

## EVALUATION OF AN EPIDEMIOLOGICAL METHOD RHEUMATOID ARTHRITIS IN LIBERIA

BY

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All current studies of rheumatoid arthritis are hindered by the lack of a precise definition of the disease. Patients in an arthritis clinic are selected, so that those with mild or short-lived forms of the disease are probably rarely seen. Because of this, better definition of rheumatoid arthritis is being sought through epidemiological studies.

Four approaches are available, either separately or in combination with one another. These include finding the prevalence rates of various factors in various populations:

- (1) History of arthritis, morning stiffness, or joint swelling (Kellgren, Lawrence, and Aitken-Swan, 1953; Rubin, Rosenbaum, and Cobb, 1956);
- (2) Polyarthritis demonstrated by physical examination;
- (3) Radiological evidence for rheumatoid arthritis;
- (4) High agglutination titres, as, for instance, with the latex-fixation test (Singer and Plotz, 1956), indicating the presence in the sera of so-called "rheumatoid factor".

Two excellent studies (Kellgren and Lawrence, 1956; Miall, Ball, and Kellgren, 1958) incorporating these four approaches emphasize the need for precise diagnostic definition for the study of comparative prevalence rates of rheumatoid arthritis in different populations, but since it is cumbersome and expensive to use all four methods, it has been suggested (Kellgren, 1958) that a serological test for rheumatoid factor alone be used to screen a population sample for rheumatoid arthritis.

Positive results of tests for the rheumatoid factor have been obtained in conditions other than rheumatoid arthritis, such as lupus erythematosus, periarteritis nodosa, and infectious hepatitis (Ziff, 1957), syphilis (Peltier and Christian, 1959), and sarcoidosis (Kunkel, Simon, and Fudenberg, 1958). Yet the study of Feldman, Mou, and Wadsworth (1958) revealed only a 0.25 per cent. incidence of positive results in what was considered a "normal" population. Kellgren and Lawrence (1956), in a study of a population sample in an industrial town in England, found 5 per cent. of men and 6 per cent. of women had positive sheep cell agglutination tests. A disturbing finding was the number of subjects with positive agglutination tests, in whom no evidence of rheumatoid arthritis was found on clinical examination. Miall, Ball, and Kellgren (1958), in a comparative study of urban and rural population samples in Wales found rheumatoid agglutination tests positive in less than 1 per cent.

Studies such as those of Feldman, Mou, and Wadsworth (1958), Kellgren, Lawrence, and Aitken-Swan (1953), Kellgren and Lawrence (1956), and Miall, Ball, and Kellgren (1958) have led to the assumption that positive serological tests for rheumatoid arthritis should be unusual in any general population. Our plan is to test this assumption through comparison of clinical and serological data in a given population said to be devoid of rheumatoid arthritis.

### Methods

The Firestone Plantations Company at Harbel, Liberia, West Africa, employs some 25,000 adult males as rubber tappers on the plantation. The subjects selected for study represent members of the families of these tappers, who appeared at one of the medical clinics

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at some time or another for any of a multitude of complaints, or who wandered by the clinic and were invited in.

The non-response rate was zero, and 230 native Liberians were examined. The sample is fairly well divided between males (121, 52.6 per cent.) and females (109, 47.4 per cent.), and among the various age groups represented (Table I). The Liberian native does not keep track of his years and his actual age is anybody's guess. With the help of Liberian nurses, likely ages were chosen and the subjects were placed in 10-year groupings.

TABLE I  
RESULTS OF F II TESTS IN 230 LIBERIANS

Age Group (yrs)	Male		Female		Total		
	No.	F II --	No.	F II --	No.	F II --	
0-9	0	—	0	—	0	—	
10-19	0	—	2	0	2	0	
20-29	13	2	10	0	23	2	
30-39	39	3	38	5	77	8	
40-49	32	4	30	3	62	7	
50-59	22	3	19	2	41	5	
60 --	15	3	10	3	25	6	
Total	No.	121	15	109	13	230	28
	Per cent.		12.4		11.9		12.2

Attempts were made to obtain the information set out in Table II. Such questions as stiffness on arising play a vital role in some studies of the incidence of rheumatoid arthritis (Cobb, Warren, Merchant, and Thompson, 1957; King and Cobb, 1958). However, information on stiffness and on other diseases was unreliable, for reasons of communication. Of the sixteen or seventeen tribes represented on the plantation, each has its own language, and the natives often cannot understand each other, much less us.

