

RHEUMATOID PLEURITIS

BY

W. C. WALKER* AND V. WRIGHT†

From the Rheumatism Research Unit, University Department of Medicine, General Infirmary, Leeds

Although there was initial reluctance to accept the concept, most authorities now believe that pleural effusion and dry pleurisy may occur as systemic manifestations of rheumatoid arthritis. This belief is based on clinical series in which the incidence of otherwise unexplained pleural effusion has been unexpectedly high (Horler and Thompson, 1959) and on several reports of granulomatous lesions in the pleura considered to be of rheumatoid origin (Bennett, Zeller, and Bauer, 1940; Gruenwald, 1948; Raven, Parkes Weber, and Price, 1948; Ellman, Cudkowicz, and Elwood, 1954; Horler and Thompson, 1959; Koepke, 1960; Schools and Mikkelsen, 1962; Hindle and Yates, 1965; Castleman and McNeely, 1965). In rheumatoid pneumoconiosis, the incidence of pleural effusion in those with the classical x-ray appearance was 12.5 per cent. (Caplan, Payne, and Withey, 1962).

It would be anticipated that controlled investigations should have revealed a greater prevalence of pleural effusion in rheumatoid subjects than in controls, but those so far undertaken have yielded conflicting results. Locke (1963) found a greater prevalence of pleural effusion in a small selected series of rheumatoid subjects than in controls, and Talbot and Calkins (1964) made a similar observation in an autopsy study. By contrast, in larger controlled investigations, pleural effusion was not found to be more common (Aronoff, Bywaters, and Fearnley, 1955; Stack and Grant, 1965).

The uncertainties surrounding pleural effusions attributed to rheumatoid disease are doubtless largely due to the difficulty in establishing a positive diagnosis and in most of the cases so far recorded this has been reached mainly by exclusion. However, Carr and Mayne (1962) have emphasized the very low glucose levels in the pleural fluids. Rheumatoid tissue has been recovered by pleural biopsy

(Heller, Kellow, and Chomet, 1956; Schools and Davey, 1960), but as a diagnostic measure this has been disappointing in the experience of others (Ward, 1961; Carr and Mayne, 1962; Mattingly, 1964; Poppius and Tani, 1964).

Despite the widely held view that attacks of dry pleurisy are more frequent in rheumatoid subjects, there is no statistical support for this in the one comprehensive controlled investigation (Short, Bauer, and Reynolds, 1957).

Several authors have reported a high incidence of pleural adhesions at autopsy (Baggenstoss and Rosenberg, 1943; Fingerman and Andrus, 1943; Aronoff and others, 1955; Sinclair and Cruickshank, 1956; Cruickshank, 1957; Talbot and Calkins, 1964). However, the histological changes have been non-specific (Sinclair and Cruickshank, 1956) and the relationship to the rheumatoid process uncertain.

Clearly several doubts remain regarding rheumatoid pleural lesions. The study here reported formed part of a comprehensive controlled investigation into the pleural and pulmonary manifestations of rheumatoid arthritis which has been recorded in detail elsewhere (Walker, 1966).

Materials and Methods

516 patients with definite or classical rheumatoid arthritis (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) were studied. 189 were new referrals to the Rheumatism Clinic of the General Infirmary at Leeds and the remainder were follow-up cases. The control group consisted of 301 patients with degenerative joint disease (DJD). 221 of them new referrals. In each case a full history was taken, a complete clinical examination done, and the arthritis carefully assessed as recorded elsewhere (Walker, 1966). Respiratory symptoms were noted and evaluated and special inquiry was made regarding previous respiratory diseases, including pneumonia, pleurisy, pulmonary tuberculosis, or other chest illness. Details of smoking habits and the occupational history were noted. All patients had a chest radiograph, which was

*Consultant Physician, Wakefield Hospitals.

†Senior Lecturer in Medicine, Consultant Physician in Rheumatology

read by one of us (W.C.W.) without knowledge of the group to which they belonged. Pleural biopsy was performed under local anaesthesia, using the Abrams punch (Abrams, 1958) when indicated. All rheumatoid patients had x rays of the hands and feet and those in the DJD group had films of the affected joints. Haemoglobin, white cell count, blood sedimentation rate (BSR), and sheep cell agglutination test (SCAT) were done in all patients, and other investigations when indicated.

