Sjögren Syndrome
mixed Conn. Tissue ds.

SLE: Systemic ~~Eng~~ Lupus Erythematus

- (i) **Chronic** once acq. will be for rest of life
- (ii) Systemic
- (iii) Autoimmune ds.
- Flares & Remissions common.

SLE m/c in:

* **Middle aged females** (♀ : ♂ = 10 : 1)

but female bias is less dramatic in children & elderly (♀ : ♂ = 2 : 1)

* m/c in African Americans & Hispanics.

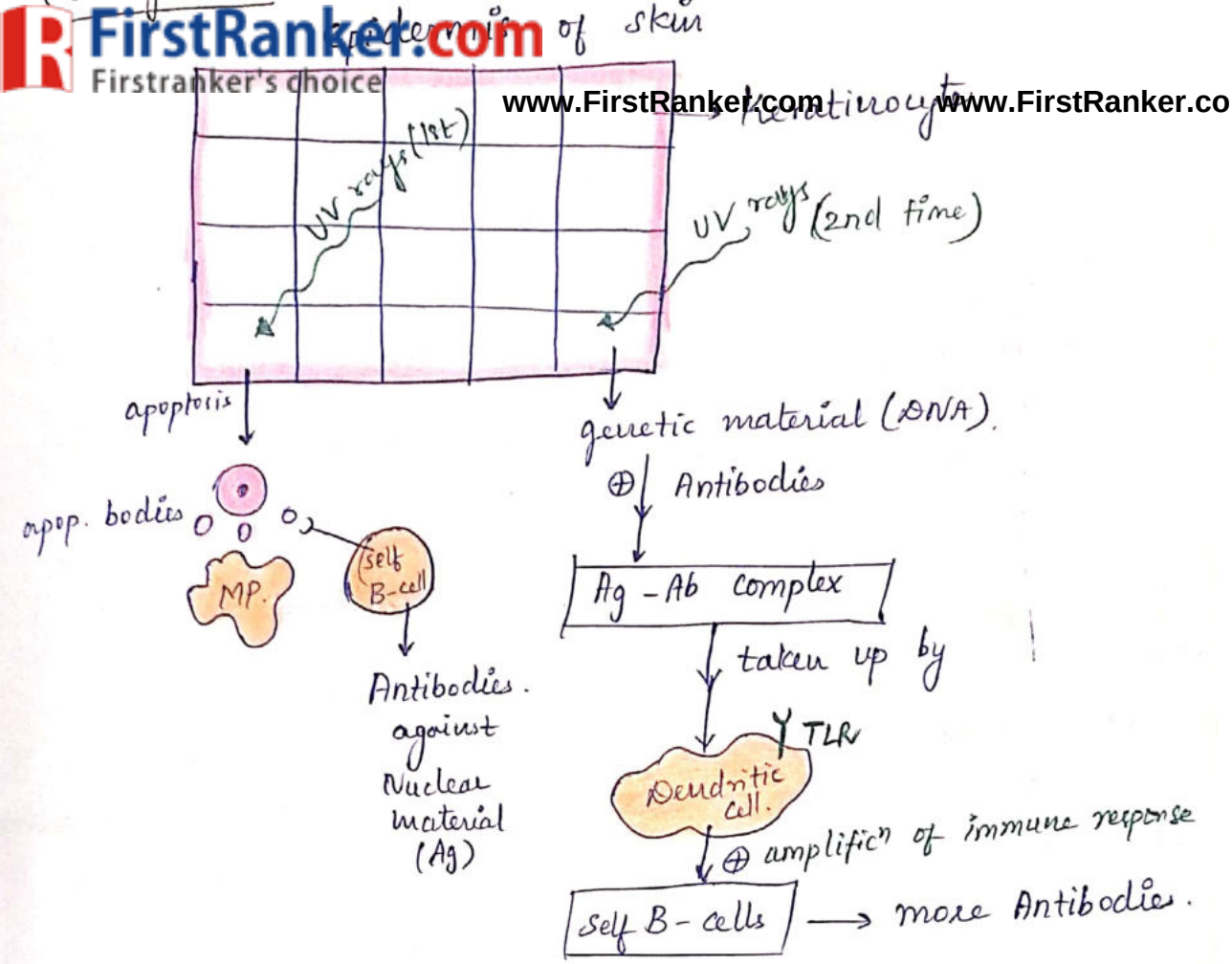
Why? estrogen ⊖ → destruc$^n$ of self reactive T-cells / B-cells.

