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ORIGINAL ARTICLES

SYSTEMIC LUPUS ERYTHEMATOSUS

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Systemic lupus erythematosus has received a very limited notice in India until late but more attention is being drawn towards it in recent years. Perusal of the Indian literature shows that articles on record are mostly comprised of individual case reports, e. g. by Konar and Banerji (1950); Mathur (1953); Rao and Reddy (1955); and Desai and Bhandarkar (1955).

It was designated as "Lupus" by Cazenave in 1851 because of the presence of destruction and scarring similar to skin tuberculosis in the lesions. The word "Erythematodes" was added to it on account of the erythema and which also differentiated it from other forms of lupus This designation "Lupus Erythematodes", though not appropriate, has persisted in the literature because of its long usage, there being no association of the disease with tuberculosis as thought of earlier. Various prefixes used by different workers to indicate its constitutional character and visceral involvement have also come under lot of criticism. For example, the prefix "Disseminated" implies spread of the disease-process from a pre-existing local focus whilst this disease is wide-spread from the very beginning with simultaneous involvement of the connective tissue all over the body. Similarly the term "Malignant" used by some has not been liked by others. It is alleged that it is unnecessarily very frightening as its course, though often malignant, can be chronic and smouldering with remissions of long duration. The adjective "Systemic" on the other hand seems justified and much more appropriate. It aptly signifies its systemic nature involving various systems at one time or the other during its course.

Early descriptions of this disease by Pierre Rayer (1857) and Thedore Biett (1828) pertained to its skin lesions only. Constitutional character was recognised

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by Kaposi (1872) and involvement of various viscera by Sir William Osler in the last decade of 19th Century. Later in 1923, changing aspect of this disorder from a localised to a generalised visceral disease was brought to lime-light by Libman and Sacks with publication of their paper entitled "A typical verrucous endocarditis". Then, Klemperer in 1942 introduced his concept of "collagen diseases" on the basis of Fibrinoid Degeneration which he found affecting principally the ground sustance of the collagenous tissues of the body in this as well as in other allied disorders like Dermatomyositis, Rheumatoid arthritis and Peri-arteritis nodosa. But the discovery of L. E. cells by Hargraves, Richmond and Morten in the year 1948 is the most important and significant development. This discovery has not only provided us with another diagnostic aid but also had led to the discovery of various other auto-immune bodies circulating in the blood. And as this serological variability has multiplied the evidence has simultaneously accumulated in favour of its being a "Hypersensitivity phenomenon of the auto-immune type". It must, however, be added that this postulation is, as yet, in a conjectural stage and its significance still remains to be assessed.

Material: Our interest in the subject got stimulated by our first two cases who got admitted under our care in 1955 as cases of skin lesions with acute illnesses, and diagnosed as systemic lupus erythematosus on subsequent follow up. Since then, 14 more cases have been collected from the Dermatologic and Medical Wards of the V. J. Hospital, Amritsar and 4 from the All India Institute of Medical Sciences, New Delhi were further added up by one of the authors (K. C. K.) who subsequently went to the Institute. These 20 cases form the material for this co-operative study. Attention to these cases was drawn by their striking clinical evidence and later on diagnosis was established by finding L. E Cells in most of these cases and by other known criteria.

The purpose of this paper is to analyse the clinical data collected, and report on the various dermatologic and medical aspects of this disease as met with in these cases.

CLINICAL ANALYSIS.

Age and Sex: Table below refers to the distribution by age and sex. Females constitute nearly 65% of our cases.

TABLE No. I (Age & Sex)

Age at onset.	10-15 yrs.	15 20 yrs.	20-25 yrs.	25-30 yrs.	30-35 yrs.	35-40 yrs.	40-45 yrs.	45-50 yrs.	Abve 50 yrs	Total	%
Male	—	2	2	1	—	—	—	1	1	7	35%
Female	1	5	4	1		—	—	1	1	13	65%

The age at on set varies from 10 to 53 years, majority of the cases falling in the age group 15-25 i. e. 13 out of 20. Its incidence as reported in the literature,

is most common during adolescence and early adult life but cases occuring from 3 months to 70 years have been reported.

