CONNECTIVE TISSUE DISEASES

Inherited /acquired disorders of connective tissue system

Collagen diseases- unacceptable term

Lupus Erythematosus

Classification

DLE - Localized

- Disseminated

SCLE

SLE Genetically distinct

Somatic mutation

Discoid Lupus Erythematosus

Autoimmune in 50%

Peak age of onset - 40 years

Relatively benign

Mainly affecting face

Characteristic histopathological,

Hematological & Serological changes

ETIOPATHOGENESIS

Genetic factors

3 genotypes according to age of onset

HLA B7,B8,CW7,DR2,DR4,DQW1

Somatic mutations at autosomal loci in lymphoid stem cell

- Forbidden clone of lymphocytes synthesizing cellular autoAB's

Environmental factors

Trauma, mental stress, sunburn,

Infection, exposure to cold,

Pregnancy,

Drugs - isoniazid, penicillin,

griseofulvin, dapsone

HISTOPATHOLOGY

- Liquefactive degeneration of basal cell layer
- Degenerative changes in connective tissue,
- Hyalinization, oedema, fibrinoid change
- Patchy dermal lymphocyte infiltrate mainly peri-appendageal

Immuno-histology

IgG, IgA, IgM & complement present at DEJ in 80% patients in skin lesions present for more than 6 weeks

Patterns

Homogenous, granular, thready

Unlike SLE

- not in uninvolved skin

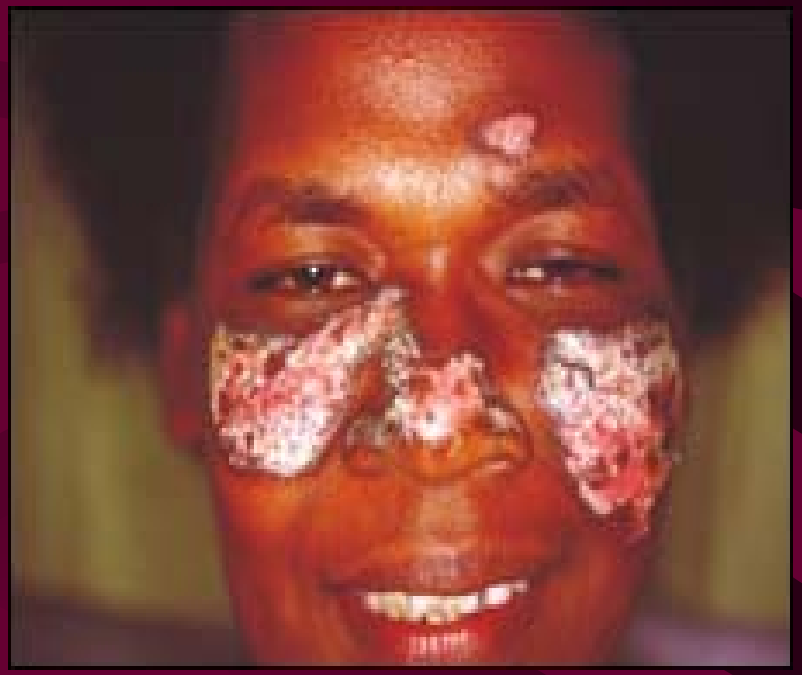
Clinical Features

Rash over face, cheeks, nose

Other sites

Scalp, ears, arms legs & trunk

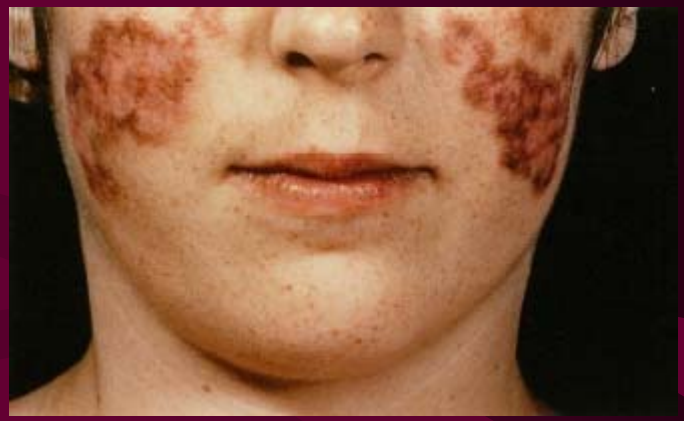
Variably sized, well defined erythematous, patches/plaques

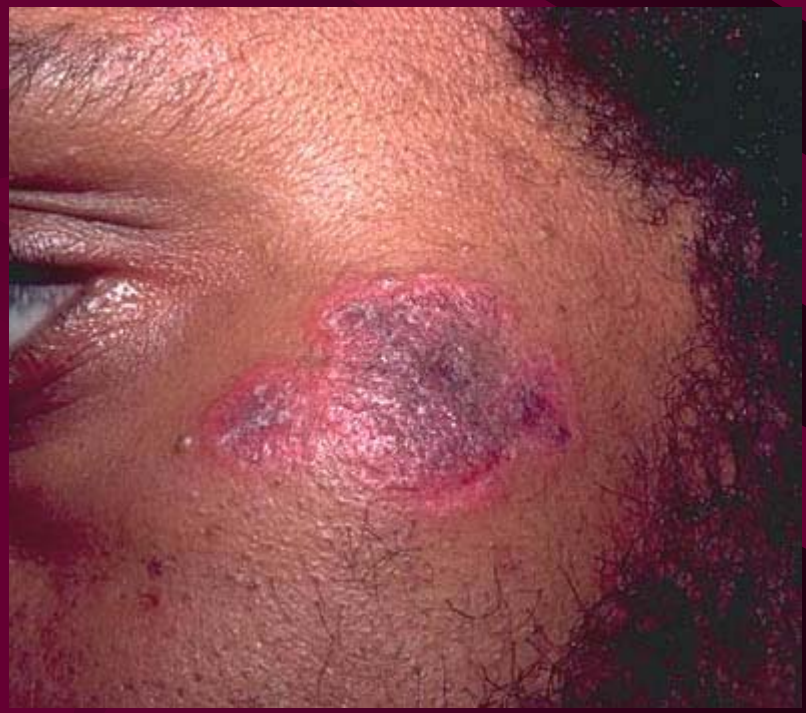


Adherent scale - removed horny plugs in dilated pilosebaceous canals – **‘Tin-tack’/‘carpet tack’ sign**

