Systemic Lupus Erythematosus

SLE

- Autoimmune disorder
- Cellular damage bcs of Auto-Abs n Immune-complexes

SLE: Etio-pathogenesis

Susceptibility Genes

- HLA II DR, DQ; Homozygous def of early complements (C1q, C'2 n C'4), female gender

Environmental Factors

- Estrogen containing OCPs, UV light exposure, EBV infection

Immune activation

- Hyper-reactivity and Hypersensitivity of T and B lymphocytes

Auto-Abs n Immune complexes

- Release of Chemotaxins, vasoactive peptides, and destructive enzymes into the tissues
- Sequestration n destruction of Ig-coated cells

SLE: Histopathology

- Skin Biopsy→ T cell infilt at DEJ, perivascular and around appendages
  → Ig deposition at DEJ
- Renal Biopsy → Class I (MMLN)
  → Class II (MesPGN)
  → Class III (FLN): A, C, A/C
  → Class IV (DLN): S/G for A, C, A/C
  → Class V (MGP)
  → Class VI (DGS)

Clinical Manifestations

- Musculoskeletal:

→ Non-erosive Polyarthritis

If erosions…..some alternative daignosis (? RA)

If monoarthritis…Ischemic bone necrosis (Steroids for SLE n not disease activity)

Hand deformity only in 10%

→ Myalgia/ Myositis ….Also consider Steroid and Anti-malarial (HCQS) myopathy

Clinical Manifestations

- Muco-Cutaneous/Lupus Dermatitis:

i) DLE ii) SCLE iii) Others

DLE→ circular, raised erythematous lesions with hyperpigmented rims & central atrophy