TABLE II  
EXAMINATION

(1) Stiffness in morning or after inactivity?		
	(a) Swelling	
(2) Wrists	(b) Motion	Normal Partial ankylosis Complete ankylosis
(3) Other manifestations—Involvement of M-P or P-I-P joints. Ulnar deviation, Subcutaneous nodules		
(4) History of yaws, syphilis, etc.		

Clinical examinations were made as outlined in Table II (2 and 3). Since the incidence of wrist involvement is high in an arthritis clinic population, the wrists of each subject were examined for swelling and impairment of motion. Other manifestations of rheumatoid arthritis sought included involvement of the metacarpo-phalangeal and proximal interphalangeal joints, ulnar deviation, and subcutaneous nodules.

Serum samples from all the subjects were shipped in ice by air to the laboratories of the Edward Daniel Faulkner Arthritis Clinic of the Columbia-Presbyterian Medical Center, New York, where they were studied by the technique of the F II tanned sheep cell agglutination (Jacobson, Kammerer, Wolf, Epstein, and Heller, 1956). The differential sheep cell test (Rose, Ragan, Pearce, and Lipman, 1948) was performed on most of the positive F II sera. Yaws is clinically prevalent on the plantation, and "V.D. Reference Laboratory" (VDRL) tests for syphilis were also done on all sera. Twenty selected serum samples were subjected to paper electrophoresis.

## Results

**Clinical.**—In the 230 subjects there was no wrist swelling. Motion was normal in 228 of 230 subjects (99.1 per cent.). None had complete ankylosis of either wrist, but two showed a partial ankylosis, one unilateral and the other bilateral. Neither of these subjects, however, showed any other clinical indications of rheumatoid arthritis. None of the 230 subjects revealed *any* of the other manifestations sought: namely, involvement of metacarpophalangeal or proximal interphalangeal joints, ulnar deviation, or subcutaneous nodules.

The clinical inquiry was extended to other areas of Liberia. Various physicians were contacted at the Firestone plantations at Harbel and Cap Palmas; Monrovia, the capital; Bomi Hills, which has two hospitals maintained by United States concerns; and the mission hospitals at Ghanta and Zor-Zor. All the physicians interviewed agreed that they had never seen a case of what they would call rheumatoid arthritis in a native Liberian.

**Serological.**—F II agglutination tests were positive in 28 (12.2 per cent.) of 230 serum samples (Table I). The positive results were about equally divided between males (15, 12.4 per cent.) and females (13, 11.9 per cent.). The percentage positive increased somewhat with increasing estimated age group. Titres ranged from 112 to one that was greater than 56,000 in a male in the 40 to 49 age group. Seven of the 28 positive titres were greater than 3,000.

Differential sheep cell agglutination tests were done on fifteen of the 28 F II positive sera. Only one was positive, in a male judged to be 75 to 80 years of age. His F II titre was 896. D.S.C. tests failed on two additional F II positive serum samples because of the persistence of heterophilic antibody after two adsorptions with sheep red blood cells.

48 of the 230 sera (20 per cent.) had positive VDRL tests, another 20 per cent. were weakly positive or equivocal, and the remainder were

negative (Table III). Nineteen of the 28 positive F II tests were in negative or equivocally positive VDRL sera. The sample with F II titre of more than 56,000 and that with positive F II and positive D.S.C. are both among the negative VDRL sera.

TABLE III  
RESULTS OF VENEREAL DISEASE REFERENCE  
LABORATORY TESTS

Result		No.	Per cent.
VDRL	+	48	20.9
	Weakly positive	50	21.7
	-	132	57.4
Total		230	100.0
F II -	with VDRL +	9	32.1
	with VDRL -	19	67.9
Total F II +		28	100.0

Of the two subjects who were found on clinical examination to have partial wrist ankylosis, the one with unilateral impairment had negative F II and negative VDRL tests, while the one with bilateral involvement had a positive F II test (titre 224) and a positive VDRL test (titre 4).

