (53.8%) had evidence of one or more current or previous pulmonary diseases: rheumatoid nodule in 1 (1%), bronchiectasis in 2 (1.9%), fibrosing alveolitis in 5 (4.8%), pneumonia in 5 (4.8%), asthma in 9 (8.7%), pleural disease in 17 (16.3%) and tuberculosis in 25 (24%). Excluding patients who were smokers or ex-smokers or who had coexistent pulmonary disease, there were 20 patients (19.2%) who had pulmonary abnormalities that could be attributed to RA: rheumatoid nodule in 1 (1%), fibrosing alveolitis in 5 (4.8%) (1 of whom also had pleural disease), pleural disease alone in 8 (7.7%), diffusion defect in 5 (4.8%) and airways obstruction in 1 (1%).

Conclusion. This study provides clinical and lung function criteria that allow a clinically useful stratification of abnormalities in relation to a spectrum of common causes of pulmonary dysfunction that need to be distinguished from pulmonary abnormalities caused by RA. Pulmonary abnormalities are common and about 20% of RA patients may have an abnormality related to RA.

S Afr Med J 1996; **86:** 829-833.

Respiratory Clinic, Rheumatic Diseases Unit and Department of Medicine, Groote Schuur Hospital and University of Cape Town

Stephen C. Morrison, M.A., M.B. B.CHIR., PH.D., F.R.C.P. (LOND.), F.R.A.C.P.

Girish M. Mody, M.B. CH.B., M.D., F.R.C.P. (LOND.), F.C.P. (S.A.)

Solly R. Benatar, M.B. CH.B., F.F.A. (S.A.), F.R.C.P. (LOND.)

Orlando L. Meyers, M.B. CH.B., M.D., F.C.P. (S.A.)

Pulmonary complications of rheumatoid arthritis (RA) were first reported in 1948.[1] These complications, also subsequently described by others, include interstitial lung disease,[1] pleurisy,[2] necrobiotic nodules,[2] nodules associated with silico-anthracosis (Caplan's syndrome),[3] obliterative bronchiolitis,[4,5] pulmonary vascular disease[6,7] and bronchocentric granulomatous lung disease.[8] An increased incidence of pulmonary infection is also found in patients with RA.[9]

Some of these manifestations of rheumatoid disease are quite uncommon, and accurate assessment of their prevalence is made difficult by differing methods of case selection in different published series. Moreover, confounding variables such as smoking habit, occupation and patients excluded because of concurrent disease present further difficulties in estimating prevalence.

The aim of this survey was to determine the prevalence and spectrum of pulmonary abnormalities in 104 patients with RA selected randomly from a rheumatic diseases unit.

Methods

Of 330 patients of mixed race with classic or definite RA[10] who were seen at the rheumatic diseases unit of the University of Cape Town, 104 were selected by means of random number tables for inclusion in this study.

A detailed cardiorespiratory history included occupational and environmental exposure to dust and foreign proteins, smoking status, present and previous drug administration, and current symptoms, including breathlessness, cough, sputum production and chest pain. The American Rheumatism Association (ARA) functional classification was applied and recorded[11] and a detailed physical examination performed.

A full blood count (Coulter-S-plus automated counter) and latex test for rheumatoid factor (slide agglutination technique, Orthodiagnostics) were performed on all patients. A titre of 80 or greater at the time of the study was considered an indication of seropositivity. Standard postero-anterior and lateral chest radiographs were taken, and the films were read independently by a respiratory physician and a radiologist, initially without reference to the clinical details. Inter-reader differences of opinion were few, and always minor. These were resolved by reference to a second respiratory physician, who had access to the patient's clinical details.

