CUTANEOUS MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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CERTIFICATE

This is to certify that the dissertation entitled "**CUTANEOUS MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS"** is a bonafide original work of **Dr. D. NITHYA GAYATHRIDEVI**, in partial fulfillment of the requirements for **M.D.BRANCH XIIA (DERMATOLOGY, VENEREOLOGY AND LEPROSY)** examination of the Tamilnadu Dr. M.G.R. Medical University to be held in March 2010.

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DECLARATION

I, **DR. D. NITHYA GAYATHRIDEVI,** solemnly declare that dissertation titled, "**CUTANEOUS MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS"** is a bonafide work done by me at Department of Dermatology and Leprosy, Madras Medical College, Chennai-3 during the period of August 2007 to September 2009 under the supervision of my **Prof. DR.D.PRABHAVATHY, M.D, D.D,** Professor and HOD, The Department of Dermatology and Leprosy, Madras Medical College, Chennai. The dissertation is submitted to Tamilnadu Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch-XII A) in DERMATOLOGY, VENEREOLOGY AND LEPROSY**.

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CONTENTS

INTRODUCTION

HIPPOCRATES, ROGERIUS, PARACELSUS, MANARDI, AMATUS LUSITANUS, SENNERT etc. are some of the early renowned Physicians who have described "LUPUS" which is derived from the Latin word which means "WOLF"[1] depicting its nature of destruction. The ulcerated skin lesions typical of this disease signify this feature as it "bites, eats away and destroys".

Lupus erythematosus (LE) was identified only as a cutaneous disease, until a century ago when emphasis was transferred from the integument to include visceral manifestations. At the beginning of this century blood vessels and connective tissues distributed throughout the body came to be implicated in the pathogenesis, which lead to the concept of "multisystem malady".[2] In 1942, KLEMPERER et al [3] were struck by the many, morphological features that were common to diseases as distinct as Lupus erythematosus, Scleroderma, Dermatomyositis, Rheumatoid Arthritis, Acute Rheumatic Fever and Poly Arteritis Nodosa and classified them as "Collagen disease" or "Collagenosis". The discovery of auto antibodies to various cellular components of different tissue in these diseases has of late given place to the concept of "autoimmune diseases".

REVIEW OF LITERATURE

HISTORICAL BACKGROUND:

In 1826 RAYER[1] described lupus erythematosus (LE) as "Flexus Sebaceui"; in 1828 BIETT[4] described the condition as "Erythema centrifuge". In 1845 HEBRA[1] described it as "Seborrhea congestiva" in which the term "butterfly rash" was used for the first time. In 1851, CAZENAVE[5] introduced the term "lupus erythematoides" meaning red wolf, in order to distinguish this disease from lupus vulgaris. KAPOSI[4] differentiated LE into two forms namely the discoid form and lupus erythematosus disseminatus.

KAPOSI[4] was the first to describe the systemic manifestation of LE (1872). WILLIAM OSLER[1] in 1903 discussed the significance of systemic manifestations and its relationships to the cutaneous lesions.

In 1925 DROCQ[6] classified lupus erythematosus (LE) into 3 major categories. In 1934 O'LEARY[6] classified LE into chronic discoid, sub acute disseminate and acute disseminate types. The discovery "LE cell phenomenon" in 1948 by HARGRAVES et al[1] paved way to the subsequent discoveries of various autoantibodies. The finding of immunoglobulin deposition at the DEJ of LE lesions by BURNHAM et al[7] in 1963 further strengthened autoimmune etiology. In 1971, COHEN and CANOSO[8] proposed the American Rheumatic Association (ARA) criteria for the classification *of* systemic lupus erythematosus (SLE), which following criticism was revised in 1982 by TAR EM et al.[9] In 1994 CASCIOLA ROSEN et al first demonstrated autoantigens that are targeted in SLE. WORTH et al demonstrated presence of 30SA TNF promoter polymorphism in SLE.

DEFINITION:

LE is a systemic autoimmune disorder associated with polyclonal B-cell activation, thought to result from interplay of genetic, environment and hormonal elements. LE is a

spectrum ranging on one end from DLE to SLE on the other end. The term SLE has been used in the past synonymously with LE to all patients suffering from this autoimmune disorder. But in our discussion SLE will be used to refer only to the patient with systemic manifestations.

AETIOLOGY AND PATHOGENESIS:

The regular manifestations of specific DLE lesions in systemic lupus erythematosus, common histological and laboratory abnormalities, immunoglobulin depositions in the involved skin, the transition of discoid lupus erythematosus to systemic lupus erythematosus, etc.[10-13] have lead to the concept that DLE and SLE have common pathogenetic mechanisms in which discoid lupus erythematosus (DLE) represents one polar expression with minimal immunological alteration and the systemic lupus erythematosus on the other end with maximal immunological alterations.[11,12]

The current concepts suggest that this is a multifactorial disorder in which there is profound disturbance of immune mechanism provoked by constitutional and environmental factors.

I. CONSTITUTIONAL FACTORS:

GENETIC PREDISPOSITION*:* A genetic role is suggested by the following observations; 1)Familial incidence (5% in the first degree relatives) [14] , 2) Concordance rate in identical twins is 65% , 3)The higher incidence of other autoimmune diseases in the patients and among family members,[16] 4) Increased association of HLA B8, B7 and DR3 in idiopathic type [17] and increased HLA DR6Y in drug induced lupus erythematosus, 5)The occurrence of linkage / disequilibrium among individual alleles at neighboring loci in some which is referred as “persistent haplotype” 6) Increased allele of TNF Alfa, IL-I, HSP 70-2 polymorphism and decreased FC receptors, increases the risk of lupus[18].

AGE, SEX AND HORMONAL FACTORS:[13] There is an increased oestrogen levels as there is an abnormal oestrogen metabolism in patients with SLE, this leads to increased number of self reactive lymphocytes and increased number of B cells which has high affinity of recognizing self DNA. This observation has a bearing on the propensity for females to develop systemic lupus erythematosus and the higher incidence between menarche and menopause and during the 3rd trimester of pregnancy, when the circulating oestrogen levels are high.[22] Women in childbearing age have 15 times more preponderance for SLE than men.[21] Female patients with DLE have noted exacerbation of the lesions during the premenstrual and menstrual periods.[13] Prolactin is immunogenic and is associated with high Anti DNA levels.

II. ENVIRONMENTAL FACTORS:

Environmental factors like viruses, drugs, UV light, trauma by interfering with the immune mechanism can precipitate or exacerbate SLE.

VIRUSES: The demonstration of Paramyxovirus like cytoplasmic tubular structure in glomerular capillaries[23] and endothelial cells of dermal blood vessels by Ken Hashimoto et al[24] suggested a possible viral aetiology. The pathogenesis behind proposed viral etiology include; 1) Virus infected cells while getting apoptised, express their Ro/SSA and related antigens towards the surface[25]. 2) An alteration of class II proteins by viral antigens, may result in preferential activation by altered self MHC class II reactive cells[26]. 3) By altering MHC class II expression there is also a molecular mimicry by viruses and auto antibodies are produced[27]. Other corroborative findings include precipitation or exacerbation of the disease following viral infection, and increased titres of antibodies against various viruses like REO viral RNA, measles, rubella, EBV, parainfluenza type 1 & 2 are seen during periods of disease

exaggeration[28,29].

DRUGS: A number of drugs have been incriminated either to produce or unmask LE. These are listed in Table-1. Hydralazine induced SLE is dose dependent, dosage <50mg/day does not induce SLE, likewise minocyclin >100 mg/day, needs 2 years of therapy to induce SLE.

Table -1

DRUGS INDUCING SLE LIKE SYNDROME

NO	TYPE OF DRUGS	NAME OF THE DRUG
1.	Cardio vascular	Procainamide, quinidine
2.	Antimicrobial	INH, penicillins, sulphonamides, griesofulvin, streptomycin, tetracyclins, nitrofurantoin
3.	Antihypertensives	Hydralazine, methyldopa, reserpine, atenolol, captopril, labetalol
4.	Antithyroid	Propylthiouracil
5.	Psychotropic	Chlorpromazine, lithium
6.	Antiepileptic	Phenytoin, sodium valproate, ethosuximide, carbamazepine, clobazam
7.	Miscellaneous	d-penicillamine, phenylbutazone, gold salts, allopurinol, PAS,ibuprofen,OCP's

Possible mechanisms hypothesized are:[30] 1) Structural similarity of the drug to the purine base of DNA, with subsequent cross-reactivity in the induction of antibody production to DNA, 2) Interaction of drugs with nuclear antigens expressing a new determinant to evoke T lymphocytes help B lymphocytes in producing antibodies, 3)Inhibition of T suppressor cell activity, 4) By genetic predisposition through an immune response gene and through slow acetylation, 5) Drugs may induce T-cell DNA hypomethylation, may cause increased auto reactivity of lymphocytes, 6)increased keratinocyte apoptosis, expose intracellular peptides on epidermal surface, enhances pro inflammatory cytokines like IFN alfa and TNF alfa[30,31].

UV LIGHT: Incidence of photosensitivity among SLE patients ranges from 32 to 37%[13], in patients with DLE from 5 to 40%[13] and in patients with sub acute cutaneous LE upto 50%[11, 31]. It has been claimed that there is increased activity of the systemic disease with sun exposure and

the degree of increased activity is related to the duration of sun exposure.[13] Kesten proposed that the local reaction to UV injury represents an isomorphic or koebner Phenomenon.[25] DLE lesions in patients with SLE have been explained to be the result of excessive damage induced by sister chromatid inducing agents, the action of which is increased by exposure to near UV light. Recent studies using monochromatic sources have confirmed that the photo reactivity lies within the sunburn range (UVB). [13]

Pathogenesis stated behind UV light includes; 1) UV light causes apoptosis of keratinocytes, which in turn makes previously cryptic peptides available for immune surveillance leading to self immunity and loss of tolerance, 2) UVB displaces intracellular Ro/SSA, LA/SSB, Calreticulin to their cell surfaces, 3) UVB induces release of CCL-27, a chemokine, activates autoreactive T Cells, IFN alfa and dendritic cells leading on to alteration of DNA, 4) UV light affects immunoregulatory cells which normally help in suppressing abnormal cutaneous inflammation[27,28,16,].

OTHER FACTORS: Hemolytic anaemia with increased anti dsDNA antibodies has been documented following the ingestion of sprouts, seeds and dietary supplements containing L-canavanin. Heavy metals like cadmium, mercury, gold, silica, trichlorethylene has also been associated with SLE. Lipogenic aromatic amines present in tobacco can induce SLE[27,28]. Lodin reported DLE following trauma (Koebner phenomenon) that included chemical burns, diathermy, scars of herpes zoster and exposure to X-rays.

III. IMMUNOLOGICAL FACTORS:

Complex interaction between various cells like B and T lymphocytes, dentritic cells, complements defects, apoptotic abnormalities, receptor defects, and aberration in chemokine secretion leads to autoimmunity.

T LYMPHOCYTE: It is postulated that in LE, varying degree of impairment of the suppressor T lymphocytes occur, leading to defect in tolerance to self antigen and over activity of B lymphocyte, followed by the production of antibodies to a wide variety of antigens, preferably to nuclear proteins. CTL cell has role both in induction and expansion phases by its increased number and surface DR antigens[23,32.]

B LYMPHOCYTE: B Cells are involved in expansion phase of pathogenesis. Production of auto antibodies against nuclear antigens and immune complexes is the hallmark of SLE, which may causes tissue damage by causing direct cell death, cellular activation, opsonization and blocking of target molecule function. The excess B cell is hypothesized to result from; 1)Primary B cell defect, 2)excess helper T Cell function, 3)increased polyclonal B cell activation and 4) genes for high responsiveness to certain auto antigens or antigens which cross-react with auto antigens. RES is less efficient in clearing circulating immune complexes, which accounts for the widespread tissue injury[27,28,32,33].

DEFECTIVE APOPTOSIS: In SLE apoptosis of peripheral blood mononuclear cells is increased and defective. Normally apoptotic cells remain intact, but in SLE apoptotic cells dissolute and release nucleoprotein there by exposing the antigen. The above factor also adds up to inherited defect of apoptotic body clearance.[34]

IDIOTYPE AND ANTI IDIOTYPE ANTIBODY: Idiotype is an antigenic determinant present on the variable region of an antibody formation. Antibodies are produced against this idiotype. So there is dysregulation of production of immunoglobulins bearing these idiotypes[35].

