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AN EPIDEMIOLOGICAL STUDY OF RHEUMATOID ARTHRITIS ASSOCIATED WITH CHARACTERISTIC CHEST X-RAY APPEARANCES IN COAL-WORKERS

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[WITH SPECIAL PLATE]

A new syndrome has been described in coal-workers (Caplan, 1953) in which rheumatoid arthritis is associated with nodular fibrosis of the lung which is radiologically similar to, but distinguishable from, the massive fibrosis appearing in complicated pneumoconiosis. A syndrome which describes an association between two pathological conditions affecting different parts of the body is usually founded on a clinical impression but is rarely studied by epidemiological methods. Such methods may determine whether the association is more than a chance occurrence of the two conditions in the same subject. This paper describes an epidemiological study of rheumatoid arthritis in a community of coal-miners in South Wales to investigate this new syndrome.

Characteristic Chest X-ray Appearances

The radiological features of progressive massive fibrosis (P.M.F.) in coal-workers' pneumoconiosis have been fully described (Fletcher *et al.*, 1949). At the beginning, ill-defined opacities develop upon a background of category 2 or 3 simple pneumoconiosis; these gradually enlarge over a period of several years to produce irregular shadows which usually become more clearly defined; ultimately the masses may occupy most of a lobe and may be associated with distortion of surrounding structures and accompanied by emphysema. An example of the early stages of the development of such a shadow is shown in Fig. 1 (see Special Plate), and a typical example of advanced massive fibrosis is shown in Fig. 2.

The type of chest lesions associated with rheumatoid arthritis in miners is strikingly different in some respects. There is a much more rapid development of numerous discrete rounded opacities scattered diffusely throughout

both lung fields. These lesions seem to appear in crops, the lesions in each crop being similar in size and rate of development. Over a period of a few months they attain a diameter of 1-2 cm., occasionally as large as 5 cm., and thereafter as a general rule they change relatively little over a period of years; they may gradually enlarge, and cavitation may occur in them; occasionally they contract to form stellate scars or they may calcify. Characteristically these lesions develop upon a background of less simple pneumoconiosis than does typical P.M.F.: whereas P.M.F. rarely, if ever, starts when there is less than category 2 simple pneumoconiosis, these "rheumatoid" lesions are often seen with a background of only category 1. Fig. 3 illustrates a typical example of the "rheumatoid" type of chest x-ray picture in a coal-miner aged 40 with a history of rheumatoid arthritis for the past eleven years. The x-ray appearances described above have been noted only in men exposed to a dust hazard and have no similarity to the interstitial pneumonitis occurring in cases of rheumatoid arthritis described by Ellman and Ball (1948).

Planning of the Investigation

The chest x-ray films used in this study were all of miners or ex-miners examined in the Rhondda Fach, a South Wales mining valley where over 95% of the mining and ex-mining population had been x-rayed (Cochrane *et al.*, 1952). In 896 cases these films had previously been classified as showing either P.M.F. (788) or clinically significant tuberculosis (108): from this group Caplan, as the first observer of the syndrome, selected all films showing the radiological appearances which he thought would be associated with rheumatoid arthritis. Twenty such films were selected. These 20 cases and a randomly selected group of 60 controls,

stratified by age and chosen from the miners whose films had been read and discarded as showing none of the characteristic appearances, were visited at their homes by a physician who was not aware of the x-ray findings. When visiting these men, a standard questionnaire was used and all joints of the arms and legs were examined in cases in which the history suggested arthritis.

To check the reproducibility of reading the chest films, all 896 films were re-read by the same observer, and to determine the inter-observer error of diagnosis of rheumatoid arthritis in field-survey work another physician visited all selected cases and any controls who had shown some evidence of rheumatoid arthritis. This small study of intra- and inter-observer error is described in the Appendix.

All men considered by either physician to have rheumatoid arthritis, and the 20 cases selected because of their characteristic chest x-ray films, were more fully investigated later. A positive diagnosis of rheumatoid arthritis was made only when at least two of the following criteria were satisfied: (1) A typical history of symmetrical polyarthritis with or without residual deformity; (2) characteristic changes of rheumatoid arthritis in the x-ray films of hands or feet; and (3) a positive differential agglutination test for rheumatoid arthritis (Rose *et al.*, 1948).

In this investigation we were particularly keen to miss no cases of rheumatoid arthritis, and as a consequence several of the men considered to be doubtfully positive when seen at their homes when investigated further either failed to fulfil the criteria or were proved to be suffering from some other arthritic condition.

Results

Prevalence of Rheumatoid Arthritis

The proportion of cases of rheumatoid arthritis found among the control group of cases of P.M.F. or tuberculosis (3%) was greater than that reported in the normal population. In the Sickness Survey (Stocks, 1949) a prevalence of 0.419% among all males and females over the age of 16 was found, and in a recent investigation of rheumatism in coal-miners in Lancashire, Lawrence and Aitken-Swan (1952) reported less than 1% of cases in the same age groups, suggesting that the prevalence of this disease among miners is no higher than in the general population, but it should be noted that massive fibrosis itself is probably less common in Lancashire than in South Wales (unpublished data, Pneumoconiosis Research Unit).

As a higher prevalence of rheumatoid arthritis was found among cases of massive fibrosis than had been expected, it was clearly necessary to determine its prevalence in miners with and without simple pneumoconiosis, and two further groups were selected in the same way as the group with P.M.F. Several doubtfully positive cases in these other x-ray groups were also fully investigated, but with negative results. Table I shows the prevalence of rheumatoid arthritis in the four x-ray groups visited.

The prevalence is very much higher in the group with characteristic chest x-ray films than in any of the other three groups. Indeed, in these cases the diagnosis of rheumatoid arthritis could have been made from the chest x-ray films alone with more than a 50% chance of being correct. The prevalence of this type of arthritis also seems to be greater in cases of P.M.F. than in miners with simple pneumoconiosis or with chest x-ray films which show no signs of pneumoconiosis.

Table II is a summary of the clinical and x-ray findings of the 20 cases with characteristic x-ray appearances and of the two cases in the P.M.F. group, and shows those who were proved to be suffering from rheumatoid arthritis. It was found that there was no close correlation between the more

typical "rheumatoid" chest x-ray film and the activity, severity, and time of onset of arthritis, or between the chest x-ray films and the radiological evidence of rheumatoid arthritis in the hands and feet. The analysis by age, dust exposure, and somatotype does, however, reveal some points of interest.