Wide follicular pits in ear

Heals with atrophy & scarring





Annular atrophic plaques

Face, neck,behind ears

Warty lesions

Nose, ear, temple, scalp

Hyperkeratotic

Arms & legs

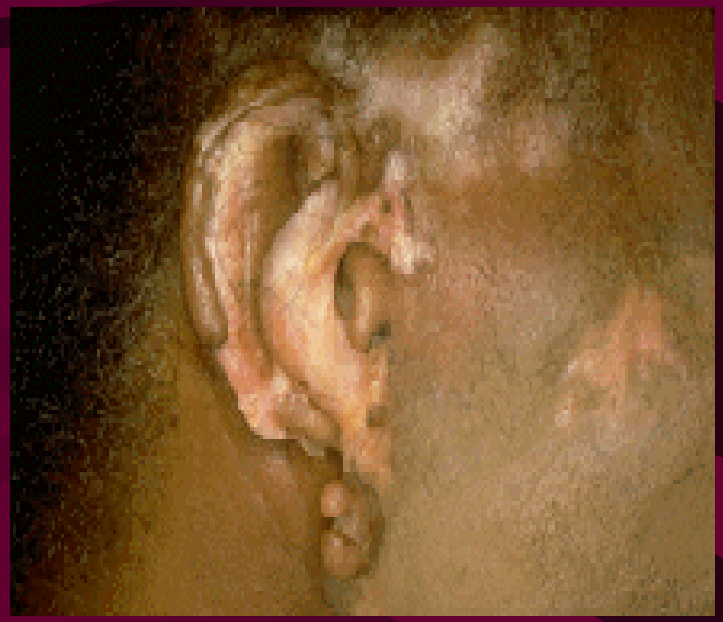
Tumid type

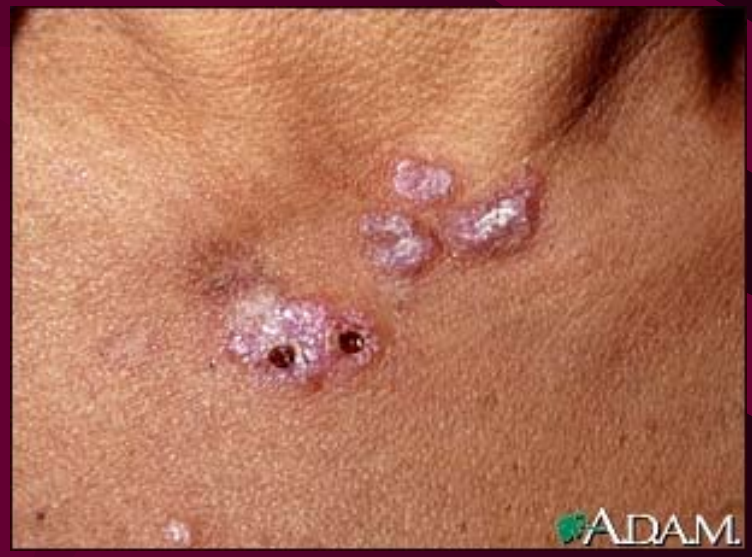
Cheek, whole limb

LE telangiectoides

Face, neck,ears

breast, hands

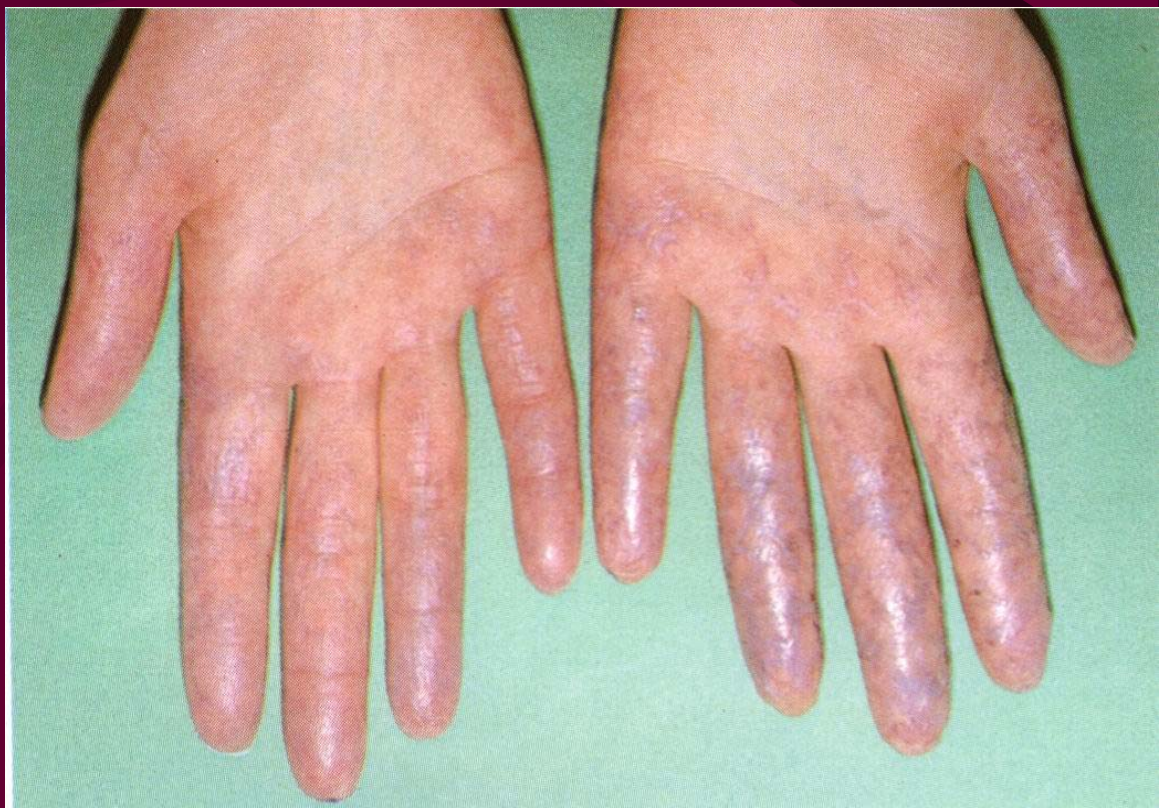




Chilblain lupus

sites- Toes, fingers, neck, Calves, knees, ears,fingers

clinically-Atrophic, spindling Hyperextensions of terminal phalanges

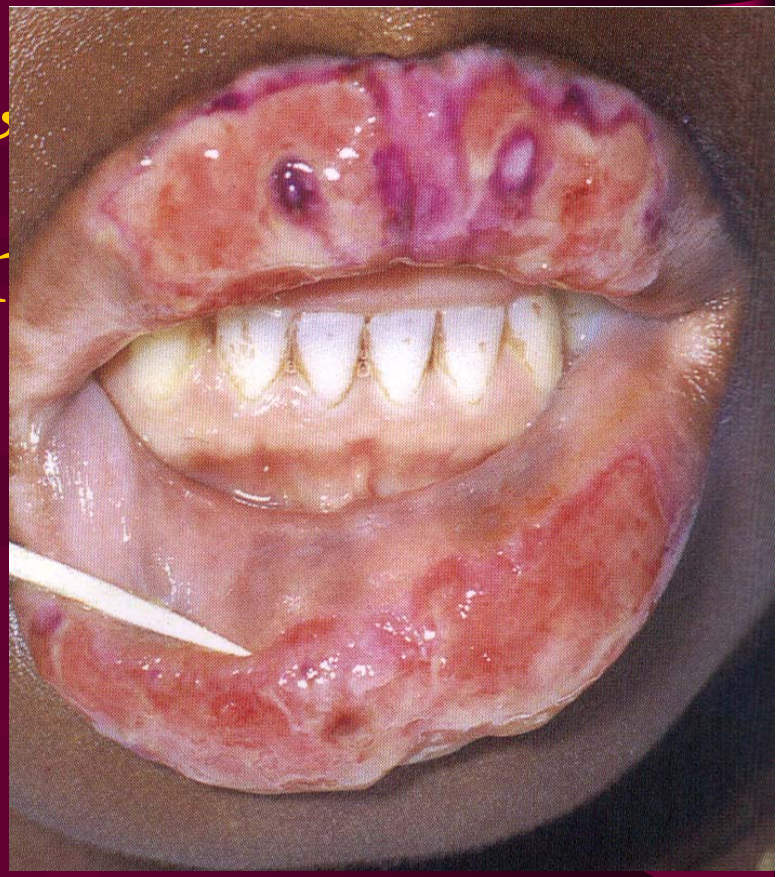


Mucus Membranes

Lips-thick, rough, red,

Superficial ulceration

& crusting



Eye lesions

Oedema & conjunctival redness

Eyelids

Infiltrated, scaly, peripheral redness

Nails

Sub ungual hyperkeratosis,

Red-blue colors of nail plate

Lab Abnormalities

↑ S.globulin - most common(55% patients)

Anemia, leucopenia, thrombocytopenia,

↑ESR

False +ve reactions for syphilis

Anti nuclear Ab’s - 35%

Differential Diagnosis

- Lichen planus
- PMLE
- Seborrheic dermatitis
- Lichen sclerosus
- Morphea
- Chilblains
- Sarcoidosis

Prognosis

Untreated - persistant

Complete remission in 50%

Scarring (57%)

Scarring alopecia (35%)

Long duration -

Raynaud's

Scalp involvement

Chilblains like lesions