COMPLEMENT DEFECTS:[36] There is both inherited and acquired complement deficiency are associated with disease. Normally complement binds to apoptotic cells which are then disposed by house keeping macrophages but when complement proteins are deficient there is a defective clearing of apoptotic cells. Complement deficiency also produce LE, probably by impaired

viral neutralization and linkage of gene foci controlling complement synthesis with those controlling the immune response.[36]

ROLE OF DENDRITIC CELLS AND IFN ALFA: Immature dendritic cells normally perform a watch dog role by capturing self antigen and keep self antigen in check. In SLE there is more plasmacytoid maturation of DC's via IFN stimulation. These mature DC's unlike immature DC's present antigen to auto reactive T-cells, there by producing antibodies[37].

TOLL LIKE RECEPTORS: Circutating DNA / Anti DNA complex trigger TLR signaling which induces proliferation of auto reactive B-Cells, IFN secretion from DC's[30,31,18].

TNF: TNF alfa secreted in response to UVR induce HLA – DR expression, stimulate NF Kappa which upregulates proinflammatory cytokines and adhesion molecules[30,18].

Other corroborative finding include the following: Detection of circulating immune complexes,[36] the deposition of immunoglobulin and complement in different tissues like kidney, skin etc.,[10] the pattern of disease expressivity correlating with the detection of specific autoantibodies, lupus like rash in graft versus host disease,[11] lymphopenia,[25] positive intradermal test on patients with autologus WBC, marked depression or absence of skin reactivity to all test antigens and finally, failure of sensitization to DNCB by majority of the patients with SLE.

The immunological aberration increases, as the spectrum moves from DLE to SLE. The possible explanation would be the presence of isolated cellmediated autoimmunity in DLE, without producing immune complexes. But, in patients with SLE, antigen antibody complexes may be the reason for multi organ involvement. However, it is the dichotomy in T suppressor cells control over the B-lymphocyte that could best explain the polar expression, though the exact pathogenic[38] mechanism not known. The various auto antibodies identified are shown in

the Table-2, and the various immunological abnormalities are enlisted in the Table-3.

Table-2

I. ANTIBODIES TO DNA AND HISTONES	
A.	ANTIBODY REACTIVE WITH DOUBLE STRANDED DNA ONLY (dsDNA)
B.	AGAINST ds AND ss DNA – 60 TO 70% OF PATIENTS WITH SLE
C.	AGAINST ss DNA ONLY
D.	AGAINST HISTONES (H, AH_2A, H_2B, H_3 AND H_4) -DRUG INDUCED LE (95-100%), SLE 30%
II	**ANTIBODIES TO NON-HISTONE NUCLEAR PROTEINS AND RNA PROTEINS**
	Sm ANTIGEN – SLE IN 30 TO 40% - MARKER ANTIBODY
	NUCLEAR RNP (N RNP) – SLE 30 TO 40%
	SSA/RO ANTIGEN – SLE 30-40%
	SSB/LA ANTIGEN – SLE 10-15%
	PROLIFERATING CELL NUCLEAR ANTIGEN (PCNA) – SLE 5% - 10%
III	KU – SLE/PM/SCLERODERMA – OVERLAP SYNDROME
	ANTIBODIES TO NUCLEOLAR ANTIGEN

Table-3

IMMUNOLOGICAL ABNORMALITIES IN SLE
ANTI DNA HISTONE ANTIBODY (LE FACTOR)
ANTI DNA ANTIBODY – SS AND DS
ANTI RNA & ANTI SM
CRYOGLOBULIN
COOMBS ANTIBODY
PLATELET, LEUCOCYTE ANTIBODY,
ORGAN SPECIFIC ANTIBODY (THYROID…ETC)
ANTIBODY TO CLOTTING FACTOR
BIOLOGICAL FALSE POSITIVITY
INCREASED TITRE OF VIRAL ANTIBODY
SERUM COMPLEMENT DEFICIENCY
DEFECTS IN CELLULAR IMMUNITY

CLASSIFICATION:

The classifications of LE by Brocq in 1925, O'Leary' in 1934, Urbach and Thomas in 1939 and Wilson and Jordon[4] in 1950 can at best be considered as anecdotal importance, since there were lacunae in the clinical and histopathological correlations. The exercise of classification is further complicated by the fact that visceral involvement may or may not be accompanied by skin changes. Based entirely upon "clinical and specific histopathological findings" of LE, Gilliam et al[11] classified cutaneous lesions of LE into,1) LE specific (or) cutaneous Lupus Erythematosus (CLE) showing specific histopathological findings and 2) LE non specific skin lesions in which histopathology is not diagnostic of LE. (Table-4)

Table -4

I. CUTANEOUS LUPUS ERYTHEMATOSUS (LE SPECIFIC SKIN LESIONS)		
A.		CHRONIC CUTANEOUS LUPUS ERYTHEMATOSUS : (CCLE)
	1.	LOCALISED DISCOID LUPUS ERYTHEMATOSUS (LDLE) (LESIONS ARE CONFINED TO HEAD AND NECK)
	2.	GENERALISED OR DISSEMINATED DISCOID LUPUS ERYTHEMATOSUS (DDLE) –(LESIONS ARE PRESENT ABOVE AND BELOW THE NECK)
	3.	HYPERTROPHIC OR VERRUCOUS DISCOID LUPUS ERYTHEMATOSUS
	4.	LUPUS ERYTHEMATOSUS PROFUNDUS (LUPUS ERYTHEMATOSUS PANNICULITIS)
B		SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS (SCLE)
	1.	PAPULOSQUAMOUS (PSORIASIFORM) SCLE
	2.	ANNULAR – POLYCYCLIC (OCCASIONALLY VESICULAR) SCLE
C.		ACUTE CUTANEOUS LUPUS ERYTHEMATOSUS (ACLE)
	1.	FACIAL (MALAR) ERYTHEMA
	2.	WIDESPREAD ERYTHEMA OF FACE. SCALP, NECK, UPPER CHEST, SHOULDERS, EXTENSOR SURFACES OF ARMS AND BACK OF HANDS
	3.	BULLOUS OR TEN LIKE ACLE

II. NON SPECIFIC BUT DISEASE RELATED SKIN LESIONS IN PATIENTS WITH LUPUS ERYTHEMATOSUS		
A.		VASCULAR LESIONS
	1.	TELANGIECTATIC LESIONS (45-65%)
	2.	DERMAL VASCULITIS (10-20%)
	3.	THROMBOPHLEBITIS (15-20%)
	4.	RAYNAUD'S PHENOMENON (15-20%)
	5.	LIVEDO RETICULARIS (10%)
	6.	CHRONIC ULCERS (2-8%)
	7.	RHEUMATOID NODULES (5-10%)
	8	PERIPHERAL GANGRENE (LESS THAN 5%)

	9.	DEGOS LIKE DERMAL INFARCTS OR ATROPHIE BLANCHE (LESS THAN 5%)
B		ALOPECIA (40-60%)
	1.	FRONTAL (“LUPUS HAIR”)
	2.	DIFFUSE (NON SCARRING)
C		MUCOUS MEMBRANE LESIONS (7%)
D		PIGMENTARY ABNORMALITIES (10%)
E.		SCLERODACTYLY (10%)
F		CALCINOAIS CUTIS (RARE)
G		URTICARIA (7 – 14%)
H		BULLOUS LESIONS (LESS THAN 5%)

This classification is again incomplete as it does not encompass other variants of cutaneous LE namely, chilblain lupus,[10] LE telangiectoides,[10] LE profundus et hypertrophicus,[10] LE tumidus,[39] and LE/LP overlap syndrome.

On the other hand, Baeur and Orfanos preferred to use the general term "LE syndrome" which comprised all types of LE disease and regarded the individual clinical picture as LE subsets. In their classification, classical LE subsets included the chronic DLE, the disseminated LE and systemic lupus erythematosus (SLE). Among the rare LE subsets few were bullous LE, LE profundus, Mixed Connective Tissue Disease, Rowell syndrome, Drug induced LE, Urticarial vasculitic LE, and ANA negative LE[39] were recently recorded in the literature.

CRITERIA FOR THE CLASSIFICATION OF SLE:

In 1964, Ropes[40] proposed the following criteria;

1) A cutaneous eruption consistent with LE. 2) Renal involvement. 3) Serositis and 4) Joint involvement.

The presence of 3 of the above mentioned 4 manifestations were considered for the classification of SLE. The diagnosis of which however required confirmatory laboratory tests.

In 1971, American Rheumatism Association[8] proposed the preliminary criteria for the classification of SLE, which, after criticism was revised in 1982 by Tan Em et al[9] (Table-5). Among the 6 cutaneous criteria initially said, Malar flush, discoid rash, photosensitivity and oral ulcers were retained and the Raynaud's phenomenon and alopecia were excluded. The revised criteria, however, was also subjected to criticism. (Table 5)

Table – 5

1982 REVISED CRITERIA FOR CLASSIFICATION OF SLE	
1.	MALAR RASH: Fixed erythema, flat or raised over the malar eminences tending to spare the naso labial fold.
2.	DISCOID RASH: Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3	PHOTOSENSITIVITY: Rash as a result of unusual reaction to sunlight by history or physician observation.
4	ORAL ULCERS: Oral or nasopharyngeal ulcerations, usually pain less
5	ARTHRITIS**:** Non erosive involving 2 or more peripheral joints characterised by tenderness, swelling or effusion.
6	SEROSITIS: (A) Pleuritis: Convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion or (B). Pericarditis: Documented by ECG or rub or evidence of pericardial effusion.
7	RENAL DISORDER: (A) Persistent proteinuria more than 5g per day or more than 3+ if quantitation not performed or (B) Cellular casts – may be RBC's, Hb, granular, tubular or mixed.
8	NEUROLOGICAL DISORDERS **:** (A) Seizures : In the absence of offending drugs or known metabolic derangements or (B) Psychosis

9	HEMATOLOGICAL DISORDER **:** **(**A) Hemolytic anemia with reticulocytosis (B) Leukopenia < 4000/cu mm on 2 or more occasions or (C) lymphopenia < 1500 / cu mm on 2 or more occasions or (D) Thrombocytopenia <1,00,000/cu mm in the absence of offending drugs
10	IMMUNOLOGICAL DISORDER : (A) Positive LE cell or (B) Anti DNA antibody in abnormal titre or (C) presence of anti Sm anti body or (D) False positive VDRL for atleast 6 months and confirmed by TPI or FTA-ABS
11	Abnormal ANA by immunoflouresence in the absence of drugs

For the purpose of identifying in clinical studies a person shall be said to have SLE, is any four or more of the 11 criteria are present serially or simultaneously, during any interval of observation.

INCIDENCE:

SLE is not a rare disease, but neither is it a common one. The average annual incidence of SLE has been estimated to be 27.5 per million population for white females and 75.4 per million for black females.[13] SCLE represents 9% of all cases of cutaneous LE[12] and DLE represents the commonest among the cutaneous LE.[42,46] Other variants of cutaneous LE seems to be extremely rare. [43,44,45,46]

AGE INCIDENCE:

Average age of onset is between the 2nd and 5th decade,[10,13] the peak incidence being between 3rd and 4th decade in DLE,[10,13] It occurs rarely in children[47,48], on the other extreme, DLE has also started at 83 years of age.[10] In the Indian study by Pandh et al[49] the majority of the patients with DLE were in the age group 21 to 40 years.

SEX INCIDENCE:

Females are predominantly affected and the female to male ratio increases as the spectrum moves from DLE to SLE. [10,13,25] In DLE the ratio ranges from 1.2:1 in the localised type[49] upto 3.8:1 in the disseminated type.[50] 70% of the patients are females in the SCLE type[31] and the ratio in ACLE ranges from 9:1[10,13] upto 15:1 in the childbearing age group. [21]

RACE:

SLE is three times more common in whites than blacks. Blacks with SLE more commonly have Sm and RNP antibodies, DLE lesions, Serositis and internal organ damage.

SYMPTOMS:

Patients with DLE are often asymptomatic, but for the most common symptom cum precipitating factor is photosensitivity. The early papular lesion of DLE may however be slightly pruritic,[13] and intolerable itching is a symptom peculiar to scalp involvement.[51,52] Pain on scratching in lesions of DLE has been explained by the carpet tack phenomenon. [53] Pain is also present in some patients with LE/LP overlap syndrome[46] and LEP. Other symptoms include symptoms of associated cutaneous and systemic lesions. [10]

DISTRIBUTION OF THE LESIONS:

The classical cutaneous LE lesions predominantly involve the face and other sun exposed areas of the body.[10,13] The DLE lesions may be solitary, multiple, localised or disseminated.[10,13] The localised type[11,53,54] is confined to the head and neck and the sites commonly affected are malar area, nose, forehead, ears, scalp and external auditory canals. SCLE is usually widespread and commonly involves the shoulder, extensor surface of the upper extremities, upper chest, upper back and neck but lesions are rarely seen below the waist.

