CLINICAL SIGNIFICANCE OF THE L.E.-CELL PHENOMENON IN RHEUMATOID ARTHRITIS*

BY

L. J. GOLDFINE,† M. B. STEVENS, A. T. MASI, AND L. E. SHULMAN

From the Connective Tissue Division, Department of Medicine, The Johns Hopkins University School of Medicine, and the Department of Epidemiology, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland

In the first few years immediately following the discovery of the L.E.-cell phenomenon by Hargraves, Richmond, and Morton (1948), L.E.-cells were found to be closely correlated with the clinical diagnosis of systemic lupus erythematosus (SLE) (Dubois, 1953; Harvey, Shulman, Tumulty, Conley, and Schoenrich, 1954; Lee, 1955; Wilkinson and Sacker, 1957; Louis and Limarzi, 1958). These early experiences with the L.E.-cell test indicated that L.E.-cells were highly specific for SLE and of great diagnostic value in this disease.

Subsequently, there were sporadic reports of finding L.E.-cells in patients with such disorders as acquired haemolytic anaemia (Lee, Michael, and Vural, 1951), glomerulonephritis (Parelhoff, 1953), and penicillin hypersensitivity (Walsh and Zimmerman, 1953). Some considered these patients to have had "false-positive" L.E.-cell tests. The interpretation of others was that these patients were merely demonstrating the initial manifestations of SLE.

In later series of patients with rheumatoid arthritis, L.E.-cells were demonstrated in a significant proportion of cases (Kievits, Goslings, Schuit, and Hijmans, 1956; Ross and Clardy, 1956; Friedman, Sickley, Poske, Black, Bronsky, Hartz, Feldhake, Recder, and Katz, 1957; Sigler, Monto, Ensign, Wilson, Rebuck, and Lovett, 1958; Goslings, Kievits, Hazevoet, Hijmans, and Cats, 1961; Monto, Rizek, Rupe, and Rebuck, 1961). Numerous attempts to correlate the presence of L.E.-cells in rheumatoid arthritis with systemic (or "lupus-like") complications have led to variable conclusions. The question whether the L.E.-cell phenomenon in these patients represented a "false-positive" reaction or was indicative of SLE remained unsettled.

In a recent study from this hospital (Stevens, Abbey, and Shulman, 1963), a clinical analysis of patients with positive L.E.-cell tests was presented; after SLE, which was the most common diagnosis, rheumatoid arthritis proved to be second in frequency. The finding of L.E.-cells in patients with rheumatoid arthritis did not correlate well with systemic complications. However, the design of the study was such that too few patients with rheumatoid arthritis appeared in the randomly-sampled control group with negative L.E.-cell tests to permit an adequate comparison with those who had L.E.-cells.

The present study was designed, therefore, to determine in a controlled manner the clinical implications of a positive L.E.-cell test in patients with rheumatoid arthritis. The clinical features of 22 patients with rheumatoid arthritis and positive L.E.-cell tests are presented and compared with those of 41 patients with rheumatoid arthritis and negative L.E.-cell tests and of 22 rheumatoid arthritis patients in whom no test had been performed. The data show that the L.E.-cell phenomenon in rheumatoid arthritis is not associated with an excess of extra-articular systemic manifestations either of the type seen in lupus erythematosus or that described in rheumatoid disease.

Material and Methods

Patients

Diagnostic Criteria.—All patients included in this study had either typical deforming polyarthritis in combination with x-ray changes compatible with rheumatoid arthritis, or symmetrical polyarthritis of greater than 6 weeks' duration associated with morning stiffness and either x-ray changes compatible with rheumatoid arthritis or typical subcutaneous nodules.

Group 1. 22 Patients with L.E.-cells.—Of 3,660 patients who had L.E.-cell tests performed during the 47-month interval from January 1, 1955, to December 1, 1958, 22 patients with L.E.-cells were found to satisfy criteria for inclusion in this study. This group was

* Supported by National Foundation Grant for Clinical Study Center in Arthritis and USPHS National Institute of Arthritis and Metabolic Diseases Graduate Training Grant Numbers TI AM 5033-09 and TI AM 5033-10, and USPHS Grant IF 3 AM-21, 397-01.