Results

Of the rheumatoid patients 73 per cent. were female and of the control patients 79 per cent. The age distribution of the two groups was reasonably comparable (Fig. 1).

Pleurisy

The number of patients giving a history of pleurisy in the two groups is shown in Table I.

TABLE I
EPISODES OF PLEURISY IN RA AND DJD
Percentage frequency in parenthesis

Diagnosis	Male	Female	Total
RA	39 (28)	68 (18)	107 (21)
DJD	4 (6)	32 (13)	36 (12)

Pleurisy was more common in the rheumatoid group and in the men the difference was significant ($t = 10.5$; $P < 0.01$).

The distribution of the attacks of pleurisy in relation to the onset of arthritic symptoms in the two groups is shown in Fig. 2 (opposite). There was no difference in the incidence of pleurisy occur-

ring more than 5 years before the onset of arthritis. Within 5 years of the onset of arthritis, however, although there was no difference between the two groups in women, attacks of pleurisy were more common in the men with rheumatoid arthritis. 1 per cent. of the men and 0.5 per cent. of the women with rheumatoid arthritis gave a history of pleurisy synchronous with the onset of arthritis. Such a history was not obtained from any patient in the DJD group. After the onset of arthritis, pleurisy was more common in the rheumatoid group in both sexes, the difference being particularly striking in the men. In the rheumatoid group two men and two women had an exacerbation of arthritis coincident with an attack of pleurisy, whereas this did not occur in the DJD group.

Pleural Effusion

Nineteen patients in the rheumatoid group had a pleural effusion either at the time of examination or during the course of their arthritis. Of these, two were due to other disease processes, but in the remainder careful investigation and observation did not reveal any evidence of an alternative cause and they were accepted as cases of rheumatoid pleural effusion, an incidence of 3.3 per cent. (in the men 7.9 per cent and in the women 1.6 per cent.). The average age at onset of the effusions was 52 years in the men and 59 years in the women. In the control group there were two patients with pleural effusion and in one of them there was no convincing evidence of any of the usual causes. The difference in the incidence of unexplained pleural effusion in

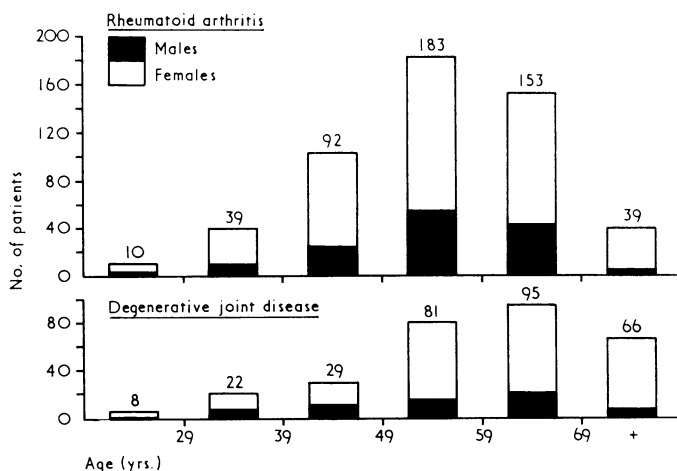


Fig. 1.—Age distribution of patients with rheumatoid arthritis and degenerative joint disease.

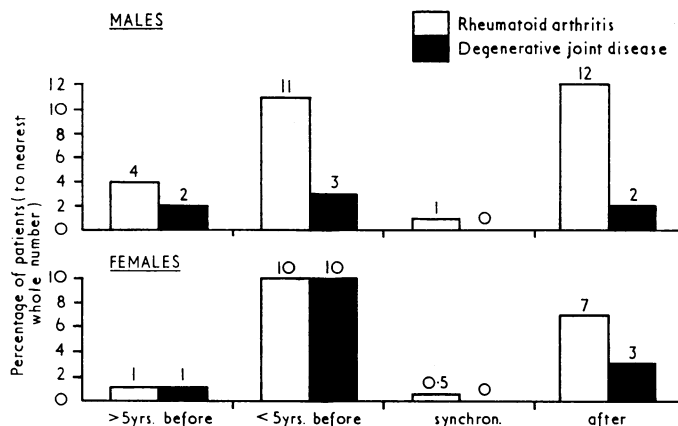


Fig. 2.—Onset of pleurisy related to onset of rheumatoid arthritis and degenerative joint disease.

the rheumatoid group compared with the control group was statistically significant ($\chi^2 = 6.1$; $P < 0.02$).