TABLE I.—Prevalence of Rheumatoid Arthritis Among Miners and Ex-miners, Analysed by Chest X-ray Appearances

| Clinical Findings | Chest X-ray Groups | | | |
|-----------------------------|-------------------------------------|---|-----------------------|--------|
| | Characteristic "Rheumatoid" Lesions | Progressive Massive Fibrosis or Clinically Significant Tuberculosis | Simple Pneumoconiosis | Normal |
| Proved rheumatoid arthritis | 11 (55%) | 2 (3%) | — | — |
| No rheumatoid arthritis | 9 (45%) | 57 (97%) | 92 | 112 |
| Total | 20 (100%) | 59* (100%) | 92 | 112 |

The difference between those with characteristic rheumatoid chest x-ray films and the control group of P.M.F. is highly significant. The difference in incidence between the P.M.F. group and the simple pneumoconiosis and normal group is exactly at the 5% level of significance.

* One patient in this group had died in the interval between the x-ray survey and this investigation.

(a) *Age*.—The mean age of men with typical "rheumatoid" chest x-ray films and with arthritis was 48.9 years, compared with 41.5 years for those with similar chest films but without arthritis. This difference is not statistically significant ($0.10 < P < 0.20$). The "rheumatoid" lung lesions may precede the onset of arthritis by several years, as is discussed later, and it is possible that a number of men with typical x-ray films and without arthritis may develop it at a later date. The average age of onset of arthritic symptoms among the proved cases was 41.7 years.

(b) *Total Dust Exposure*.—The total duration of dust exposure has a mean of 22.6 years in the proved cases, as opposed to 16.3 years in those without arthritis. This difference is statistically significant ($0.01 < P < 0.02$). Age and total length of exposure to dust are of course correlated, and by making allowance for this fact it should be possible to throw some light on which is more closely related to the arthritis. The mean age of the proved rheumatoid arthritis cases can be compared with that of those without arthritis when the length of dust exposure has been allowed for, and, similarly, the duration of dust exposure standardized for age can be compared in the two groups. When this is done there is no significant difference between the two groups either in age ($0.60 < P < 0.70$) or in dust exposure ($0.10 < P < 0.20$), but whereas length of dust exposure, which previously was significant, now becomes just less than significant, all suggestion of a difference in age has vanished. Thus the dust exposure might be a factor differentiating the two groups, and age probably only so far as it is related to dust exposure. This difference, however, is not established with any degree of confidence.

(c) *Stone Dust Exposure*.—When analysed according to years of exposure to stone dust some interesting results are forthcoming. Taking the group with characteristic "rheumatoid" x-ray films and the control group of P.M.F. cases, we find there is no statistically significant difference between their exposure to stone dust, though it is possible that such a difference is present but not revealed in these relatively small groups. In the group with typical "rheumatoid" x-ray films, however, there are nine men who have had exposure to stone dust, and seven of these occur in the group of eleven who have proved rheumatoid arthritis. Two occur in the group without arthritis. The probability of this occurring fortuitously is 8%. Of these nine men, five have had a stone dust exposure of three years or more, and all these have rheumatoid arthritis. The probability of this occurring fortuitously is only 3%. The significance, if any, of this curious finding will be determined only when further cases of this syndrome are investigated. It is of interest to note that Collis and Yule (1933),

TABLE II.—Summary of Clinical Findings and Industrial Histories of 20 Cases with "Rheumatoid" Chest X-ray Films and 2 Cases with P.M.F.

| No. | Age (Years) | History of Rheumatoid Arthritis | Differential Agglutination Test (Rose) | X-ray Diagnosis of Rheumatoid Arthritis | | | | Lowest E.S.R. (Westergren) mm. Fall in 1 Hour | Middlebrook-Dubos Agglutination Test (1:8 positive) | Somatotype Index | Age of Onset of Arthritis (Years) | Years of Dust Exposure Before X-ray | | | |
|--|-------------|---------------------------------|--|---|-------------|------------|------------|---|---|------------------|-----------------------------------|-------------------------------------|----------------|------|----------------|
| | | | | Hands | | Feet | | | | | | Stone | Stone and Coal | Coal | Total |
| | | | | Observer A* | Observer B* | Observer A | Observer B | | | | | | | | |
| <i>Cases with Proved Rheumatoid Arthritis with "Rheumatoid" Chest X-ray Films</i> | | | | | | | | | | | | | | | |
| 1 | 72 | + | + | 3 | 3 | 3 | 3 | 40 | — | 107.8 | 47 | — | — | 34 | 34 |
| 2 | 60 | + | + | 2 | 2 | 2 | 2 | 36 | + | 114.4 | 58 | 8 | — | 26 | 34 |
| 3 | 58 | + | — | 1 | 2 | 2 | 2 | 39 | — | 99.4 | 48 | — | — | 22 | 22 |
| 4 | 50 | + | — | 1 | 1 | 0 | 0 | 30 | — | 111.5 | 45 | 3 | — | 19 | 22 |
| 5 | 49 | + | + | 1 | 0 | 0 | 0 | 6 | + | 105.3 | 47 | 18 | — | 9 | 27 |
| 6 | 46 | + | + | 0 | 1 | 0 | 1 | 20 | N.R. | 108.9 | 44 | — | 1 | 25 | 26 |
| 7 | 43 | + | + | 1 | 1 | 2 | 2 | 5 | + | 108.6 | 37 | — | — | 11 | 14 |
| 8 | 41 | + | + | 0 | 0 | 0 | 0 | 16 | + | 104.3 | 39 | 3 | — | 17 | 19 |
| 9 | 40 | + | + | 0 | 1 | 0 | 0 | 13 | + | 100.5 | 38 | — | 2 | 19 | 19 |
| 10 | 40 | + | + | 1 | 1 | 2 | 2 | 21 | + | 113.7 | 29 | — | — | 15 | 15 |
| 11 | 39 | + | + | 0 | 1 | 2 | 2 | 14 | — | 95.3 | 27 | — | 12 | 5 | 17 |
| | Mean 48.9 | | 72.7% positive | | | | | Mean 21.8 | 50% positive | Mean 106.3 | Mean 41.7 | | | | Mean 22.6 yrs. |
| <i>Cases without Proved Rheumatoid Arthritis with "Rheumatoid" Chest X-ray Films</i> | | | | | | | | | | | | | | | |
| 12 | 50 | — | — | 0 | 0 | 0 | 0 | 30 | — | 99.3 | — | — | — | 23 | 23 |
| 13 | 48 | +(?) | — | 0 | 0 | 0 | 0 | 23 | + | 98.7 | 47(?) | — | — | 15 | 15 |
| 14 | 45 | — | — | 0 | 0 | 0 | 0 | 4 | — | 105.5 | — | — | — | 20 | 20 |
| 15 | 44 | — | — | 0 | 0 | 0 | 0 | 7 | + | 111.7 | — | — | — | 20 | 20 |
| 16 | 40 | — | — | 0 | 0 | 0 | 0 | 1 | — | 105.6 | — | — | — | 14 | 14 |
| 17 | 39 | — | — | 0 | 0 | 0 | 0 | 6 | — | 99.4 | — | — | 2 | 12 | 13 |
| 18 | 38 | — | — | 0 | 0 | 0 | 0 | 5 | + | 105.3 | — | 1 | — | 19 | 20 |
| 19 | 35 | — | — | 0 | 1 | 0 | 0 | 56 | — | 100.0 | — | — | — | 10 | 10 |
| 20 | 35 | — | N.R. | 0 | 0 | 0 | 0 | N.R. | N.R. | 102.4 | — | — | — | 12 | 12 |
| | Mean 41.5 | | | | | | | Mean 16.5 | 37.5% positive | Mean 103.1 | | | | | Mean 16.3 yrs. |
| <i>Cases with Proved Rheumatoid Arthritis with P.M.F. Chest X-ray Films</i> | | | | | | | | | | | | | | | |
| 1 | 41 | + | + | 2 | 2 | 2 | 2 | 85 | — | 93.8 | 30 | — | 4 | 8 | 12 |
| 2 | 49 | + | + | 1 | 1 | 2 | 2 | 5 | — | 94.0 | 48 | — | — | 26 | 26 |