† Present address: Department of Rheumatology and Physical Medicine, Middlesex Hospital, London.

obtained by a review of L.E.-cell tests and a subsequent analysis of the clinical record of each with a positive preparation. Of the 22 patients with L.E.-cells fulfilling the criteria for rheumatoid arthritis, ten were out-patients at the time of the positive L.E.-cell test; and the remaining twelve were in-patients.

Group 2. 41 Patients with Negative L.E.-cell Tests.—All control patients were selected from the index of discharge diagnoses of hospital in-patients. The index code for "rheumatoid arthritis" included not only patients with rheumatoid arthritis fulfilling our criteria but also patients in whom rheumatoid arthritis was included in the differential diagnosis. These latter patients, as well as those with variant forms of rheumatoid disease and juvenile rheumatoid arthritis, were excluded.

An attempt was made to obtain two control patients with negative L.E.-cell tests for each L.E.-cell positive patient matched by year; the desired number of patients could not be obtained, but after review of all indexed cases in 1957, only three less than the number required in this year were found, *i.e.* 41 instead of 44.

Group 3. 22 Patients with No L.E.-cell Test.—This group was included to evaluate a possible selection bias existing in those patients who had an L.E.-cell test performed. Patients were obtained from the same indexed hospital source as those in Group 2, and again, an attempt was made to obtain twice as many patients, matched on a yearly basis, as in Group 1. This was not possible, however, because it was increasingly difficult in 1956 and thereafter to obtain patients who had not had an L.E.-cell test performed.

Clinical Analysis

The hospital record on each of the 85 patients was summarized in detail and the data obtained at the time of the L.E.-cell test was analysed. In those patients in whom no test was performed (Group 3), the time of admission in the year selected for study was chosen arbitrarily.

Since Group 1 (L.E.-cell positive patients) was composed of out-patients as well as in-patients, these two sub-groups were analysed separately; any differences are presented.

The L.E.-cell tests were performed in the Special Haematology Laboratory of this hospital according to the method of Zinkham and Conley (1956) which was instituted as routine procedure in 1955. All other laboratory data were obtained from the general hospital laboratories. Tests for rheumatoid factor were not performed routinely during this period; and insufficient data were thus available for including such results in this analysis.

Statements of statistical significance are made only on the basis of the χ^2 analysis, using Yates' correction or, when mean values were compared, the "t" test.

Results

Age and Sex.—The majority of patients in each group proved to be women over the age of 40 years (Table I).

Women comprised three-quarters of those with L.E.-cells and approximately two-thirds of the control group. There were, therefore, no significant differences between the groups with respect to age or sex.

TABLE I
AGE, SEX, AND RACE OF PATIENTS

Group				1	2	3
L.E.-cell Test				Positive	Negative	No Test
No. of Patients				22	41	22
No. of Negroes				8	4	1
No. of Females				16	27	14
Age (yrs)	< 30			0	1	0
	30-39			2	4	1
	40-49			8	10	5
	50-59			8	14	7
	60-69			3	9	6
	70+			1	3	3
Mean				52	53	58
Range				34-73	20-75	35-86

Race.—A significant difference was found among the three groups with respect to race. Eight of the 22 patients with L.E.-cells, which included six of the ten out-patients, were Negroes, compared with four of 41 patients with a negative L.E.-cell test and one of 22 patients with no test. This difference was thus explained by the predominance of Negroes in the out-patients of Group 1.

Character of Joint Disease.—Clinical evidence of active inflammatory joint disease was present in more than one-half of the patients in Groups 1 and 2. On the other hand, only eight of 22 patients who had not had an L.E.-cell test performed (Group 3) had clinical signs of joint inflammation (Table II, opposite). It might appear, therefore, that active disease was the indication for obtaining an L.E.-cell test. However, these differences among the three groups were not statistically significant.