Spirometry was assessed by means of the flow volume loop, performed with a wedge spirometer and XY recorder (med-Science 570). The best of three satisfactorily performed manoeuvres was used and response to bronchodilator was assessed. All 104 patients were able to perform spirometry satisfactorily. Functional residual capacity (FRC) was measured by the helium dilution method (Expirograph, Godart). Total lung capacity (TLC) and residual volume (RV) were calculated from this test, which was performed once only; 5 patients were unable to co-operate fully. Transfer factor for carbon monoxide (TLCO) and transfer coefficient (KCO) were obtained by the single-breath method (Carbon Monoxide Transfer test, PK Morgan). The mean of two adequately performed measurements, 5

minutes apart and corrected for haemoglobin level, was used.[12] Three patients were unable to sustain the required 10-second breath hold, but satisfactory results were obtained in 101 patients. Maximum inspiratory (MIP) and expiratory mouth pressures (MEP) were performed at RV and TLC respectively, according to the method of Black and Hyatt,[13] in which the patient was required to sustain maximal effort against the pressure gauge for at least 1 second; the best of three such measurements was taken. All measurements were expressed as percentages of predicted values based on each subject's age, sex, height and weight.[12,14-17]

Pulmonary function tests were interpreted by a respiratory physician without reference to the clinical or radiographic data. The presence and severity of airflow obstruction, restrictive abnormality, or both together was determined by examining the flow volume loop and full volume data. In the case of TLCO, KCO, MIP and MEP, the severity of abnormality was assessed individually for each test. The criteria used to interpret the pulmonary function tests are given in Table I.

Table I. Criteria for interpretation of pulmonary function tests

Abnormality	General criteria	Grade	Specific grading criteria
Airway obstruction	Appearance of flow-volume loop, plus specific criteria	Mild	Deviation of more than 2 standard deviations below or above predicted values for any of the following: FEV_1/FVC ratio, PEFR, MEF50, FEV, with normal FVC, RV*, FRC*, TLC*, RV/TLC ratio* with normal TLC
		Moderate	FEV_1/FVC ratio 50 - 65%, or MEF50 < 40% predicted
		Severe	FEV_1/FVC ratio < 50%
Response to bronchodilator	–	Nil	No increase in FEV, or FVC
		Slight	0 - 10% increase in FEV, or FVC
		Marked	> 10% increase in FEV, or FVC
Restrictive pattern	Appearance of flow-volume loop, plus specific grading criteria	Mild*	Deviation of more than 2 standard deviations below predicted values for any of the following: FVC, FRC, TLC
		Moderate*	FVC or TLC 40 - 60% predicted
		Severe	FVC or TLC < 40% predicted
TLCO, KCO, MIP, MEP	–	Minimal	60 - 80% of predicted value but within 2 standard deviations
		Mild	Deviation of more than 2 standard deviations below predicted value, but > 60% predicted value
		Moderate	40 - 59% predicted value
		Severe	< 40% predicted value

* No obstruction must be present if reduced FVC is the only criterion for diagnosis of restriction.
FEV_1 = forced expired volume in 1 second; FVC = forced vital capacity; PIFR = peak inspiratory flow rate; PEFR = peak expiratory flow rate; MEF50 = maximum expiratory flow at 50% FVC; RV = residual volume; FRC = functional residual capacity; TLC = total lung capacity; TLCO = transfer factor for carbon monoxide; KCO = transfer coefficient; MIP = maximum inspiratory pressure; MEP = maximum expiratory pressure.

Contingency analysis (chi-square) was used to test for possible relationships between variables; where expected cell sizes were less than 5, Fisher's exact test was used.

Results

Clinical information (Table II). The mean age of the patients was 51.1 years (range 21 - 80 years) and the mean duration of RA was 12.4 years (range 1 - 50 years). The female/male ratio was 2.3:1. Sixty-three patients (60.6%) were seropositive at the time of the study, although a total of 80 patients (76.9%) had at some time been seropositive and 31 patients (30.7%) had subcutaneous nodules. Nodules were significantly commoner in men ($P = 0.013$). Twenty-five patients were in ARA functional classes 3 or 4,[11] and 16 of these were over 50 years old. Age, duration of RA, seropositivity rate and functional class did not differ significantly between men and women. The mean (SD) haemoglobin levels were 14.0 (SD 1.9) g/dl for men, and 12.4 (SD 1.7) g/dl for women.