Risk of SLE - 6.5% in localised DLE

22% in Disseminated

Treatment

General measures

- Photoprotection

Topical Steroids

Resistant cases - I/L steroids (lips, mouth, ears)

I/L Interferons

CO2 laser

Pulsed dye laser

Argon laser (telangiectatic type)

Oral therapy

Antimalarials

Chloroquine sulphate 200mg B.D

Reassessed at 6 weeks

Side effects

Corneal deposits, retinopathy, pigmentation of nails & legs, bleaching of hair, Exfoliative dermatitis, Myopathy, neuropathy, mental disturbances

HCQS(Hydroxychloroquine)

400-800mg B.D

75% patients respond

Oral steroids- if antimalarials fail

Prednisolone 5-15mg/day help in joint pains & scalp involvement

Others

B-carotene 50mg TDS

Clofazamine 100mg/day

Dapsone 100mg/day

Etretinate 1mg/kg/day

Methotrexate

Thalidomide(100-200/day)

Cyclophosphamide (50-200mg/day)

Gold salts(6-9mg/day)

Phenytoin 100mg TDS

Subacute cutaneous lupus Erythematosus

10% LE patients

Non scarring papulosquamous (2/3)

Annular polycyclic lesions (1/3)

Resolve with grey-white hypopigmentation & telangiectases

- Follicular plugging & hyperkeratosis not prominent

-Non scarring alopecia & photosensitivity(50%)

-50% fulfill ARA criteria for SLE (arthritis MC)

-Fever, malaise & CNS involvement frequent

Mild renal disease

Lesional subepidermal Ig deposition(60%)