Patients included here, by definition, had clinically well-established joint disease. This was further confirmed when patients were classified by x-ray stage of disease (Steinbrocker, Traeger, and Batterman, 1949): three-fourths of the patients in each group were found to have moderate to severe joint

L.E.-CELLS IN RHEUMATOID ARTHRITIS

155

TABLE II
CHARACTER OF JOINT DISEASE

Group	1	2	3
L.E.-cell Test	Positive	Negative	No Test
No. of Patients	22	41	22
Joint Disease	Clinically Active Arthritis	27	8
	Stage of x-ray Changes	8	4
	I, II III, IV	31	17
Subcutaneous Nodules	11	16	9

Two patients in Group 2 and one patient in Group 3 did not have x rays.

disease (Stages III and IV) characterized by destruction of cartilage and bone, joint subluxation, and ulnar deviation in addition to the periarticular osteoporosis and narrowed joint spaces characteristic of Stages I and II. X rays were available in every case except two of the negative test group and one of the no test control group.

Subcutaneous Nodules.—Eleven of 22 patients with L.E.-cells, sixteen of the 41 in the negative test group, and nine of the 22 in the no test group were found to have subcutaneous nodules. When patients with and without nodules were compared, irrespective of L.E.-cell test, no differences were found with respect to age, sex, race, or clinical and laboratory features.

The occurrence of subcutaneous nodules was not a function of duration of disease (Figure). There were only three patients with disease of less than 1 year's duration, and none of these had nodules. However, there were seven patients with disease of greater than 24 years' duration who did not have nodules; and, as shown in the Figure, there was no progressive increase in the occurrence of subcutaneous nodules with increasing duration of disease.

Duration of Disease.—No significant difference in mean duration of disease was found when patients with L.E.-cells were compared with controls (Table III).

Figure.—Incidence of subcutaneous nodules by duration of disease.

TABLE III
DURATION OF DISEASE

Group	1	2	3
L.E.-cell Test	Positive	Negative	No Test
No. of Patients	Total	41	22
	Out-patients		
Mean Duration of Disease (yrs)	12.5	10.2	12.4
S.E.	± 2.3	± 1.63	± 1.50

However, while in-patients with L.E.-cells had disease averaging 18.6 yrs in duration, out-patients with L.E.-cells had a mean duration of disease of only 5.2 yrs. This difference is highly significant ($P < 0.01$), as is the difference between the in-patients with L.E.-cells and the in-patient controls ($P < 0.02$).

Clinical Features.—Systemic involvement was infrequent in all three groups and was no more frequent among patients with L.E.-cells than controls (Table IV).

Except for one patient with pleurisy and another with non-bacterial pneumonitis, clinical manifestations commonly associated with SLE were lacking in the L.E.-cell positive group. However, seven control patients had unexplained low-grade fever and two others had a macular erythematous skin rash. One patient had psoriasis. In none of the 85 patients was there a typical butterfly rash or evidence of renal disease. The only two patients with cardiac disease were controls with rheumatic mitral insufficiency.

Reticulo-endothelial involvement was the most prominent finding, with splenomegaly in five patients and generalized lymphadenopathy in six. Two of those with splenomegaly had Felty's syndrome.

Finally, such "rheumatoid-like" features as leg ulcers and peripheral neuritis were not found in any patient.

Laboratory Investigations (Table V, opposite)

Anaemia.—Five patients with L.E.-cells and sixteen controls had an anaemia for which no cause other than rheumatoid arthritis was found. There was no evidence of a haemolytic process in any patient. Two additional patients with a negative L.E.-cell test had an iron deficiency anaemia

secondary to menorrhagia. There were thus no differences between the L.E.-cell positive patients and their controls with respect to the occurrence of anaemia. Moreover, the mean haematocrits of the three groups were remarkably similar.