Also in middle aged females > children, elderly (estrogen levels)

What is SLE? Type III Hypersensitivity

Antibodies directed against Host DNA → Ag-Ab complex formed & deposits in multiple tissues → Activation of Complement ↓ damages Tissues

Test to find out levels of $C_1$-$C_9$ ← $CH_{50}$, $C_3$, $C_4$ values will be low




## Explanation

UV rays hit Keratinocyte, resulting in Apoptosis.

↓

Delay in clearing of Apoptotic bodies

↓

self reactive B-cells exposed to Nuclear Ag

↓

~~Ag~~ ~~Ab~~ Antibodies ~~complex~~ formed, Now if again UV ....

↓

Ag - Ab complex formed which is taken up by TLR of Dendritic cells resulting in

↓

Amplificn of Immune Response, so more B-cells (self). are activated & Thus more Ag - Ab complex.

↓

Ag - Ab complex reaches blood, deposits & ~~activates~~ Complement → SLE

b associated with SLE why?

In SLE, Ag-Ab complexes are formed.

↓

Which should be cleared by Complements by ② mechanism

↓

| $C_3b$ – acts as Opsonin | CR1 - in RBC (RBC ⇆ CR1) |
|---|---|
| * $C_3b$ deposited on Ag-Ab complex ↑ phagocytosis by Macrophages. | * CR1 attaches to Ag-Ab & carries it to spleen where its phagocytosed. |

But in Eaely complement def., This 1st mech. will be defective & will result in SLE..

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## CLINICAL FEATURES: Non specific & ⑪ Specific features.

### Non specific:

(i) fever
(ii) Weight loss.
(iii) Fatigue
(iv) LAD (Lymph ADenopathy).

} → Common for ds. in which there is activatn of Immune System

(v) secondary Raynaud phenomenon

⇓

Vasoconstrictn due to arteriospasm resulting White → Blue → Red color changes of finger tip & Nose.

① Malar Butterfly Rash:

* seen in acute SLE
* in face on exposure to sunlight (cheek bones)

② Discoid Rash: (like a wolf bite).
↳ Thats why this ds. is named "LUPUS"

* Chronic SLE
* Discoid/Ocular, erythmatous, scaling often scaring

③ Rash upon exposure to sunlight:

④ Oral (or) Naso pharyngeal ulcers:

⑤ Arthritis

⑥ Serositis.

⑦ Psychosis (or) Seizures.

⑧ Renal Damage. (m/c cause of death in SLE).

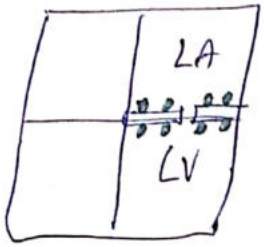
- Nephrotic syndrome
  - * proteinuria
  - ↓
  - membranous Glomerulonephritis
- Nephritic syndrome
  - * HTN, Hematuria
  - ↓ proliferative
  - diffuse Glomerulonephritis

Leukopenia. death.

Ab against Blood cells (Type II Hypersensitivity)

⑨ Libman-Sacks endocarditis

↳ small vegetatn on both sides of mitral valve.




⑩ ANA Antibody (Anti Nuclear Ab)

↳ sensitive but not specific. (bcoz its also present in other Auto immune disorders)

⑪ Anti-ds DNA & anti-Sm. (smith) Abs.

→ These ② Abs are specific for SLE

→ Also used to detect prognosis bcoz these ② predict renal involvement which is a mjr. cause death in SLE

⑪ Antiphospholipid Ab

* When proteins are bound to Phospholipid epitopes are revealed & they become antigenic. Ab. are secreted against it.

* ③ Antiphospholipid Ab

(i) Anti cardiolipin Ab → False ⊕ve test in syphilis (VDRL & RPR).

