

RHEUMATOID ARTHRITIS IN LIBERIA

WITH AN ASSESSMENT OF SEROLOGICAL FINDINGS

BY

W. HIJMANS, H. A. VALKENBURG, A. S. MULLER, AND S. GRATAMA

From the Research Laboratories, Department of Rheumatology, University Hospital, Leiden, The Netherlands, and the Hospital of the Firestone Plantations Company, Cavalla Plantation, Cape Palmas, Liberia

The potential value of demographic studies for investigating the aetiology of rheumatoid arthritis is generally accepted. In a recent review Scotch and Geiger (1962) accordingly propose to give a high priority to descriptive epidemiology. In this respect a total absence of rheumatoid arthritis in a given population could be as important as an increased prevalence. It is unfortunate from this point of view that definite rheumatoid arthritis has been reported to occur with the same frequency in all seven Northern European populations studied by means which allow mutual comparison (De Graaff, Laine, and Lawrence, 1963) and that a total absence of this disease has never been convincingly demonstrated. Malawista, Boies, and Seides (1959), however, mention that Liberia is said to be devoid of rheumatoid arthritis, basing this conclusion on their own experience and on the opinion of various physicians working in other areas of that country. Our observations do not support this conclusion, because they show that rheumatoid arthritis does occur in the indigenous population, and in view of the bearing of these observations on the epidemiological aspects of this disease it seems justifiable to present the details of a fully-established diagnosis of rheumatoid arthritis in a native Liberian girl and to describe our findings in two Liberian adults suffering from the same disease. The general conditions prevailing in the region where the first patient originated have already been described by one of us (Gratama, 1957).

The assessment of the serological findings was made against the results obtained in the local control population, whose sera had become available as part of a study on the epidemiology of the rheumatoid factor (Valkenburg, 1963a; Valkenburg and Hijmans, 1961).

Material and Methods

The sera were stored frozen and care was taken that no thawing occurred during their transportation to Leiden, where the tests were performed.

The Waaler-Rose test was carried out with human erythrocytes and the latex-fixation test with Dow polystyrene latex particles, 0.81 μ in diameter. The details of these procedures have been described elsewhere (Valkenburg, 1963b).

The immunofluorescence test for the detection of antinuclear factor (A.N.F.) was done with human leucocytes, as suggested by Alexander, Bremner, and Duthie (1960), although in our hands different results have been obtained (Hijmans, 1963).

Case Reports

Case 1, a girl about 13 years old, of the Kelepo tribe, visited the out-patients' department of the hospital of the Firestone Plantation Company at Cape Palmas, Liberia, because of a traumatic eye lesion. On further clinical examination a severe polyarthritis with deformities and contractures of practically all the peripheral joints was observed (Fig. 1).



Fig. 1.—Case 1, showing polyarthritis in both hands.

Multiple subcutaneous nodules were present on the medial side of both knees and on the lateral part of both feet.

Routine laboratory examinations did not reveal any specific abnormalities: urinalysis was negative, the haematological findings were non-contributory, and the electrocardiogram was normal.

Special studies of the serum yielded the following information. The total protein content was 5.3 per cent. Quantitative paper electrophoresis showed the relative content of albumin to be 40.1 per cent. and the relative level of gamma globulin 36.4 per cent. The Meinel reaction and Kahn test were strongly positive. The Wassermann reaction was negative. The Waaler-Rose test was positive in a titre of more than 2,048. The latex-fixation test was negative. The A.N.F. test was strongly positive.

An x-ray photograph of the hands showed advanced erosive polyarthritis with ankylosis (Fig. 2).



Fig. 2.—Case 1, x-ray of right hand, showing advanced erosive arthritis with osteoporosis and ankylosis.

A nodule was removed from the left knee. The histological appearance was that of a typical rheumatoid lesion with central necrosis and fibrinoid alteration, palisading, and peripheral infiltration with mononuclear cells (Fig. 3).