White Blood Cell Count.—The frequency of leucopenia was significantly greater in patients with L.E.-cells than in the controls ($P < 0.05$). Six of the 22 L.E.-cell positive patients as compared to four of 63 controls had a white cell count of less than 5,000 cells/mm.³. Three of those with L.E.-cells and two controls had white cell counts below 3,000 cells/mm.³

None of the patients with L.E.-cells had an unexplained leucocytosis. There was, however, one patient in this group with an *E. coli* urinary tract infection who had a raised white cell count which returned to normal after antibiotic therapy. In contrast, there were twelve control patients with unexplained leucocytosis. With the exception of two patients in Group 2 who had white cell counts of 19,000 and 20,200 cells/mm.³ respectively, the leucocytosis among the controls was of modest degree (10,000 to 13,000).

Finally, when mean white cell counts for the three groups were compared, patients with L.E.-cells were found to have a significantly lower value than the controls ($P < 0.01$).

Serum Globulin.—Four of 21 patients with L.E.-cells and three of 41 controls had a serum globulin greater than 3.9 g. per cent. Although this difference was not significant, the mean serum globulin (3.30 g. per cent.) for patients with L.E.-cells was significantly higher than that (2.80 g. per cent.) for the controls ($P = 0.02$). In view of this finding, patients with L.E.-cells were analysed with regard to the in- and out-patient subgroups, but mean serum globulin for out-patients (3.40 g. per cent.) did not

TABLE IV
CLINICAL FEATURES

Group	1	2	3
L.E.-cell Test	Positive	Negative	No Test
No. of Patients	22	41	22
Clinical Features	Fever	0	2
	Skin rash	0	0
	Pneumonitis, pleurisy	2	0
	Lymphadenopathy, generalized	1	1
	Splenomegaly (Felty's syndrome)	2 (1)	1 (1)
	Rheumatic valvular disease	0	1
Renal disease, cytooid bodies, myositis, Raynaud's phenomenon, peripheral neuritis, leg ulcers			
	0	0	0

* One patient had psoriasis.

L.E.-CELLS IN RHEUMATOID ARTHRITIS

157

TABLE V
LABORATORY INVESTIGATIONS

Group											1	2	3
L.E.-cell Test											Positive	Negative	No Test
No. of Patients											22	41	22
Laboratory Investigations	Anaemia										5	11	5
	Leucopenia										6	2	2
	Leucocytosis										0	8	4
	Thrombocytopenia										1	0	0
	Raised erythrocyte sedimentation rate										17 (of 21)	26 (of 39)	13 (of 19)
	Hyperglobulinaemia										4 (of 21)	2 (of 29)	1 (of 12)
	Biologic false-positive serological test for syphilis, chronic										0	1	0
	Mean haematocrit (per cent.)										40	41	42
	Mean erythrocyte sedimentation rate (mm./hr)										25	24	24
	White blood cell count/mm. ³												
Mean										6,000	8,300	7,800	
S.E.										±570	±550	±940	
Serum globulin (g. per cent.)													
Mean										3·30	2·80	2·80	
S.E.										±0·17	±0·14	±0·27	

Anaemia = haematocrit <40 in males; <37 in females.
 Leucopenia = white blood cell count <5,000/mm.³
 Leucocytosis = white blood cell count >10,000/mm.³
 Thrombocytopenia = <150,000 platelets/mm.³
 Raised Erythrocyte Sedimentation Rate = erythrocyte sedimentation rate (Wintrobe) >20 mm./hr.
 Hyperglobulinaemia = serum globulin 4 g. per cent. or greater.

differ significantly from that for in-patients (3.30 g. per cent.) despite the preponderance of Negroes in the clinic population.

Other Features.—A raised erythrocyte sedimentation rate was a frequent occurrence in all groups—seventeen of 21 patients with L.E.-cells and 39 of 58 controls. The mean corrected rate for each group was essentially the same.

Only one patient (with L.E.-cells) had thrombocytopenia with a platelet count of 35,000/mm.³

Only one patient (with a negative L.E.-cell test) had a chronic biologic false-positive test for syphilis.

No other laboratory abnormalities were found.