[13,31]ACLE may manifest as malar erythema of the face or as generalised morbilliform eruption. [13,54]Hypertrophic lesions mainly manifest on the upper extremities. [45] LEP predominantly involve the face, abdomen, buttocks, upper arm, thighs and breast. [10,56] LE/LP overlap syndrome predominantly involve the acral areas palms, soles, face and less commonly the trunk.[37,57] Chilblain lupus predominantly involve the digits, calves and heels.

MORPHOLOGY AND COURSE:

DISCOID LUPUS ERYTHEMATOSUS (DLE): [10-13] Starts as an erythematous papule or scaly patch and on evolution is characterised by well demarcated erythematous scaly, disc shaped or irregular plaque with follicular dilatation and keratotic plugging. When the plug comes out, the prickly under surface resembles "Carpet tacks" or "Cats tongue", which is very characteristic of DLE.[52] There is an active infiltrated margin with peripheral hyperpigmentation. The lesions have a tendency to spread peripherally and the central area heals with hyper, hypo or more commonly depigmentation, telangiectasia, and atrophy. Scarring with depigmentation is a characteristic feature of DLE and it persists indefinitely. Size varies and lesions may remain active for months or years together. Scarring of the concha of the ear as a sign of DLE has been stressed by Rebra[58] and SAM Shuster. [57,58,59] DLE lesions that occur only on the head and (or) neck are referred to as localized DLE whereas DLE occurring both above and below the neck are referred to as generalized DLE. Various other types of localized DLE includes, patch, warty, non itchy hyperkeratotic, papulonodular lesions, annular lesions, acneiform lesions, rosacea like. Likewise, morphological types of disseminated DLE include annular variant, lupus erythematosus gyratus repens, bullous lesions, linear lesions, arteritic lesions.

Oral mucosal involvement has been reported to occur in 3% to 25% of DLE patients,[19,60] while other mucosa like conjuctival, nasal, vulval, perianal are rarely involved. The sites of predilection within the mouth are buccal mucosa and the palate but the gingiva may also be

involved. The lesions of localised LE have a predilection for the vermillion border of the lip which presents as cheilitis or as superficial ulcer or as crusting. While silvering or whitening of the vermillion border of the lip is a pathognomonic sign of DLE,[51] early lesions appear as, superficial painless erythematous patches or plaques with telangiectasia and may exhibit atrophy, erosion or ulceration. Chronic lesions typically show sharply marginated irregular atrophic plaques with scalloped radiating white striae and telangiectasia. Nasal mucosa is involved in 9% of patients. Erythema in vulva is seen in 5%. In the eye they produce velvety edema and redness. Erythematous plaques occur on lower eyelid in 6% which may be associated with scaring of conjunctiva and symblepharon[60,61].

Rarer presentations include vesicles, bullae,[10] DLE in nail causing nail dystrophy and cutaneous horns.[61] Scarring alopecia is the end result of scalp lesions. Rare complications include calcinosis[10,62] and neoplastic changes[10,49] like basal cell epithelioma or squamous cell carcinoma.

LE PROFUNDUS/LE PANNICULITIS/KAPOSI–IRGANG DISEASE: Kaposi in 1883 first described the subcutaneous nodules in LE. In 1940, Irgang introduced the term LE profundus.[63] Two third of LEP patients had DLE lesions. The lesions are usually non tender, firm, subcutaneous nodules which are sharply defined, one to several centimeters in size. The overlying skin may be normal but is frequently drawn inward [51] with saucerized depression. Ulceration may occur spontaneously [51] while, atrophy, scarring and cosmetic deformity may ensue as the nodules resolve. This condition occurs most often in the absence of associated internal diseases. LEP presented as discrete breast nodules - lupus mastitis, that simulated breast carcinoma on mammogram. [51]

HYPERTROPHIC LE /VERRUCOUS LE: [45] It was first described by Behcet in 1942, as hypertrophic LE. Later, Vitto et al coined them as verrucous variant of DLE. Clinically the

lesions often resembled keratoacanthoma, prurigo nodularis, Lichen planus or fibrokeratoma. The clinical course is marked by chronicity and absence of regression of lesions and resistance to therapy.

LE HYPERTROPHICUS ET PROFUNDUS: [10] Described by Behcet, starts as a violaceous, scaly, tender lesion. It rapidly enlarges and develops a warty hypertrophic surface with coarse adherent scales that form a hard brown black tar like plaque with rolled border and central crateriform atrophy. This name is ambiguous as the pathology does not reveal any LEP features.

LE TUMIDUS: [39] Lesions are of violet red colour, the epidermis appears normal and there is little or no follicular plugging. The patches are well defined, raised and soft.

LE TELANGIECTOIDES:[10] Described by Radcliffe Crocker in 1888, is characterised by persistent blotchy reticulate telangiectasia and heals with punctate atrophic scarring. Scaling is absent.

CHILBLAIN LUPUS: [44] Described first by Jonathan Hutchinson in 1888, which is characterised by lesions of purplish blue discoloured patches or plaques on toes, fingers and face with little hyperkeratosis. The pulp of the fingers becomes atrophic but does not ulcerate. Patients usually have Ro antibody positivity and abnormal peripheral circulation and rarely cryofibriginogens or cryoagglutinins.

ROWELL'S SYNDROME: [10] Described by Rowell in 1963.This is unusual variant with transitions between SCLE and EMF. [30] The syndrome was described in DLE but it also occurs in SLE. It starts as a papule and later form rings with vesicles at the edge. Intense forms may

show bulla, necrosis and ulceration. When the syndrome occurs in DLE, the lupus band test is positive in the discoid lesion and negative in EMF lesion. They characteristically have speckled ANA pattern and anti La positivity.

LE/LP OVERLAP SYNDROME/RUBRIC LP: This refers to a condition in which the skin lesions present clinical, histologic and/or immunopathologic characteristics that may be typical for both or either of the disease at the same time. [46] It is usually not possible to assign a diagnosis of LE or LP alone. The lesions are characterised by large circumscribed atrophic patches and plaques with hypopigmentation and a livid red to violet colour, mild hyperpigmentation at the borders, minimal silvery scaling, fine telangiectasia and occasionally tending towards ulceration.[37,46] Transient bullae and verrucous changes may occasionally develop.[37] The lesions have a chronic course.

SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS: (SCLE) [11,39,55] In 1977 Gilliam[31] introduced the term SCLE to describe a distinct type of cutaneous LE, which had been described in the past as superficial disseminated LE, subacute disseminated LE,[11] pityriasiform LE,[11,] maculo papular photosensitive LE,[11] and annular vesicular erythema.[11] Approximately 85% of all SCLE patients report of photosensitivity. It erupts as a small erythematous scaly papule that evolves into a psoriasiform lesion or extends peripherally to form annular or polycyclic figurate configuration. The lesions tend to involve large confluent areas in contrast to the individual lesions that tend to remain separate and well circumscribed in DLE. Follicular plugging is not a prominent feature. Greyish hypopigmentation is usually seen in the centre of the annular lesions that are bordered by erythema and superficial scales. Vesiculo bullous lesions are present sometimes. The lesions heal without scarring. Residual hypo or depigmentation and telangiectasia may be present which resolve in months to years. Mucous membrane ulcers occur in 39% of patients particularly in patients with systemic manifestations. More than 50% have non scarring alopecia. Other associated cutaneous findings in uncomplicated cases include facial telangiectasia, livedo reticularis, periungual telangiectasia, vasculitis and cutaneous sclerosis. Most patients have mild systemic complaints and 50% satisfy ARA criteria[54,55].

ACUTE CUTANEOUS LUPUS ERYTHEMATOSUS : (ACLE)[11,54,55] The classic malar butterfly rash or the more extensive morbilliform eruptions occurs at sometime in 30 to 40% of patients with SLE. ACLE is typically characterised by abrupt onset of confluent symmetrical erythema and edema over malar eminences and last few hours or days, which frequently coincides with the activity of disease. If it extends over bridge of nose it completed the body of classical butterfly rash but sparing nasolabial fold. Lesions do not leave a scar. Vesiculation, superficial ulceration and crusting develop if the edema is severe and healing with hyper-pigmentation is common. This acute edematous, erythematous eruption occurs most frequently

after exposure to sunlight. The more widespread acute morbilliform or exanthematous eruption may resemble drug eruption which is also referred as “photosensitive rash”

DRUG INDUCED LE:[27,28]: Skin lesions are less common.[29] Drugs like dapsone, sulphonamides and griseofulvin can produce chronic cutaneous LE. [10] In contrast to classical SLE, drug induced SLE is uncommon in blacks, has HLA-DR4 association, CNS and renal system is infrequently involved, low anti DNA antibodies, normal serum complement levels and more frequent association with antihistone antibodies. ACLE, Polyserositis, hepatomegaly, polyarthritis, lymphadenopathy and pulmonary infiltration do rarely occur.

BULLOUS LE:[27,28] First description by Haradway in 1889.[68] Bullous LE is apparently systemic in most cases. [69] It may be the sole manifestation of LE. Typically the lesions have little, if any, surrounding erythema, induration or inflammation. Usually erythema follows the rupture of the vesicle with ulceration and possible infection and scarring. [69] Bullous skin lesions that can be seen in LE patients can be specific or nonspecific. Specific bullous lesions can be seen with, TEN like SCLE and ACLE, vesiculobullous annular SCLE, bullous DLE. LE non specific bullous lesions included DA like cutaneous LE and Epidermolysis bullosa like cutaneous LE.

NEONATAL LE: LE in neonates may occur at birth, within few hours or upto 6 weeks. [52,71,72] This disorder is by transplacental passage of maternal antibodies. Cutaneous manifestations are seen in 50% of cases. Most common finding is erythematous, scaly eruption confined mostly to head and neck. Lesions over orbital skin called as Racoon sign or Owl eye. Rashes improve within few months with residual dyspigmentation.[72] Systemic involvement like congenital heart block, hematological and hepatic manifestations are common. Neonates are Ro/SSA antibody positive in which 52 KDa protein and 60 KDa protein of Ro antibody are responsible for CHD and cutaneous lesions respectively[27].

CHILDHOOD LE:[72,73] DLE is rare in children. The common age of occurrence is between 8 and 10 years of age. Lesions are the same as adults[52] but they encounter severe disease and often associated with hepatosplenomegaly and lymphadenopathy. Other types of CLE are also rare.

SLE IN PREGNANCY:[27,28] Fertility is not affected but there are more chances of recurrent abortion and poor fetal outcome particularly when associated with APLS. Renal function detoriates if it has already affected.

SLE IN ELDERLY:[27,28] It is associated with HLA DR3, increased incidence of lung disease and anti Ro and La antibody.

ANTIPHOSPHOLIPID ANTIBODY SYNDROME: This is a procoagulant syndrome. This in SLE is associated with recurrent abortions, thrombosis, ulcer, livido reticularis, purpura, ecchymosis, retinal changes. This occurs due to interruption in protective function of beta2 microglobulin against coagulation.

URTICARIAL VASUCLITIC LE: [39] This is probably an LE subset with sense of combination of SCLE with leukocytoclastic vasculitis. Clinically there are patches of erythema as well as persistent urticaria with some hyperpigmentation and purpura.

COMPLEMENT DEFICIENCY LE: [36] Deficiency of early components of complement especially C_2 is well known. 60% of the persons with C_2 deficiency may be affected with SLE or DLE. Striking feature is the presence of LE like rash involving sun exposed areas. Laboratory abnormalities and systemic associations are minimal.

ANA NEGATIVE SLE: [39] Malar rash and annular type of lesions may be prominent. Photosensitivity and oral ulcerations are common and the systemic involvement is usually less and hence prognosis is good.

URTICARIAL PLAQUE:[51] The commonest manifestation. It is a reddish purple plaque, relatively fixed in shape and time, showing no atrophy or scaling, and occurs usually on the face. It occurs in both cutaneous and systemic LE. In the systemic form a more acute violaceous, urticarial, papular lesion that look like hives except for their violaceous colour occurs that lasts only for few days and disappears without scarring. Urticaria in SLE is usually the cutaneous expression of the underlying circulating immune complex. Chronic urticaria may be a presenting manifestation of LE but is very uncommon.

ALOPECIA (40 to 60%):[11,54] Scarring alopecia is a sequlae of DLE. Diffuse non scarring alopecia occurs during the acute toxic exacerbation of systemic disease. A receding frontal hair line with broken hairs has been called "lupus hair" which is seen in 6% of patients.. [11,54] Other causes of non scarring alopecia may include drugs, stress and telogen effluvium.