The readings of the x-ray films of the hands and feet are scored as follows: 0=normal or doubtful changes of rheumatoid arthritis; 1=minimal changes of rheumatoid arthritis; 2=moderate changes of rheumatoid arthritis; 3=marked changes of rheumatoid arthritis. N.R.=no record.
* Observers A and B, see Appendix.

who analysed the Registrar-General's Decennial Supplement for 1921-3, found a remarkably increased mortality from a wide range of diseases in men exposed to a silica risk. This included a fourfold increase in the mortality rate from chronic rheumatic conditions.

(d) *Somatotype*.—It is often said that rheumatoid arthritis affects people of asthenic build. In this series anthropometric measurements were made, using the body index suggested by Rees and Eysenck (1945), which is

$$\frac{100 \times \text{stature in cm.}}{6 \times \text{mean chest diameter in cm.}}$$

Analysis shows that the group with typical "rheumatoid" chest x-ray films but without arthritis are similar in body build to the control cases with P.M.F., but those with arthritis have a higher mean "body index"—that is, they are of a more asthenic type. This difference may be a sampling effect, but if it is justifiable to assume that all the cases with typical "rheumatoid" chest films have some factor predisposing to the development of arthritis (see under Discussion) then this predisposing factor is not related to somatotype, and the difference in body build is probably secondary to the rheumatoid arthritis.

Clinical Investigations

Clinical examination, the x-ray appearances of peripheral joints, the erythrocyte sedimentation rate, and the differential agglutination test all indicated that the type of arthritis seen in these miners differs in no way from rheumatoid arthritis in other people. Of the 12 men who gave histories suggestive of rheumatoid arthritis, positive differential agglutination tests were obtained in eight. No positive result was obtained in any case without a history of polyarthritis. These findings agree with those found in other series of rheumatoid arthritis in males, and would not be expected in other arthritic conditions, with the possible exception of disseminated lupus erythematosus (Ball, 1952).

The Middlebrook-Dubos agglutination test was also carried out. This test, which is based on the agglutination by tuberculous patients' serum of sheep's red cells sensitized to tuberculin, seems to be of limited value except in research into the pathogenesis of tuberculosis, the false positives and false negatives being so numerous that the significance of the result in any individual case cannot be determined. In this series we found 8 positive results (agglutination to a titre of 1:8) in 18 sera tested (44%). In a series of 133 cases of early progressive massive fibrosis, agglutination to a titre of 1:8 occurred in only four cases (3%). This suggests that the lesions in the lungs are a form of tuberculosis, and there is other evidence which supports this, but both the Middlebrook-Dubos and the Rose agglutination test are based on the agglutination of sensitized sheep's cells by human serum, and may be interrelated.

Sputa or laryngeal swabs were cultured for tubercle bacilli in all cases, but there was only one positive (No. 8), and in his case morphologically atypical tubercle bacilli were isolated, which, however, produced tuberculosis on guinea-pig inoculation.

One man of 72 years (Case 1) has died since this investigation was made. His arthritis dated from 1926 and caused him to leave coal-mining in 1928 after having worked 25 years underground, chiefly as a collier. The significant clinical findings are shown in Table II, and x-ray films of his chest and hands are shown in Figs. 4 and 5. A summary of the post-mortem examination conducted by Dr. D. Rivers is given below.

Post-mortem Findings in Case 1

External Appearances.—The body was that of a well-nourished elderly male with numerous coal-pigmented scars present on the hands and forearms and pitting oedema of the lower limbs. Characteristic periarticular swellings and gross deformities of rheumatoid arthritis were present in the elbows, wrists, knees, and ankles. There was subluxation and severe ulnar deviation at all metacarpo-phalangeal joints

of the left hand, with spindling of the proximal interphalangeal joints; the right hand showed much less deformity, but changes typical of severe rheumatoid arthritis. The small toes of both feet had been amputated and there was pronounced lateral deviation of both large toes. No rheumatoid nodules were present.