Thirty-six per cent. of the men with effusions had chronic bronchitis compared with 22 per cent. of the total male rheumatoid population, but this was not a significant difference. Other rheumatoid lesions were known to be present in four cases. One had interstitial lung disease, one Caplan's syndrome, and two others non-pneumoconiotic intra-pulmonary rheumatoid nodules, proven histologically. No other respiratory diseases were more frequent in those with pleural effusion.

There was no significant difference in the age at onset, the extent of the arthritis, or the functional grade in those with and without pleural effusion. The duration of arthritis in those with effusions was slightly longer than in the group as a whole. Subcutaneous nodules were present in eight men and two women in the pleural effusion group, 73 per cent. and 33 per cent. respectively. In the rheumatoid population, 44 per cent. of men and 25 per cent. of women had subcutaneous nodules. None of the women in the pleural effusion group had any other systemic manifestations of rheumatoid disease. Of the eleven men, one had splenomegaly compared with five of the remaining men in the rheumatoid population, one had a myopathy compared with three other proven cases, three had pericarditis, one of them a year after the effusion, and no other example of pericarditis was encountered amongst men in the whole series.

There was no difference in the haemoglobin levels of the men with effusions compared with the male rheumatoid population. In the women a haemoglobin level of less than 12.6 g./100 ml. was present

in 67 per cent. (4 of 6) of the effusion group compared with 44 per cent. of the rheumatoid group. There was no difference in the BSR.

Comparing the results of the SCAT in the pleural effusion group with the rheumatoid population as a whole, no significant difference was apparent. Three patients with pleural effusion had L.E.-cells in the peripheral blood, but there was no other evidence of systemic lupus erythematosus.

A low serum albumin was more common (9 of 14, 64 per cent.) in the effusion group than in the total rheumatoid population (41 of 212, 19 per cent.) This was a significant difference ($\chi^2 = 15.1$; $P = < 0.01$). The serum globulin levels were similar in the two groups.

There was no difference in the severity of the radiographic changes in the hands and feet between the two groups.

Of those with pleural effusion, 24 per cent. were non-smokers compared with 45 per cent. of the total rheumatoid population. Men who smoked more than ten cigarettes daily for more than 20 years were equally common in the pleural effusion group and the total male rheumatoid population (Table II).

TABLE II
SMOKING HABITS AND PLEURAL EFFUSION

Group	No. of Cigarettes Daily (per cent.)	
	11-20	>20
Pleural with Effusion	36	18
Total RA	33	14

Only one in the effusion group had been exposed to noxious dusts (a furnace cleaner in an iron

foun dry), compared with 10 per cent. of the total rheumatoid population.

Temporal Relations

The relationship between the time of development of the effusion and the onset of the arthritis in nineteen patients (seventeen from the series, two specially referred) is shown in Table III. The effusion came first in one man, preceding the arthritis by a period of at least 6 weeks. In four (18 per cent.), the effusion occurred synchronously with the arthritis. The onset was regarded as synchronous if either occurred within 4 weeks of the other. In half of the cases the effusion either preceded or developed within 5 years of the arthritis. The remainder occurred after varying intervals and some developed in very long-standing cases. In four the effusion was accompanied by an exacerbation of arthritis and in one it occurred very shortly after the appearance of subcutaneous nodules.

TABLE III
ONSET OF EFFUSIONS RELATED TO ONSET OF RA—22
EPISODES IN 19 PATIENTS

Sex	Before	Synchronous	Years after			
			>5	6-10	11-20	>20
Male ..	1	2	5	2	4	2
Female ..	0	2	1	1	1	1
Total ..	1	4	6	3	5	3

In one man and one woman there were no symptoms attributable to the pleural effusions, both being detected by routine chest radiography. Either unilateral or bilateral pleuritic pain occurred in ten men and five women. Dyspnoea of varying severity occurred in seven men and three women, three men and three women had cough, and in one man and one woman fever was known to occur. The majority of cases, therefore, had symptoms, pleuritic pain being the commonest.

Characteristics of Effusion

The effusion was bilateral in four, on the left side in six, and on the right side in twelve. The size of the effusions varied from small collections, producing little more than obliteration of the costophrenic angle, to a radiographic opacity involving about half of the hemi-thorax. In most cases there was a moderate amount of fluid involving between one third and one half of the hemi-thorax.

