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THE L.E. CELL: SIGNIFICANCE AND RELATION TO COLLAGEN DISEASE

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The lupus erythematosus (L.E.) cell phenomenon has been available for clinical application for over a decade. It is timely that the usefulness of this unique system be reviewed in a large general hospital. Of considerable practical importance in medicine is the evaluation of the L.E. cell in the light of the natural history of systemic lupus erythematosus (S.L.E.) as well as in the interpretation of the "false negative" and "false positive" reactions.[3,4]

It was the purpose of the present study to examine the records of all the patients from Henry Ford Hospital who demonstrated the L.E. cell phenomenon during the past ten years. As a counterpart, the records of all of the patients with collagen diseases (S.L.E., polyarteritis nodosa, scleroderma, dermatomyositis, rheumatoid arthritis, rheumatic fever and discoid lupus erythematosus) were reviewed in reference to the occurrence of the L.E. cell phenomenon. These observations have utilized long term observation to clarify relationship of the L.E. cell to the clinical disorders.

It has been suggested that the finding of one authentic L.E. cell establishes a positive result and a diagnosis of S.L.E. Others have required that five or more L.E. cells in a count of 500 polymorphonuclear leukocytes be present for a positive test.[1] In the patients reported in this review the L.E. cell test was performed on bone marrow specimens until 1955; after this time peripheral blood (two-hour blood clot) preparations were employed.[5]

In 1950 a total of 18 L.E. cell preparations from bone marrows were done at the Henry Ford Hospital; since then, the number of tests has been mounting through the years to approximately 3000 in 1959. This figure will exceed 4000 in 1960 (Fig. 1). Since 1954 the incidence of S.L.E. has averaged 20 to 25 patients a year. This chart must be interpreted in light of our changing concepts of S.L.E., the use

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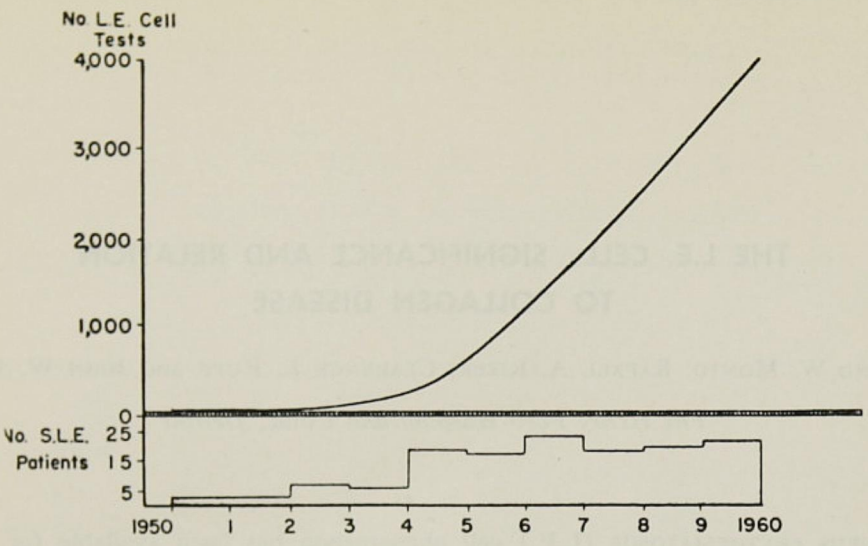

Figure 1

The number of L.E. cell tests performed in relation to the number of patients diagnosed yearly with S.L.E.

of peripheral blood L.E. techniques and a 20 per cent increase in new patient registrations between 1955 and 1960. The performance of the L.E. test in large numbers in diversified diseases other than S.L.E. has afforded an unusual opportunity for the clinical evaluation of this phenomenon.

Table 1 lists the diseases commonly considered to be of connnective tissue origin. Two of 51 tested patients with discoid L.E. demonstrated the phenomenon. One of the two subsequently developed S.L.E. and an L.E. cell count greater than five. All patients diagnosed as S.L.E. (156) were tested. L.E. cells were not found in 22 cases, a percentage of 14.0. When the patients demonstrating only one to four L.E. cells are included as "negative" the percentage reaches 26.3. Although the L.E. cell phenomenon was noted in scleroderma, dermatomyositis, polyarteritis and rheumatic fever at the frequency seen in Table I, the number of L.E. cells did not exceed five. In rheumatoid arthritis (R.A.) L.E. cells in varying numbers were found in 68 of 455 patients tested, a percentage of 15.2.