speckled IgG

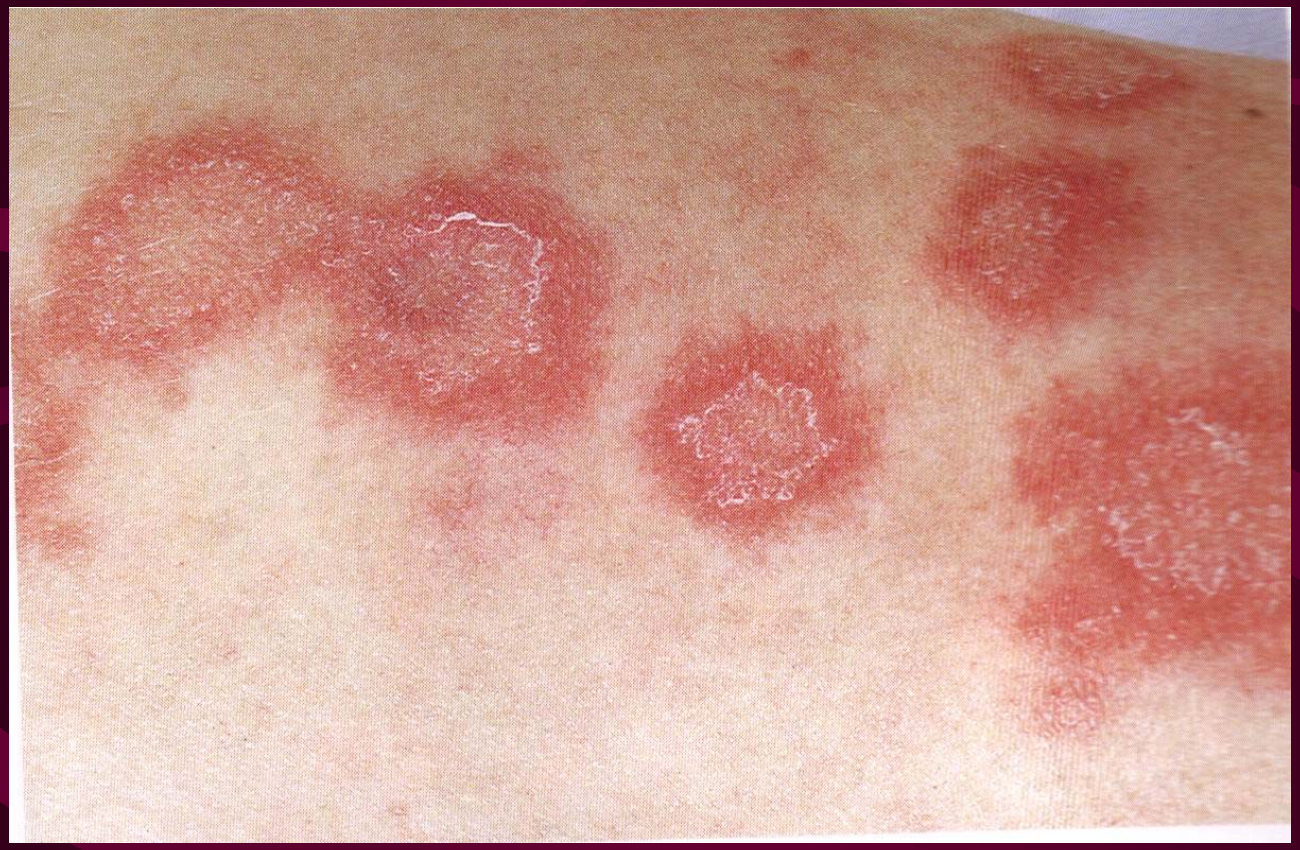
Drugs

Hydrochlorthiazide

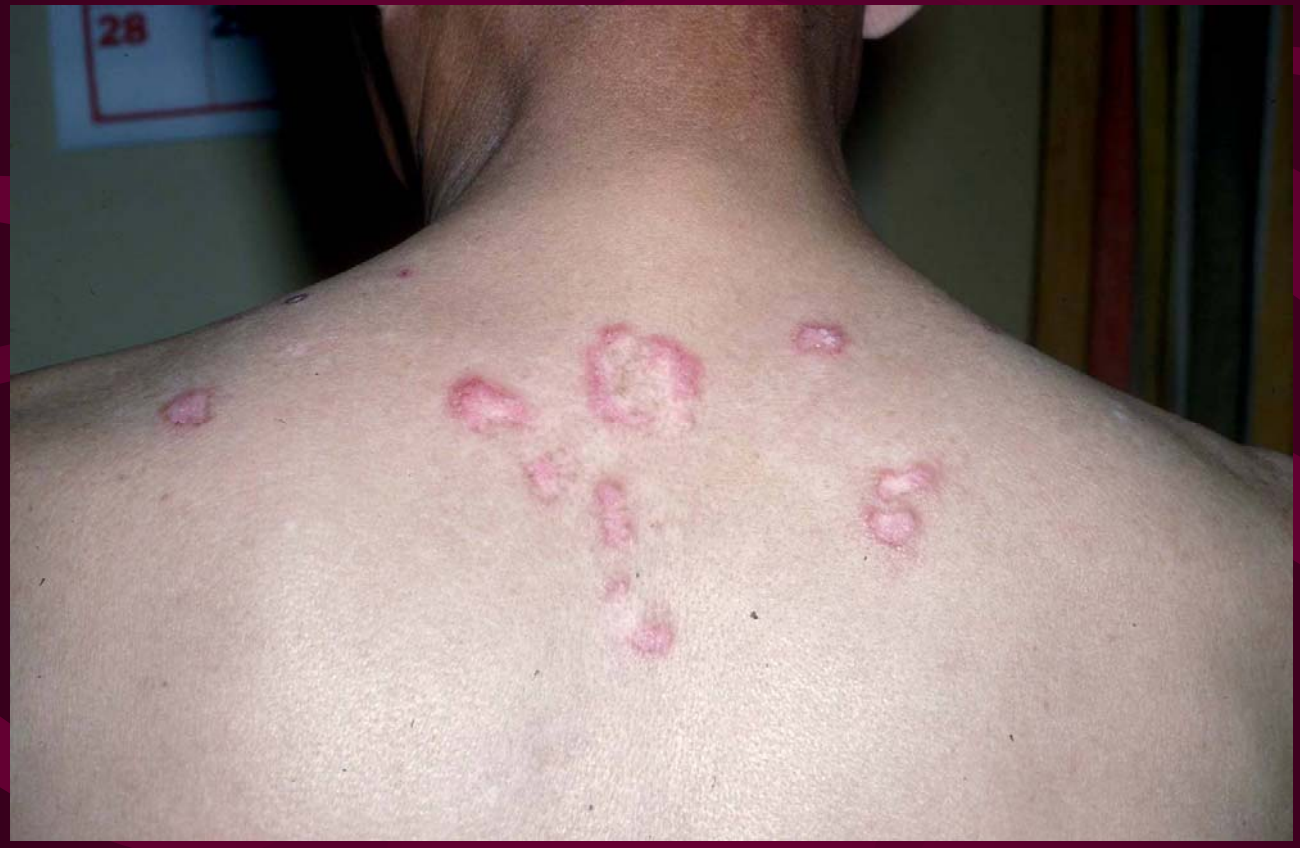
Griseofulvin

PUVA

Subacute Cutaneous Lupus Erythematosus



Subacute Cutaneous Lupus Erythematosus



Treatment

- Sunscreens
- Topical steroids
- Antimalarials
- Oral steroids
- Etretinate, Dapsone
- Cyclosporine, oral gold