PHOTOSENSITIVITY REACTIONS:[51] Photosensitivity reactions include atrophic scaling plaques, fixed urticarial plaques, transient urticarial papules and a persistent violaceous flush over the face and 'V' of the neck. The lesions may persist for hours, days or weeks. Photosensitivity reactions may cause fatal exacerbation of the disease. Although, most photosensitive patients react to the sunburn portion of the UV spectrum, but rarely to blue green radiation emitted by fluorescent lamps[54].

VASCULAR LESIONS (50-70%):[11,54] Three types are commonly seen namely linear telangiectasia involving the posterior nail fold and cuticle, erythematous polyangular macules and lastly papular telangiectasia (45-65%). Discrete papular telangiectasia on the palms and finger is characteristic sign of SLE.[51] Discrete erythema with or without scaling is sometimes observed over the interphalangeal and large joints and the periorbital tissues.[51]Centrifugal annular erythema is rarely seen.[10]

RAYNAUD'S PHENOMENON: [51] (30%) May precede or follow LE lesions. Digital gangrene and ulceration may be produced by severe Raynaud's phenomenon.

DERMAL AND SUBCUTANEOUS VASCULITIS: Dermal vasculitis may produce palpable purpura occurring in the lower extremities, small dermal ischaemic infarcts with ulcerations, peripheral gangrene, painful subcutaneous nodules, chronic and recurrent ulcers, especially in the legs and forearms (2-8%) and livedo reticularis (10%).[11]Purpura can also occur secondary to thrombocytopenia and steroid therapy. [10]

ATROPHIE BLANCHE: The lesions closely resembling malignant atrophic papulosis.[10] Small splinter haemorrhages are rarely seen. [13]

SUBCUTANEOOS NODULES (Rheumatoid nodules 5-10%):[11,54] Usually non tender and cartilagenous in consistency and may occur over the proximal inter phalangeal joints, elbow, dorsum of the wrists, extensor surface of the extremities and occiput.

RECURRENT SUPERFICIAL AND DEEP THROMBOPHELBITIS: (5%-10%) May be an early sign of SLE. [51]

GENERALISED HYPERPIGMENTATION: This may be seen[11,54] in 10%.

BULLOUS LESIONS:(< 5%) Including haemorrhagic bullae can occur in LE.[11,54]

MUCOUS MEMBRANE LESIONS: They are often histologically LE specific usually occur during acute flares of the disease and painless.[10,11,51] Palate is most commonly involved followed by cracked edematous crusted lips. Mucosal haemorrhage, painful erosions, shallow ulceration surrounded by erythema, gingivitis and palatal erythema may also occur as nonspecific lesions. Nasal septal, vulva and perianal ulcers may rarely occur, especially during disease activity.

SCLERODACTYLY:(10%[11]) Sclerodactyly and clubbing is rarely seen.[10]

OTHERS: Erythema multiforme may also be an expression of increased disease activity in SLE.[51] Calcinosis can develop in subcutaneous tissue, muscle and periarticular structures in longstanding disease.[11] Other rare manifestations include poikiloderma atrophicans vasculare, erythromelalgia, pyoderma gangrenosum and panniculitis. Allergic reactions like allergic dermatitis, rhinitis, asthma or food or drug allergies have a higher than normal incidence in SLE. [13]

OVERLAP SYNDROMES: Variable signs of more than one disease are shared in this condition for example, Dermatomyositis and LE. [27] In some cases such a differentiation is not seen and in such cases, a diagnosis of undifferentiated connective tissue disease seems warranted. [74]

MIXED CONNECTIVE TISSUE DISEASE: Was first described by Sharpe et al in 1971.[74] The most common presentations include Raynaud's phenomenon, joint pain and cutaneous LE. [75] Among the cutaneous LE, the majority have chronic discoid LE, minority have SCLE, and rarely have ACLE, LEP and others.[75] Sharpe et al found lupus like rash, SCLE and DLE in upto 50% of cases. The defining feature of this disease is high titre of haemagglutinating antibody to the ribonuclease sensitive component of extractable nuclear antigen (ENA). [51,76]

SJOGREN SYNDROME: This syndrome also can have LE lesions and immunological findings of LE syndrome. [30]

SENEAR USHER SYNDROME:[77] The exact categorization as a distinct subset of Pemphigus erythematosus or LE or co-existence of Pemphigus erythematosus and LE is still under debate though Chorzelski et al[78] had concluded that in the majority of cases reported, there is co-existence of pemphigus erythematosus and LE, both clinically and immunologically.

SYSTEMIC MANIFESTATIONS IN LUPUS ERYTHEMATOSUS: Various studies show different percentage incidence of various organ involvement.[10,11,13,21,33,47,79] Constitutional symptoms include fever, myalgia, malaise, weakness, anorexia, weight loss etc.

MUSCULOSKELETAL SYSTEM:[13,79] This is the commonest system to be involved. Arthritis without erosion or deformity, migratory polyarthritis, joint effusions, persistent arthralgia with stiffness, and aseptic necrosis of the bone occur. One of the hall mark of lupus joint symptom is more symptom and less deformity. Myopathy and lupus foot are rare occurrence.

CARDIOVASCULAR SYSTEM:(50%)[79] Pericarditis, pericardial effusion, myocarditis, conduction defects, cardiac failure, heart murmurs, Libmann Sack endocarditis, hypertension, cardiomegaly etc.

RESPIRATORY SYSTEM:(45%)[79] Pleurisy, pleural effusion, pneumonia, pulmonary vasculitis, etc.

RENAL SYSTEM:(53%)[79] Hematuria, localised, diffuse and membranous glomerulonephritis, nephrotic syndrome etc.

CENTRAL NERVOUS SYSTEM:(26%)[79] Peripheral neuritis, convulsions, psychosis, hemiparesis, aphasia, cranial nerve palsies, subarachnoid haemorrhage, Guillain Barre syndrome, chorea and others.

GASTROINTESTINAL SYSTEM:(53%)[79] Nausea, vomiting, diarrhoea, ulcerative colitis, dysphagia, abdominal pain, hepatomegaly(25%), splenomegaly(10%), jaundice etc.

LYMPHATIC SYSTEM: Generalised lymphadenopathy (59%).[79]

EYE INVOLVEMENT: [13] Cytoid bodies, exudation, haemorrhage, arteriolar narrowing, conjunctivitis, episcleritis, papilloedema, optic atrophy etc.

BONE CHANGES: These include avascular necrosis, cysts and sclerosis.

INTER RELATIONSHIP AND IMPLICATION OF CUTANEOUS LE IN SLE[76]:

Cutaneous LE can be acute, subacute or chronic and scarring or non scarring. DLE is on the benign end of the LE spectrum and SLE is on the other pole. All variations occur between the cutaneous and systemic form of the disease and the host immune response is critical in disease expression. There is a 'Grey area' between DLE and SLE as defined by ARA criteria.[54] In this area are those patients who have DLE with mild serological or clinical symptoms of systemic disease. The chronic cutaneous lesion in DLE and SLE are identical clinically and histologically. [51,80] DLE is the presenting manifestation in approximately 2 to 10% of the patients with SLE and. approximately 15-20% of the patients with SLE[4,10,13,42] eventually have DLE lesions.[10,13,54,55] Females developing DLE before the age of 40 years and those with HLA B8 are more prone to develop SLE. [17] Patients with DDLE and DLE lesions below the neck, have more frequent clinical and laboratory abnormality suggestive of SLE. [50,81,82] Patients with DLE develop SLE particularly after exposure to sun light, X-ray, chronic infection or drugs. 30

to 50% of DLE patients intermittently exhibit abnormal lab findings such as leucopenia, increased ESR, mild anemia etc. Nearly all patients with DLE and extra cutaneous disease have positive ANA test.[34]

SLE patients with DLE lesions usually have a better overall prognosis than those patients who do not have DLE and these patients rarely develop renal insufficiency. [47,54,70,82,83] It is impossible to predict whether a DLE patient will eventually go in for SLE or not from the morphological or clinical picture of DLE alone. [51]

About 50% of the patients with LEP go in for SLE[56]. [84]SCLE manifests in approximately 10% of the SLE patients and 50% of patients with SCLE satisfy the ARA criteria for SLE. [55]ACLE is the commonest of the specific cutaneous LE to be the presenting manifestation of SLE[10] and 30 to 40% of SLE patients have ACLE at sometime of the disease.[55] It reflects the activity of the systemic disease. The presence of overlapping cutaneous features of DLE and SCLE may point towards the presence of probable development of SLE. [85]The prognosis in SLE worsens when the spectrum moves from the DLE to ACLE.

DIFFERENTIAL DIAGNOSIS: [10,11,13,51]

DLE needs to be differentiated from polymorphic light eruption, seborrheic dermatitis, psoriasis, acne rosaceae, tinea faciei, granuloma teenei, leishmania recidivans, sarcoidosis and others. Scarring alopecia due to DLE should be differentiated from lichen plano pilaris and pseudopelade of Brocq. SCLE should be differentiated from psoriasis and psoriasiform syphilide. ACLE should be differentiated from erysipelas, leprosy in reaction, Senear-Usher syndrome, Sweet's syndrome, drug eruption and others. Bullous LE should be differentiated from eruption and others. Bullous LE should be differentiated from erythema multiforme, pemphigus, pemphigoid and other bullous dermatosis. LEP should be differentiated from other causes of panniculitis especially connective tissue panniculitis and Weber-Christian disease.

HISTOPATHOLOGY:

The histopathologic features of LE are well known and are usually considered to be diagnostic. [10-13] But different clinical types cannot be reliably distinguished on histological grounds alone.[12] It is opined that most of the Pathologists had not tried to separate the different LE subsets, the primary reason being, they considered the variations in the findings to be related to the age of the lesion, the more aged showing more changes.

DLE lesions show hyperkeratosis, keratotic plugging (both follicular and extrafollicular), epidermal atrophy, liquefaction degeneration of basal cells, squamatization of basal cell layer,[88] thickening of the basement membrane zone (BMZ), edema of the papillary dermis, and lymphohistiocytic, mononuclear and macrophage infiltrate. Liquefaction degeneration of the basal cell has been considered as the most important finding in the diagnosis of cutaneous LE[12,88] The lymphohistiocytic infiltrate is patchy and distributed around the blood vessels, appendages and also independently in the papillary and reticular dermis,

rarely extending upto the subcutaneous fat. The infiltrate may extend into the appendageal epithelium with vacuolation and liquefaction degeneration of the basal cells, which in the absence of epidermal basal cell degeneration may be diagnostic.[88] [88] Civatte bodies (Dyskeratotic cells) and incontinence of melanin into the upper dermis and increased production of melanin are usually seen.[88] Dermal edema, fibrinoid deposits and focal dermal hemorrhage may be present. Increased deposits of acid mucopolysaccharide also been observed in special stains. Excepting for fibrinoid deposit, these changes are characteristically seen in DLE. Atypical keratinocytes may be seen occasionally in chronic lesions of DLE.

In ACLE, the lesions show sparse dermal infiltrate, focal liquefaction degeneration of basal cells and upper dermal edema. Epidermal necrosis may be noted in severe forms[12.] In SCLE, the hydropic degeneration of the basal cells and edema of the dermis are more pronounced than DLE lesions,[12] but the hyperkeratosis is less and inflammatory infiltrate independent and around the appendages is confined to the upper third of the dermis only.[87] The oedema may be severe enough to produce clefts and even vesicles between the epidermis and dermis.[12] Focal extravasation of erythrocytes and fibrinoid deposits may be seen. The presence of hyperkeratosis, BMZ thickening, extensive follicular damage, dense leukocytoclastic infiltrate and involvement of the deep dermis favoured the diagnosis of DLE. While minimal changes of this type and sparing of the follicles and deep dermis favoured the diagnosis of SCLE. Liquefaction degeneration was considered as one of the unimportant factor in the diagnosis of SCLE. They concluded that irrespective of the age of the lesion, the two subtypes can be distinguished in that the lesions of SCLE were superficial with slight follicular involvement, while those of DLE were more extensive and deeper.

LEP shows septal and lobular panniculitis composed of lymphoid cells, plasma cells and histiocytes[56] occasionally forming germinal centers, necrobiotic changes with fibrinoid

deposits, vascular changes like thrombosis, perivascular fibrosis and calcification are rarely seen.[12] The overlying epidermis and dermis may show DLE changes or changes of verrucous type i.e. hyperkeratosis, hyperplasia and papillomatosis. [56]

In LE/LP overlap syndrome, some may show findings suggestive of LP, some LE and in some both. It appears that on histological grounds clear differentiation may be impossible and only the subsequent evolution may make a diagnosis possible.[90]

In bullous LE, bulla is subepidermal.[69] Mucosal LE shows parakeratosis or hyperkeratosis, liquefaction degeneration of basal cell layer, degeneration of collagen and dense inflammatory cells in the submucosa, sometimes in a perivascular pattern.