Table I

INCIDENCE OF L.E. CELL PHENOMENON IN DISEASES OF CONNECTIVE TISSUE

	Total	Tested	L.E. Phenomenon
Discoid lupus erythematosus	102	51	2
Systemic lupus erythematosus	156	156	134
Scleroderma	38	12	3
Dermatomyositis	35	26	3
Polyarteritis	48	39	3
Rheumatic fever	151	28	11
Rheumatoid arthritis	891	455	68

Table II

PATIENTS DEMONSTRATING FIVE OR MORE L.E. CELLS WITH DIAGNOSES OTHER THAN S.L.E.

Rheumatoid arthritis	18	Parkinsonism	1
Pulmonary tuberculosis	1	Aplastic anemia, benign thymoma	1
Chronic dermatitis	1	Chronic hepatitis	1
Chronic lymphocytic leukemia	1	Necrotizing papillitis of the kidney	1
Erythrocytic leukemia	1	Pelvic abscess and pyelonephritis	1
Hodgkin's disease	1	Hydralazine reaction	1

Table 2 lists 29 patients with diseases other than S.L.E. demonstrating five or more L.E. cells. The criteria for rheumatoid arthritis were those of the American Rheumatism Association. It is to be emphasized that we have listed as R.A. those patients presenting a classic clinical picture of R.A. without clinical and laboratory evidence of S.L.E.[2] The largest number (32) of L.E. cells seen in a patient not considered to have S.L.E. occurred in one with R.A.

Disease other than S.L.E. with incidence of four or less L.E. cells are tabulated in Table 3. There were more than 147 patients in 35 disease categories. R.A. again comprised a major part of this group. The high incidence of connective tissue disorders as well as auto-immune and vascular diseases is noted.

Table III

PATIENTS DEMONSTRATING FOUR OR LESS L.E. CELLS WITH DIAGNOSES OTHER THAN S.L.E.

Connective tissue diseases		Arteriosclerotic heart disease, generalized	
Rheumatoid arthritis	50	arteriosclerosis	5
Rheumatic fever	11	Psychoneurosis	3
Polyarteritis	3	Metabolic diseases (gout, porphyria)	3
Dermatomyositis	3	Malignant diseases (leukemia, carcinoma,	
Scleroderma	3	sarcoma)	4
Undifferentiated collagen diseases	2	Laennec's cirrhosis	2
Discoid L.E.	1	Osteoarthritis	2
Hydralazine reaction	1	Polyserositis (Armenian disease)	2
Idiopathic thrombocytopenic purpura	2	Chronic pulmonary fibrosis	1
Acquired hemolytic anemia	2	Sarcoidosis	1
Pernicious anemia	1	Brachial neuritis	1
Infections (septicemia, S.B.E.,		Pancreatitis and duodenitis	1
bronchopneumonia, virus)	11	Parkinsonism	1
Miscellaneous skin diseases (erythema		Menopausal syndrome	1
multiforme, urticaria, chronic		Myeloid metaplasia	1
dermatitis, etc.)	7	Irritable colon	1
Miscellaneous kidney diseases (pyelonephritis,		Endometriosis	1
chronic glomerulonephritis, nephrosis)	9	Calcific pericarditis	1
Miscellaneous vascular disorders		Toxic nodular goiter	1
(Raynaud's, thrombophlebitis)	5	No final diagnosis	6

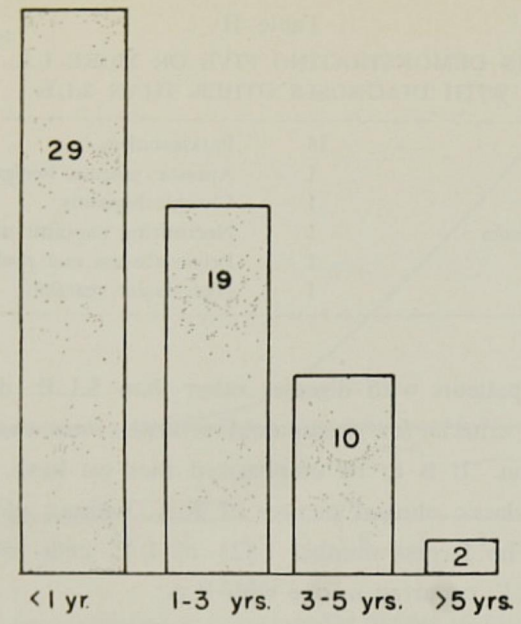

Figure 2

Patients demonstrating five or more L.E. cells with diagnoses other than S.L.E.—period of observation.