Drug Therapy.—In view of the significantly lower mean white cell counts among patients with L.E.-cells compared with controls, the groups were analysed with respect to drug therapy. It was found that significantly more control patients (26 of 63) than L.E.-cell positive patients (three of 22) were receiving antirheumatic agents which could have had a potential depressant effect upon the myeloid series ($P < 0.05$). Furthermore, none of the ten patients with L.E.-cells and only four of the 22 controls who were treated with corticosteroids had an unexplained leucocytosis. Therefore, neither the increased frequency with which leucopenia and lower mean white cell counts occurred among patients with L.E.-cells nor the increased frequency

of leucocytosis among controls could be satisfactorily explained on the basis of drug administration.

Drug reactions were no more frequent among patients with L.E.-cells than among controls. Five of thirteen patients in Group 1 who had received gold had a history of a gold reaction as compared with seven of 21 controls. With regard to all other drugs, there were only three additional instances of hypersensitivity reaction among the L.E.-cell positive patients and ten among the controls.

Discussion

The finding of L.E.-cells in patients with rheumatoid arthritis had given support to the concept that SLE and rheumatoid arthritis were closely related disorders. However, neither the frequency with which L.E.-cells occur in rheumatoid arthritis nor the clinical implications of this finding have been satisfactorily determined.

All patients included in this study had, by definition, advanced rheumatoid arthritis, with destructive x-ray changes (Stages III and IV) in more than three-quarters of the group. The pattern of joint involvement in all patients would meet the 1958 ARA criteria (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) for "definite" or "classical" rheumatoid arthritis. (However, these designations have been intentionally avoided in view of the ARA exclusion pertinent to Group 1, based on the presence of L.E.-cells.) Although fewer patients in Group

III (no L.E.-cell test performed) had active articular inflammation at the time of the evaluation, there was no significant difference between patients with L.E.-cells and controls in this regard when either clinical signs or raised erythrocyte sedimentation rate were considered. This is in contrast to the observations in patients with SLE which have shown L.E.-cell positivity to be more closely associated with periods of disease activity than with remissions (Rothfield and Pace, 1962). Therefore, the character of joint involvement in patients with L.E.-cells was indistinguishable from that found in controls.

Moreover, subcutaneous nodules, the hallmark of rheumatoid disease, occurred no more frequently among those patients with L.E.-cells than in controls. This data would be in agreement with the observations of Kievits and others (1956), but differs from the correlation of nodules with positive L.E.-cell tests reported by other workers (Friedman and others, 1957; Willkens and Decker, 1963). Furthermore, when patients with subcutaneous nodules were compared with patients without nodules, irrespective of L.E.-cell testing, no significant differences were found. As noted by Sharp, Calkins, Cohen, Schubart, and Calabro (1964), there was no increased frequency of nodules with increasing duration of disease.

It should be emphasized that the patients presented here had, by definition, well-established rheumatoid arthritis. It is in such patients that one would anticipate finding such extra-articular complications as peripheral neuritis, leg ulcers, myopathy, arteritis, and Felty's syndrome. At the outset, one major reason for selecting a control group in which no L.E.-cell test had been performed was to evaluate whether or not a test was done only in patients who had such complicating systemic disease. The infrequent occurrence of systemic complications in all groups, regardless of L.E.-cell testing, was not only surprising but also indicated in this hospital the lack of any clinical bias in performing an L.E.-cell test in patients with rheumatoid arthritis.

In contrast to the original report of Kievits and others (1956), splenomegaly was not more frequent among patients with L.E.-cells. Moreover, Felty's syndrome, which was so prominent in the select series of patients reported by Friedman and others (1957), was found in only two of our patients. One of these had L.E.-cells and the other was a control in whom no test was performed. In no instance was there clinical evidence suggesting vasculitis.