Fifty-two patients were current smokers, 17 ex-smokers and 35 non-smokers. Mean cigarette consumption in smokers and ex-smokers was 20.1 pack-years, and a smoking history was significantly commoner in men ($P = 0.003$).

The occurrence of dyspnoea in 31 patients could be attributed to anaemia, lung or heart disease in 29 patients, some of whom were also smokers or ex-smokers; the remaining 2 were current smokers and did not have any other predisposing factor. Productive cough was present in 7 patients, all of whom had either bronchiectasis or a history of smoking. Twelve patients kept either pigeons or budgerigars and 1, a grindstone operator, was exposed to silica dust; in none of these 13 patients could any disease be attributed to their exposure.

Five patients had digital clubbing, of whom 2 had fibrosing alveolitis and 1 bronchiectasis. No cause of the clubbing was apparent in the remaining 2 patients; 1 of these had evidence of previous pleurisy on the chest radiograph, while the other had valvular heart disease.

A total of 47 patients had received gold preparations (oral or intramuscular) and/or d-penicillamine. No relationship was found between any abnormality of the respiratory system and administration of these drugs.

Prevalence of pulmonary disease. The clinical, radiographic and physiological findings were used together to determine the prevalence of lung disease in the study population, and the results are given in Tables II and III.

One asymptomatic patient had evidence of a cavitating rheumatoid nodule on the chest radiograph, which regressed spontaneously on serial follow-up examinations.

Bronchiectasis was present in 2 patients (1.9%), 1 with Kartagener's syndrome and the other with chronic suppurative lung disease following pulmonary tuberculosis.

Fibrosing alveolitis was diagnosed in 5 patients (4.8%), all of whom had a diffuse pulmonary infiltrate on the chest radiograph, with honeycombing in 3 patients. All 5 patients had crackles on auscultation, 2 had clubbing and 1 had clinical evidence of pulmonary hypertension. There was no significant association with gender or with the presence of subcutaneous nodules or seropositivity. Only 2 of the patients had received gold preparations or d-penicillamine. Four of the 5 patients had airways obstruction, 3 of whom were smokers. The predominant pulmonary function abnormality was restriction of lung volumes ($P = 0.008$). Severe reduction of TLCO was present in 2 of the 4 patients in whom it could be measured.

Table II. Profile of patients with disease affecting the lungs

Patient grouping	*N*	Diff inf	Prod cough	Birds/ dust	Sm	Dysp- noea	Club- bing	Mean age (yrs)	Male	Mean durat RA (mo.)	Class 3/4	Nod	Sero- pos	Drugs	Obstn	Restn	TLCO abn	KCO abn	MIP abn	MEP abn
All patients	104	8	7	13	69	31	5	51.1	32	148	25	31	63	47	31	11	57	21	10	31
Lung nodules	1	0	1	0	1	0	0	46.0	1	216	0	1	1	0	0	0	0	0	0	1
Bronchiectasis	2	0	2	0	1	1	1	33.5	0	156	2	1	2	1	1	1	2	1	0	0
Alveolitis	5	5	0	0	3	4	2	54.8	2	158	2	2	4	2	4	3	4	3	1	1
Pneumonia	5	0	1	1	3	3	0	53.2	1	121	3	2	4	1	2	1	2	1	0	1
Asthma	9	1	1	0	8	5	1	52.9	3	118	2	2	4	4	9	0	2	1	1	1
Pleural disease	17	3	4	3	12	6	2	54.8	7	175	5	7	12	7	6	5	13	6	1	5
Tuberculosis	25	4	2	4	18	7	0	53.6	10	177	6	7	16	9	9	6	14	4	3	8

Numbers, except where indicated, refer to numbers of patients with each characteristic. The 6 columns on the right of the table indicate pulmonary function abnormalities. Diff inf = diffuse infiltrate on CXR; Sm = smokers or ex-smokers; Durat RA (mo.) = duration of rheumatoid arthritis in months; Class 3/4 = patients in functional classes 3 or 4; Nod = patients with subcutaneous nodules; Drugs = therapy with gold or d-penicillamine; Obstn = airways obstruction; Restn = restrictive abnormality; abn = abnormality.