ELECTRON MICROSCOPIC EXAMINATION:[12]

EMS of the specific cutaneous lesions of LE show marked vacuolation in the cytoplasm of the basal cells, numerous greatly elongated narrow cytoplasmic projections in to the dermis with surrounding basement membrane. The basal cells progress to disintegration with necrosis of the cytoplasm, giving the impression that the basal cells are the primary site of change in cutaneous LE. The colloid bodies appears as homogenous eosinophilic ovoid bodies, of 20 nm in diameter filled with filaments of 6 to 8 nm in diameter. They are largely located in the papillary dermis but sometimes are seen in the lower epidermis. They contain fibrin, immunoglobulin and complement.[90]

CUTANEOUS IMMUNO FLOURESCENCE TEST (LUPUS BAND TEST-LBT):

In 1963, Burbham et al first reported the presence of immunoglobulin (Ig) at the dermo-epidermal junction (DEJ) in patients with LE. [7] Cormane (1964) pointed out Ig and complement (C) deposition at DEJ in clinically normal skin of patients with SLE.[91] The test entails the Direct Immunoflourescence (DIF) testing of involved and uninvolved sun exposed skin for the purpose of diagnosis, and of uninvolved sun protected skin for the purpose of prognosis. For this purpose skin biopsy specimen is transported in Micheli's medium and incubated with fluorescent tagged IgG/IgM and viewed under fluorescent microscope[26].

All three major immunoglobulin classes (Ig G, M, A) and a variety of complement components may be present in the subepidermal deposits. The pattern is usually granular, thready, stippled and continuous, but may be homogenous in a small percentage. Stippled band occurs in uninvolved skin, thready band in new lesions and homogenous band in older lesion. IgM and IgG are most frequently detected in the subepidermal deposit while properdin along with fibrin is also deposited occasionally.[26,27]

When involved skin were tested, Ig and complement deposition are seen between 50% to 90% of the specimens in DLE, between 50% to 94% in SLE and around 60% in SCLE. [92] When uninvolved sun exposed skin were tested, it was almost negative in DLE, and was positive in 81% to 90% with SLE and 26% with SCLE. [92] When uninvolved sun protected skin was tested, 50% to 83% of specimens were positive in SLE, 46% in SCLE and was negative in DLE.[92] The basement membrane phenomenon can be demonstrated in uninvolved skin in patients with transitory type of DLE. The percentage of positive LBT in uninvolved, sun protected skin is correlated with the severity of renal involvement. In addition, the deposits in normal skin may be found in SLE patients who lack skin involvement altogether. [93]

HISTOLOGICAL DIFFERENTIAL DIAGNOSIS:[12]

Lichen planus, polymorphous light eruption of the plaque type, lymphocytic lymphoma, lymphocytoma cutis and lymphocytic infiltration of Jessner. Bullous LE should be differentiated from EMF, dermatitis herpetiformis, bullous pemphigoid and other bullous dermatoses with subepidermal bulla.

LABORATORY ABNORMALITIES OF LE:

The lab abnormalities increase as the spectrum moves from DLE to SLE. Before investigations are planned they can be categorized as biochemical abnormalities, ANA pattern and its titre, investigations pertaining to systemic involvement.

BIOCHEMICAL ABNORMALITIES:

Since ACLE is usually the scene of SLE the lab abnormalities parallel those of SLE. Literature report shows leukopenia in 37%, thrombocytopenia in 21%, anaemia in 75%, raised serum gamma globulin in 29%, LE cell was positive in 83%, VDRL shows false positivity in 25%, while rheumatoid factor and positive coomb's test was seen in 37% and 15% respectively. Cryoglobulins are most often present in patients with lupus nephritis, raynaud's phenomenon, gangrene while APL antibodies are seen in patients with repeated abortion, gangrene, thrombosis anywhere, livedo reticularis. Complement levels are low in patients with lupus nephritis [26,27,94,95].

In patients with SCLE leucopenia was seen in 19%, anaemia in 15% increased ESR in 59%, LE cell test positivity in 56%, increased gamma globulin in 30%, false positive VDRL in 30%, Rheumatoid factor positivity in 17%, ANA in 30% and Anti DNA in 57%[94,95]

Studies of abnormal lab values in DLE has shown leucopenia in 12.5%, anaemia in 30%, thrombocytopenia in 5%, increased ESR in 26%, increased serum globulin in 29%, positive RF in 15%, false positive VDRL in 5%, positive LE cell phenomenon in 1.7%, positive ANA in 35%, positive cryoglobulin in 2.5%. The diversity of results in all these spectrum is due to the spectrum of disease per se in its pathogenesis[26,94] It has been established however,

that patients in whom the disease changes from DLE to SLE have persistent multiple abnormal lab findings from the beginning. This is in contrast to cases of simple DLE in which most abnormal lab findings, if present at all are transient more over, no single lab abnormality value in a patient with DLE can tell whether there will be an conversion to SLE or not.

ANA PATTERN:

ANA are family of auto antibodies directed against contents of cell nucleus like dsDNA, ENP (extractable nuclear proteins), Histone, nuclear RNA. ANA titre measures the pattern and amount of auto antibodies. Substrates used are rat liver, mouse liver and human laryngeal cells (Hep-2 cells). The pattern depends on the type of antibodies and substrate used. Hep-2 cells are widely used now a days for its high specificity and sensitivity.[26,27] Patient's serum is incubated with Hep-2 cells along with the fluorescence tagged auto antibody and viewed under fluorescence microscope. Then the pattern is compared with standardized charts. Various other quantitative methods as mentioned above are also used, which measures antibody in titres[90,92].

Various types of ANA pattern (table 6) using Hep-2 cells are seen which includes homogenous, fine speckled, discrete speckled, nucleolar pattern. Nucleolar pattern is further divided into homogenous speckled and clumpy shows pattern of ANA, associated antibodies, their target antigen and their significance.[26,93,95] Homogenous ANA pattern is equivalent to LE factor and it's the most common pattern seen in SLE. Peripheral rim pattern is most commonly associated with active disease, while peripheral shrunken pattern is most commonly seen in patients with lupus nephritis.[26,92,93] Peripheral shrunken pattern is seen 1-2 wks before disease exacerbation and it is an indicator of poor prognosis. Presence of anti Sm antibody indicates lupus nephritis. LE cell test which was used a decade ago is obsolete now.

Table 6

PATTERN	TARGET SITE	ASSOCIATED ANTIBODIES	ASSOCIATED DISEASES	CLINICAL SIGNIFICANCE
Homogenous	Chromatin	Antihistone	Drug induced SLE	less alopecia, less anemia ,less CNS &Renal problems
		Anti DNA	SLE	
Rim Peripheral	Chromatin Nuclear membrane	Anti DNA, Anti laminin	SLE	Peripheral Shrunken – Poor Prognosis lupus nephritis
Line Speckled	Nuclear RNP	Anti Sm	SLE	More Specific, associated with Renal, CNS Vasculitis
		Anti La/SSB	Rowells Syndrome	
		Anti Ro/SSB		Photosenitivity, serositis, CLE, Chilblain lupus, Neonatal LE with heart block
		Anti KU SCL-70	Scleroderma	
Discrete Speckled	Chromatin	Anticentromear	CREST	
Nucleolar	Nucleolar RNP	Anti U3RNP	Scleroderma	
	Nucleolar	Anti RNA Polymerase		
	Components	Anti Pm SCI		

INVESTIGATIONS PERTAINING TO SYSTEMIC INVOLVEMENT:

As SLE involves almost all viscera, investigations are done depending upon the symptoms. All base line investigations like LFT, RFT, urine routine, USG abdomen, CXR, ECG is done. Expanded modes of investigations are done on individual needs which are shown in table 7.

Table 7

S.NO	PATHOLOGY	INVESTIGATION
1	CNS symptoms	CT, MRI
2	Gangrene, ulcer	APL levels
3	Livedo reticularis	Cryoglobulins
4	Repeated abortions	Cold agglutinins, APL
5	Cardiac	ECHO
6	Respiratory	CXR, HRCT
7	Lupus nephritis	Renal biopsy, 24 hrs urine protein,C3, C4 levels
6	Lupus retinopathy	Retinoscopy, angiography
7	GIT	Endoscopy
8	Avascular bone necrosis	MRI, lupus anticoagulant

All the above investigations are considered and treatment and follow up are made based on them since SLE is a multi systemic disease.

TREATMENT:

LE may subside spontaneously or remain as a minimal problem or progress with resultant scarring, so therapy should be as conservative as possible and should be a multi disciplinary approach. Treatment can be divided into general care, treatment of the disease proper.

General care includes education to the patients and family regarding the nature of progression of the disease, avoidance of phototoxic drugs, pregnancy complications. Avoidance of sun exposure is one of the mainstays of treatment, which includes photoprotective clothings, and using sunscreens of SPF>30[28]. Counseling regarding good hygiene, early treatment of infections, avoidance of precipitating factors like stress, alcohol should be stressed.

Both topical and systemic drugs are used depending upon the need. Class I steroids like clobetasone propionate 0.05 % can be given as BD dose for 2 wks (or) Betamethasone dipropionate 0.05% twice weekly for 2 wks followed by 2 wks rest can be given for severe leison to minimize the side effects.[27] Intralesional triamcinalone acetonide 2.5-5mg / ml can be given upto 3 ml in patients with DLE which is more resistant and hyperkeratotic[26,27,96].

Since the first use of quinacrine hydrochloride in 1940, antimalarials has been used as the mainstay of treatment for the disseminated type of cutaneous LE, DLE, SLE, LEP and other types and for cases resistant to topical steroids[28]. Chloroquine sulphate in the dose of 4mg /kg (or) 200 mg BD initially for 2-3 wks followed by 200 mg OD can be prescribed[27]. Progress is assessed after 6 wks and if there is improvement, the drug is continued for not more than 6 months, due to the serious toxic effects like retinal damage[97,26]. A dose related side effect may ensure. Hydroxy chloroquin may be preferred for its less ocular toxicity. This drug is used in 6.5 mg/kg dose for 6-8 wks then tapered and may be continued for 1 year[27,95,96]. Quinacrine can

also be used in a dose of 100 mg/day for 4-6 wks. 75% of the patients are helped by antimalarials but 50% show relapse in 6 months of stopping the treatment. A careful ophthalmic examination should be performed prior to treatment and 3-4 months interval, while on antimalarials[97].

Immunosuprressants and cytotoxic drugs are used in patients with extensive, skin diseases which are severely symptomatic and in whom there is severe systemic involvement. Steroids in the form of pulse methyl prednisolone (or) Prednisolone 1-2 mg/kg can be given[97,98]. Later once the desired response is attained steroid is stopped by tapering. Various other steroid sparing drug and combination drugs can be used in patient to reduce the side effects of steroids and in patient who are not responsive to steroids alone.

Azathioprine a steroid sparing drug in a dose of 1.5 – 2 mg /kg/ day, mycophenolate mofetil a purine analogue in a dose of 2.5 – 3mg/day, methotrexate 15-20 mg/wk, cyclophosphamide 500-700mg/m^2, cyclosporine 2-5 mg/kg are various other immunosuppressants are used in severe cases. [97,98,27] Leflunomide which is an inhibitor of denovo pyrimidine synthesis used in rheumatoid arthritis can also be used here.

Various other non immune suppressive like dapsone can be started in a dose of 50mg/d and can be raised up to 100mg/d[98,99]. Retinoids in the form of isotretinoin and acetretin in the dose of 0.5-2mg /kg/day and 10-50mg/d respectively is used.

Thalidomide a TNF alfa inhibitor is tried in refractory cases in the dose of 100-300mg/d[98]. Lenolidomide, a thalidomide analogue is more efficacious but with equal side effects. Other drugs like gold, clofazamine, Vitamin E, Pheytoin, sulfasalazine are also in use.

Recently advanced biologicals like Anti TNF alfa medication (i.e) Itarnacept, Adalimumab, Infliximab can be tried in recalcitrant LE but these agents are also well known to

induce both SLE and CLE. Biologicals like Rituximab, a genetically engineered monoclonal antibody of CD20, Eprutuzumab, a monoclonal antibody against CD22 B Cell antigen, Bisulimumab, a monoclonal antibody to B lymphocyte stimulation, Abatacept ,a fusion protein which modulates T cell activation by blocking costimulator signals, Efalizumab monoclonal IgG antibody directed against CDla/LFA can also be tried for resistant cases. IVIg in the dose of 2g/kg/day over 2-5 days acts by neutralizing antibody[26,27,98]. Stem cell transplant and anti B cell antibodies are now tried experimentally.[27,28,98]

Physical methods like freezing with liquid nitrogen, CO_2 snow sometimes results in clearing, painting with TCA has also been used with some success. Treatment of systemic disease largely depends on the system involved and the extent of involvement. The main stay of treatment of systemic diseases includes immunosuppressants and biologicals [26,27].