Internal Appearances.—Pleural adhesions were present in both sides of the chest. Both lungs were enlarged and there was some bullous emphysema at the apices and along the free margins. The cut surface of the right lung showed a group of circumscribed fibrous nodules in the apex of the upper lobe, some of which were joined by narrow bands of black fibrous tissue. These fibrous lesions were 1–2 cm. in diameter, were almost entirely black in colour, but had a whorled appearance formed by thin concentric laminae of yellowish-white fibrous tissue. A number of similar lesions were scattered throughout the rest of the lung, and in addition there were numerous small dust-pigmented fibrous nodules varying from 1 to 2 mm. in diameter. Most of both the larger and the smaller lesions showed central softening and necrosis, but there was no definite caseation or other evidence of tuberculosis. The left lung showed essentially similar appearances, and in the lower part of the upper lobe there was also a large mass of black dust-pigmented fibrosis measuring 5 cm. across its greatest diameter. Central softening and necrosis were present in this mass, but again there was no definite evidence of tuberculosis. Both lungs showed a moderate number of soft-coal-dust foci uniformly distributed throughout their parenchyma, and both were congested and oedematous. The mediastinal lymph nodes were enlarged, black, and firm. There was some cardiac enlargement with right ventricular hypertrophy and atheroma in the main pulmonary arteries and their smaller branches. The liver, spleen, and kidneys were very congested. All other organs appeared normal.

Microscopical Appearances.—The histological features of the predominant type of lung nodule were essentially similar. Each had a large amorphous eosinophilic centre with numerous cholesterol clefts, and in some of them patchy calcification was present. This zone was surrounded by dense collagenous fibrosis, the inner layers of which were hyalinized, and the ghost structure of collagen could be identified towards the periphery of the central zone. In some lesions this central zone consisted of completely hyalinized collagen. A large amount of coal dust was distributed between the fibres of collagen and throughout the centres of the lesions.

Sections of the large mass in the left lung showed it to consist of largely hyalinized dense collagen containing areas of eosinophilic necrosis and cholesterol clefts and heavily impregnated with coal dust. No definite histological evidence of tuberculosis was identified in sections of the nodules or the mass, and no acid-fast bacilli could be found in Ziehl-Neelsen preparations.

Comment.—The cause of death was considered to be congestive cardiac failure due to coal-workers' pneumoconiosis. Though the macroscopical and microscopical appearances of the individual lung lesions are often seen in cases of P.M.F., and the rounded nodules are similar to those described by Gough (1947) as infective nodules, it is unusual to find them so large, so sharply circumscribed, or so numerous and widely distributed as in this case. The pathological evidence supports the contention that the lesions are unlikely to differ in aetiology from that of P.M.F., but material from a case in the active phase is essential to establish this more firmly. It is probable that the lesions described here were active about the time of onset of this man's arthritis 27 years ago, and the appearances are now those of a completely healed infection.

Discussion

This investigation has confirmed the observation that a particular type of radiological appearance in the chest x-ray films of coal-miners is closely associated with the presence of rheumatoid arthritis.

P.M.F. in coal-workers is generally regarded as tuberculosis modified by the presence of coal dust (Gough, 1947; Fletcher, 1948). How do these typical "rheumatoid" lung lesions differ from ordinary P.M.F.? The pathology of this syndrome has been studied at necropsy in only one radiologically characteristic case, but necropsies have recently been performed on seven cases of rheumatoid arthritis in coal-workers with chest films similar to, but less typical than, those described in this series, and evidence of active tuberculosis was found in five of them. The only two men with "rheumatoid" lung lesions who have had a positive sputum culture in life were noted to have morphologically atypical bacilli which, however, produced tuberculosis in guinea-pigs on inoculation.

In spite of the two types of lung lesions tending to merge into one another, we can say in general of the "rheumatoid" lesions that from the radiological point of view there is comparatively little simple pneumoconiosis relative to the time of appearance of the lesions; from the industrial point of view exposure to stone-dust inhalation seems important; from the bacteriological point of view the tubercle bacilli may be abnormal; and from the pathological point of view the lesions are individually similar to the infective nodules commonly found in the neighbourhood of the fibrotic masses of P.M.F. but are larger, more numerous, more discrete, and more widespread than are usually seen in complicated pneumoconiosis.

We have reported here only the results of an investigation in one mining valley, but a number of other cases of this syndrome have been studied. One most interesting finding concerns the time relationship between the development of rheumatoid arthritis and the development of the characteristic "rheumatoid" chest x-ray appearances. It seems likely that in most cases the onset of arthritic symptoms coincides with the development of the lung lesions. In some cases, however, the characteristic x-ray appearances may precede the arthritis by several years, and one case has been found of a miner who developed rheumatoid arthritis six years before his first chest x-ray film was taken; this showed simple pneumoconiosis. The next film, taken five years later, showed the typical "rheumatoid" appearances.

It has been shown that there is probably an increased prevalence of rheumatoid arthritis among cases of P.M.F. On the evidence available it is not possible to state whether the P.M.F. predisposes to rheumatoid arthritis, or whether rheumatoid arthritis predisposes to P.M.F., or whether the factors predisposing to rheumatoid arthritis also predispose to P.M.F. This problem can only be investigated epidemiologically by determining the attack rates of rheumatoid arthritis in men with and without massive fibrosis. It is nevertheless of interest to seek an explanation of the association of rheumatoid arthritis with these characteristic "rheumatoid" lung lesions, and there are at least three possible explanations of this association.

The simplest hypothesis is that the changes in the lung are merely one manifestation of the rheumatoid syndrome and are unrelated to typical P.M.F. Kellgren (1952) has suggested that the inflammatory lesion in the connective tissues in rheumatoid arthritis may be due to collagen breakdown, and it is possible that such changes in the lungs would be made more radio-opaque by the migration of dust-laden phagocytes to these areas of inflammation. This hypothesis is possible, but it is improbable for the following reasons: (a) Such lesions, even if less obvious, would have been seen at necropsy in non-miners. (b) There is some clinical and post-mortem evidence that the lesions are tuberculous. (c) Similar radiological findings have never been reported in association with rheumatoid arthritis. No similar cases were found among non-miners in the Rhondda Fach scheme, where almost 90% of the adult population of 20,000 people were x-rayed (Cochrane *et al.*, 1952).