Table III. Pulmonary function values, expressed as percentage predicted. Actual values are given for ratios

Patient grouping	*N*	FEV_1	FVC	FEV_1/ FVC	PEFR	PIFR	MEF50	RV	FRC	TLC	RV/ TLC	TLCO	KCO	MIP	MEP
All patients	104	85	87	77	107	95	96	123	109	97	37	77	95	110	90
Non-smokers	35	87	86	80	114	88	107	128	111	100	37	87	106	113	86
Ex-smokers	17	81	83	77	99	95	80	123	103	94	40	74	97	112	96
Smokers	52	85	89	75	105	99	95	120	109	97	36	73	86	107	91
Males	32	83	88	74	107	108	91	97	92	90	34	73	86	110	89
Females	72	86	87	79	107	89	98	134	116	100	38	79	98	109	91
Lung nodules	1	114	118	76	176	196	166	98	111	105	29	111	98	126	73
Bronchiectasis	2	42	46	79	58	54	55	136	89	66	47	44	85	123	122
Alveolitis	5	63	68	74	85	92	44	118	101	83	43	39	62	113	100
Pneumonia	5	75	80	72	86	86	64	132	109	99	41	78	96	112	96
Asthma	9	69	81	66	84	88	48	147	118	100	44	83	98	116	105
Pleural disease	17	77	80	75	103	96	85	118	107	92	41	69	90	118	90
Tuberculosis	25	80	83	75	101	97	84	110	97	91	37	75	95	114	92

Abbreviations as for Table I.

Five patients (4.8%) had radiographic evidence of past or present pneumonia. In 1, this took the form of a chronic bilateral necrotising pneumonia, in the absence of a history or other evidence of tuberculosis, while a second had collapse and consolidation of the right middle lobe. The remaining 3 had areas of atelectasis on the radiograph. Only the patient with necrotising pneumonia had restriction of pulmonary function, and 2 others, both smokers, had airways obstruction.

Nine patients were diagnosed as having bronchial asthma, all of whom had reversible airways obstruction. TLCO was normal in 7; the 2 in whom an abnormal TLCO was obtained had additional lung disease to account for it — previous tuberculosis, in 1, and fibrosing alveolitis in the other.

Seventeen patients (16.3%) had evidence of past or present pleural disease on the chest radiograph. A small pleural effusion was present in 2, apical pleural capping in 12, and nonspecific pleural shadows in 3. There was no significant association between pleural abnormality and gender, seropositivity or subcutaneous nodules. Eight of these patients had coexistent cardiopulmonary disease, viz. tuberculosis in 5 (1 of whom also had fibrosing alveolitis), previous pneumonia in 2 and cardiac disease in 1. Pleural disease in 9 patients may therefore be attributable to RA. The predominant pulmonary function abnormality in the patients with pleural disease was restriction of lung volumes, which was present in 5 of the 17 patients. This association was significant ($P = 0.016$) and remained so even when the patients with previous tuberculosis were excluded. Airflow obstruction was present in 6 patients, but 5 of these were smokers and the sixth had cardiac disease. Eleven patients gave a history of having received treatment for pulmonary tuberculosis, while a further 14 had radiographic evidence of previous tuberculosis. Therefore 25 patients (24.0%) were considered to have had tuberculosis in the past. There was a significant association between a restrictive pulmonary function abnormality and tuberculosis ($P = 0.022$).

Pulmonary function abnormality. As shown in Table II, more patients exhibited abnormalities of pulmonary function than had clinically and radiologically diagnosed lung disease. Airways obstruction was present in a total of 31 patients (29.8%). The association between obstruction and smoking was significant ($P = 0.044$); 25 of the 69 smokers and ex-smokers had obstruction compared with only 6 of the 35 non-smokers. The obstruction in the 6 non-smokers was not severe. The clinical details of these 6 patients were as follows: 2 patients had had previous pulmonary tuberculosis, 1 of whom was also asthmatic; 2 patients had cardiac disease (1 had a coronary artery bypass graft with cardiomegaly and 1 had hypertension and mitral incompetence with a dilated left ventricle); 1 patient, who had a 12.5% increase in FEV_1 post bronchodilator, had a

unilateral radiolucent lung. The remaining patient, whose airways obstruction was not responsive to bronchodilator, and whose TLCO was 82% of the predicted value, had no obvious cause of airways obstruction and may have had bronchiolitis obliterans. Eleven patients, all of whom had pulmonary disease (Table II), had evidence of a restrictive pulmonary function defect.