AIM OF THE STUDY

1. To study the incidence of SLE in Government General Hospital, Chennai during the period between August 2007 to September 2009.

2. To study the incidence of various cutaneous spectrum of SLE.

3. To study the age and sex incidence.

4. To study the commonest site of lesions in various spectrum.

5. To study the precipitating and exacerbating factors.

6. To study the various mucocutaneous presentations.

7. To study relevant laboratory abnormalities.

8. To study the associated disorders.

9. To study the histopathological features and Immunofluorescence pattern.

MATERIALS AND METHODS

45 cases of systemic lupus erythematosus were collected from the patients attending the Skin & Rheumatology department, Govt. General Hospital, MMC from August 2007 to September 2009.

Patients who either fulfilled ARA criteria (or) ANA positivity were included in our study. A detailed history regarding the onset, progress, precipitating (or) exacerbating factors, recurrence, number, size, morphology, distribution and sequelae of the lesions was obtained. Symptoms related to cutaneous lesions and internal systems were noted in all cases. In all female patients detailed menstrual and obstetric history was taken to look for anti phospholipid syndrome. Detailed laboratory investigations including biopsy were done.

Then depending on the above information conclusions and discussions were formulated. All these patients were followed up for 2 years and the patients were categorized according to their clinical features into the following groups.

1. Chronic Cutaneous Lupus Erythematosus (CCLE): It include (a) Discoid LE (DLE) Characterised by well defined erythematous plaques with thick adherent scales and keratotic plugging, peripheral hyperpigmentation and central hyper, hypo (or) depigmentation, atrophy, telangiectasia, and scarring. It was subdivided into localised type, when lesions were restricted to head and neck and disseminated type (DDLE) when lesions were present elsewhere also, and (b) Lupus erythematosus panniculitis, characterised by well defined, firm, non tender, subcutaneous plaques with normal (or) indrawn overlying skin and with (or) without ulceration. Presence of DLE lesion elsewhere was taken as confirmatory evidence for the diagnosis.

2. Subacute Cutaneous Lupus Erythematosus (SCLE) Characterized by annular (or)

polycyclic erythematous plaques with superficial scales (or) psoriasiform lesions, having a tendency to coalesce to form large confluent areas with hypo pigmentation in the centre and erythematous scaly margins without scarring.

3. Acute Cutaneous Lupus Erythematosus (ACLE) characterised by acute erythema with oedema and confined mostly to the malar area (or) other sun exposed areas. It lasts for few days to weeks and heals with hyperpigmentation. The lesions are sometimes generalised with morbilliform (or) exanthematous eruptions and are characteristically associated with other cutaneous lesions and systemic manifestations.

The morphological description given above was taken as "Classical form" for each specific group.

Biopsy of the skin lesions was done in all patients to confirm the clinical diagnosis of Lupus Erythematosus (LE). The characteristic and diagnostic histopathological findings in LE are, 1) Hydropic degeneration of the basal cells of the epidermis (or) the follicles, 2) Patchy lymphohistiocytic infiltrate both independently and around the blood vessels and appendages.

3) Degenerative changes in connective tissues like hyalinization, oedema, mucin and fibrinoid change.

In addition to the above findings the presence of following histopathological features were taken as suggestive evidence for specific clinical type.

DLE – Hyperkeratosis, keratotic plugging both follicular and extrafollicular, epidermal atrophy, depth of inflammatory infiltrate extending upto the deeper dermis and mucin deposits.

SCLE – Absence (or) minimal keratotic plugging, no epidermal atrophy, vesicular

changes in active borders, focal hydropic degeneration of basal cells and sparse inflammatory infiltrate confined to the upper third of the dermis, dermal edema, extravasation of RBC's and dermal fibrinoid deposits

ACLE – Increased degree of hydropic degeneration of basal cells, sparse dermal cellular infiltrate and upper dermal oedema and rarely epidermal necrosis.

All case selected were examined clinically to rule out any systemic manifestations. Depending upon the systemic symptoms patients were investigated in detail pertaining to the system suspected to be involved.

CBC, platelet count, urine for albumin, sugar and deposits, RFT, LFT, CRP, VDRL, RF, CXR, and ECG were done to all patients. APL antibodies were done in all suspected patients. Delivered new born of SLE mother were screened for heart block. Patients with symptoms suggestive of renal problems and vasculitis were investigated for C3 and C4 levels. Renal biopsy was also done for few patients as suggested by nephrologist. Doppler was done for lower limb vessels for patients with gangrene and legulcer. Direct Immunofluorescence and Indirect Immunofluorescence (IDIF) were done in few patients. With all the above methodologies and investigation, results were formulated and conclusions were drawn.

OBSERVATION & RESULTS

I. INCIDENCE OF SLE:

Total number of patients attended skin op between August 2007 to September 2009	52,369
Total number of patients with SLE	45
Incidence	0.08%

II. DISTRIBUTION OF THE CASES IN THE DISEASE SPECTRUM:

Total no. of cases	**CCLE**		**SCLE**	**ACLE**
	DLE	**LEP**		
45	16 (39.92%)	1 (2.86%)	3 (8.48%)	25 (47.94%)

In our study out of total 45 cases, majority of them were ACLE, followed by CCLE and SCLE.

III. AGE INCIDENCE:

Age	CCLE		SCLE	ACLE	Total	Percentage
	DLE	LEP				
11-20	4	-	-	4	8	17.77%
21-30	8	-	2	10	20	44.44%
31-40	3	1	1	9	14	31.11%
41-50	1	-	-	2	3	6.66%

75.55% of the patients were between the age group 20 to 40 years. Out of them, 42.22% were ACLE patients, 26.66% were CCLE patients and 6.33% were SCLE patients.

IV.SEX INCIDENCE:

	CCLE		SCLE		ACLE		TOTAL	
Sex	M	F	M	F	M	F	M	F
Number of cases	2	15	0	3	4	21	6 (12%)	39 (88%)

In our study male: female ratio is 1:7

V.PRECIPITATING / EXACERBATING FACTORS:

Factors	Number of cases	Percentage
Sunlight	14	55%
Drugs	2	4.44%
Infections	5	11.11%
Mental stress	2	4.44%
Physical exertion	5	11.11%
Pregnancy	1	2.22%
Menstruation	2	4.44%
Others	1	2.22%

Sunlight was a precipitating / exacerbating factor in 55% of cases. Cotrimoxazole and ibuprofen were the drugs which precipitated SLE in each one patient. No exacerbating or precipitating factors seen in 26.66% patients.

VI. PRIMARY PRESENTATION:

Primary Presentation	with mucocutaneous problems only	with systemic problems only	both
Number of patients	20 (45%)	18 (40.47%)	7 (14.53%)

Patients primarily presenting only with mucocutaneous problems was seen in 45% of patients and in patients primarily presenting with only systemic problems was seen in 40.47% and both in 14.53% of patients.

VII. PATIENTS PRIMARILY PRESENTING WITH MUCOCUTANEOUS PROBLEMS ONLY:

Symptoms	Number of cases	Percentage
Photosensitivity	9	47.91%
Non scaring Alopecia	5	26.08%
Oral ulcer	4	21.73%
Urticaria	1	4.34%
Leg ulcer	1	4.34%

Photosensitivity was the most common cutaneous symptom seen in 47.91% followed by diffuse non scarring alopecia in 26.08% and oral ulcer in 21.73% of patients.

VIII: PATIENTS PRIMARILY PRESENTING WITH SYSTEMIC PROBLEMS ONLY:

Symptoms	Number of patients	Percentage
Fever	8	45.45%
Arthralgia	6	35.71%
Oliguria	2	9.09%
Recurrent abortion	1	4.54%
Irregular menstruation	1	4.54%

Fever was the most common systemic symptom seen in 45.45% followed by arthralgia in 35.71% of patients.

IX. PHOTOSENSITIVITY IN DIFFERENT SPECTRUM OF DISEASE:

Symptom	CCLE	SCLE	ACLE
Photosensitivity	7 (41.17%)	3 (100%)	20 (80%)

Photosensitivity was seen in 100% of patients with SCLE, 80% of patients with ACLE and 41.17% of the patients with ACLE.

X. CLINICAL PRESENTATION DURING FOLLOW UP:

Follow up duration	Patients initially presenting with cutaneous & later with systemic symptoms	Patients initially presenting with systemic symptoms & later with cutaneous symptoms
<6 months	7 (35%)	10 (55.55%)
6months -1yr.	8 (40%)	4 (22.20%)
1yr-1.5 yr.	3 (15%)	3 (16.55%)
1.5yr-2yrs	2 (10%)	1 (5.55%)

Among the patients who initially presented with cutaneous symptoms, 75% of them developed systemic symptoms within first year of follow up. In patients who initially presented with systemic symptoms 77.75% of them developed cutaneous symptoms with in 1 year.

XI. ASSOCIATION OF SKIN LESIONS OF ARA CRITERIA WITH THE OTHER ARA CRITERIAS:

	Skin ARA criterias			
Other ARA criterias	Malar rash	DLE lesions	Photosensitivity	Oral ulcer
Arthritis	5	6	9	8
Renal criteria	1	1	2	2
Neuropsychiatric criteria	3	2	5	2
Hematological criteria	4	8	11	7
Immunological criteria	10	7	14	14

Photosensitivity was the most common ARA skin criteria associated with other ARA criterias followed by oral ulcer and malar rash. Both photosensitivity and oral ulcers were commonly associated with immunological criteria.

XII. DISTRIBUTION OF CUTANEOUS LESIONS:

Sites involved	CCLE	SCLE	ACLE	TOTAL
Only sun exposed area	3	-	5	6
Both sun exposed & non exposed area(disseminated)	3	3	3	10
Localised to head & neck	11	-	18	29

Among the CCLE patients, 64.70% of the patients had localised DLE lesions, 35.30% of them had disseminated type. Among the SCLE patients all had disseminated lesions. Among the ACLE patients 72% had localised lesions and 28% had disseminated type.

XIII. MUCOSAL LESIONS:

Mucosa involved	CCLE	SCLE	ACLE	Percentage
Palatal erosions or ulcers	4	2	13	83.30%
Erosions and crusting of lips	1	1	5	25%
Gingival erosions	-	-	1	3.57%
Conjuctiva	-	-	1	3.57%

Palatal involvement was the commonest in 83.30% of patients followed by erosions and crusting of lips. In patients with lip involvement vermilion border was blurred by crusting but the lesion did not extend beyond it.

XIV.MORPHOLOGY AND SEQULAE OF LESIONS:

Among the CCLE patients 33.66% of the patients had classical plaque lesions of DLE, 1.22% had verrucous DLE, and 1.22% had follicular plugging in the ears. 1.22% had LEP lesions, which was well defined, firm subcutaneous plaques that later ulcerated resulting in scarring. 60% of the patients with DLE lesions ended with depigmentation and scarring, 40% with hyperpigmentation and 15.55% with scarring alopecia.

In patients with SCLE, 66% of them had classical papulosquamous lesions and 33% of them had annular scaly plaques. These annular scaly plaque lesions initially started as individual plaques which later, coalesced to form large polycyclic scaly plaques. All SCLE lesions healed in due course without scarring.

In ACLE patients with maculopapular rash, initially rash started in sun exposed area later on spread to whole of the body. Maculopapular rash, malar rash and butterfly rash were seen in 37%, 13.33% and 13.33% resp. Patient with bullous SLE had lesions throughout the body.

XV. INITIAL CLINICAL PRESENTATION:

	LE specific skin lesions			**LE non specific skin lesions**	**Both**
Total number of cases	CCLE	SCLE	ACLE	7 (30.43%)	4 (17.39%)
	5 (19.11%)	3 (13.04%)	4 (17.39%)		

52.28% of patients presented with LE specific skin lesions as initial manifestation, 30.43% with LE non specific skin lesions as initial manifestation and both as initial manifestation in 17.39% patients.

XVI. SPECTRUM OF LE SPECIFIC SKIN LESIONS:

LE specific skin lesions		**Number of patients**	**Percentage**
ACLE	Malar rash	17	68%
	Butterfly rash	1	4%
	Maculopapular rash	6	24%
	Bullous lesions	1	4%
SCLE	Annular	1	33.33%
	Papulosquamous	2	66.66%
	Localised	11	64.70%

CCLE	Generalised	6	35.29%
	Verrucous	1	5.88%
	LEP	1	5.88%

Among ACLE patients, malar rash was commonly seen in 68% followed by maculopapular rash in 24%. In SCLE patients 66.66% had papulosquamous lesions, 33.33% had annular lesions. Among the CCLE lesions localised type is most commonly seen in 64.70% of patients followed by generalised type in 35.29%.