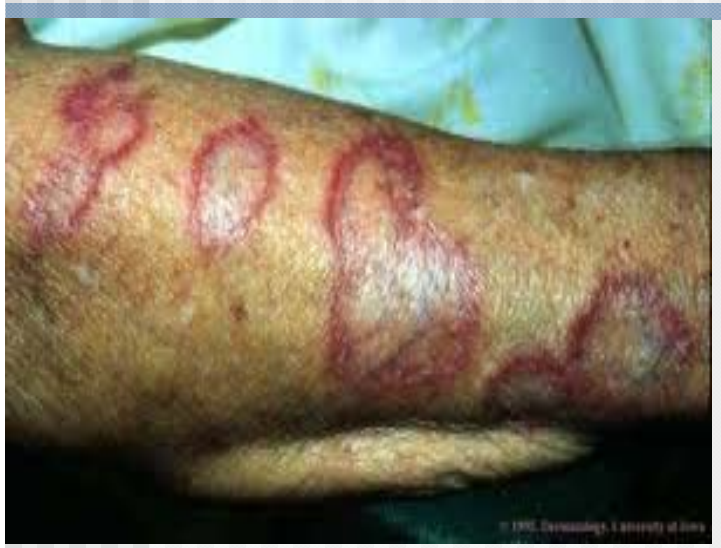
→ 5 % of pts with DLE…..have SLE

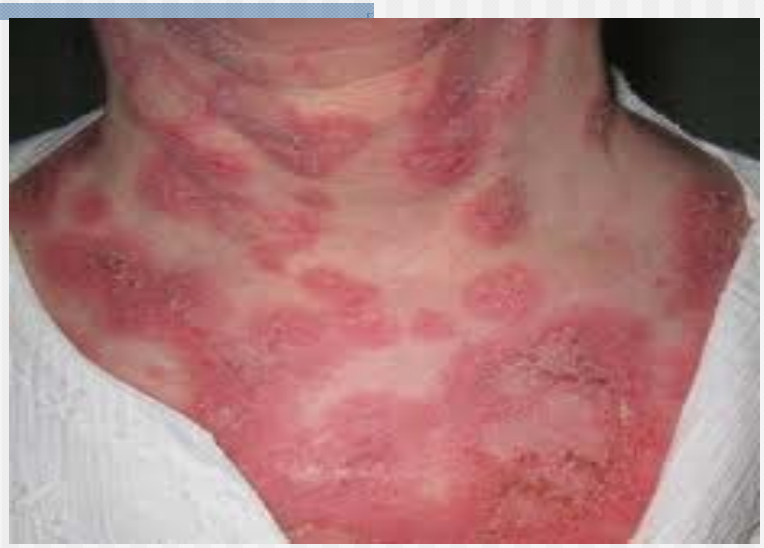
→ 20% Of pts with SLE…..have DLE

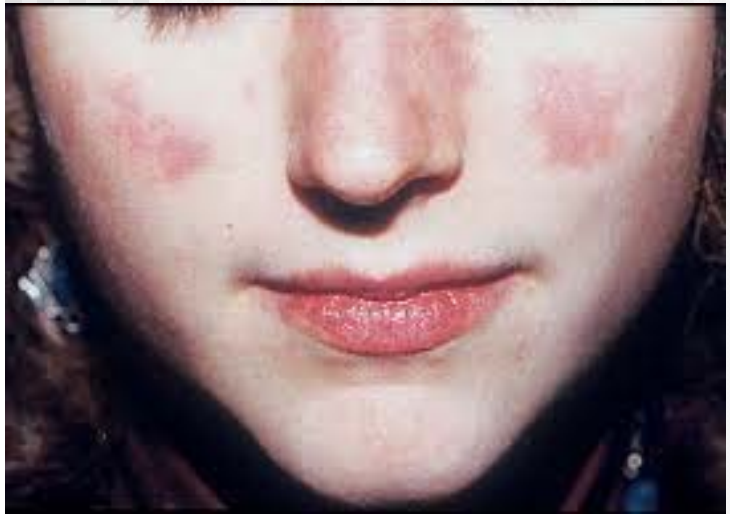
Photosensitivity→ V-region of neck, upper back, extensor surfaces of arms

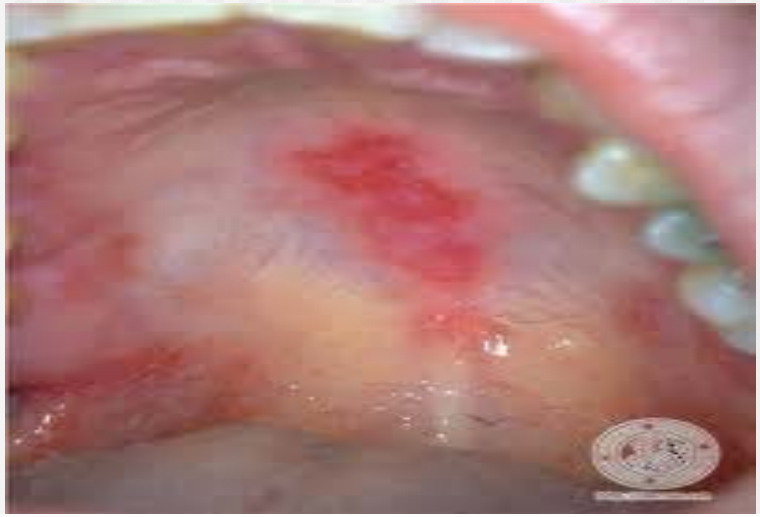
Malar Rash & recurrent oral ulcers

Clinical Manifestations









Clinical Manifestations

- Renal/ Lupus Nephritis:

All pts to have urine analysis

Kidney biopsy if active urinary sediments/ proteinuria

Histologic Class I-VI

Class IV→ESRD in 2 years (if untreated)

Better prognosis for Nephrotic synd as compared to Nephritic synd

Clinical Manifestations

- CNS/ PNS:

Unexplained Psychosis→ At Presentation, during Acute flare-up n …Steroid induced (1st week and > 40 mg/d of prednisolone)

Unexplained seizures

ATM

Mononeuritis Multiplex, Peripheral neuropathy

Clinical Manifestations

- Vascular occlusion:

TIA, CVA, ACS

CVA…. Vasculitic, aPL-Ab(APLA synd), Libman-Sachs endocarditis asso.