In 57 patients the TLCO was reduced — severely in 5, moderately in 9, mildly in 10 and minimally in 33. One patient with mild reduction and 9 with minimal reduction were non-smokers who had not had TB. Of these 10 patients 3 had cardiac disease with cardiomegaly. Of these, 1 had aortic incompetence, 1 mitral incompetence and 1 had had a previous coronary artery bypass graft. One further patient had previously had pneumonia, and had residual pleural and pulmonary shadows on the chest radiograph, and 1 had a unilateral radiolucent lung with mild airflow obstruction. The remaining 5 patients had no obvious explanation for the reduced TLCO. The KCO was abnormal in 21 patients, all of whom were smokers.

Abnormalities of MIP and MEP occurred in 10 and 31 patients respectively, but these were mild or minimal in all cases, and no clinical association could be found.

Altogether, 56 of 104 patients (53.8%) had one or more abnormalities of the respiratory system based on clinical, radiographic or pulmonary function data. Fourteen of these patients were diagnosed as having pulmonary disease related to RA, i.e. rheumatoid nodule in 1 patient, fibrosing alveolitis in 5 patients (1 of whom also had pleural disease) and pleural disease alone in 8 patients. A further 6 patients had abnormality of pulmonary function which could not be explained by clinically or radiographically apparent disease — fixed airways obstruction in 1 patient and reduced TLCO in 5 patients. It is therefore possible that a total of 20 patients had pulmonary pathology attributable to rheumatoid disease.

Discussion

Pulmonary complications are frequently reported in RA, but their prevalence varies depending on the selection of patients, the investigations performed, and the criteria used in the interpretation of investigations, particularly pulmonary function tests. Estimates of prevalence of interstitial lung disease, for example, varied from 1.1% when radiological criteria only were employed[18] to 41% when pulmonary function criteria were used.[19] The prevalence of interstitial lung disease based on the presence of diffuse reticulonodular radiographic shadows was 4.8% in the present study, which is in close agreement with the 4.5% of 309 patients reported by Jurik *et al.*[20] and the 5% of 155 patients reported by Hyland *et al.*[21] Since a further 4.8% of our patients had an abnormal gas transfer value not attributable to smoking or other clinically apparent disease, it is likely that the prevalence of interstitial lung disease in RA may be underestimated if pulmonary function tests are not included in the diagnostic work-up of patients. Indeed the inclusion of lung biopsy, even in patients without infiltrates on radiographs, may increase the prevalence to even higher levels.[22] This view is supported by Yousem *et al.* who reported on the lack of correlation between radiographic and histological findings.[23] The use of high-resolution computed tomography of the chest has also been shown to help detect early lung disease in RA[24] and it has a high sensitivity for the diagnosis of interstitial lung disease.[25] A recent survey, which included broncho-alveolar lavage, reported a prevalence of interstitial lung disease of 15% in unselected RA patients.[26] Treatment with gold salts, penicillamine and other disease-modifying anti-rheumatic drugs has been reported to cause interstitial lung disease,[23,27] but no such association was noted in this study or by Whorwell *et al.*[26]