XVII. SPECTRUM OF LE NONSPECIFIC SKIN LESIONS:

Lesions		**Number of patients**	**Percentage**
Diffuse non scarring alopecia		22	48.88%
Nail changes		10	22.22%
Mucosal lesions		10	22.22%
Icthyosis		4	8.88%
Vasculitis	Urticarial vasculitis	2	4.44%
	Purpura	2	4.44%
	Leg ulcer	1	2.22%
	Gangrene	1	2.22%
Acanthosis nigricans		2	4.44%
LE/ LP overlap		1	2.22%
Anetoderma		1	2.22%

Diffuse non scarring alopecia was the most common nonspecific skin lesion seen in 48.88% followed by, nail changes in 22.22%, mucosal lesions in 22.22%. Among the patients with vasculitis 4.44% of them presented with urticarial lesions, 4.44% with purpura, 2.22% with leg ulcer and 2.22% with gangrene. Icthyosis was seen in 8.88%, acanthosis nigricans in 4.44% cases, and LE /LP overlap in 2.22% of patients. Other than the above said lesions 4.44%

of the patients had palmar exfoliation.

XVIII. ASSOCIATED SYSTEMIC MANIFESTATIONS:

Systemic involvement	**Number of patients**	**Percentage**
Fever	31	92.42%
Arthralgia	10	22.44%
Psychiatric	10	22.22%
Lupus nephritis	2	33.33%
Lymphadenopathy	5	11.11%
Respiratory system	4	8.88%
Neurological	2	4.44%
Conjunctivitis	1	2.22%

Fever was the most common symptom seen in 68.88% followed by musculoskeletal symptoms in 26.66% and psychiatric symptoms in 22.22%.

XIX.HISTOPATHOLOGY:

Majority of our study patients HPE of specific lesions showed features suggestive specific for LE. Characteristic LE specific skin lesions common to all spectrum like hyperkeratosis was seen in 66.44%, liquefaction degeneration of basal cells in 100%, periappendageal infiltrate in 34%, perivascular infiltrate in 28% of patients .

In patients with ACLE various other HP features other than the common features mentioned above like sparse inflammatory infiltrate and upper dermal edema as documented in literature was seen in 56% and 16% resp. Extravasated RBC's seen in 26% of patients. Patient with ACLE had bullous lesions which showed subepidermal bulla.

In patients with SCLE focal liquefactive degeneration was seen in 66.66%, sparse upper dermal infiltrate in 66.66% and upper dermal edema in 33.33%.

In DLE patients follicular plugging was seen in 58%, keratotic plugging in 51%, colloid bodies in 50%, dense and deep dermal infiltrate was seen in 51%, periappendageal infiltrate in 48% , more melanophages in 33%, perivascular infiltrate in 29% of patients.

Patients with urticarial vasculitis showed inflammatory infiltrate predominantly within and around small blood vessels mainly of neutrophils and also leukocytoclastosis. A case of LEP showed minimal atrophy of epidermis, inflammatory infiltrate cell collection in dermis and septilobular lymphohistiocytic infiltrate in sub cutis. In patient with LE/LP overlap, hypertrophic DLE lesions showed features of lichen planus, but ulcerative DLE lesions showed features of SCC, like individual cell keratinisation and keratin pearls.

XX. LABORATORY CRITERIA OF ARA IN VARIOUS SPECTRUMS OF SLE:

Lab criteria	CCLE	SCLE	ACLE	%
Anemia (Hb %<10gm/dl)	6	3	9	40%
Leucopenia (<4000/mm^3)	1	2	4	15%
Thrombocytopenia(<1,00,000/mm^3)	-	-	2	4.44%
Lymphopenia(<1500/mm^3)	-	-	4	15%
Persistent Proteinuria	-	-	2	13.33%
24 hrs urine protein >150mg	-	-	2	33.33%
ANA positivity	12	3	25	94%
dsDNA positivity	2	3	14	83%
False positive VDRL	1	1	4	18%
Immunofluorescence positivity	-	-	3	100%

Laboratory ARA criteria was fulfilled by most of the patients in ACLE spectrum. Two patients confirmed to have lupus nephritis in biopsy. Abnormal levels of both IgG and IgM APL antibody was documented in 3 patients. SGOT and SGPT were deranged in 6 patients. ANA was positive in 100% of SCLE patients, 70% of CCLE patients and 100% of ACLE patients .

XXI. INDIRECT IMMUNOFLOURESCENT PATTERN:

TYPES/PATTERNS OF ANA	NO OF PATIENTS
Homogenous	2
Speckled	1

All the 3 patient's samples sent for Indirect IF and Direct IF were positive. In IDIF 2 of them showed homogenous pattern and 1 showed speckled pattern.

DISCUSSION

In this study, among the total 52,369 new patients attending skin op GGH, Chennai, during the study period of August 2007 to September 2009, total number of patients with SLE was 45. The incidence of SLE in our study is 0.08% as compared to incidence of 0 .01 to 0.12% in literature[27]. F.B.Yab et al[100] study showed an incidence of 46.5%, 38.8%, 12.7%, and 2% of ACLE, CCLE, SCLE, LEP respectively, which is comparable with our study of 47.94%, 39.92%, 8.48% and 2.86% of ACLE, CCLE, SCLE, LEP respectively.

In Binoy.J.Paul et al[101] study youngest and oldest patient seen were 16 years and 63 years resp. In our study youngest patient documented was 15 years and oldest patient was 50 years. In Binoy.J.Paul[101]and Malaviya et al[102] studies average age was 21.6 years and 23 years resp. which is 22 years in our study. In Vaidhia et al[103] and Masi et al[104] studies 58% were between the age group of 20 to 30 years, but our study showed 62%.

In Malaviya et al[102] study female: male ratio is of 8:1 which is nearer to our study of 7:1. Burning sensation and erythema were the most common symptoms among patients, which is 63.63% & 42.42% respectively. Photosensitivity was the most common symptom in SCLE patients and pain is the most common symptom in LEP patient as documented in literature.[27]

Sunlight, infections, drugs, pregnancy, menstruation, stress are among the few well document precipitating (or) exacerbating factors that have been described in the literature[27]. Photosensitivity was observed in 52% in Allkes et al[105] study done in PGI and 54.4% in Nazarinia et al[106] study, which is comparable with our study of 55%. Co-trimoxazole and ibuprofen precipitated SLE in each one patient, which is also observed in literature.[27,28] Among the 45 patients, 26.66% of patients did not relate their disease with any exacerbating (or) precipitating factors. Familial incidence of SLE has been reported but with rarity[27,28].

In our study, history of SLE was present in a patient's sister, while another patient had an elder sister with Dermatomyositis. One patient had alopecia and another had hypothyroidism. Rheumatoid arthritis was seen in one of the patient's first degree relative. All these associations state a positive correlation of HLA association and autoimmunity in the pathogenesis of SLE[28].

In Fung et al[107] study, 44.52% presented only with mucocutaneous symptoms as primary complaints which is consistent with our study of 45%. Binoy.J.Paul[101] et al observed primary presenting complaints as photosensitivity in 78% of his study patients, non scarring alopecia in 60%, malar rash in 57%, which is comparable with our study of 80%, 57.77% and 60% resp.

Fung et al [107] showed arthritis as primary presenting complaint in 44% while Binoy.J.Paul[101] showed it as 66% which is comparatively high than our study of 34%. Fever was primary presenting complaint in 56.6% of patients in Binoy.J.Paul[101] study which is high compared to our study of 45.44%. Renal manifestations as initial presentation were seen 6% , 8% and 7.4% of Ester et al[108], Malaviya et al[102], Radhamadavan et al[109] study groups respectively, but in our study group it was 9.09%.

Photosensitivity as a symptom is seen in 70% - 80% of ACLE patients, 60% -70% of SCLE patients and 40% of CCLE patients as per literature.[27,28] In our study it was 88%, 100% and 43% of ACLE, SCLE and CCLE patients respectively.

Among the 20 patients who initially presented with mucocutaneous symptoms 75% of them developed systemic symptoms within one year and another 25% of them within next one year. Among 18 patients who presented with systemic symptoms initially, 77.75% of them developed cutaneous symptom within one year.

Photosensitivity is the most common ARA skin criteria associated with other ARA

criteria as given in the literature[27]. Photosensitivity is most commonly associated with 36.65% of hematological criteria and 21.5% of immunological criteria.

In our study distribution of the lesions were same as described in the literature.[28] In 16 patients with DLE 73.64% had lesions localised to the head and neck, 26.46% had disseminated type. This is compatible with the study of Millard and Rowell[21]. Binoy.J.Paul et al [101] observed 18.17% had DLE lesions over the scalp which is nearer to our study of 17.7%. Involvement of the concha of the ear has been stressed as an important clue in the diagnosis of DLE by Rebra and Sam shuster[67], in our study 17% patients had ear involvement. In SCLE, ACLE and LEP, lesions involved the classical sites as described in the literature[27].

Patients with ACLE, SCLE and CCLE had 43.21%, 28.62% and 28.17% of mucosal involvement resp. In our study majority of ACLE patients had mucosal involvement followed by SCLE and ACLE as described in literature[28]. Malaviya et al[102]documented oral involvement in 64% in his study as compared to 62% observed in our study. Among the mucosa, palate was involved in 83.30% of patients, lips in 25% and gingiva in 3.57%. Crusting of lips was the most common manifestation in patients, with lip involvement and characteristically spare vermillion border as described in the literature[28].

Morphology and sequelae of lesions were classical in the majority of the patients, in all the three spectrum as described in literature.[27,28] In DLE patients majority of them had plaque like lesions which ended with scarring as described in literature.[27] Few of the patients also had verrucous lesion, follicular plugging lesion in the ear which is also described in literature[27]. In our study two third of SCLE patients had papulosquamous lesions and one third had annular lesions, both these types of lesions did not end in scarring as described in the literature[28]. Vesiculation in active border seen in SCLE patients as in literature is not documented in our study.[46]

In ACLE patients with maculopapular rash, initially rash started in sun exposed area later on spread to whole of the body. In our study of ACLE patients, classical lesion as described in litrature of ACLE patients like facial erythema, butterfly rash(sparing naso labial fold), generalised exanthematous rashes were described.[28] LE/LP overlap turning in to SCC is seen in one patient, bullous lesion in one patient and LEP in one patient all of them had their morphology similar as described in literature[27,28]

As per Gilliam classification of specific and non specific lesions, specific skin lesions are comparatively common than non specific skin lesions in our study. Kapadia et al[110], Weysback et al[111] and Vaidhiya et al [112]who showed specific skin lesion in 55%, 53%, 50% respectively, which is comparable to our study of 54.33%. In Binoy.J.Paul et al[101] study, malar rash was seen in 28%, butterfly rash was seen in 26% of patients and maculopapular rash was seen in 20%. In our study malar rash, butterfly rash and maculopapular rash were seen in 37%, 35%, 18% respectively. Though only few presented with LE specific skin lesions initially, in due course of follow up, majority of them developed LE specific skin lesions.

Allkesh et al[105] and F.B.Yab et al[100] studies showed facial erythema in 80% and 86% respectively which is observed as 82% in our study. Out of 25 patients with ACLE 24% had butterfly rash, which is consistent with literature.[27] Masi et al[104] documented malar rash in 80% of patients which is observed as 76.52% in our study. Allkes et al[105] observed bullous SLE in 10% of their patients which is high compared to our study of 2.22%.

Zeevi et al[113], Allkes et al[103] showed diffuse non scarring alopecia in 86% and 85% of patients respectively, which comparable to our study patients with 85%. It was observed that the severity of hair loss was proportional to the disease activity, as also observed by Zeevi et al.[113] Nail changes were seen in 15% of patients as compared to 25% in literatures.[28] Nail changes documented in our study included ragged cuticle in 42%, paronychia in 25%, nail

dystrophy in 16%, melanonychia in 6% and beau's lines in 11%. The above nail changes were documented in the literature.[28] In our study among the above findings ragged cuticle was seen in most of the patients.

Non specific mucosal lesions are seen in 26% of patients in literature[28], but in our study it was 22.22%. In Allkes et al [105]study vasculitis presented as urticaria in 10% of patients, as purpura in 8%, as leg ulcer in 10%, and as gangrene in10% of patients, but in our study it was 4.44%, 4.44%, 2.22% and 2.22% respectively. Among the 2 patients with urticarial vasculitis 1 patient had renal involvement and low complement levels which states that the urticaria may be due to immune complex mediation. Association of hypocomplementemia was documented with lupus nephritis and urticaria in literature.[27,28] Patients with leg ulcer, was also associated with urticarial vasculitis . LE/ LP over lap was seen in 1 patient, who turned into SCC later, which is a rare documentation in literature[28].