Systemic lupus Erythematosus

-Systemic association of immunological abnormality with pathological changes in various organs

-Particularly Skin, joints & vasculature

- F:M 8:1

-Age of onset - 38 years

Etiopathogenesis

Unknown

Genetic factors

HLA - B8, DR3, A1, DR2, DQ

Auto antibodies

Non organ specific humoral auto AB's

- hallmark of SLE

Anti ds DNA & Anti Sm Ab's

- More specific

Antinuclear & Anti Sm Ab's

- More common

Environmental factors

- Silicone implants, heavy metals, mercury, gold, & trichloroethylene
- Infections, stress, hormonal factors
- UV radiation
-Virus - Myxovirus
- Drugs –n Hydralazine, minocycline anticonvulsant, procainamide

Histopathology

Hyperkeratosis without parakeratosis

liquifactive degeneration of basal cell

Edema in dermis with vesicle formation

at DEJ

Perivascular lymphocyte infiltration

Immuno Histology

Predominantly IgG, IgM, IgA with complement

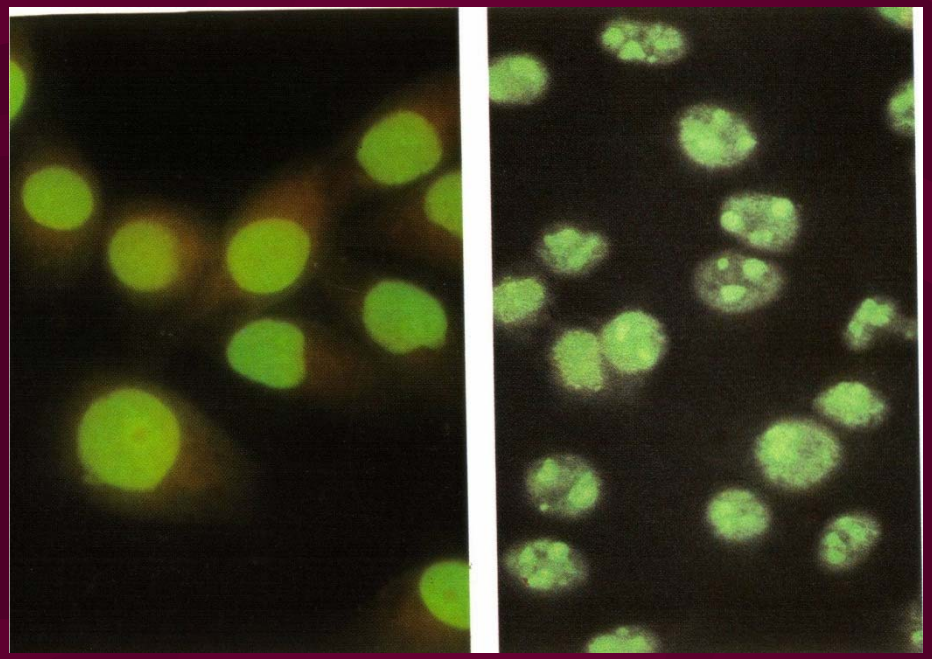
C1,C3 at DEJ in 80% patients

Uninvolved skin from exposed area - 75%

Uninvolved unexposed skin +ve in 50%

Immunoflurosence patterns

Homogenous	stippled	thready
↓	↓	↓
Old lesions	Uninvolved skin	New lesions



Internal organs

Characteristic microscopic features

Haematoxylin bodies in heart valves

Periarterial fibrosis

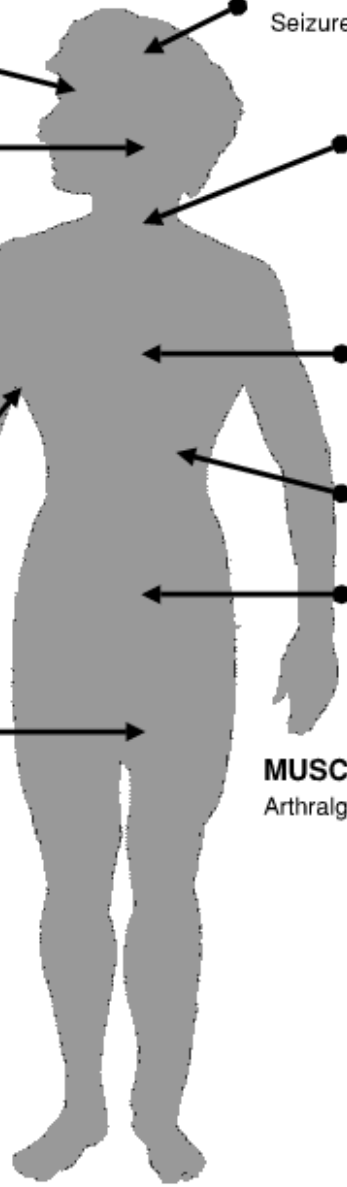
Wire-loop lesions in kidney

Clinical Features

- Arthritis
- Cutaneous changes
- Renal abnormality
- Psychiatric disturbance
- Serological findings
- Pericarditis
- Pleurisy
- Abdomen pain
- PUO, Menstrual disturbances, Raynaud’s