- Resp.:

Pleuritis (with or without effusion)

ILD

Intra-alveolar hemorrhage

Clinical Manifestations

- Cardiac:

Pericarditis (MC)

Myocarditis

Fibrinous endocarditis of Libman-Sachs

(Valvular insuff or embolic events)

- Hemat:

NCNC Anemia of Chr ds, Hemolytic anemia

Leukopenia

TCP

Clinical Manifestations

- GIT:

Autoimm Peritonitis

Hypertransaminasemia

Mesenteric vasculitis….. Ischemia, bleeding, perforation, sepsis

- Ocular:

Sicca synd & non-sp. Conjunctivitis

Retinal vasculitis

Optic neuritis

Diagnostic Criteria: ACR (4/11)

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers
5. Non-erosive arthritis (≥ 2 joints)
6. Serositis
7. Renal…. > 0.5 g/d proteinuria or cellular cast
8. Neurologic….unexplained psychosis/seizures
9. Hemat….hemolytic anemia, leukopenia, TCP
10. Immunologic…Anti-dsDNA, Anti-Sm, aPL Ab
11. ANA (absence of drugs known to induce)

Lab tests

- For diagnosis:

1. ANA: + in 95% of cases
2. Anti-dsDNA: specific for SLE, Lupus Nephritis, high titers during Ac. Flare-up
3. aPL Ab: not specific for SLE, venous/arterial thrombosis, fetal loss, TCP
4. Std (routine) lab tests

Lab tests

- For Ac. Flare-up

1. Tests that indicate status of organ involved such as Hb, Pl count, KFT, Urine R/M, LFT
2. Others → Anti-dsDNA titer, C'3 complement levels, Anticardiolipin Ig G

Treatment

- Non-life threatening events/ Potentially reversible organ damage
  - Arthralgia/ Arthritis

NSAIDs: renal dysfun esp if asso lupus nephritis

Antimalarials: retinal toxicity, ototoxicity, Peripheral neuropathy

Systemic steroids (low dose-0.07-0.3mg/Kg)

Methotraxate: BM suppression, pulm fibrosis

Treatment

- Malar rash/ Discoid rash/ Photosensitivity/ Oral ulcers

Topical sunscreen (SPF at least 15): contact dermatitis

Systemic retinoids: congenital fetal anomalies

Topical glucocorticoids

Methotraxate : BM suppression, Pulm fibrosis, hapatotoxic

Treatment

- Life-threatening SLE
  - Proliferative forms of Lupus Nephritis (Class III, IV & V)

Methyl Pred. 1g iv q 24h X 3d

f/b Oral Pred. 0.5-1 mg/Kg qd X 4-6 weeks f/b

Oral Pred. 5-10 mg qd (low dose maintenance)

+

Cyclophosphamide 500mg/m^2 monthly X 6 mths

eatment

de-effects of therapy:

ystemic glucocorticoids→

nfections

HTN & volume overload

sychosis

Hyperglycemia

Osteoporosis

eatment

de-effects:

yclophosphamide→

M suppression

Gonadal failure

Hemorrhagic cystitis

a urinary bladder

Alopecia

eatment

- eventive therapies: usually for S/E of eroids n cytotoxic agents
- H. Influenza n Pneumococcal vaccine
- T/t for Osteoporosis, HTN n Dyslipidemia
- revention of UTI (adeq fluid intake n local ygiene)

ognostic factors

erum Creatinine > 1.4 mg%

TN

ephritic synd >> Nephrotic synd

PL Ab + status

eading causes of death→ systemic disease

E n Special Situations

- egnancy n Lupus→
- ecurrent fetal losses: LMWH increases hances of fetal survival
- High chances in aPL Ab+ status or Nephritis
- Higher steroid requirement as placental ehydrogenase deactivates prednisolone
- Neonatal lupus (skin rash + heart blocks)
- S/E of prednisolne on fetus: LBW, CNS