Few other associated skin lesions were also seen in our study which includes icthyosis in 8.88%, acanthosis nigricans 4.44% and anetoderma in 2.22% patients. The above findings though rare, are documented in literature[27].

Associated systemic findings were most commonly seen in ACLE patients as in literature.[28] Allkes et al[105] study observed fever and arthralgia in 92.67% and 22.4% respectively which is comparable with our study of 92.42% and 22.44%. Binoy.J.Paul et al[101] and Malaviya et al[102] studies observed lupus nephritis in 35% as compared to 33.33 % in our study. Ester et al [108]and Radha Madhavan et al [109]studies showed renal symptoms as initial complaints in 6 & 7.4% respectively but in our study it was 4.04%.

Respiratory problems were seen 26% in Nazarinia et al[106] study which is comparatively higher than our study of 8.88%. Dubois et al[115], Vaidiya et al [103] and Radhamadavan et al [109]

observed 25% of neuropsychiatric manifestations in their patients which is nearer to our observation of 26.52%. Among 12 patients with neuropsychiatric manifestations 4.32% had seizures and 40% had psychiatric problems. Psychiatric manifestations included depression, anxiety neurosis and obsessive compulsive neurosis. Lymphadenopathy was documented as 50% in literature [28] but in our study it was11.11%. Conjunctivitis observed in our study was a rare documentation in the literature.[27]

HPE DISCUSSION

Characteristic HP skin changes of LE specific skin lesion as in literature,[27,28] like hyperkeratosis, liquefaction degeneration of basal cells periappendageal infiltrate , perivascular infiltrate is seen in majority of patients. Varying mosaicism of these features are seen in 3 major spectrum of LE specific skin disease[35].

It is described in literature[28] that, follicular plugging , keratotic plugging, extensive basal cell degeneration, dense pigment incontinence, patchy inflammatory infiltrate around and independent of appendages and dense deep dermal infiltrate is seen more commonly in DLE than in SCLE or ACLE[35].The above finding is consistent with our study like extensive basal cell degeneration in 100%, follicular plugging is seen in 74% of patients, keratotic plugging in 65%, dense pigment incontinence in 82%, dense deep dermal in filtrate in 70% and periappendageal infiltrate in 68% of patients.

Focal liquefaction degeneration of basal cells, dermal edema and sparse inflammatory infiltrate in upper dermis (as against the deep dermal infiltrate of DLE lesions) which are all common documentation in SCLE patients in literature, [35] were also documented in our study. Other uncommon literature[35] findings like atrophic epidermis, vesicular changes in active borders, extravasation of RBC's and fibrinoid deposits were not encountered in our study.

As per literature[35] reports hyperkeratosis is less striking in ACLE than in DLE and SCLE, this finding is consistent with our study.[125] Upper dermal sparse inflammatory cell, and upper dermal edema, which is a common finding documented in literature[35], was frequently encountered in our study. Focal liquefactive degeneration which is a common finding in literature,[35] is seen in only few of our study patients. Histopathological feature of bullous SLE is consistent with the literature[35]. Severe forms of ACLE may have epidermal necrosis and the clinical lesion may resemble TEN.[35] The above finding, which was a rare entity, has not been encountered in our study.

In patients with urticarial vasculitis histopathological examination showed inflammatory infiltrate predominantly within and around small blood vessels mainly of neutrophils and also leukocytoclastosis. A case of LEP showed minimal atrophy of epidermis, inflammatory infiltrate cell collection in dermis and septilobular lymphohistiocytic infiltrate in subcutis. In patient with LE/LP overlap, hypertrophic DLE lesions histopathologically showed features of lichen planus, but ulcerative DLE lesions showed features of SCC like, individual cell keratinisation and keratin pearls. All the above findings documented in our study were also seen in literature.[35]

LABORATORY FINDINGS

As reviewed in the literature[28], most of the laboratory abnormalities have been attributed to the autoantibodies produced against the various components of different tissues. Binoj.J.Paul et al [101]study showed raised ESR in 65.43%, anemia in 42% and leucopenia in 13% in his patients, which is observed as 63.34%, 42%, and 15.55% respectively in our study. Thrombocytopenia was seen in 17.2% & 12.22% of Ester et al[108] and Yokohari et al[114] studies respectively, which is 4.45% in our study. False positive VDRL was seen in 23% of Jarallah et al [112] patients, but in our study it was 18%.

In Allkes et al[105] study 26.67% had abnormal 24 hrs urine protein excretion which is comparable to 33% in our study. Grade III lupus nephritis was observed in 49.7% of Nazarinia et al[106] study as compared to our study of 50%. C3 and C4 levels were found low in 45% of patients in Arfaj et al [115]study as compared to 66% of patients in our study. Rheumatoid factor was positive in 19% in Binoj.J.Paul[101] et al study as compared to 11.11% in our study. All 6 patients who had suspicion of antiphospholipid antibodies were investigated with IgG and IgM levels of APL. 50% among them had abnormal levels which is same as that of Arfaj et al study[115].

ANA was done for all the patients. Binoj.J.Paul et al [101]and Nazarinia et al[106] studies showed ANA positivity in of 93% and 94% respectively, which is almost correlating with our study of 94%. ANA positivity in literature[28] in various spectrum like DLE, SCLE and CCLE are 30%-40%, 60% and 85% respectively. But in our study it was 70%, 100% and 100% in CCLE, SCLE and ACLE respectively. dsDNA was positive in 83% as also shown by Arfaj et al [115]and Nazarina et al.[106] DIF and IDIF were done for 3 patients. All three patients specimen sent for lupus band test and IDIF, showed positive results. Two patients of IDIF positivity showed homogenous pattern and one patient showed speckled pattern. Patient with speckled pattern had lupus nephritis. Among the lab criterias of ARA, ANA was the most common criteria seen in 94% of patients, followed by dsDNA in 83% of patients, anemia in 40% of patients and leucopenia in 15% of patients. Maximum lab criterias were fulfilled by patients in ACLE spectrum as described in the literature.[27,28]

SUMMARY & CONCLUSIONS

- The incidence of SLE during the period of August 2007 to September 2008 is 0.08%.

- ACLE is the commonest spectrum followed by CCLE and SCLE.

- Commonest age group falls between 20 to 30 years. Youngest age documented was 15 years and oldest age was 50 years.

- Female preponderance was seen in all types of spectrum.

- Sunlight is the commonest among the precipitating and exacerbating factor followed by infections, physical/mental stress, drugs, pregnancy and menstruation.

- Familial history of other associated autoimmune disease states that, genetic back ground is an important contributing factor.

- Diffuse hair loss and photosensitivity are common among the cutaneous symptoms. Palatal ulcer is the most common mucosal symptoms and it is commonly associated with ACLE. Fever and arthralgia are the most common symptoms among the systemic symptoms.

- Among the patients who initially presented with cutaneous symptoms most of them developed systemic symptoms in first year of follow up likewise patients who initially presented with systemic symptoms majority of them developed cutaneous symptoms with in 1 year.

- Among the clinical skin criterias of ARA, photosensitivity is the most common criteria. Photosensitivity and malar rash are among the ARA skin criteria to have more correlation with other ARA criteria.

- Localised DLE is the most common type among the CCLE group. SCLE lesions are widespread and ACLE lesions are more commonly seen over the sun exposed area.

- Among the specific lesions, malar rash and DLE are commonly encountered. Among the non specific skin lesions diffuse non scarring alopecia is the most common finding documented.

- Few rare observations in our study are LEP, bullous SLE, anetoderma, urticarial vasculitis, purpura, gangrene and acanthosis nigricans. LE/LP over lap turning into SCC, which is a rare entity, is encountered in our study.

- ACLE spectrum is the commonest to be associated with systemic disease.

- Majority of the patient's HP feature in various spectrum of SLE is consistent with that of literature. All the three patient's samples sent for DIF and IDIF are positive.

- Maximum laboratory abnormalities are seen in ACLE spectrum. Among the lab criterias of ARA, Anemia, leucopenia and ANA positivity are the most common lab abnormalities observed.

PROFORMA

Case No	Name	Age
RC No	Sex	
Occupation	Address	Date

Chief Complaints

Cutaneous	Extra Cutaneous.

History of presenting illness

Elaborate the symptoms

Site	Onset	duration
Progression	regression	

PPT factors –

Photo sensitivity	Food	Infections
Stress	Mental	Physical
Trauma	Drugs-Duration / name of drug	
Menstruation	pregnancy	Others

H/O Constitutional symptoms

H/O Implants

H/O Raynaud's phenomenon

H/O heavy metal exposure – Type of metal – duration.

H/O Shortening of fingers / ulceration

H/O hair loss – re growth present / absent

H/O urticaria

H/O Purpura, nodules, papules

H/O Pigmentation, bullae

H/O Oral ulcers

H/O difficulty in swallowing

H/O nasal symptoms

History related to systemic involvement

H/O Joint pain / deformity

H/O suggestive of CVS movement

H/O CNS involvement

H/O Psychiatric disturbances

H/O Respiratory tract involvement

H/O Hematuria / loin pain

H/O Ocular symptoms

Past History

Treatment History:

Family history	-	Other family members affected
	-	Any other connective issue disorder
Personal	-	H/O abortion
	-	H/O Premenstrual flare
	-	H/O Perinatal mortality / Morbidity

G/E	anaemia	jaundice	clubbing	lymphadenopathy

BP	HR	RR	Edema	Built

CVS - SIS2 /any other murmurs

RS - NVBS / any added sounds

Abd

CNS

Joints

Dermatological examination

MORPHOLOGY – SKIN

Erythema	Malar rash	Papule	Patch
Plaque	atrophy	scaling	scarring
Edema of face	chronic ulcer	telengiectasia	urticaria
Purpura	Raynaud's	Icthyosis	Discoid rash

Bulla	Pyoderma gangrenosum	Acanthosis nigricans
Follicular papules	nodules	Thrombophlebitis
gangrene	relapsing condritis	pigmentary abnormalities

Others

HAIR		non scarring
	Alopecia	lupus hair
		Scarring

NAIL	splinter hemorrhage	ragged cuticle	red lunula
	ridging	onycholysis	Others

MUCOSA	oral	nasal
	Vulval	perianal
	Others	

BLOOD

HB%	TC	DC	platelets

ESR

RFT

LFT

CRP	VDRL	HIV
ANA		ANA Pattern
dsDNA		Anti DNA antibody
Other Auto antibodies		Serum Complement levels
RA factor		ACL Antibodies

Others

URINE

Albumin	Sugar	Deposits

24 hrs urine protein excretion

Skin biopsy

Immunoflourescence	Indirect	Direct

ECG	ECHO
CXR	others

Expert opinion

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KEY TO MASTER CHART

M	: Male
F	: Female
ppt	: Precipitating factor
agg	: Aggravating factors
ESR	: Erythrocyte sedimentation rate
Drg	: Drugs
D	: Disseminated
L	: Localised
sun	: Sunlight
ps	: Physical stress
MS	: Mental stress
pmf	: Premenstrual flare
INF	: Infections
alc	: Alcohol
preg	: Pregnancy
pneu	: Pneumonia
LN	: Lupus nephritis
NP	: Neuropsychiatric
conj	: Conjuctiva
pal	: Palate
UV	: Urticarial Vasculitis
pur	: Purpura
NSA	: Non scarring alopecia
SA	: Scarring alopecia
Nc	: Nail changes
AN	: Acanthosis nigricans

gang : Gangrene

ANE : Anetoderma

ANU : Annular

PSq : Papulosquamous

Lu : Leg ulcer

Ic : Icthyosis

ABBREVIATIONS

SLE	:	Systemic Lupus Erythematosus
DLE	:	Discoid Lupus Erythematosus
SCLE	:	Subacute Cutaneous Lupus Erythematosus
ACLE	:	Acute Cutaneous Lupus Erythematosus
DDLE	:	Disseminated Discoid Lupus Erythematosus
DIF	:	Direct Immuno Fluorescence
IDIF	:	InDirect Immuno Fluorescence
LE/LP	:	Lupus Erythematosus/ Lichen Planus overlap
LEP	:	Lupus Erythematosus Panniculitis
TNF	:	Tumour Necrosis Factor
INF	:	Interferon
dsDNA	:	Double Stranded DNA
ENA	:	Extractable Nuclear Antigen
LBT	:	Lupus Band Test
DEJ	:	Dermo Epidermal Junction
BMZ	:	Basement Membrane Zone
Ig	:	Immunoglobulin
EMF	:	Erythema Multi Form