Discarding the first hypothesis, then, the second explanation of the association is that the pathological changes reflected in the x-ray film may play the part of a chronic septic focus, one of the many other postulated factors in the

W. E. MIALL AND OTHERS: RHEUMATOID ARTHRITIS ASSOCIATED WITH
CHARACTERISTIC CHEST X-RAY APPEARANCES IN COAL-WORKERS

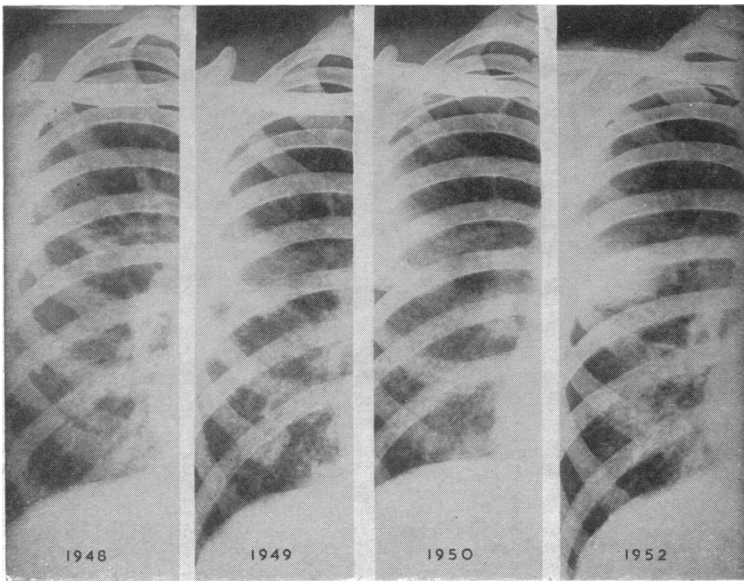


FIG. 1

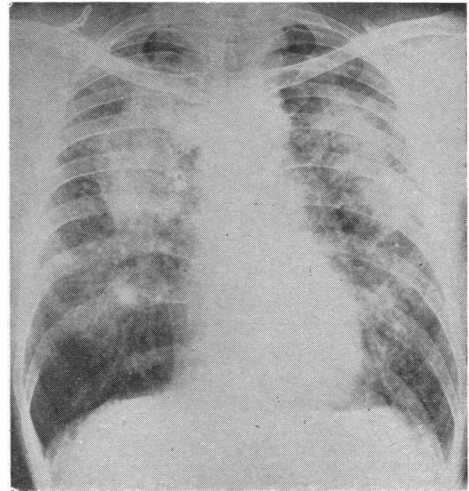


FIG. 2

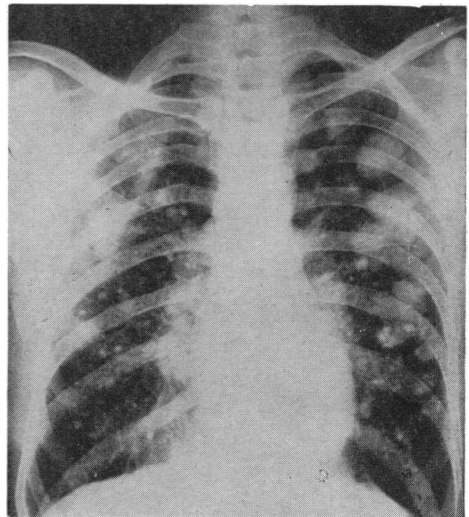


FIG. 3

FIG. 1.—The gradual development of a typical massive fibrosis opacity in the right mid-zone.

FIG. 2.—A typical example of advanced massive fibrosis.

FIG. 3.—A typical example of "rheumatoid" appearances.

FIG. 4.—Coal-miner aged 72 (Case 1) with rheumatoid arthritis of 26 years' duration.

FIG. 5.—Same case as Fig. 4, showing advanced changes of rheumatoid arthritis in both hands.

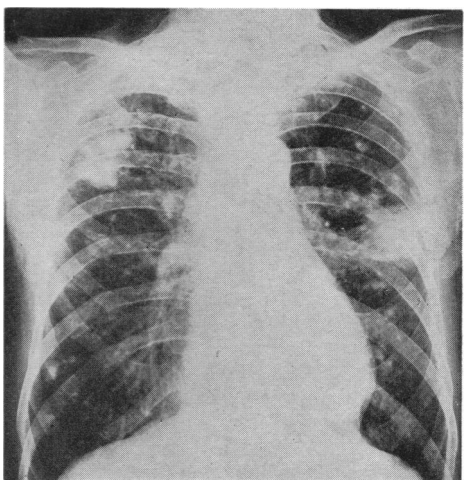


FIG. 4

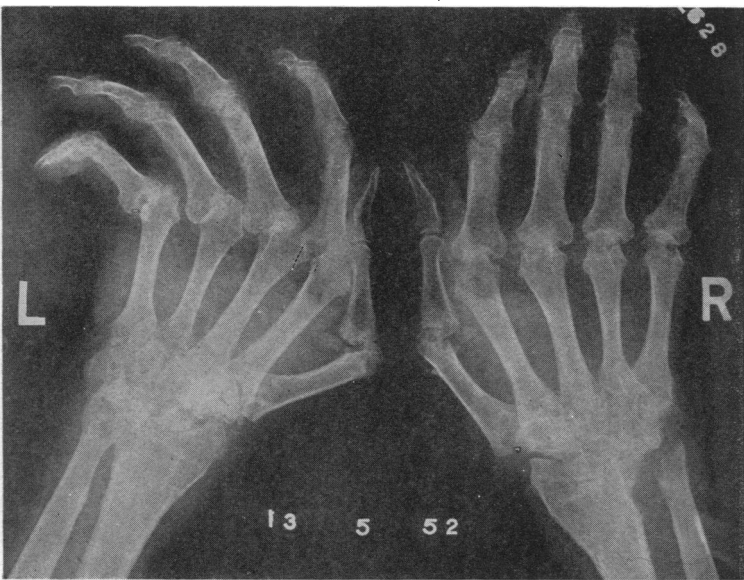


FIG. 5

MICHAEL HARTY: BLOOD SUPPLY OF THE FEMORAL HEAD

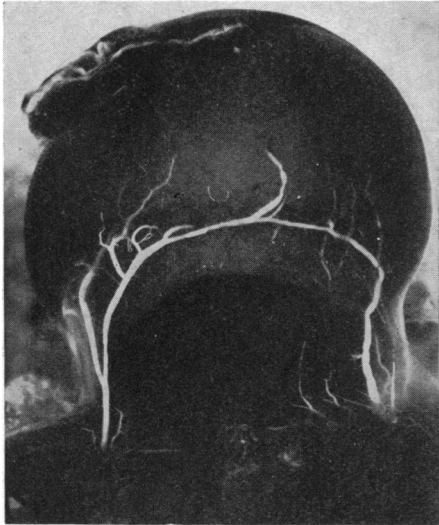


FIG. 1.—Infant femur (×3). Inferior aspect of head and neck, showing anastomosis between anterior and inferior retinacular vessels.