E n Special Situations

upus n APLA synd→

/o venous or arterial thrombosis and/or
ecurrent fetal losses & aPL + at least on
wo separate occasions

Mx : long-term Anticoag,Target INR= 3.0

Microvascular thrombotic crisis (TTP/HUS)

Tissue damage in Brain n Kidney, high
nortality, usually young pts with Nephritis

/t : Plasma exchange/Plasmapheresis ; No

ug induced Lupus

NA + with fever, arthritis, rash n serositis

ff^{ed} from SLE as….dsDNA only rarely +

….less female predilection

….resolves over weeks

after offending drug withdrawn

ug induced Lupus

rugs....

nticonvulsants→ Carbamazepine, Phenytoin

ntipsychotics→ Lithium

ntithyroid→ PTU

ntiHTN→ ACEI, Thiazides, β-blockers, Hydralazine

nti-arrhythmics→Procainamide, Propafenon

perimental therapies for SLE

gainst T cell-B cell interaction:

nti CD40L Ab, Anti CTLA4-Ig fusion prot.

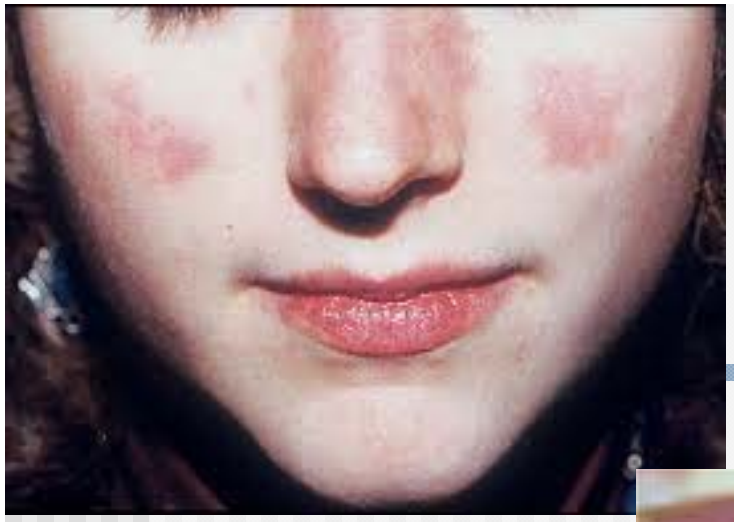
nti CD20 Ab

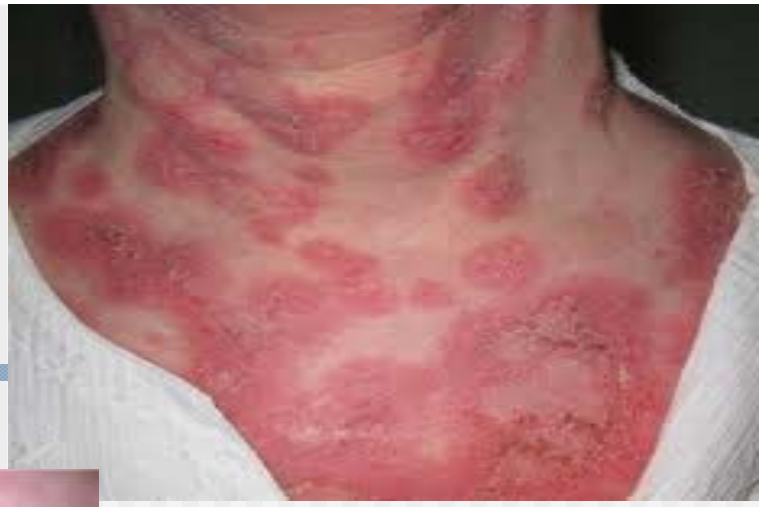
gainst Complement syst:

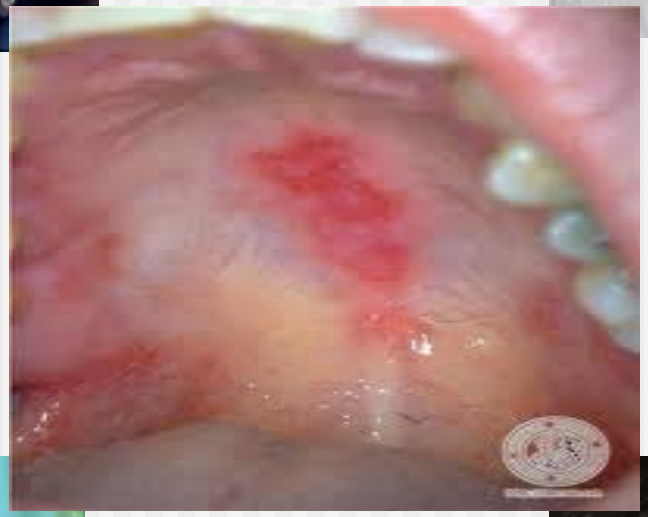
nti C'5 Ab

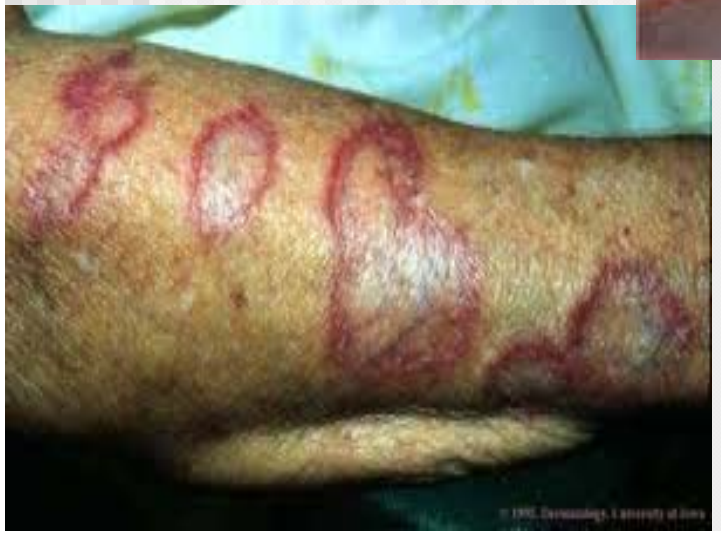
ARE YOU DONE WITH SLE(EPING) ???

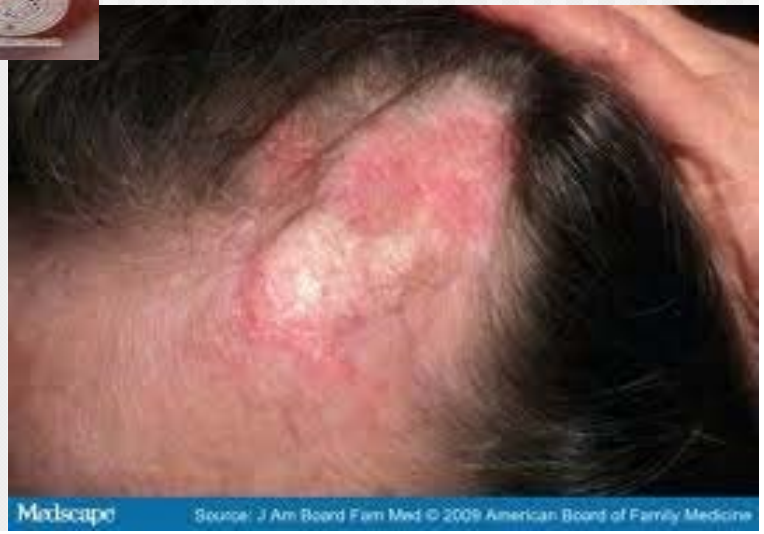
ANY QUESTIONS ?







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