The First Manifestation: Information regarding the first manifestation of the disease at its onset is given in the table (Table No. 2) below. Nine cases, in our series.

TABLE 2 (First Manifestation)

		No. of Cases
1. Polyarthritis or arthralgia	...	9
2. Upper respiratory tract	...	4
3. Skin eruptions	...	4
4. Fever	...	1
5. Ocular	...	1
6. Glandular enlargement	...	1
	Total	20

Started with polyarthritis, 4 with symptoms pertaining to upper respiratory tract, 4 with cutaneous lesions, 1 with fever, 1 with ocular symptoms and 1 with glandular enlargement in the neck. It is well known that disease may start differently in different persons and dysfunction in any system may be the presenting feature.

Clinical Features in Order of Frequency: The clinical features as presented by our cases varied. They are summarised and given in the table (Table No. 3) below in order of frequency.

TABLE No. 3 (Clinical features in order of frequency)

Clinical features	Total No. of cases	%
1. Fever	20	100%
2. Anaemia	20	100%
3. Cutaneous lesions	18	90%
4. Arthritis	16	80%
5. Involvement of heart	10	50%
6. Pleuro-pulmonary involvement	9	45%
7. Lymph node enlargement	8	40%
8. Mucous membrane involvement	8	40%
9. Neuro-psychiatric symptoms	6	30%
10. Renal symptoms	7	35%
11. Gastro-intestinal symptoms	6	30%
12. Hepatic enlargement	4	20%
13. Splenic enlargement	2	10%
14. Eye involvement	1	5%

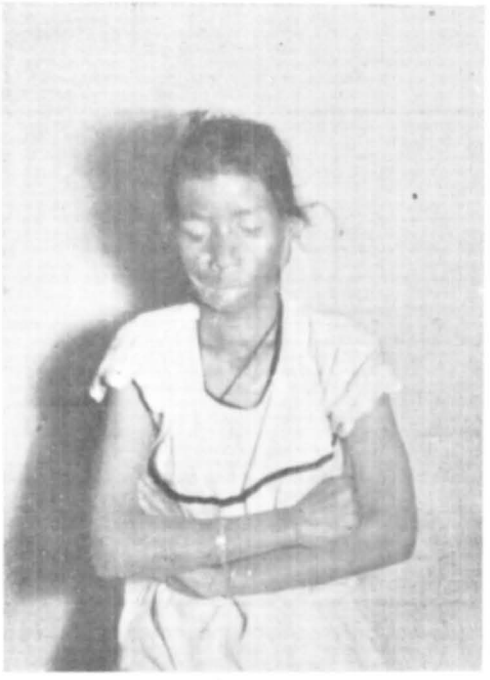
Fever and Anaemia: Fever, which was of irregular type occuring in bouts and anaemia which was present at one or the other stage of the disease were present in all the cases.

Rash : Incidence of rash in our series was rather high compared to other workers. It may, however, be emphasized that disease can exist without skin lesions as has happened in 2 of our cases. It is likely that many cases without rash have escaped notice. Of the rashes noticed, various types that met with are given in the table (Table No. 4) below.

TABLE 4 (Skin lesions)

Type	No. of cases
1. Erythemato-Squamous	7
2. Erythemato-oedematous lesions	7
3. Diffuse erythema (Butter-fly distribution)	3
4. Transient erythematous patches	1
5. Erythemato-squamous patches admixed with superficial and pigmented scars	1
6. Vesiculo-bullous	1
7. Petchiae and ecchymotic areas	1
8 Urticarial	1
9. Pigmented macules and patches	1
10 Alopecia	1
11. Discolouration of nails	2

Variability in character of the rash and its distribution is marked. Almost all types of skin lesions described in the literature were met with except painful nodules of Osler, Erythema multiforme, erythema nodosum like lesions and chronic



Photagraph 1

Photograph 2

ulceration on the legs. Some cases showed combinations of these different lesions. Pictures of few of our cases are reproduced, for types of skin lesions.