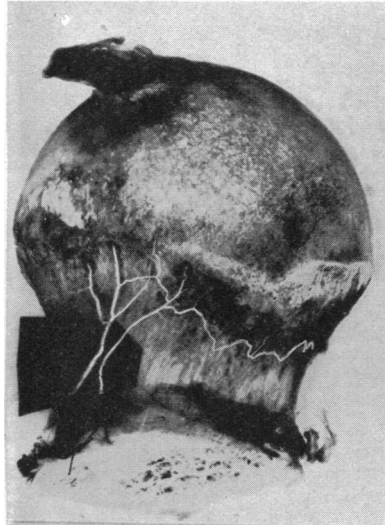


FIG. 2.—Posterior view of femoral neck. Arteries injected, and black paper under pedunculated retinaculum.

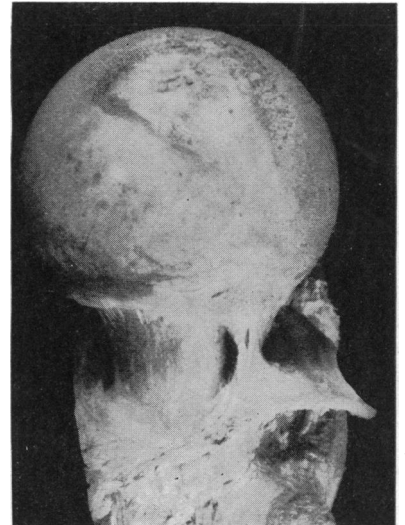


FIG. 3.—Postero-inferior retinaculum from below.

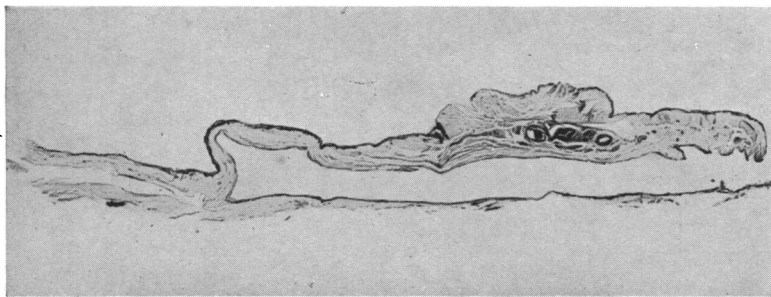


FIG. 4.—Section of retinaculum and periosteum of neck, with blood vessels in pedicle. (×3.)

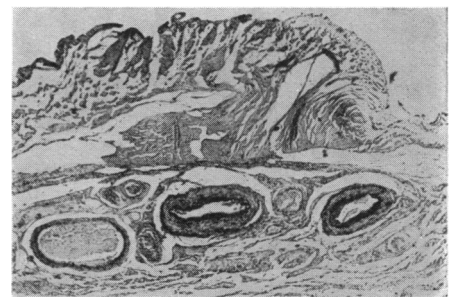


FIG. 5.—Vascular region, showing two thick-walled arteries and one vein. (×18.)

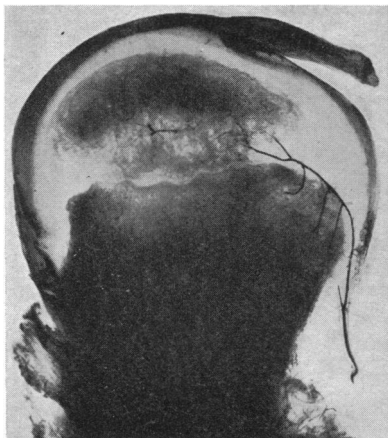


FIG. 6.—Injected retinacular artery to epiphysal centre and recurrent branches to juxta-epiphysal region. (×2.)

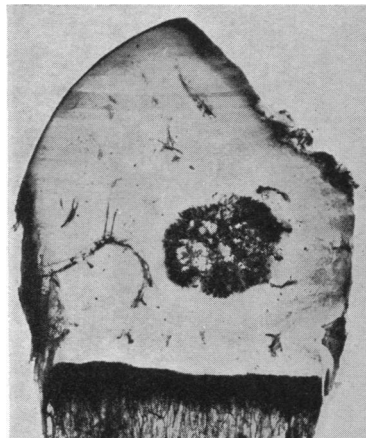


FIG. 7.—Indian ink injection showing increased concentration of blood vessels at the juxta-epiphysal "line." (×4½.)

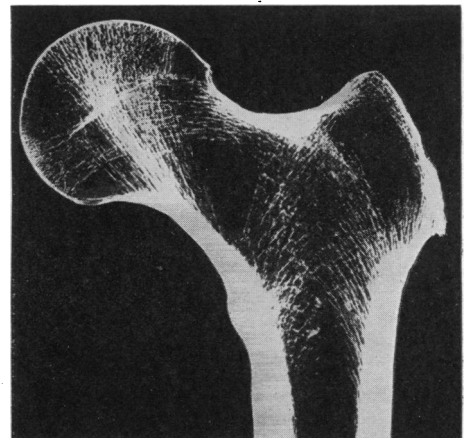


FIG. 8.—Skiagram of femoral segment, illustrating the superior and inferior triangles at the junction of head and neck.

aetiology of rheumatoid arthritis. Against this hypothesis we have the fact that in one case the arthritis preceded the development of typical "rheumatoid" lung lesions by more than six years, and in other cases there may be a latent period of as much as 11 years between the development of the typical lung lesions and the onset of arthritis.

It is possible, therefore, that neither of these hypotheses is correct and that there is some other factor which is causally related to both the arthritis and this type of "rheumatoid" lung lesion—for example, a more fundamental generalized abnormality of tissue reaction to dust and infection.