An important distinguishing feature between patients with SLE and those with rheumatoid arthritis is the frequent occurrence of glomerulonephritis

in lupus and its virtual absence in rheumatoid arthritis. In none of the 85 patients here reported, regardless of the L.E.-cell test, was there clinical or laboratory evidence of glomerular disease. Urinary sediments were normal and proteinuria was lacking except in the single individual with a urinary tract infection due to *E. coli*. The significance of the more frequent occurrence of abnormal urinary sediment among Kievits' patients with L.E.-cells than among controls remains obscure, for in view of their follow-up data 5 years later (Goslings and others, 1961) such findings could not be associated with any progressive renal disease.

Of interest in this regard is the more recent report of fourteen patients with severe deforming rheumatoid arthritis (Willkens and Decker, 1963), in which case selection was based upon the presence of anti-nuclear factor. L.E.-cells were demonstrated in eight individuals. Proteinuria was noted in half the group, five of the seven patients with proteinuria being among those with L.E.-cells. The clinical picture was not that of glomerulonephritis in any instance; and in two patients with proteinuria and L.E.-cells who came to autopsy no evidence of membranous changes was found. Both patients had nephrosclerosis and, in one, acute arteritis and pyelonephritis were found as well. Pathological lesions most compatible with the diagnosis of SLE were not present in any organ. The lack of renal disease in our patients would, therefore, be in agreement with the observations of most investigators and with the pathological data of Pollak, Pirani, Steck, and Kark (1962).

In contrast to these observations and the results of the present investigation is the report by Ross and Clardy (1956) of renal disease occurring in sixteen of eighteen patients with rheumatoid arthritis and L.E.-cells. Subsequent follow-up data on this group would be of the utmost importance since, at the time of evaluation, these patients were at an early stage of disease (Stages I and II) and for the most part lacked the destructive joint changes so characteristic of our patients (Stages III and IV). The difficulty in distinguishing early rheumatoid arthritis from SLE manifested predominantly by articular involvement is a major clinical problem which may be reflected in these authors' observations.

The observations presented here would fail to support the concept that the L.E.-cell phenomenon in rheumatoid arthritis implies "lupus-like" disease. Of interest are the two features which were significantly different in patients with rheumatoid arthritis and L.E.-cells compared with controls.

(1) The average white blood cell count in patients with the L.E.-cell phenomenon was lower than in

controls and, furthermore, there was also an increased frequency of leucopenia. Although leucopenia occurred more frequently among those with L.E.-cells, it was no more severe in this group than in controls. In none of the three groups could the occurrence of white cell depression be related to current or past therapy. While leucopenia is a frequent feature of SLE, previous studies have paid relatively little attention to this finding in rheumatoid arthritis except when it has occurred in a setting of Felty's syndrome. However, in the selected series of patients with advanced rheumatoid arthritis and antinuclear factor described by Willkens and Decker (1963), a white blood cell count of less than 5,000 cells/mm.³ was a prominent finding in half the cases, five of whom were among the eight patients with L.E.-cells.

(2) The serum globulin level was higher in those patients with L.E.-cells than in the controls. Nevertheless, the frequency of marked hyperglobulinaemia was the same for these patients and control patients. This increase in serum globulin could not be explained by the greater proportion of Negroes among those with L.E.-cells. In fact, when mean serum globulin levels were determined from Negroes and whites, the values were surprisingly similar.

With data such as these, one may certainly question the basis for separating patients with rheumatoid arthritis and L.E.-cells from those with negative tests on other than theoretical grounds. Certainly, except for the trend toward leucopenia and hyperglobulinaemia, "lupus-like" features are noticeably absent.

Even as regards the L.E.-cell test *per se*, differences exist between patients with rheumatoid arthritis and those with SLE. As shown previously (Zimmer and Hargraves, 1952; Monto and others, 1961; Stevens and others, 1963), the degree of positivity of the L.E.-cell test is generally less in those with rheumatoid arthritis than in SLE. In only three of the 22 patients in Group 1 were numerous L.E.-cells found on testing. In three others, only a single L.E.-cell was noted after careful re-examination, while in the majority the preparation showed a small number of L.E.-cells and variable amounts of extracellular material.