The fluid on aspiration was serious in all but one case with a purulent effusion.

Differential cell counts, done on the pleural fluid in thirteen cases, were predominantly lymphocytic in six, polymorphs predominated in three and in the

remaining four there was a mixed-cell population.

The glucose levels in twelve specimens of pleural fluid from eight patients are shown in Table IV.

TABLE IV
GLUCOSE LEVELS IN PLEURAL FLUID IN EIGHT PATIENTS

Patient No.	mg./100 ml.
1	112, 122, 105
2	0
3	65
4	16
5	80, 85
6	120
7	60
8	40, 60

In one case no glucose was present and in another the level was very low at only 16 mg./100 ml. In a third the initial level was 40 mg./100 ml. but 2½ months later the level had increased to 60 mg./100 ml. In the remainder the initial level was 60 mg. or more. In one case the level was followed serially over a period of 10 months; it was above 100 mg./100 ml. on each occasion.

Protein levels in the pleural fluid were estimated in seven cases; they varied from 3·7 to 5·5 g./100 ml., figures merely indicating that the effusion was an exudate.

In eight patients the SCAT was carried out on both the blood and the pleural fluid (Table V).

TABLE V
SCAT TITRES IN PLEURAL FLUID AND BLOOD IN EIGHT
PATIENTS

Patient No.	Pleural Fluid	Blood
1	512, 512, 256	128
2	negative	negative
3	256	256
4	1024	256
5	negative	negative
9	512	32
6	512	512
7	negative	negative

In three cases the SCAT was negative in both. In three of the remaining five cases there was more than a one-tube difference in the titres, that in the pleural fluid being higher than in the blood.

Pleural Pathology

Punch biopsy of the parietal pleura was performed in eleven cases considered to have a rheumatoid pleural effusion and in one with pleural thickening. The pathological changes found will be reported separately. In four cases the biopsy was regarded as giving positive help in diagnosis.

Treatment

In two of the nineteen cases, oral corticosteroid therapy was given specifically because of the pleural

effusion, and in both resolution occurred shortly afterwards. In one case intra-pleural corticosteroid therapy was given without any obvious benefit. Single or repeated aspirations were employed for treatment purposes in nine cases.

Natural History

In thirteen the effusion resolved within 3 months, but in one of these there was a recurrence 12 months later. In four the effusion was unduly persistent. In one the duration has been over 2 years so far, with only temporary improvement after aspiration. In a second the effusion persisted for 18 months before finally resolving. In one man the effusion persisted for 15 months and during this time he developed severe pleural thickening, which resulted in gross restriction of respiratory movement on that side and associated dyspnoea. Decortication had to be performed, which relieved his symptoms. A fourth patient, a man with empyema, had persistent pleural fluid for 5 years, until he died as a result of renal papillary necrosis.

Three more of the nineteen patients died, the first as a result of cardiac tamponade from pericardial effusion, the second from lobar pneumonia on the opposite side to that of the effusion, and the third from amyloidosis.

Discussion

This investigation has demonstrated a significantly higher incidence of pleural effusion in the rheumatoid population than in the control group, a result at variance with the findings of Aronoff and others (1955) and Stack and Grant (1965). However Aronoff and others (1955) x-rayed their patients only when clinically indicated and used as a control group patients referred to hospital for chest radiography. Stack and Grant (1965) reviewed the chest radiographs of rheumatoid patients taken at their first attendance at a rheumatic clinic and therefore would only detect cases who had a pleural effusion at that time. In the present study account has been taken of pleural effusion occurring at any time during the natural history of the rheumatoid process and cases covering a wide spectrum have been included in the review. Moreover, in none of the previous controlled investigations has a comparison been made with patients in whom there is no known association with respiratory disease.