Photograph 3

Photograph 4

Articular Pattern: Brunt of the disease next fell on joints. Of the 20 cases 16 showed joint involvement which was mainly of rheumatoid arthritis type and seen in 13 cases, Ac. Rheumatic arthritis type seen in 1 case and arthralgia only seen in 2 cases. The incidence of arthropathy recorded by various workers is from 77% (Jessar et. al. 1953) to 93.8% (Hill L. C., 1957).

Cardiac Involvement: This was the next most common clinical manifestation, being present in 10 cases. The table below (Table No. 5) shows various types of the cardiac involvement. Pericardium was the seat of involvement in 4 cases.

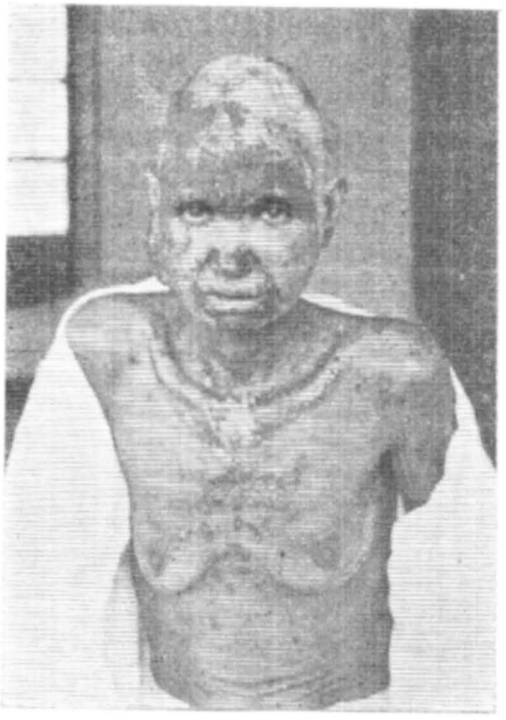
It was of fibrinous pericarditis type in 2 cases and in both of them there was uraemia. In the remaining 2 cases it was pericarditis with effusion and was due to actual involvement of the serous cavity by the disease process itself. In all the above 4 cases there was clinical radiological and electrocardiographic evidence. The skiagram (Photograph 6) and E. C. G. of one case are reproduced.

Endocardium was the seat of involvement in 1 case. This patient had clinical evidence of aortic leak and enlargement of heart on x-ray.

TABLE 5 (Cardiac Involvement)

No.	Type	No. of cases
1.	Pericardial involvement	4
	i. Fibrinous Pericarditis—2	
	ii. Pericarditis with effusion—2	
2.	Endocardial involvement	1
3.	Myocardial involvement	1
4.	Enlarged Heart shadow on x-ray	4
	i. With abnormal E. C. G. changes—1	
	ii. With normal E. C. G.—2	
	iii. E. C. G. not done—1	

One patient devloped sinus tachycardia and went into circulatory failure. This was probably due to myocardial involvement. Inspite of steroids in a very heavy dose and other symptomatic treatment, this patient could not be saved.

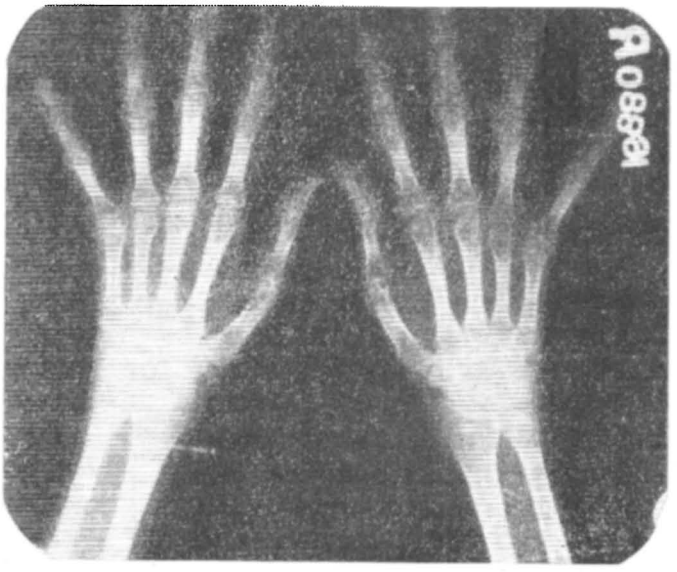


Photograph 5

In the remaining 4 cases heart was found to be enlarged radiologically only. One of these cases showed E. C. G. changes (i. e. generalised poor voltage and flattening of T waves) but she was severly anaemic at this stage, and both these

radiological and E. C. G. changes could be explained on the basis of anaemia. In the other 2 cases E. C. G. was normal while in another case E. C. G. was not done.