Even more impressive than the differences in degree of L.E.-cell positivity in patients with SLE and rheumatoid arthritis is the widely discrepant frequency with which L.E.-cells are found in the two disorders. While the vast majority of patients with SLE have the L.E.-cell phenomenon demonstrable at some time during the course of their disease,

L.E.-cells occur infrequently among individuals with rheumatoid arthritis. Despite the increasing tendency to perform L.E.-cell tests in this hospital (as evidenced by the difficulty in obtaining control patients for this study who had no test performed), only 22 individuals with rheumatoid arthritis and L.E.-cells were found during the 47-month interval. Furthermore, of seventy patients with rheumatoid arthritis currently attending our clinic, only two have been found to have L.E.-cells. Such differences are difficult to explain if the L.E.-cell phenomenon is a reflection of a single pathogenetic mechanism common to both disorders.

Summary

Clinical analyses of the following groups of patients with rheumatoid arthritis are presented:

- (1) 22 patients with L.E.-cells;
- (2) 41 patients with a negative L.E.-cell test;
- (3) 22 patients who had no test performed.

Patients with rheumatoid arthritis and L.E.-cells were remarkably similar to those in the two control groups with regard to inflammation of joints, duration of arthritis, and presence of subcutaneous nodules. Systemic involvement of any sort was remarkably infrequent in all groups of patients and occurred no more frequently in those with L.E.-cells than in the rest.

Leucopenia was more frequent, and the mean white blood cell count was lower in the patients with L.E.-cells. Also, the mean serum globulin level was higher in this group. These were the only statistically significant differences observed and were of small magnitude.

It would appear from these data that there is little justification on clinical grounds for considering rheumatoid arthritis with L.E.-cells to be either an entity distinct from rheumatoid arthritis, or a variant of systemic lupus erythematosus.

REFERENCES

- Dubois, E. L. (1953). *Arch. intern. Med.*, **92**, 168.
 Friedman, I. A., Sickley, J. F., Poske, R. M., Black, A., Bronsky, D., Hartz, W. H., Jr., Feldhake, C., Reeder, P. S., and Katz, E. M. (1957). *Ibid.*, **46**, 1113.
 Goslings, J., Kievits, J. H., Hazevoet, H. M., Hijmans, W., and Cats, A. (1961). "Atti del X Congresso del Lega Internazionale contro il Reumatismo", Vol. 1, p. 328.
 Hargraves, M. M., Richmond, H., and Morton, R. (1948). *Proc. Mayo Clin.*, **23**, 25.
 Harvey, A. M., Shulman, L. E., Tumulty, P. A., Conley, C. L., and Schoenrich, E. H. (1954). *Medicine (Baltimore)*, **33**, 291.