Paper electrophoresis was done on ten high-titred F II positive serum samples and ten F II negative samples. Both groups revealed varying amounts of globulin increase especially in the beta and gamma fractions. The findings were heterogeneous and non-specific.

### Discussion

A significant number of positive serologic reactions (F II test) for rheumatoid factor were found in a population which is virtually devoid of clinical rheumatoid arthritis. Yet only one positive sheep cell agglutination test was found in fifteen F II positive sera. In rheumatoid arthritis, there is generally a good correlation between F II and sheep cell tests. Kunkel and others (1958) found similar test discrepancies in the sera of patients with sarcoidosis. The difference in results with the two test systems is as yet unclear. The F II test seems to be less specific for rheumatoid factor than the sheep cell test, but whether or not it is more sensitive remains to be seen.

Peltier and Christian (1959) found 11 per cent. positive F II tests in syphilitic sera, again with negative sheep cell tests. One-third of the positive F II sera in our study also had positive VDRL tests, and yaws has a high clinical incidence in Liberia, but, since the specificity of the VDRL test for syphilis in this population is unknown, no

assumption can be made as to either the prevalence of yaws itself or the incidence of positive serologic reactions for rheumatoid factor in true yaws sera.

Positive F II sera were about equally divided between males and females in almost all age groups. This is in contradistinction to positive results in the sarcoid patients of Kunkel and others, where females predominated.

The problem of specificity of the various tests for the rheumatoid factor has raised many questions concerning definitions of rheumatoid arthritis which rely on serological testing. At any rate, the F II test has shown itself to be a poor screening method in the epidemiology of rheumatoid arthritis.

### Summary

(1) 28 (12.2 per cent.) of 230 serum samples from native Liberians showed positive results to F II tanned sheep cell agglutination tests. Positive serologic reactions were almost equally divided between males and females. Differential sheep cell agglutination tests were done on fifteen of the F II positive sera, and in all but one the results were negative.

(2) The population sample was devoid of clinical rheumatoid arthritis. Information on previous medical history was unreliable because of language difficulties.

(3) Nine of the 28 positive F II tests were associated with positive VDRL tests.

(4) The F II tanned sheep cell agglutination test appears inadequate in screening for rheumatoid arthritis.

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**Evaluation d'une méthode épidémiologique pour  
l'arthrite rhumatismale en Libéria**

**RÉSUMÉ**

(1) Sur 230 échantillons de sérums des indigènes Libériens, 28 (12,2%) donnèrent une réaction positive d'agglutination des globules rouges tannés F II de mouton. Le nombre des réactions sérologiques positives fut presque le même chez les hommes et chez les femmes. On procéda à des réactions d'agglutination différentielle des globules rouges de mouton sur 15 sérums F II positifs, et le résultat ne fut positif que dans un seul cas.

(2) Il n'y eut pas d'arthrite rhumatismale clinique parmi la population de l'échantillon étudié. Des renseignements concernant les antécédants médicaux furent sans valeur, en raison des difficultés de langue.

(3) Sur les 28 réactions F II positives, neuf furent associées à des réactions de VDRL positives.

(4) La réaction d'agglutination des globules rouges

tannés F II de mouton est insuffisante pour décélérer l'arthrite rhumatismale.

**Valoración de un método epidemiológico para  
la artritis reumatoide en Liberia**

**SUMARIO**

(1) Sobre 230 muestras de sueros de indígenas librianos, 28 (12,2%) dieron una reacción positiva de aglutinación de eritrocitos curtidos F II de oveja. Las reacciones serológicas positivas se repartieron casi igualmente entre hombres y mujeres. Se efectuaron reacciones de aglutinación diferencial de eritrocitos de oveja con 15 sueros F II positivos, obteniéndose tan sólo un resultado positivo.

(2) No hubo casos de artritis reumatoide clínica en la muestra de la población estudiada. Datos recogidos sobre los antecedentes médicos fueron sin valor en vista de dificultades de idioma.

(3) Sobre las 28 reacciones F II positivas, nueve fueron asociadas a reacciones de VDRL positivas.

(4) La reacción de aglutinación de eritrocitos curtidos F II de oveja no es adecuada para descubrir la artritis reumatoide.