As these "rheumatoid" lung lesions in miners can develop several years before, concurrently with, or several years after the onset of arthritis, the suggestion is that there may be a particular type of tissue reaction to dust and tuberculosis in the lungs of miners who are predisposed to the development of rheumatoid arthritis. Recent work on adrenal cortical hormones and their relationship to rheumatoid arthritis and to tissue reaction suggests that this may be part of the explanation.

A.C.T.H. and cortisone are known to diminish the inflammatory response to trauma and chemical irritants (Shapiro *et al.*, 1951), to diminish the tuberculin reaction (Long and Miles, 1950; Long *et al.*, 1951; Pickering, 1952), and to inhibit the migration of dust cells in animals receiving intratracheal injection of powdered quartz (Harrison *et al.*, 1952). The formation of silicotic granulomata after intraperitoneal injection of powdered quartz is inhibited or diminished by cortisone in some experimental animals (Magarey and Gough, 1952; Schiller, 1953). These are the effects of excess A.C.T.H. and cortisone. Methods of assaying the levels of circulating A.C.T.H. and cortisone are not yet sufficiently developed to indicate whether these hormones are diminished in cases of rheumatoid arthritis; but Venning, Johnson, and Rose (1951) demonstrated a lowered excretion of certain groups of adrenal steroids in cases of rheumatoid arthritis, and Pearse (1950) found pituitary changes in patients dying with active rheumatoid arthritis, which he considered secondary to adrenal dysfunction. It is possible that rheumatoid arthritis may be related to adrenal or pituitary function, but, as Pickering (1952) points out, there is apparently no increased prevalence of this condition in cases of Addison's disease and Simmonds's disease, and it is therefore unlikely that it is simply due to a pituitary or adrenal defect; but such a defect may contribute to its aetiology, and, similarly, may contribute to the type of tissue reaction causing these "rheumatoid" lung lesions.

Summary

An epidemiological investigation of a syndrome in which rheumatoid arthritis is associated with characteristic chest x-ray appearances in coal-workers is described.

The widespread nodular fibrosis shown in these x-ray films is radiologically distinguishable from typical progressive massive fibrosis, but the available evidence suggests that the aetiology of both types of lesion is similar.

The prevalence of rheumatoid arthritis among cases with these characteristic chest x-ray films is over 50%; among cases of P.M.F. it was found to be 3%; whereas no cases were found in two similar groups of miners with and without simple pneumoconiosis.

The significant epidemiological, clinical, and pathological findings are given, and some possible explanations of the relationship between the "rheumatoid" lung lesions and the arthritis are discussed.

We wish to acknowledge our indebtedness to our colleagues in the Pneumoconiosis Research Unit for much helpful criticism and advice, and particularly to Dr. J. C. Gilson, the director; to Drs. C. M. Fletcher and R. F. Mahler, until recently members of the Unit; and to Dr. D. Rivers, who supplied the report on the pathology of this syndrome. The x-ray films of the peripheral

joints were kindly read for us by Dr. J. H. Kellgren and Dr. J. Sharp, of the Manchester Rheumatism Research Centre; the differential agglutination tests were performed by Dr. J. Ball, of the same unit; and the Middlebrook-Dubos tests were carried out by Dr. Geraint James and Dr. F. O'Grady at the Middlesex Hospital. It is a pleasure to record our thanks to them, and to the miners who so willingly co-operated in this survey.

APPENDIX

(a) *Intra-observer Error in Reading Characteristic Chest X-ray Appearances.*—All 896 films were read twice by the same observer. On the first occasion 20 films were selected as showing these typical appearances and divided into four groups—A, B, C, and D—group A being the most typical, group D the least typical. On the second occasion 27 films were selected, and divided in three groups only—A+B, C, and D. On the second reading, 16 of the 20 original films were reselected; only one of the four cases not reselected on this occasion was a proved case of rheumatoid arthritis, but 11 new cases not previously selected were added in this group; clinically none of these was a case of rheumatoid arthritis, but none was fully investigated in hospital. Of the 16 selected on each occasion, 13 were allotted to the same subgroups as previously. These results are shown in Table III.

TABLE III.—*Intra-observer Error in Reading "Rheumatoid" Chest X-ray Films in Miners*

| | | Second Reading | | | | Total |
|---------------|--------------------------------------|----------------|----|----|--------------------------------|-------|
| | | A and B | C | D | Not Selected on Second Reading | |
| First reading | "Rheumatoid" Chest X-ray Appearances | | | | | |
| | A and B .. | 5 | 1 | — | — | 6 |
| | C .. | 1 | 6 | — | 2* | 9 |
| | D .. | — | 1 | 2 | — | 5 |
| | Not selected on first reading | — | 4† | 7† | — | — |
| Total .. | | 6 | 12 | 9 | — | — |

Cases selected on first reading were all fully investigated.
 * One of these cases had proved rheumatoid arthritis, the other three not selected on second reading were not suffering from rheumatoid arthritis.
 † These 11 cases selected on second reading but not selected on first reading all had no clinical evidence of rheumatoid arthritis, but were not fully investigated in hospital.

(b) *Intra-observer Error in Clinical Diagnosis of Rheumatoid Arthritis under Field-survey Conditions.*—Two observers visited cases at an interval of about three months. In this study 20 men with characteristic x-ray films and 5 men without characteristic x-ray films but thought by Observer A to be possible cases of rheumatoid arthritis were visited by both doctors. Table IV shows the result of this investigation. It will be seen that both observers agreed on the clinical grading of 20 of the 25 men, but both thought two were cases of

TABLE IV.—*Inter-observer Error in the Clinical Diagnosis of Rheumatoid Arthritis in the Field*

| Observer A | | Clinical Grade | Observer B | | | | Total |
|------------|-------------|----------------|------------|----------|----------|----------|-------|
| | | | Certain | Probable | Possible | Negative | |
| Observer A | Certain .. | 7 (7) | — | — | — | 7 (7) | |
| | Probable .. | 1 (1) | 3 (1) | — | — | 4 (2) | |
| | Possible .. | — | — | 1 (1) | 4 (2) | 5 (3) | |
| | Negative .. | — | — | — | 9 (1) | 9 (1) | |
| Total .. | | 8 (8) | 3 (1) | 1 (1) | 13 (3) | 25 (13) | |

The numbers in parentheses indicate proved cases of rheumatoid arthritis.
 Certain=Typical history+marked residual signs.
 Probable=Typical history+minimal residual signs.
 Possible=Typical history+no residual signs.

rheumatoid arthritis when this diagnosis was not substantiated, and both thought one case normal when in fact he was suffering from rheumatoid arthritis. Observer A saw 16 cases he thought positive, of which 12 were later proved cases, and 9 he thought negative, of which 1 was later a proved case. Observer B saw 12 cases he thought positive, of which 10 proved to be so, and 13 cases he thought negative, of which 3 were later proved cases. Such disagreement as occurred

is partly explicable by the desire to find very early cases of a disease in which the earliest symptoms and signs are not usually clearly defined.