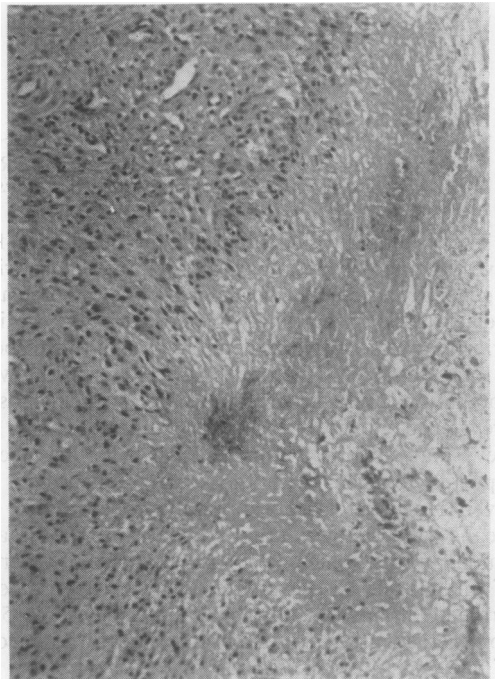


Fig. 3.—Case 1, biopsy of nodule, showing typical rheumatoid lesion.

The specimen contained a cavity with marked villous hypertrophy of the lining, fibrin deposits on the surface, and mononuclear infiltration (Fig. 4, opposite).

The family history was negative, but a latex-fixation test of the patient's father gave a reaction with a titre of over 10,000, the Waaler-Rose test being negative. Both tests were negative in the patient's mother and sister.

Case 2, a woman about 50 years old, presented the typical clinical picture of rheumatoid arthritis with swollen and tender wrists, metacarpophalangeal joints, elbows, and knees. The x-ray photograph of the hands showed a narrowing of several joint spaces with erosions, deformities, and subluxation (Fig. 5, opposite). The latex-fixation test was positive in a dilution of 10,000. The Waaler-Rose test reached a titre of 1:64. The A.N.F. test was strongly positive.

Case 3, a man about 40 years old, was admitted because of a painful, swollen, hot right knee. Further findings included a slight ulnar deviation and flexion contracture of the proximal interphalangeal joints. Radiological examination showed a narrowing of the joint spaces with juxta-articular osteoporosis.

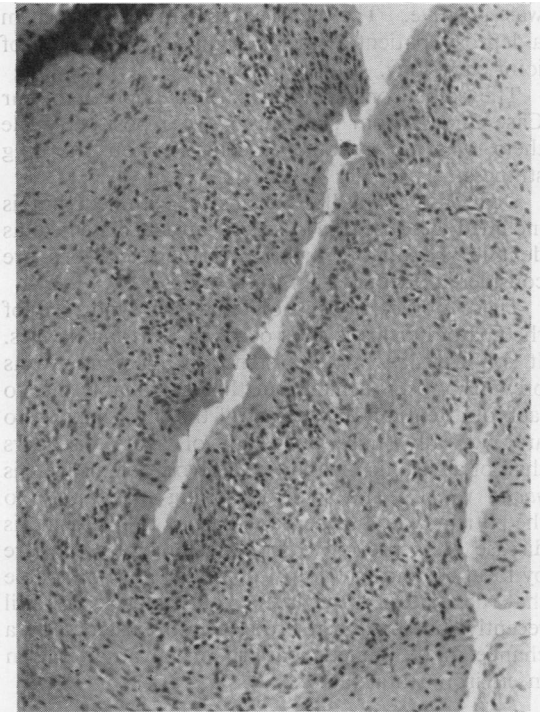


Fig. 4.—Case 1, biopsy of nodule, showing a lining with fibrin deposits and mononuclear infiltration.