Pleuro-Pulmonary Involvement : Was present in 9 cases. Incidence of Involvement of this viscera is also quite frequent i. e. 45% in our series. Lung parenchyma alone was involved in 3 cases, pleura alone in 1 case but pleura as well as lung parenchyma both were involved in the remaining 5 cases. X-ray's of these patients were very interesting, but all could not be included for want of space. Only 3 skiagrams are reproduced (Photographs 7, 8, 9). Their description in brief is as under :

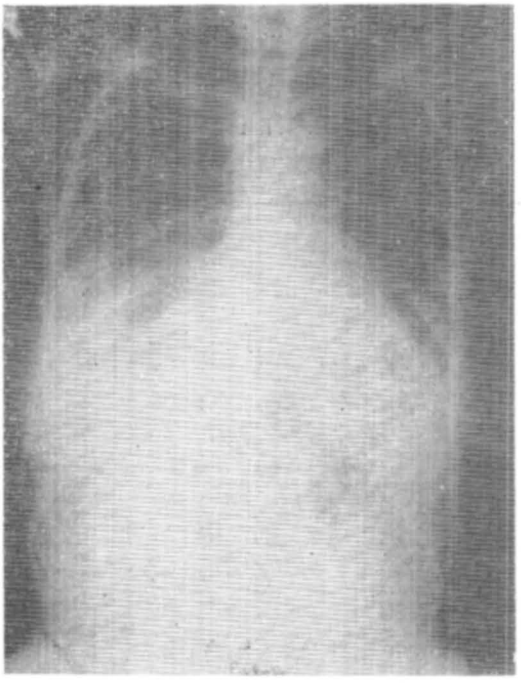


Photograph 5A

The lesions appeared as opacities near or continuos with the mediastinum in two cases, it was quite big (Photograph No. 8) and even diagnosed as a mediastinal tumour. This shadow disappeared completely in subsequent x-rays. In other case the opacities were of smaller size, but later on became denser. In two cases it appeared as patchy parenchymatous lesions in both the lower lung fields only. In still another case it appeared as patchy parenchymatous lesions in both the lower lung fields only. In still another case, it appeared as consolidation in lower part of the lung field on either side (Photograph No. 7). In the sixth case it there was a patch in the outer part of the right lung-field and in the seventh case was seen as a healed streaky fibrotic lesions with a few calcified spots in the right upper lung (Photograph No. 7). At least in four of these cases the lesions progressed assuming streaky character later on, this goes to show that the pathology in the lungs is mainly interstitial

Lymph Node Enlargement was seen during the course of the disease in 8 cases. In 7 of them enlarged glands were of varying size from that of pea to an

almond, non-tender, discrete and not very firm. In one case there was a matted group of glands in submandibular region. This last patient died of generalised tuberculosis subsequently after steroid therapy.



Photograph 6

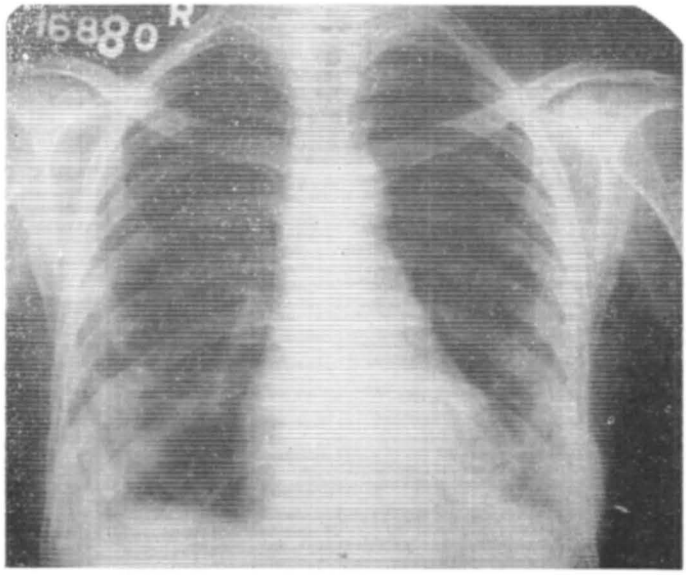
Mucous Membrane Involvement was also present in 8 cases. Three cases had scaly erythematous patches on lips. Two cases had pigmented macules on the inter-dental region of the buccal mucous membrane. In one case there was extensive superficial ulceration of the lips, buccal mucous membrane, tongue, oropharyngeal and upper respiratory tract. The remaining two cases had bleeding from various sites as gums, nose and rectum.