Although all those with pleural effusions were carefully investigated for an alternative cause, this does not prove that the effusions were due to the rheumatoid process. It has been suggested that

tuberculosis (Miall, 1955), pyogenic infections (Lewis-Faning, 1950), and pulmonary embolism (Cobb, Anderson, and Bauer, 1953) are more common in rheumatoid subjects, and such factors require consideration. In this series, evidence of tuberculous infection was not more frequent in the rheumatoid than in the control group; a history of pneumonia was more common but most of the attacks occurred before the onset of arthritis (Walker, 1967); venous thrombosis was also more common but there was a striking predominance of females affected (9:1) in contrast to the male predominance in pleural effusion. There is therefore no evidence to suggest that any of these conditions accounted for the greater prevalence of pleural effusion, but on the other hand such observations do not establish that they were rheumatoid in nature. However, it is difficult to reach an alternative conclusion when consideration is given to the available evidence. Firstly, this series has demonstrated an excess of otherwise unexplained pleural effusions in rheumatoid subjects compared with a control group, whereas the incidence of "explained" pleural effusions was virtually identical in the two groups (0.4 and 0.3 per cent. respectively). Secondly, rheumatoid granulation tissue in the pleura has been reported by several authors, and in all but one of the cases described pleural effusion has been present. Thirdly, careful study did not reveal an alternative explanation. More patients in the effusion group had L.E.-cells in the peripheral blood, but there was no other evidence of systemic lupus erythematosus and they were considered to be examples of rheumatoid arthritis with L.E.-cells.

One of the objects of this investigation was to evaluate criteria for diagnosis in the examination of rheumatoid pleural effusion. The differential cell count was not helpful. Carr and Mayne (1962) emphasized the very low glucose level in the pleural fluid, but in the present series a level of 40 mg. or less was found in only three of the eight patients in whom the investigation was done. Moreover, in three other patients with levels of 65 mg./100 ml. or more, subsequent histological examination of the pleura undertaken either at autopsy or after decortication did not reveal evidence of an alternative pathological process. There was no correlation between low pleural glucose levels and the histological findings in the pleura at biopsy, and serial readings in three patients did not suggest that they were dependent on the duration of the effusion. The glucose levels in this series were not examined in the fasting state, since the figures of Carr and Mayne (1962) did not indicate that this influenced the results in those with very low levels.

Rodnan, Eisenbeis, and Creighton (1962) showed that occasionally tests for rheumatoid factor were positive in joint fluid and negative in the blood. The titre of rheumatoid factor in the pleural effusion and serum was therefore compared in eight patients. In three with a positive SCAT in the blood, a higher titre was present in the pleural fluid. It is possible that such a finding might be of diagnostic value but more cases require to be studied, including a group of rheumatoid patients with effusion due to other causes.

The findings on pleural biopsy will be discussed elsewhere. This technique yielded information of positive value more frequently in this series than has been suggested by previous investigators. However in over half the cases only non-specific changes were present.

These studies indicate that investigation of the pleural fluid and pleural biopsy does not permit a positive diagnosis of rheumatoid pleural effusion in more than a proportion of cases. A very low pleural glucose level is certainly helpful but normal levels are found in some cases.

In many cases, therefore, the diagnosis will largely depend on exclusion of other causes and on suggestive clinical features such as the pleural effusion accompanying the onset of the arthritis or occurring with an exacerbation of arthritis. About one-fifth are bilateral and in a similar proportion intrapulmonary rheumatoid lesions are present.

In this series resolution of the effusions occurred within 3 months in thirteen of the nineteen cases compared with seven of thirteen described by Carr and Mayne (1962). The effusions were unduly persistent in four patients. Hitherto, little stress has been laid on possible complications of rheumatoid effusions, apart from residual pleural thickening which has usually been minimal. However, in two cases, major pleural complications ensued and these were the only examples in the series in which lesions regarded as intra-pulmonary rheumatoid nodules were present. In one case pleural thickening was so extensive that decortication was required to relieve dyspnoea. In the second there was an empyema which persisted for 5 years until his death and there were good grounds at autopsy for believing that the initial pleural pathology had been rheumatoid in nature. This case is reminiscent of that described by Cudkowicz, Madoff, and Abelman (1961). The pleural space may well have become infected for reasons similar to those accounting for pyarthrosis in rheumatoid arthritis (Kellgren, Ball, Fairbrother,

and Barnes, 1958) and distinct from the pyopneumothorax which may result from rupture of subpleural rheumatoid nodules (Hindle and Yates, 1965; Davies, 1966).

The one patient who received intra-pleural corticosteroids did not benefit. In the two patients who received oral corticosteroids the pleural effusions resolved quite rapidly, but it is uncertain whether this was the result of treatment.