Discussion

The final classification of a disease is only possible if its cause and pathogenesis are known. In the absence of this knowledge a diagnosis had to be founded on a combination of data obtained by clinical observation and/or laboratory analysis. The number of positive criteria is a measure of the degree of certainty of the diagnosis, whereby the contribution of each criterion depends on its sensitivity and its specificity. Rheumatoid arthritis is a good example of this situation. On the initiative of the American Rheumatism Association, diagnostic criteria have been prepared, and these are being revised and modified periodically (Kellgren, 1963). In addition to several categories, which together present the full evolution of this disease, there is a list of exclusions which comprises a number of known diseases, each of which has one or more characteristics, which may also be associated with rheumatoid arthritis. One has to remember, however, that there may be other syndromes mimicking rheumatoid arthritis which have not yet been studied from this point of view. This may occur particularly in regions where rheumatoid



Fig. 5.—Case 2, x-ray of right hand, showing osteoporosis, narrowing of joint spaces with erosions, and subluxation.

arthritis does not constitute a major health problem and has therefore received little attention. In the absence of a proven adequate list of exclusions in such areas, the diagnosis of rheumatoid arthritis will be acceptable only in a fully-established case. This will require an assessment of the significance of the applied criteria in the local population, as the specificity of such criteria depends on their frequency in these control groups.

Our first case fulfils the requirements for inclusion in the group "Classical Rheumatoid Arthritis" (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959). All eight criteria which were tested are positive, but there is no reliable information on the presence of morning stiffness and the synovial fluid was not analysed. In addition, the test for A.N.F. is strongly positive.

The value of the serological findings was assessed against those in 88 patients' sera obtained locally at

random, in fifty sera from female inmates of the New Hope leprosy settlement, and in 86 sera from members of the hospital staff, all of whom belonged to the indigenous population. The results of the serological tests (presented in detail in Tables I and II) show that they can be used for diagnostic purposes in the area. The results obtained in the leprosy patients have been tabulated separately, because (according to Schubart, Cohen, and Calkins, 1959) a relatively increased incidence of positive latex-fixation tests can be expected in lepers; we have been unable to confirm this finding either in this series or in a study conducted in Nigeria (Valkenburg, 1963a; Valkenburg and Hijmans, 1961).

The percentage of positive results in the Waler-Rose test is 6.2 per cent., if the limit of positivity is taken at 1:32. The corresponding figure for the latex-fixation test is 4 per cent. at a dilution of 1:320. Strictly speaking, the results of the Waler-Rose test do not meet the requirements of the A.R.A. criteria, because according to these rules positive tests should not occur in more than 5 per cent. of normal controls. We believe, however, that in our case the results can be taken into account for two reasons. First, most of our control cases are diseased and it is known that higher figures are found in diseased controls than in normal controls. Secondly, the titre in our patient was extremely high, which increases its specificity. An equally high titre was found in two controls, both of whom belonged to the group recruited from the hospital staff.

So far the test for A.N.F. has not been incorporated in the diagnostic criteria for rheumatoid arthritis, but the figures obtained in this study show that it may be used successfully for this purpose. Of 183 sera tested, two were weakly positive and one

was positive. The positive specimen came from a leprosy patient with no signs or symptoms of joint pathology.

The same consideration can be applied to our Case 2, in whom six criteria were positive while there was no reliable information on morning stiffness.

Our Case 3 was less extensively studied, but is included because the disease can be classified as definite rheumatoid arthritis if the exclusions are considered adequate for this region.

These observations show that the syndrome of rheumatoid arthritis does occur in Liberian natives. It is not clear why its existence in this country has previously been denied, but this is probably due to lack of attention on the part of the physicians, who are naturally more observant of acute disorders than of a chronic illness with a favourable prognosis *quoad vitam*. The same reasoning may apply to the patient, who has perhaps learned to live with his disease or is prevented from seeking medical care by local custom or taboo. It is also not impossible that rheumatoid arthritis did not in fact occur until recently, but has been brought into existence by a change in the genetic pattern or by an alteration in environmental factors.

Summary

Because of the important information to be gained from demographic studies, the details are presented of the first fully-established case of rheumatoid arthritis in a native girl in Liberia, a country formerly said to be devoid of this disease. Two additional adult patients are also discussed. The serological findings, which included tests for rheumatoid and antinuclear factors, were compared with those in a large number of local control subjects.