- Kievits, J. H., Goslings, J., Schuit, H. R. E., and Hijmans, W. (1956). *Ann. rheum. Dis.*, **15**, 211.
- Lee, S. L. (1955). *J. Mt Sinai Hosp.*, **22**, 74.
- , Michael, S. R., and Vural, I. L. (1951). *Amer. J. Med.*, **10**, 446.
- Louis, J., and Limarzi, L. R. (1958). *J. chron. Dis.*, **8**, 596.
- Monto, R. W., Rizek, R. A., Rupe, C. E., and Rebuck, J. W. (1961). "L.E. Cell: Significance and Relation to Collagen Disease". In "Inflammation and Diseases of Connective Tissue: A Hahneman Symposium", ed. L. C. Mills and J. H. Moyer, p. 200. Saunders, Philadelphia.
- Parelhoff, M. E. (1953). *Sinai Hosp. J. (Baltimore)*, **2**, no. 2, p. 12.
- Pollak, V. E., Pirani, C. L., Steck, I. E., and Kark, R. M. (1962). *Arthr. and Rheum.*, **5**, 1.
- Ropes, M. W., Bennett, G. A., Cobb, S., Jacox, R., and Jessar, R. A. (1959). *Ann. rheum. Dis.*, **18**, 49.
- Ross, S. W., and Clardy, E. K. (1956). *Sth. med. J. (Bgham, Ala.)*, **49**, 553.
- Rothfield, N. F., and Pace, N. (1962). *New Engl. J. Med.*, **266**, 535.
- Sharp, J. T., Calkins, E., Cohen, A. S., Schubart, A. F., and Calabro, J. J. (1964). *Medicine (Baltimore)*, **43**, 41.
- Sigler, J. W., Monto, R. W., Ensign, D. C., Wilson, G. M., Jr., Rebuck, J. W., and Lovett, J. D. (1958). *Arthr. and Rheum.*, **1**, 115.
- Steinbrocker, O., Traeger, C. H., and Batterman, R. C. (1949). *J. Amer. med. Ass.*, **140**, 659.
- Stevens, M. B., Abbey, H., and Shulman, L. E. (1963). *New Engl. J. Med.*, **268**, 976.
- Walsh, J. R., and Zimmerman, H. J. (1953). *Blood*, **8**, 65.
- Wilkinson, M., and Sacker, L. S. (1957). *Brit. med. J.*, **2**, 661.
- Willkens, R. F., and Decker, J. L. (1963). *Arthr. and Rheum.*, **6**, 720.
- Zimmer, F. E., and Hargraves, M. M. (1952). *Proc. Mayo Clin.*, **27**, 424.
- Zinkham, W. H., and Conley, C. L. (1956). *Bull. Johns Hopk. Hosp.*, **98**, 102.

Importance clinique du phénomène LE dans l'arthrite rhumatismale

RÉSUMÉ

On présente des analyses cliniques de groupes suivants de malades atteints d'arthrite rhumatismale:

- (1) 22 malades avec cellules LE;
- (2) 41 malades au test pour cellules LE négatif;
- (3) 22 malades chez qui on n'a pas procédé au test.

Les malades atteints d'arthrite rhumatismale au test pour cellules LE positif se distinguaient peu de ceux dans les deux groupes témoins en ce qui concerne l'inflammation articulaire, la durée de l'arthrite et la présence des nodules souscutanés. Toute atteinte généralisée était fort rare dans tous les groupes des malades et ne survenait pas plus souvent chez ceux qui avaient des cellules LE que chez les autres.

La leucopénie était plus fréquente et la valeur leucocytaire moyenne plus basse chez les malades qui présentaient le phénomène LE. De même, le taux sérique de la globuline était plus élevé dans ce groupe. C'étaient les seules différences statistiquement appréciables que l'on avait observé et leur magnitude était faible.

Ces faits semblent indiquer qu'on a peu de raisons cliniques pour considérer l'arthrite rhumatismale avec des cellules LE comme une entité distincte de l'arthrite rhumatismale ou comme une variante du lupus érythémateux disséminé.

Significado clínico del fenómeno LE en la artritis reumatoide

SUMARIO

Se presentan análisis clínicos de siguientes grupos de enfermos con artritis reumatoide:

- (1) 22 enfermos con células LE;
- (2) 41 enfermos con el fenómeno LE negativo;
- (3) 22 enfermos en quienes no se hizo el test.

Los enfermos con artritis reumatoide y con células LE se distinguieron poco de los en los grupos testigos respecto a la inflamación articular, la duración de la artritis o la presencia de nódulos subcutáneos. Implicación sistémica de cualquier suerte en todos los grupos de enfermos fué rara y no ocurría con más frecuencia en los con células LE que en los demás.

La leucopenia fué más frecuente y el valor leucocitario medio más bajo en los enfermos que presentaron el fenómeno LE. Asimismo, el valor sérico de la globulina fué más alto en este grupo. Estas fueron las únicas diferencias estadísticamente apreciables observadas y su magnitud fué poca.

Estos hechos parecen indicar de que hay pocas razones clínicas para considerar la artritis reumatoide con células LE como una entidad distinta de la artritis reumatoide o como una variante del lupus eritematoso diseminado.