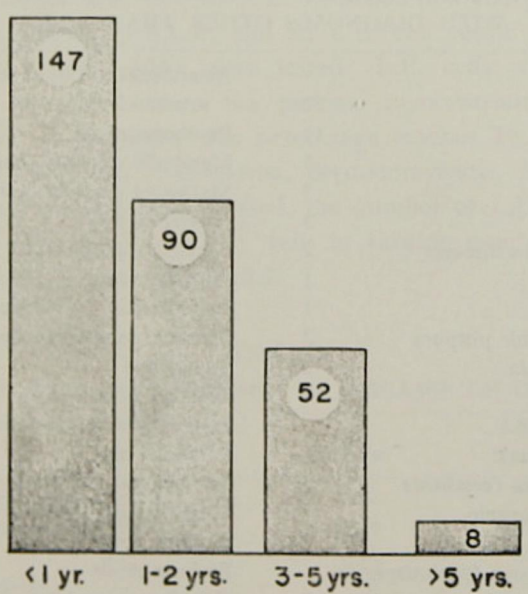

Figure 3

Patients demonstrating four or less L.E. cells with diagnoses other than S.L.E.—period of observation.

Because of the natural history of S.L.E., it was imperative to obtain observations on the progress of the group of patients not considered to have S.L.E. but demonstrating the L.E. phenomenon. Figure 2 incidates the period of observation on 29 of these patients with five or more L.E. cells, and Figure 3 indicates that on the 147 patients with four or less L.E. cells. During the period of follow-up only one of these patients was considered possibly to have S.L.E. on the basis of necropsy findings. This patient, with generalized Hodgkin's disease, demonstrated "onion-skinning" in the spleen and plasmacellular interstitial nephritis. In this study, the tissues were not surveyed with antiglobulin fluorescent microscopy. It has been estimated that approximately two-thirds of patients with S.L.E. not under hormonal therapy will demonstrate relapse in a three-year interval. Less than 50 per cent of this group of patients received steroid therapy.

Figure 4 indicates the time interval required for patients with S.L.E. to develop five or more L.E. cells. Of 17 patients with no L.E. cells when the clinical diagnosis of S.L.E. was made, 11 demonstrated five or more cells in six months, two in 9 months, one in 12 months, one in 22 months, and one in 36 months. The time interval required for patients having originally but one to four L.E. cells with the clinical diagnosis of S.L.E. to develop five or more L.E. cells was as follows: less than one month, three patients; less than one year, three patients; one to three years, six patients; and more than three years, three patients.

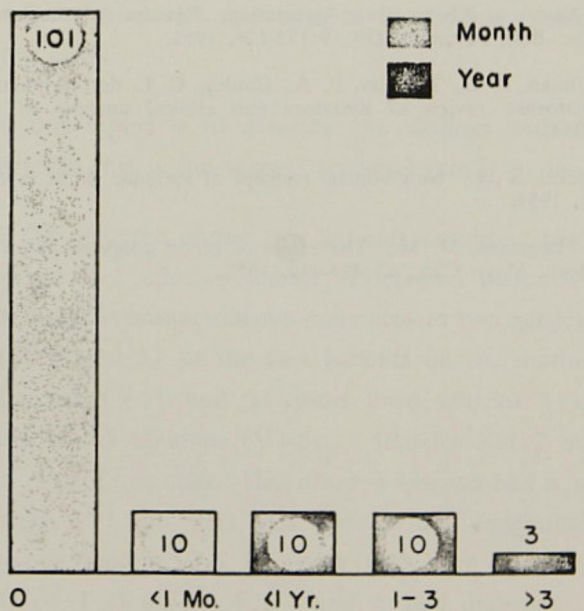

Figure 4

Time interval required for patients with a diagnosis of S.L.E. to develop five or more L.E. cells.

Summary And Conclusions

The specificity and sensitivity of the L.E. cell phenomenon were evaluted by a large and lengthy retrospective study in a general hospital. The incidence of S.L.E. does not appear to be increasing. The L.E. cell phenomenon was observed in 310 patients; 176 or 57 per cent of these patients were not considered to fulfill the clinical or laboratory criteria of S.L.E. Of this group, 70 patients (40 per cent) were categorized as having a connective tissue disease in which rheumatoid arthritis was dominant. Every patient demonstrating more than 32 L.E. cells was found to have S.L.E. L.E. cells were not found in 22 patients (14 per cent) believed to have S.L.E. Of the patients with five or more L.E. cells, 28 (25.6 per cent) were not believed to have S.L.E. On the basis that five or more cells constitute a "positive" test, in a series of 10,000 preparations less than 0.3 per cent were considered "false positives."

It is concluded that L.E. cell phenomenon, while a characteristic of S.L.E. lacks both specificity and sensitivity as a diagnostic test. At present, with generally available techniques, the diagnosis of S.L.E. can be made most accurately by considering all factors, both clinical and laboratory, of which the L.E. cell phenomenon is of major importance.

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