GENERALISED SYSTEMS

Weight loss, Fever, Fatigue, Aching, Weakness



EYE
Retinal exudates, Blindness, Conjunctivitis

CENTRAL NERVOUS SYSTEM
Seizures, Paralysis, Psychiatric Disorders, Neuropathies

SKIN COVERING
Baldness, Discoid L.E., Butterfly rash, Raynaud's Syndrome, Photosensitivity, Mucosal ulcers of Nose, Mouth and Vagina

BLOOD
Decreased platelets, Abnormal Autoantibodies

LINING MEMBRANES
Pericarditis, Pleurisy, Endocarditis

KIDNEY
Renal Failure, Proteinuria, Oedema, Hypertension

LYMPHADENOPATHY
Spleen enlargement

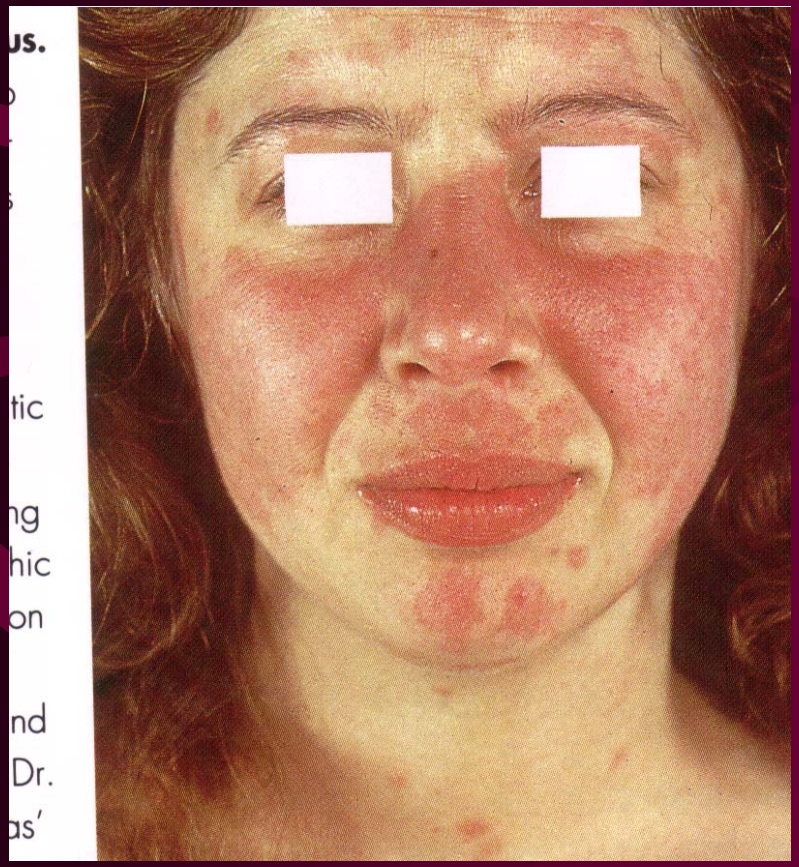
GASTRO-INTESTINAL TRACT
Poor appetitie, Vomitting, Diarrhoea

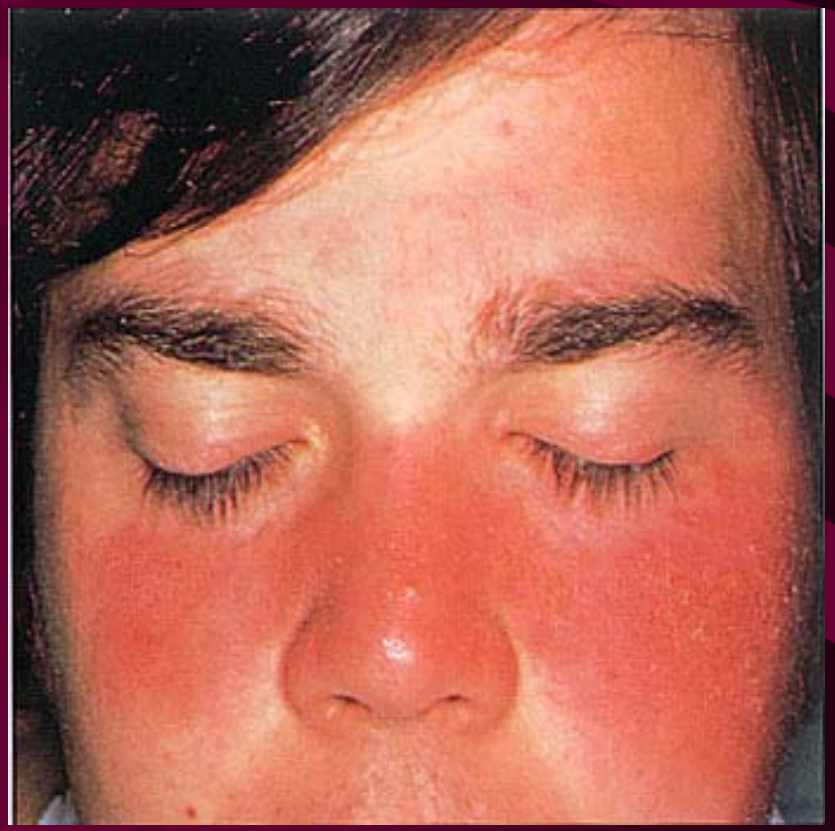
REPRODUCTIVE
Menorragia, Amenorrhoea, Prematurity, Stillbirths