The prevalence of pleural involvement varies from 5% for pleural effusion,[2] to 21% for pleuritic chest pain[29] to 75% for pleural abnormalities in postmortem studies of patients with longstanding RA.[30] An analysis of the chest radiograph in 309 RA patients in Denmark showed evidence of previous pleurisy in 18.8% and pleural effusion in 0.6%.[20] A large British study of 516 RA patients recorded a history of pleurisy in 21%, and 3.3% had pleural effusion which was attributed to RA.[29] We found pleural abnormalities in 17 patients (16.3%), but these may be attributed to RA in only 9 patients (8.7%) who did not have any coexistent cardiopulmonary diseases. However, it is possible that some of these patients may have had previous asymptomatic pleural involvement caused by tuberculosis without evidence of parenchymal involvement, but this cannot be determined with certainty. Hyland *et al.*[21] did not find any evidence of an increased prevalence of pleurisy in RA. However, the characteristic changes in the pleural fluid in RA provide convincing evidence that it is a definite entity.[31]

A significant reduction in the pulmonary gas transfer has been reported in RA,[19,28,32,33] although Hyland *et al.*[21] failed to detect any difference between 155 RA patients and 95 controls. The prevalence of abnormal TLCO was 23.8% and 41% in the studies of Davidson *et al.*[32] and Frank *et al.*[19] respectively. We found a reduction in TLCO in 54.8% of our patients but the majority were smokers or ex-smokers. A relationship between smoking and a reduction in TLCO has been reported in other studies.[21,34] We found that only 6 (5.8%) of our patients did not have any other contributory factors for a reduction in the diffusion capacity. These patients may have had occult interstitial or pulmonary vascular disease. A similar low prevalence of an abnormal TLCO was reported by Banks *et al.*,[35] who found a reduced TLCO in 6 (2.2%) of 264 RA patients in the absence of clinical or radiographic evidence of lung disease.

Airways obstruction was reported in 32% and 61% of patients by Geddes *et al.*[36] and Collins *et al.*[37] respectively, but a large Canadian study failed to detect any increase compared with controls.[21] Acute obliterative bronchiolitis with a poor prognosis was reported in a series of 6 patients by Geddes *et al.*[4] Progressive obstructive disease of the peripheral airways in 6 lifetime non-smokers with RA, with documentation of the histological abnormalities, was reported by Begin *et al.*[38] We detected airflow obstruction in 31 (29.8%) of our patients but the majority were smokers. Only 1 patient had airflow obstruction which could not be related to asthma, smoking or any other disease; this patient may have had bronchiolitis obliterans.

The association of infection with RA has been noted in several reports.[9,39-41] A fourfold increase in mortality over an age- and sex-matched general population has been

reported as a result of respiratory infections in RA.[42] Tuberculosis is common in the coloured population of South Africa and was noted in 25 (24%) of our RA patients. A Danish radiographic study report showed evidence of healed tuberculosis in 9.1%, with a significant increase in 17.2% of the RA men compared with 6.1% in male controls.[20] We found that 6 patients (5.9%) had evidence of previous pneumonia and 2 (1.9%) had bronchiectasis. Bronchiectasis was detected in 16 (3.1%) of 516 patients reported by Walker and Wright.[43] A recent high-resolution computed tomography study of 20 patients with radiological evidence of interstitial lung disease and 20 controls without interstitial lung disease detected bronchiectasis in 6 patients with interstitial lung disease and 4 controls without interstitial lung disease, suggesting that bronchiectasis is more common than previously recognised.[44]

Pulmonary manifestations such as pleural involvement and interstitial lung disease have been reported to occur more commonly in association with nodules and a positive rheumatoid factor.[43] However, in our survey there was no relationship between these manifestations and the prevalence of nodules and seropositivity.

In conclusion, pulmonary involvement is common in RA and was detected in 20 patients (19.2%). It is possible that the true prevalence is higher; some of the abnormalities noted in smokers and patients with other diseases (such as tuberculosis) may be due to a combination of factors, including RA, but this cannot be determined with certainty. The pulmonary abnormalities attributable directly to RA were pleural involvement (7.7%), interstitial lung disease (4.8%), gas transfer defect in the absence of clinicoradiographic evidence of disease (4.8%), airways obstruction in the absence of clinicoradiographic evidence of disease (1%), and pulmonary nodule (1%).

Our study provides a perspective on the spectrum of lung disease that may be found in patients with RA in a developing country. It also demonstrates how the use of simple clinical, radiographic and lung function data can be used to stratify abnormalities in a clinically useful manner.