TABLE I
RESULTS OF LATEX-FIXATION TEST IN 224 LIBERIAN SERA

Titre	<20	20	40	80	160	320	640	1,280	2,560	>2,560	Total
Total Number	211	4	0	0	0	3	2	2	2	0	224
Subgroup with Leprosy	48	0	0	0	0	1	0	0	0	1	50

TABLE II
RESULTS OF WAALER-ROSE TEST IN 224 LIBERIAN SERA

Titre	<4	4	8	16	32	64	128	256	512	1,024	2,048	>2,048	Total
Total Number	190	10	5	5	5	4	0	1	2	0	0	2	224
Subgroup with Leprosy	40	1	2	2	2	2	0	0	1	0	0	2	50

The authors wish to thank Dr. H. de Jager for his reports on the pathological specimens and Dr. J. Kiewit de Jonge for his efforts to provide adequate transport of the serum samples. They are indebted to Dr. K. H. Franz, medical director of the Firestone Health Services in Liberia, for his permission to collect the blood samples for this investigation and to KLM Royal Dutch Airlines for extra services rendered. The assistance received from the New Hope leprosy settlement is gratefully acknowledged.

REFERENCES

- Alexander, W. R. M., Bremner, Joan M., and Duthie, J. J. R. (1960). *Ann. rheum. Dis.*, **19**, 338.
- Graaff, R. de, Laine, V., and Lawrence, J. S. (1963). In "The Epidemiology of Chronic Rheumatism", ed. J. H. Kellgren, vol. 1, p. 228. Blackwell Scientific Publications, Oxford.
- Gratama, S. (1957). *Docum. Med. geogr. trop. (Amst.)*, **9**, 237.
- Hijmans, W. (1963). In "The Epidemiology of Chronic Rheumatism", ed. J. H. Kellgren, vol. 1, p. 82. Blackwell Scientific Publications, Oxford.
- Kellgren, J. H. (editor) (1963). "The Epidemiology of Chronic Rheumatism", vol. 1. Blackwell Scientific Publications, Oxford.
- Malawista, S. E., Boies, L. R., Jr., and Seides, S. W. (1959). *Ann. rheum. Dis.*, **18**, 305.
- Ropes, Marian W., Bennett, G. A., Cobb, S., Jacox, R., and Jessar, R. A. (1959). *Ibid.*, **18**, 49.
- Schubart, A. F., Cohen, A. S., and Calkins, E. (1959). *New Engl. J. Med.*, **261**, 363.
- Scotch, N. A., and Geiger, H. J. (1962). *J. chron. Dis.*, **15**, 1037.
- Valkenburg, H. A. (1963a). In "The Epidemiology of Chronic Rheumatism", ed. J. H. Kellgren, vol. 1, p. 74. Blackwell Scientific Publications, Oxford.
- (1963b). *Ibid.*, p. 330.
- and Hijmans, W. (1961). In "Atti del X Congresso della Lega Internazionale contro il Reumatismo", vol. 2, p. 749. Minerva Medica, Turin.

L'arthrite rhumatismale en Libéria, avec l'évaluation des résultats sérologiques

RÉSUMÉ

En raison de l'importance des données dérivées des études démographiques, on présente ici en détail le premier cas confirmé d'arthrite rhumatismale chez une jeune indigène en Libéria, pays où l'existence de cette maladie avait été déniée. On discute aussi le cas de deux autres malades adultes. Les résultats sérologiques, comprenant la recherche des facteurs rhumatismal et anti-nucléaire, sont comparés à ceux obtenus chez de nombreux sujets locaux, servant de témoins.

Artritis reumatoide en Liberia, con valoración de los resultados serológicos

SUMARIO

En vista de la importancia de los datos obtenidos en estudios demográficos, se presenta aquí detalladamente el primer caso confirmado de artritis reumatoide en una chica indígena en Liberia, país en que hasta ahora la existencia de tal enfermedad fué denegada. Se discuten también dos otros casos de enfermos adultos. Se comparan los resultados serológicos, que incluyen investigaciones de los factores reumatoide y anti-nuclear, con los obtenidos en numerosos sujetos locales que sirvieron de testigos.