MUSCULOSKELETAL
Arthralgias, Arthritis and Myalgias

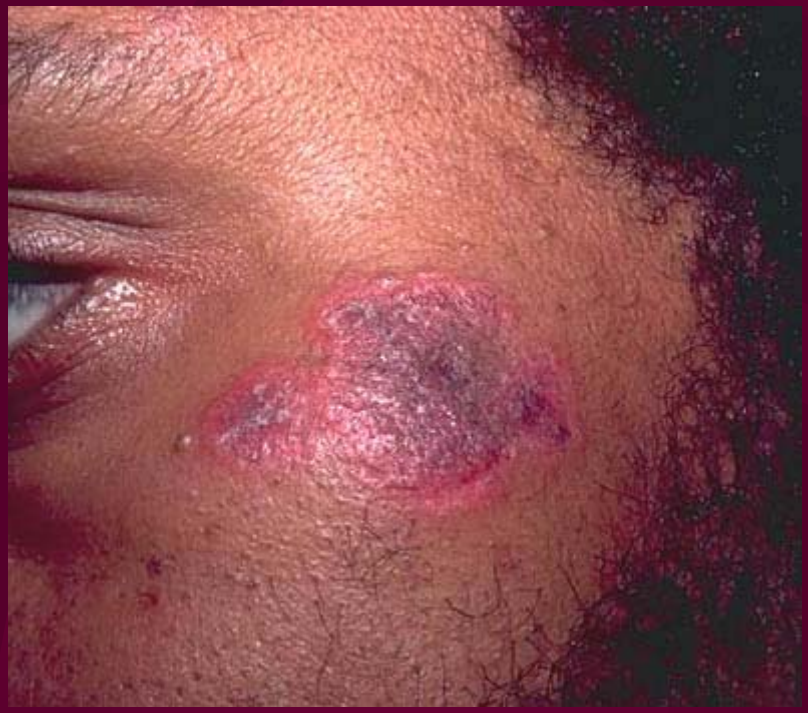
American Rheumatism Association Criteria for SLE