The reason for the striking male predominance in this and previously-reported series remains obscure. It is of interest that more men with pleural effusion in this series had chronic bronchitis than in the rheumatoid population as a whole, and noteworthy that effusions occurred in as many as 12.5 per cent. of those with the classical x-ray appearance of Caplan's syndrome (Caplan and others, 1962). These observations raise the possibility that environmental factors may play a part, but if this is so it is surprising that there was no correlation between prolonged smoking and pleural effusion in this series.

In keeping with the findings of others, the effusion tended to develop in the sixth decade. As might be anticipated, subcutaneous nodules were more common in those with pleural effusion than in the rheumatoid population, particularly in men. In addition, the only three examples of pericarditis in men encountered in the whole series occurred in patients with pleural effusion. This suggests a correlation between involvement of the pleura and pericardium in rheumatoid arthritis and two recent reports are in keeping with this (Beck and Hoffbrand, 1966; Berger and Seckler, 1966). There was, however, no evidence of a correlation with any other systemic lesions. The severity of the arthritis as assessed clinically and radiologically did not differ in those with pleural effusion when compared with those without, and the haematological and serological findings were also similar. A low serum albumin was more frequent in the patients with pleural effusion than in the rheumatoid population, and analysis revealed that there was a correlation between a low serum albumin and the presence of subcutaneous nodules.

The greater frequency of a history of pleurisy in men with rheumatoid arthritis compared with the control group and the temporal relationship to the arthritis was of interest in view of the comparable findings in those with pleural effusion. Such retrospective information suggests, although it does not establish that dry pleurisy occurs as a systemic manifestation of rheumatoid arthritis.

Summary and Conclusions

516 patients with definite or classical rheumatoid arthritis have been studied clinically, radiographically, and serologically in order to evaluate the pleural manifestations more fully. 301 patients with degenerative joint disease were simultaneously investigated to serve as a control group. Pleurisy was more common in the rheumatoid group, particularly in men. There was strong evidence to support the view that pleural effusion may occur as a manifestation of rheumatoid disease. Unexplained effusion was significantly more frequent in the rheumatoid group, especially in men, and occurred particularly in cases of nodular rheumatoid arthritis. Intra-pulmonary lesions of rheumatoid origin were often present and pericarditis seemed to be an associated feature in men.

Methods for establishing an early definitive diagnosis of rheumatoid pleuritis were assessed.

Very low glucose levels in the pleural fluid were less frequently present than previously suggested, but pleural biopsy was helpful in 42 per cent. In some patients the sheep cell agglutination titre was higher in the pleural fluid than in the blood. The effusions usually appeared to be benign, but were unduly persistent in four patients and resulted in major pleural complications in two. There was no evidence that smoking or exposure to noxious dusts were aetiological in the pleural effusions in these patients.

Although clearly all cases must be thoroughly investigated for an alternative aetiology, our experience indicates that pleural effusion developing in patients with rheumatoid arthritis seen at a rheumatism clinic is most likely to be due to the rheumatoid disease.

We are grateful to Dr. O. H. J. Maxwell Telling and Dr. M. R. Jeffrey for allowing us to study patients under their care.