The authors are grateful to the late Dr H. S. Myers for reading the chest radiographs, Mrs J. Etheridge and staff for performing the pulmonary function tests, the medical superintendents of Groote Schuur and Princess Alice Orthopaedic Hospitals for permission to publish patient information, and the Medical Research Council of South Africa for financial support.

REFERENCES

1. Ellman P, Ball RE. 'Rheumatoid disease' with joint and pulmonary manifestations. *BMJ* 1948; **2:** 816-820.
2. Horler AR, Thompson M. The pleural and pulmonary complications of rheumatoid arthritis. *Ann Intern Med* 1959; **51:** 1179-1203.
3. Caplan A. Certain unusual radiological appearances in the chest of coal-miners suffering from rheumatoid arthritis. *Thorax* 1953; **8:** 29-37.
4. Geddes DM, Corrin B, Brewerton DA, Davies RJ, Turner-Warwick M. Progressive airway obliteration in adults and its association with rheumatoid disease. *Q J Med* 1977; **46:** 427-444.
5. Herzog CA, Miller RR, Hoidal JR. Bronchiolitis and rheumatoid arthritis. *Am Rev Respir Dis* 1981; **124:** 636-639.
6. Kay JM, Banik S. Unexplained pulmonary hypertension with pulmonary arteritis in rheumatoid disease. *Br J Dis Chest* 1977; **71:** 53-59.
7. Armstrong JG, Steele RH. Localised pulmonary arteritis in rheumatoid disease. *Thorax* 1982; **37:** 313-314.
8. Bonafede RP, Benatar SR. Bronchocentric granulomatosis and rheumatoid arthritis. *Br J Dis Chest* 1987; **81:** 197-201.
9. Walker WC. Pulmonary infections and rheumatoid arthritis. *Q J Med* 1967; **142:** 239-251.
10. Ropes MW, Bennett GA, Cobbs S, Jacox R, Jessar RA. 1958 revision of the diagnostic criteria for rheumatoid arthritis. *Bull Rheum Dis* 1958; **9:** 175-176.
11. Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. *JAMA* 1949; **140:** 659-662.
12. Cotes JE. *Lung Function: Assessment and Application in Medicine.* 4th ed, rev. London: Blackwell, 1979.
13. Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. *Am Rev Respir Dis* 1969; **99:** 696-702.
14. Grimby G, Soderholm B. Spirometric studies in normal subjects. III. Static lung volumes and maximum voluntary ventilation in adults with a note on physical fitness. *Acta Med Scand* 1963; **173:** 199-206.
15. Bass H. The flow-volume loop: normal standards and abnormalities in chronic obstructive pulmonary disease. *Chest* 1973; **63:** 171-176.
16. Schoenberg JB, Beck GJ, Bouhuys A. Growth and decay of pulmonary function in healthy blacks and whites. *Respir Physiol* 1978; **33:** 367-393.
17. Wilson SH, Cooke NT, Edwards RH, Spiro SG. Predicted normal values for maximal respiratory pressures in caucasian adults and children. *Thorax* 1984; **39:** 535-538.
18. Patterson CD, Harville WE, Pierce JA. Rheumatoid lung disease. *Ann Intern Med* 1965; **62:** 685-697.
19. Frank ST, Weg J, Harkleroad LE, Fitch RF. Pulmonary dysfunction in rheumatoid disease. *Chest* 1973; **63:** 27-34.
20. Jurik AG, Davidsen D, Graudal H. Prevalence of pulmonary involvement in rheumatoid arthritis and its relationship to some characteristics of the patients. *Scand J Rheumatol* 1982; **11:** 217-224.
21. Hyland RH, Gordon DA, Broder I, *et al.* A systematic controlled study of pulmonary abnormalities in rheumatoid arthritis. *J Rheumatol* 1983; **10:** 395-405.