1.Malar Rash

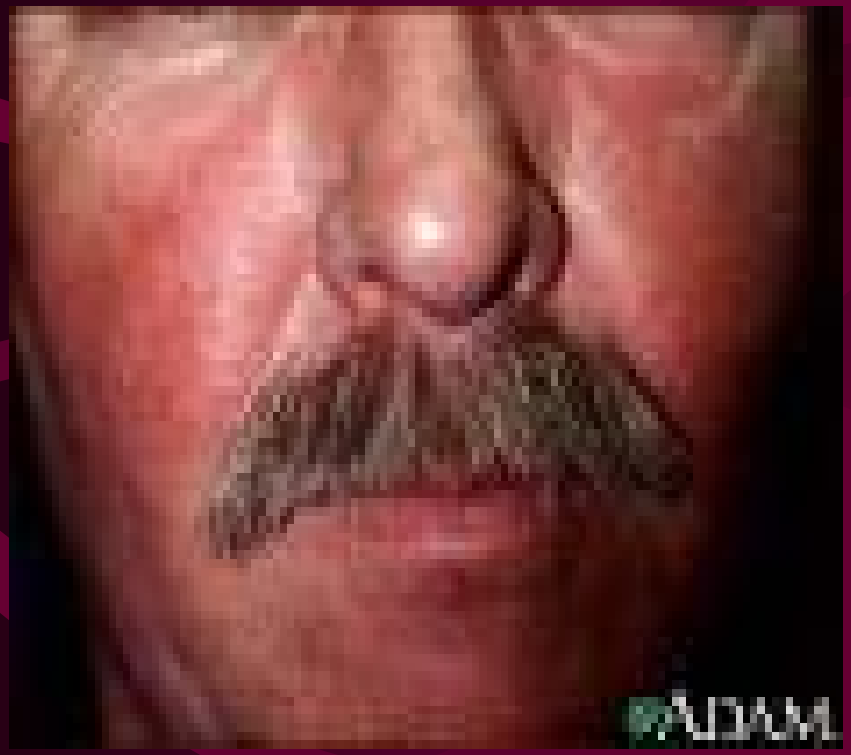


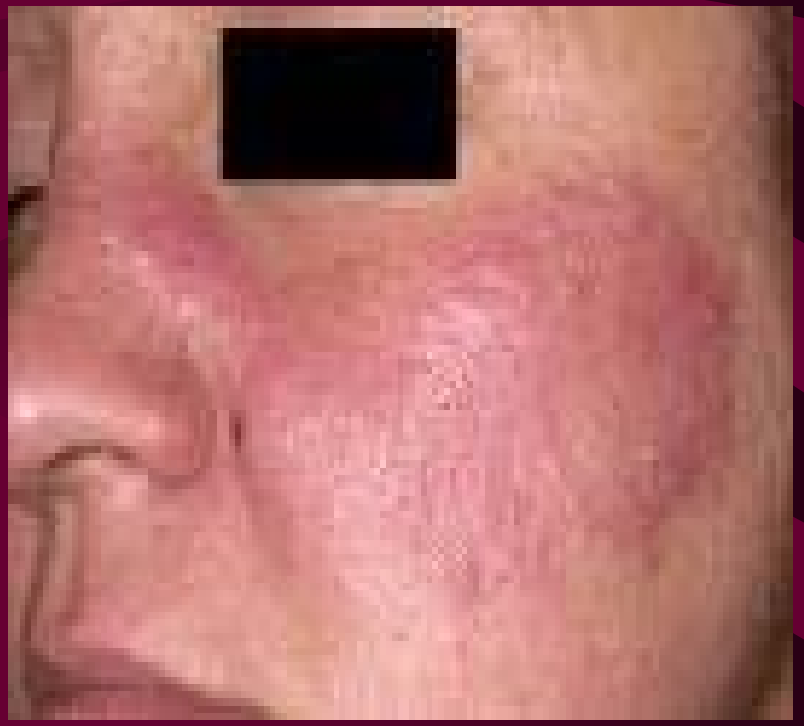


2. Discoid rash

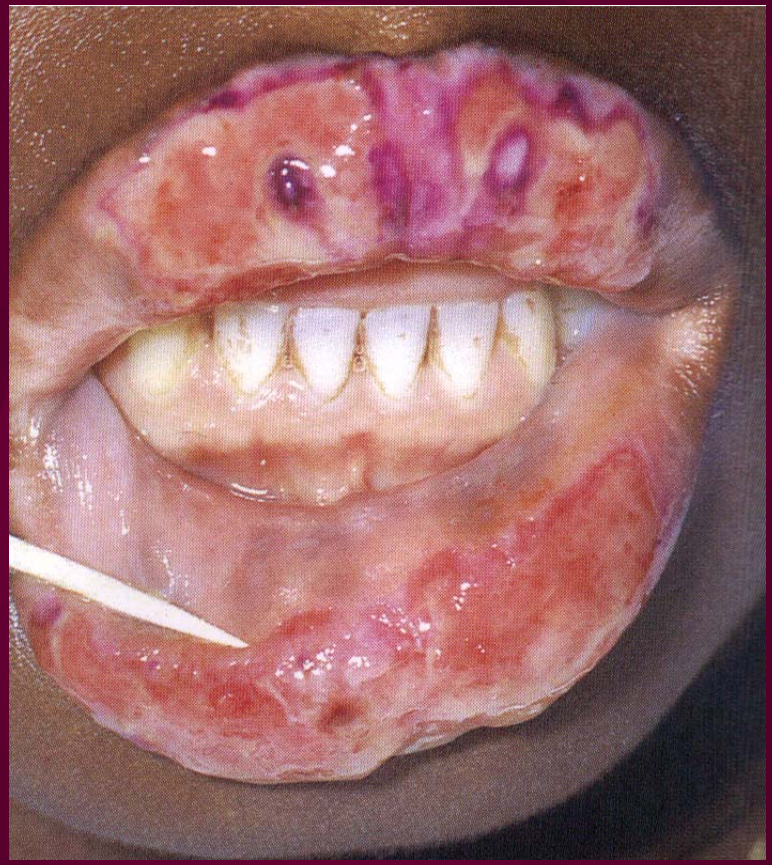


3. Photosensitivity

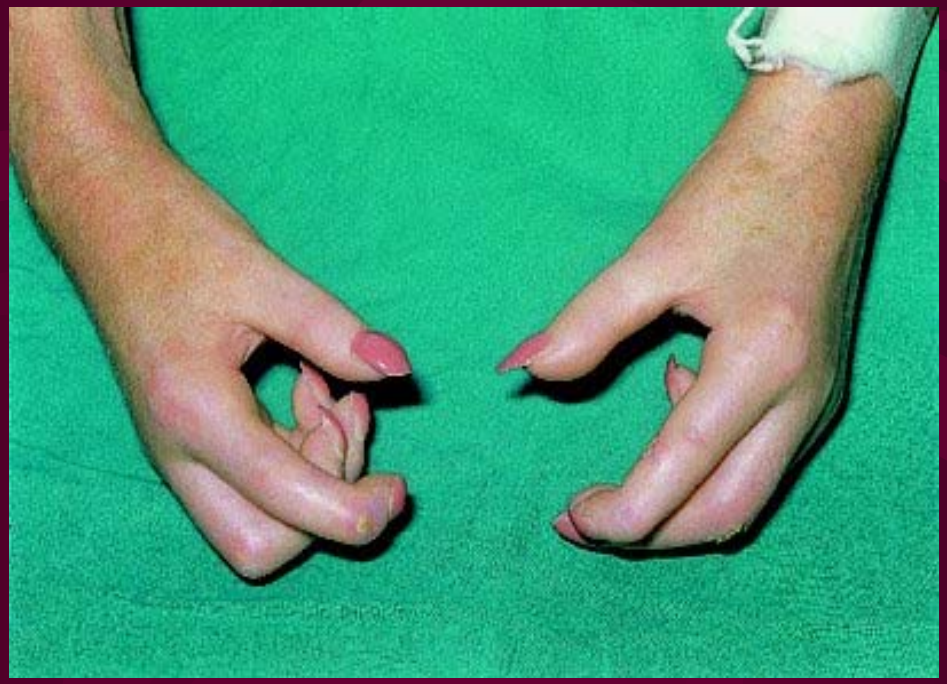




4. Oral ulcers - Palate



5. Non erosive arthritis



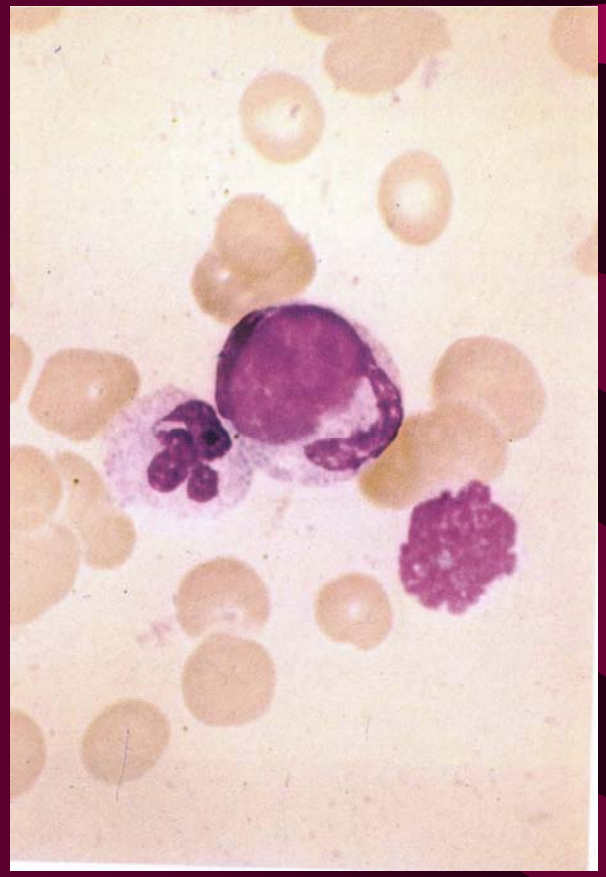
6. Serositis-Pleurisy/ pericarditis

7. Renal disorder (Persistent proteinuria >0.5g/d or cellular casts)
8. Neurological disorder - seizures/ psychosis
9. Hematological - Hemolytic anemia, leucopenia, thrombocytopenia
10. Immunological - LE cells, anti DNA Ab, anti Sm Ab
11. Antinuclear Ab's

Lab Investigations

LE cell Test (80%)

LE cells are polymorph with ingested nuclear material from degen. WBC's (those of an Ab to deoxyribonucleoprotein)



Treatment

Optimal function with minimal disease

General - Photoprotection

Steroids - Prednisolone 60mg/day,

↓ 10- 15mg/d

Chloroquine/HCQS - Less useful

Immuno suppressives - Azathiophine, Cyclophosphamide

Plasmapheresis ,Cyclosporin, Methotrexate