Neuro-Psychiatric Involvement: This was present in 6 cases. Four patients had frank psychotic symptoms. One had just impairment of memory only. Another complained of attacks lasting for a minute or so during which he would become lifeless and inert. Once this patient fell down unconscious also during an attack.

One of the patients with psychotic symptoms also had severe grand-mal fits and two showed residual hemiplegic signs.

Renal Iuvolvement: Evidence of renal involvement was present in 7 cases. Clinical picture in 4 of these cases was that of chronic Nephritis leading to uraemia and death in 3. In the remaining three cases examination of urine just showed presence of a few R. B. Cs., pus cells, rare granular and hyaline casts.

Gastro-Intestinal Symptoms: Six patients complained of Gastro-intestinal symptoms which were mainly of the dyspeptic nature. Repeated stool examination in these cases revealed no significant finding.



Photograph 7

Hepatic Enlargement: Liver was found enlarged in 4 cases. In one case it was due to circulatory failure. Liver function tests done in the remaining 3 cases were normal.

Splenic Enlargement was present in 2 cases.

Eye Involvement was present in only 1 case, the clinical pattern being that of chronic irido-cyclitis.

LABORATORY INVESTIGATIONS

Besides routine laboratory investigations of R. B. C. count; Haemoglobin estimation; W. B. C. count; differential leuococyte count; stool examination, urine examination, determination of E. S. R. following other investigations were carried out in these cases:—

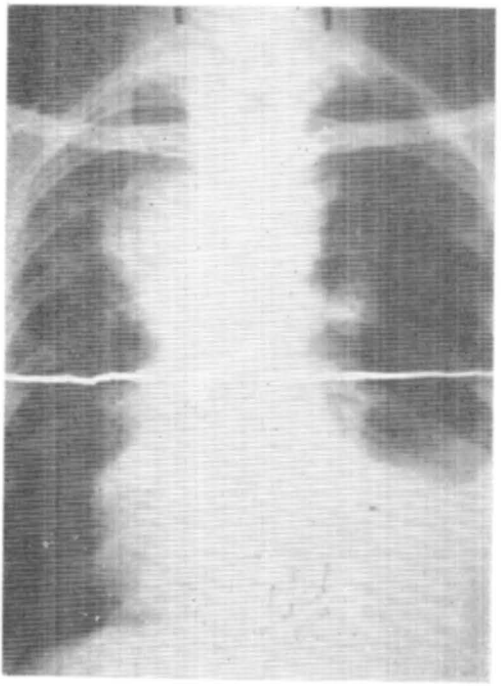
(a) Serum proteins.
(b) Serological tests for syphilis.
(c) L. E. Cell test.

Other investigations like blood urea, liver function test, skin biopsy, various investigations for a bleeding disorder like bleeding time, clotting time, platelet count and prothrombin time etc. were also carried out in cases wherever necessary.

Anaemia was the most common haematological finding being present in all the cases. It was of moderate to severe degree. Haemolytic anaemia, an uncommon

though a well recognised manifestation, was not encountered in any of our cases.

Leucop.nia i. e. count below 5000 c.mm. at some stage of the disease, was present only in 6 cases.