REFERENCES

- Abrams, L. D. (1958). *Lancet*, **1**, 30 (A pleural-biopsy punch).
- Aronoff, A., Bywaters, E. G. L., and Fearnley, G. R. (1955). *Brit. med. J.*, **2**, 228 (Lung lesions in rheumatoid arthritis).
- Baggenstoss, A. H., and Rosenberg, E. F. (1943). *Arch. Path.*, **35**, 503 (Visceral lesions associated with chronic infectious (rheumatoid) arthritis).
- Beck, E. R., and Hoffbrand, B. I. (1966). *Ann. rheum. Dis.*, **25**, 459 (Acute lung changes in rheumatoid arthritis).
- Bennett, G. A., Zeller, J. W., and Bauer, W. (1940). *Arch. Path.*, **30**, 70 (Subcutaneous nodules of rheumatoid arthritis and rheumatic fever).
- Berger, H. W., and Seckler, S. G. (1966). *Ann. intern. Med.*, **64**, 1291 (Pleural and pericardial effusions in rheumatoid disease).
- Caplan, A., Payne, R. B., and Withey, J. L. (1962). *Thorax*, **17**, 205 (A broader concept of Caplan's syndrome related to rheumatoid factors).
- Carr, D. T., and Mayne, J. G. (1962). *Amer. Rev. resp. Dis.*, **85**, 345 (Pleurisy with effusion in rheumatoid arthritis, with reference to the low concentration of glucose in pleural fluid).
- Castleman, B., and McNeely, B. U. (1965). *New Engl. J. Med.*, **272**, 1069 (Case records of the Massachusetts General Hospital. Weekly clinico-pathological exercises. Case 23—1965).
- Cobb, S., Anderson, F., and Bauer, W. (1953). *Ann. rheum. Dis.*, **12**, 323 (Length of life and cause of death in rheumatoid arthritis) (Abstract).
- Cruickshank, B. (1957). *Proc. roy. Soc. Med.*, **50**, 462 (Rheumatoid arthritis and rheumatoid disease).
- Cudkowicz, L., Madoff, I. M., and Abelmann, W. H. (1961). *Brit. J. Dis. Chest*, **55**, 35 (Rheumatoid lung disease. A case report which includes respiratory function studies and a lung biopsy).
- Davies, D. (1966). *Thorax*, **21**, 230 (Pyopneumothorax in rheumatoid lung disease).
- Ellman, P., Cudkowicz, L., and Elwood, J. S., (1954). *J. clin. Path.*, **7**, 239 (Widespread serous membrane involvement by rheumatoid nodules).
- Fingerman, D. L., and Andrus, F. C. (1943). *Ann. rheum. Dis.*, **3**, 168 (Visceral lesions associated with rheumatoid arthritis.)
- Gruenwald, P. (1948). *Arch. Path.*, **46**, 59 (Visceral lesions in a case of rheumatoid arthritis).
- Heller, P., Kellow, W. F., and Chomet, B. (1956). *New Engl. J. Med.*, **255**, 684 (Needle biopsy of the parietal pleura).
- Hindle, W., and Yates, D. A. H. (1965). *Ann. rheum. Dis.*, **24**, 57 (Pyopneumothorax complicating rheumatoid lung disease).
- Horler, A. R., and Thompson, M. (1959). *Ann. intern. Med.*, **51**, 1179 (The pleural and pulmonary complications of rheumatoid arthritis).
- Kellgren, J. H., Ball, J., Fairbrother, R. W., and Barnes, K. L. (1958). *Brit. med. J.*, **1**, 1193 (Suppurative arthritis complicating rheumatoid arthritis).
- Koepke, J. A. (1960). *Wis. med. J.*, **59**, 739 (Rheumatoid pleuritis: report of a case).

- Lewis-Faning, E. (1950). *Ann. rheum. Dis.*, **9**, Suppl. "Report of an inquiry into the aetiological factors associated with rheumatoid arthritis".
- Locke, G. B. (1963). *Clin. Radiol.*, **14**, 43 (Rheumatoid lung).
- Mattingly, S. (1964). *Ann. phys. Med.*, **7**, 185 (The lungs and rheumatoid arthritis).
- Miall, W. E. (1955). *Ann. rheum. Dis.*, **14**, 150 (Rheumatoid arthritis in males. An epidemiological study of a Welsh mining community).
- Poppius, H., and Tani, P. (1964). *Acta tuberc. pneumol. scand.*, **44**, 310 (Non-tuberculous pleurisy).
- Raven, R. W., Weber, F. Parkes, and Price, L. W. (1948). *Ann. rheum. Dis.*, **7**, 63 (The necrobiotic nodules of rheumatoid arthritis).
- Rodnan, G. P., Eisenbeis, C. H., and Creighton, A. S. (1962). *Arthr. and Rheum.*, **5**, 316 (On the occurrence of rheumatoid factor in synovial fluid).
- Ropes, M. W., Bennett, G. A., Cobb, S., Jacox, R., and Jessar, R. A. (1959). *Arthr. and Rheum.*, **2**, 16 (1958 Revision of diagnostic criteria for rheumatoid arthritis).
- Schools, G. S., and Davey, W. N. (1960). *Univ. Mich. med. Bull.*, **26**, 1 (Needle biopsy of the parietal pleura).
- and Mikkelsen, W. M. (1962). *Arthr. and Rheum.*, **5**, 369 (Rheumatoid pleuritis).
- Short, C. L., Bauer, W., and Reynolds, W. E. (1957). "Rheumatoid Arthritis". Harvard University Press, Cambridge, Mass.
- Sinclair, R. J. G., and Cruickshank, B. (1956). *Quart. J. Med.*, **25**, 313 (A clinical and pathological study of sixteen cases of rheumatoid arthritis with extensive visceral involvement.)
- Stack, B. H. R., and Grant, I. W. B. (1965). *Brit. J. Dis. Chest*, **59**, 202 (Rheumatoid interstitial lung disease).
- Talbot, J. A., and Calkins, E. (1964). *J. Amer. med. Ass.*, **189**, 911 (Pulmonary involvement in rheumatoid arthritis).
- Walker, W. C. (1966). "The Lungs in Rheumatoid Arthritis". M. D. Thesis, Edinburgh.
- (1967). *Quart. J. Med.*, **36**, 239 (Pulmonary infections and rheumatoid arthritis).
- Ward, R. (1961). *Lancet*, **2**, 1336 (Pleural effusion and rheumatoid disease).