(c) *Inter-observer Error in Reading Characteristic X-ray Changes of Rheumatoid Arthritis in the Hands and Feet.*—Two observers from the Manchester Rheumatism Research Centre kindly read the films of the hands and feet of the 20 cases with typical "rheumatoid" chest x-ray films. Their readings are plotted against each other in Table V. In read-

TABLE V.—*Inter-observer Error in X-ray Diagnosis of Rheumatoid Arthritis*

| | | Second Observer | | | | |
|----------------|--------------------|--------------------|--------|----------|--------|-------|
| | | Normal or Doubtful | Slight | Moderate | Marked | Total |
| First Observer | Normal or doubtful | 8 (1) | 4 (3) | — | — | 12 |
| | Slight | 1 (1) | 3 (3) | 1 (1) | — | 5 |
| | Moderate | — | — | 1 (1) | — | 1 |
| | Marked | — | — | — | 1 (1) | 1 |
| | Total | 9 | 7 | 2 | 1 | 19 |
| <i>Hands</i> | | | | | | |
| First Observer | Normal or doubtful | 12 (4) | 1 (1) | — | — | 13 |
| | Slight | — | — | — | — | — |
| | Moderate | — | — | 5 (5) | — | 5 |
| | Marked | — | — | — | 1 (1) | 1 |
| | Total | 12 | 1 | 5 | 1 | 19 |
| <i>Feet</i> | | | | | | |

The numbers in parentheses indicate proved cases of rheumatoid arthritis.

ing the films of the hands there was agreement in 13 of the 19 cases, but in 5 cases one observer noted changes (3 of which were osteoporotic changes only) which were not noted by the other observer; in the remaining case the difference was only one of degree. In reading the films of the feet, however, there was agreement in 18 of the 19 cases. Table V also indicates that the x-ray changes in the feet seemed less likely to be present than in the hands, but when present they were more severe. In this series, four cases of proved rheumatoid arthritis had no changes in the x-ray films of the feet, whereas only one case had no changes in the x-ray films of the hands; nevertheless, among these 11 cases of rheumatoid arthritis six had moderate or marked changes in the feet, whereas only two had moderate or marked changes in the hands. Typical x-ray changes of rheumatoid arthritis were never read by either observer in this series for any case which had no other clinical evidence of arthritis; there was one case of proved arthritis which both observers agreed had no x-ray changes in the hands or feet. This study would have been improved if a normal control bone had been used when each film was taken. Many films were read as "doubtful" because osteoporosis cannot be accurately assessed without such a control.

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BLOOD SUPPLY OF THE FEMORAL HEAD

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[WITH SPECIAL PLATE]

Towards the close of the eighteenth century William Hunter had raised London to the position of one of the best anatomy schools in Europe. He visited Albinus, the celebrated Dutch anatomist, in 1748, and admired his injected anatomical specimens. On returning to London, Hunter developed and elaborated this technique, and many of his original examples are preserved in the Hunterian Museum at the University of Glasgow. This collection contains a number of illustrations of the *circulus articuli vasculosus*, which Hunter had described originally in 1743.

Materials and Methods

The injected specimens used in this investigation were removed from recent post-mortem bodies or from the anatomical dissecting-rooms. They were dehydrated and cleared in oil of wintergreen (methyl salicylate). Red lead and starch were employed for the intra-arterial injections in Figs. 1 and 2 and indian ink was used for Figs. 6 and 7.

Circulus Articuli Vasculosus.—Since Hunter's original description, this vascular articular anastomosis has been given various anatomical situations. In his account Hunter states, "All round the neck of the bone there is a great number of Arteries and Veins, which ramify into smaller Branches and communicate with one another by frequent Anastomoses like those of the mesentery." These vessels he placed by the margins of the articular cartilages in the subsynovial tissues (Figs. 1 and 2). Some more recent accounts put the *circulus articuli vasculosus* at the attachment of the joint capsule to the bone. This attachment may coincide approximately with the margin of the articular cartilage in those diarthrodial joints which permit little movements, such as the joints between the intervertebral articular facets. In the adult femoral neck, however, the regions are separated by from 2 to 5 cm. The head of the femur derives its main blood supply from the subcapital anastomosis, as the contribution via the ligamentum teres is, at any age, limited to a small medial segment of the head of the femur. Davies (1946), when discussing the dynamics of haemarthrosis, emphasized the richness and superficial position of the capillary fringe in the synovial membrane.

Retinacula.—The arterial circle at the base of the femoral head is supplied by arteries situated on the neck of the femur between the synovial membrane and periosteum. The vessels are concentrated postero-inferiorly, superiorly, and occasionally anteriorly. The synovial membrane covering these vascular bundles is thrown into longitudinal ridges, to which the term "retinacula" was first applied by Weitbrecht, of St. Petersburg, in 1742. The postero-inferior retinaculum is a very definite structure in the human femur, and shows as a duplication of synovial membrane measuring 1 cm. or more in 76% of specimens examined (Figs. 2, 3, and 4). This pleat of synovial membrane always contains medium-sized arteries, situated at the attachment to the periosteum of the neck or anywhere along the pedunculated area (Figs. 2, 4, and 5).

The Pericapsular Anastomosis.—The afferent arteries to the retinacular vessels are derived from another anastomosis on the capsular attachment towards the base of the neck. This pericapsular corona, which is part of the trochanteric anastomosis, gets its blood supply from the ascending branches of the medial femoral circumflex, the superior gluteal, the obturator, and profunda femoris arteries, as well as from small communications from the acetabular marginal