Photograph 8

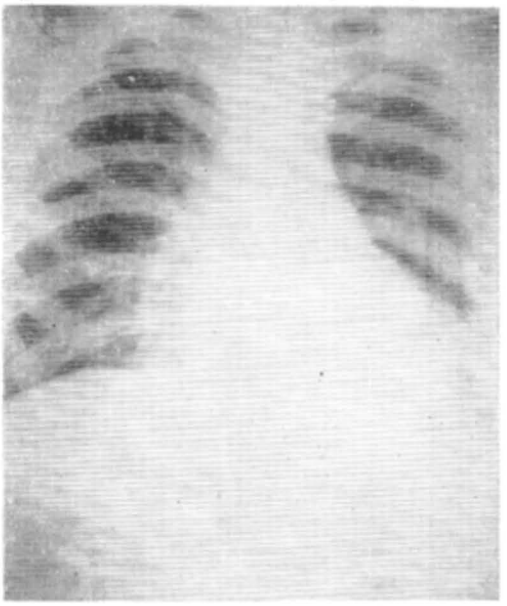
Platelet count was done in 10 cases. It was below 40000/c.mm. in one case In the remaining 9 cases it varied from 110,000 to 176,000 per c.mm.

Serum Proteins were estimated in 19 cases. Total protein value was within normal range in 18 cases and reduced in one. Serum globulin was 3% or more than 3% in 16 cases, 2.9% in 1 case, 9.8% in 1 case and 2 5% in 1 case, while albumin varied from 3.1% to 3.5% in 13 cases, was 2.8% in 3 cases, was 2.4% in 1 case and 2.1% in 2 cases.

S. T. S. Blood for serological tests for syphilis was examined in 16 cases. Only 3 cases showed positive S. T. S.

L. E. Cell Test. This is an important diagnostic aid, but could be carried out in 17 cases only because of the fact that attention to the nature of the disease was some times drawn only in retrospect in the process of continued search for proper diagnosis. The technique employed was that described by Magath and Winkle. Improved L. E. Cell test technique described by Lempert and Berlyne was employed in some of the cases. The test was found positive in as many as 13 cases. Two patients in whom it was negative were in remission at that time. But there is also

one case in whom L. E. Cell test was performed twice and both times it was positive, although when performed second time she was in remission. This clearly shows that remission is not always accompanied by negativation of the test.



Photograph 9

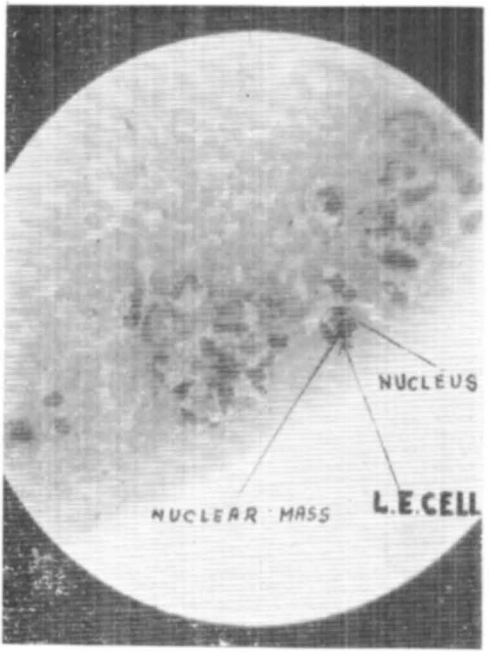
Haserick (1951) found L. E. cell test to be negative in 5 to 10% of undoubted cases of systemic lupus erythematosus. False positive L. E. Cell tests, on the other hand, though rare are also met with (e g. they are found in severe drug reactions particularly to penicillin, rarely to a lesser degree in chronic discoid form, rheumatoid arthritis, in certain disease due to auto-immunization, disorders associated with hyper-globulinaemia and the course of various hypersensitisation processes.

DISCUSSION

There are a few significant observations made during our study which require discussion.

Firstly, attention is drawn to the protean clinical manifestations which the disease can assume. As a matter of fact, it can masquerade any disease and no system is immune from its on-slaught. Its true nature may not be evident till late stages and even then it may be missed. This diagnostic failure is amply borne by records of our cases which make it quite an interesting study from this aspect. Various diagnoses under which these patients were treated outside and even by some of us initially in a few instances were rheumatoid arthritis, Ac rheumatic fever, Brucellosis, mediastinal tumour, Herpes Zoster, Bleeding disorder, Tubercular adenitis, Pericarditis or pleurisy.