La pleurite rhumatismale

On étudia 516 cas d'arthrite rhumatismale classique ou "définie" du point de vue clinique, radiologique et sérologique pour évaluer d'une manière plus détaillée les manifestations pleurales. En même temps on étudia 301 cas d'affection articulaire dégénérative en guise de témoin. L'atteinte pleurale était plus fréquente chez les malades atteints d'arthrite rhumatismale, en particulier chez les hommes. Il y eut de sérieux indices permettant de penser que l'épanchement pleural pouvait se produire en tant que manifestation de la maladie rhumatismale. Un épanchement inexplicé fut significativement plus fréquent dans le groupe ayant une arthrite rhumatismale, particulièrement chez les hommes, surtout en cas d'arthrite rhumatismale nodulaire. Des lésions pulmonaires d'origine rhumatismale furent souvent trouvées et une péricardite sembla être un caractère associé chez les hommes.

On évalua des méthodes pour établir un diagnostic précoce et certain de pleurite rhumatismale. On trouva moins souvent qu'on ne le pensait des taux très bas de glucose dans le liquide pleural, mais dans 42 pour cent des cas la biopsie pleurale fut utile. Chez quelques malades le taux de la réaction de Waaler-Rose était plus élevé dans le liquide pleural que dans le sang. Les épanchements paraissaient généralement bénins, mais chez quatre malades ils persistèrent assez longtemps et chez deux d'entre eux ils entraînaient des complications pleurales majeures. On ne trouva pas d'indices permettant d'impliquer la responsabilité du tabac ou de poussières nocives comme étiologie des épanchements pleuraux.

Bien que, naturellement, on doive explorer à fond tous ces malades en vue d'une autre étiologie, notre expérience prouve que l'épanchement pleural survenant chez les malades ayant une arthrite rhumatismale vus dans un service de rhumatologie est vraisemblablement dû à la maladie rhumatismale.

La pleuritis reumatoide

Se estudiaron 516 casos de artritis reumatoide clásica o "definida" clínica, radiológica y serológicamente para valorar de una manera más detallada las manifestaciones pleurales. Al mismo tiempo se estudiaron 301 casos de afección articular degenerativa, que sirvieron de testigos. La lesión pleural fue más frecuente en enfermos con artritis reumatoide, en particular del sexo masculino. Existieron datos importantes para indicar que el derrame pleural puede producirse en función de la enfermedad reumatoide. Un derrame sin explicación fue significativamente más frecuente en el grupo con artritis reumatoide, especialmente en hombres y particularmente en casos de artritis reumatoide nodular. Se encontraban a menudo lesiones pulmonares de origen reumatoide y una pericarditis parecía ser un rasgo asociado en los hombres.

Se valoraron los métodos para establecer un diagnóstico pronto y cierto de pleuritis reumatoide. Muy bajas cifras de glucosa en el líquido pleural fueron encontradas con una frecuencia menor que la indicada anteriormente, pero en un 42 por ciento de los casos la biopsia pleural fue útil. En algunos enfermos las cifras de la reacción de Waaler-Rose fueron más altas en el líquido pleural que en el suero. Los derrames parecieron generalmente benignos, pero en cuatro enfermos persistieron bastante tiempo y en dos de ellos llevaron a mayores complicaciones pleurales. No se encontraron indicios implicando el tabaco o el polvo nocivo en la etiología de los derrames pleurales en estos enfermos.

Es claro que todos estos casos merecen una investigación completa en busca de otra etiología, pero nuestra experiencia indica que un derrame pleural ocurriendo en un enfermo con artritis reumatoide y visto en un servicio de reumatología se debe muy probablemente a la enfermedad reumatoide.