22. Cervantes-Perez P, Toro-Perez AH, Rodriguez-Jurado P. Pulmonary involvement in rheumatoid arthritis. *JAMA* 1980; **243:** 1715-1719.
23. Yousem SA, Colby TV, Carrington CB. Lung biopsy in rheumatoid arthritis. *Am Rev Respir Dis* 1985; **131:** 770-777.
24. Steinberg DL, Webb WR. CT appearances of rheumatoid lung diseases. *J Comput Assist Tomogr* 1984; **8:** 881-884.
25. Kelly CA, McDonagh J, Heycock C, Griffiths ID, Owen JP. High resolution computed tomography in the assessment of interstitial lung disease in rheumatoid arthritis. *Br J Rheumatol* 1992; **31:** suppl 2, 96.
26. Gilligan DM, O'Connor CM, Ward K, Moloney D, Bresniham B, Fitzgerald MX. Bronchoalveolar lavage in mild and severe rheumatoid arthritis. *Thorax* 1990; **45:** 591-596.
27. Cannon GW. Pulmonary complications of antirheumatic drug therapy. *Semin Arthritis Rheum* 1990; **19:** 353-364.
28. Whorwell PJ, Wojtulewski JA, Lacey BW. Respiratory function in rheumatoid arthritis. *BMJ* 1975; **2:** 175.
29. Walker WC, Wright V. Rheumatoid pleuritis. *Ann Rheum Dis* 1967; **26:** 467-474.
30. Baggenstoss AH, Rosenberg EF. Visceral lesions associated with chronic infectious (rheumatoid) arthritis. *Arch Pathol* 1943; **35:** 503-516.
31. Kelly CA. Rheumatoid arthritis: classical rheumatoid lung disease. *Ballieres Clin Rheumatol* 1993; **7:** 1-16.
32. Davidson C, Brooks AG, Bacon PA. Lung function in rheumatoid arthritis. A clinic survey. *Ann Rheum Dis* 1974; **33:** 293-297.
33. Oxholm P, Madsen EB, Manthorpe R, Rasmussen FV. Pulmonary function in patients with rheumatoid arthritis. *Scand J Rheumatol* 1982; **11:** 109-112.
34. Wilson RH, Meador RS, Jay BE, Higgins E. The pulmonary pathologic physiology of persons who smoke cigarettes. *N Engl J Med* 1960; **262:** 956-961.
35. Banks J, Banks C, Cheong B, *et al.* An epidemiological and clinical investigation of pulmonary function and respiratory symptoms in patients with rheumatoid arthritis. *Q J Med* 1992; **85:** 795-806.
36. Geddes DM, Webley M, Emerson PA. Airways obstruction in rheumatoid arthritis. *Ann Rheum Dis* 1979; **38:** 222-225.
37. Collins RL, Turner RA, Johnson AM, Whitley NO, McLean RL. Obstructive pulmonary disease in rheumatoid arthritis. *Arthritis Rheum* 1976; **19:** 623-628.
38. Begin R, Masse S, Cantin A, Menard HA, Bureau MA. Airways disease in a subset of nonsmoking rheumatoid patients. Characterization of the disease and evidence for an autoimmune pathogenesis. *Am J Med* 1982; **72:** 743-750.
39. Huskisson EC, Hart FD. Severe, unusual, and recurrent infections in rheumatoid arthritis. *Ann Rheum Dis* 1972; **31:** 118-121.
40. Editorial. Infection in rheumatoid disease. *BMJ* 1972; **2:** 549-550.
41. Baum J. Infection in rheumatoid arthritis. *Arthritis Rheum* 1971; **14:** 135-137.
42. Monson RR, Hall AP. Mortality among arthritics. *J Chron Dis* 1976; **29:** 459-467.
43. Walker WC, Wright V. Pulmonary lesions and rheumatoid arthritis. *Medicine* 1968; **47:** 501-520.
44. McDonagh J, Greaves M, Wright AR, Heycock C, Owen JP, Kelly C. High resolution computed tomography of the lungs in patients with rheumatoid arthritis and interstitial lung disease. *Br J Rheumatol* 1994; **33:** 118-122.

Accepted 30 Aug 1995.