Secondly, familial incidence though reported in the literature is not so common. This series includes an instance in which a brother and a sister got afflicted with this malady, one after the other.



Photograph 10

Thirdly, ocular involvement, which is present in one of our cases and was a presenting feature, manifested itself as Iridocyolitis. This went on relentlessly though punctuated with remissions and relapses. It, ultimately, ended up with irregular narrowed pupils, posterior synechiae, complicated cataract and deterioration of the vision. Steroid therapy which was administered only at the later stages of her illness could not arrest the progress of this complaint. Though this complication has been described in number of cases in relation to Rheumatoid arthritis, spondylitis ankylopoetiea and even Ac. rheumatic fever, only a few cases of iridocyclitis as ocular involvement are on record in connection with systemic lupus erythematosus.

Fourthly an overall prognosis in this disease is, yet another problem which requires further study. This is too small a series to draw any conclusions regarding prognosis of the span of life as well as of the individual complaint. Out of these 20 cases we lost touch with four. Of the remaining 16 cases 9 died after a period of illness varying from 3 months to 22 years. The cause of death in 3 was kidney involvement and uraemia. In 1 involvement of myocardium and consequent circulatory in failure 1 involvement of central nervous system and status epilepticus, in 1 due to extensive ulceration of the mucous membrane of the oropharyngeal and

upper respiratory tract. In another 2 cases the exact cause of death could not be determined with certainty because they died at their homes, whilst our 9th case died of generalised tuberculosis, probably as a result of steroid therapy. This flaring up of a hidden tubercular focus in cases of systemic lupus erythematosus after treatment with steroids is well known.

The ominous nature of the kidney involvement which does not respond to steroid therapy is also an established fact. But the intractability of the ulceration of the mucous membrane and lack of its response to steroid therapy has not been mentioned in the literature. The uiceration of the mucous membrane in our cases persisted inspite of steroid therapy in quite a heavy dosage even though skin lesions on the rest of the body surface disappeared. This patient ultimately succumbed to his illness because of this complication leading to inanition and toxaemia.

It may further be pointed out that the most serious and over-whelming symptoms were those of myocardial involvement and convulsive seizuers. Our two patients with these symptoms died within a period of 1½ to 3 months.

Last of all, we come to the most vexed problem of its etiology. As the purpose of this paper is not to discuss this aspect we shall remain content by referring to an important observation made by other workers as well as by us in 4 of our cases regarding the role that pregnancy, parturition, or abortions may have to play in this connection. For example, the pregnancy not only precipitated the relapse in 4 of our cases but also it is felt that it initiated the disease in at least two.

SUMMARY

Clinical analysis of 20 cases of systemic lupus erythematosus is presented.

Familial incidence in which a brother and a sister got afflicted with this maiady one after the other is reported.

Attention is drawn to the protean clinical manifestations which the disease can assume.

Fever and anaemia were the most common clinical features, being present in all the cases. Brunt of the disease next fell on joints, heart, respiratory tract, lymph-nodes, mucous-membrane and nervous system.

Rash of almost all types described in the literature except erythema multiforme, erythema-nodosum like lesions, and chronic ulceration on the legs were met with. Intractibility of the ulceration of the mucous-membrane to steroid therapy is pointed out.

Pericardium was more often the seat of involvement than mayocardium and endocardium.

Though the lesions assumed various types of radiological appearances when lung-paranchyma was involved with this disease process, pathology seems to be mainly interstitial.

Incidence of involvement of the nervous system in this series is also quite considerable i.e. nearly 32%, the most common manifestation being psychotic symptoms.

Ocular involvement which was present in our case and presented as chronic iridocyclitis is reported.

Attention is also drawn to the pregnancy as a factor precipitating relapses in 4 cases and even initiating the disease in 2.

The fact that the clinical remission is not always accompanied by negativation of the L. E. Cell test is born out in one of the cases. This L. E. cell test was negative in 4 of the 16 cases in which this test was performed.

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