(ii) Lupus Anticoagulant → Falsely elevated PTT is obtained due to this Ab

(iii) Anti-β2 glycoprotein I

→ APA ⊕ Hypercoagulable state.

↓ produces

(i) DVT (ii) Hepatic v. Thrombosis (iii) Cerebral Thrombosis

(iv) placental Thrombosis

→ Requires Life long Anticoagulatn.

→ Although pt. has Hypercoagulable state, He/She will have false elevated PTT due to APA.

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DRUG INDUCED SLE:

→ Hydralazine, Procainamide, Isoniazid.

* Anti Histone Ab (a Type of ANA) is characteristic of drug induced SLE.
* CNS & CP involvement rare.
* Removal of drug usually results in remission

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Rx:

(i) Avoid Sunlight (why? pathogenesis).

(ii) Glucocorticoids (to cure flares)

(iii) Other Immunosuppressive agents

But now, Rx. Syst. survival ⇒ >90%

↳ (or) due to excess corticosteroids.

* Renal failure & infecⁿ (due to leucopenia - ↓ immunity) are m/c causes of death.

* late death - may be due to Accelerated Coronary Atherosclerosis.

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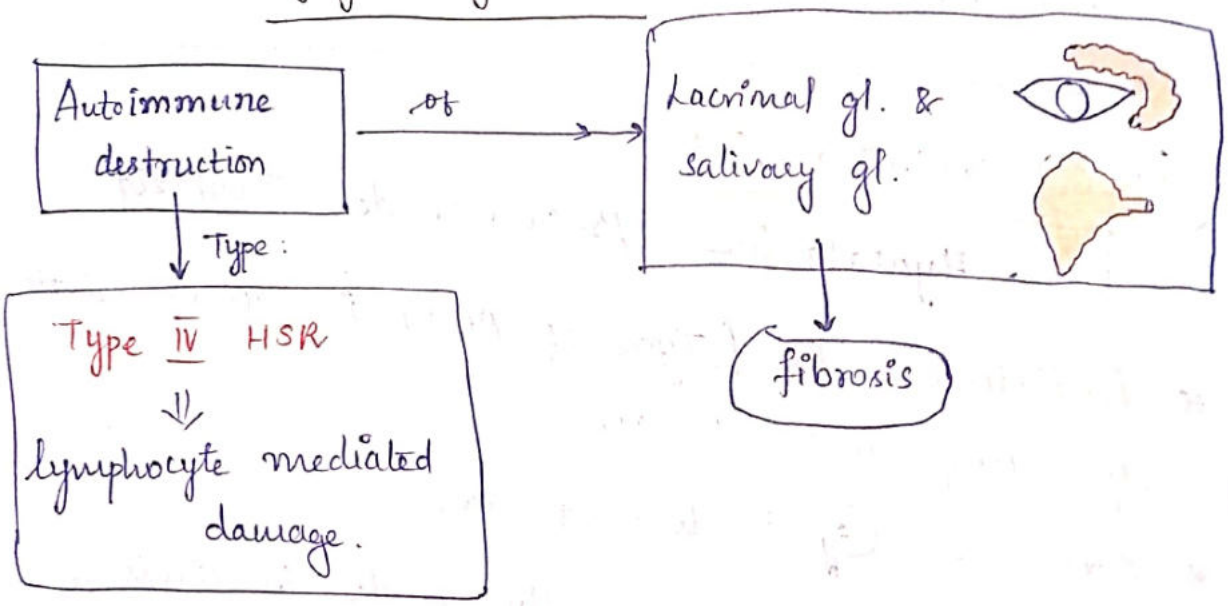
II) Sjögren Syndrome :




Classical presentation: "CAN CHEW A CRACKER, DIRT IN MY EYES"

↳ * Dry eyes, Dry mouth (due to destrucⁿ of lacrimal & salivary glands)

* Recurrent dental caries. in an older woman.
(absence of saliva → Bacteria easily grow)

* Also extraglandular manifestatⁿ.
(Joints, CNS, skin)

with ... ds.) (OR) associated with another Autoimmune ds. :

↓

* especially Rheumatoid Arthritis

* Rheumatoid factor often present in these pt. even in primary ds. → used for Δ^sis.

↓

Boaz present in Sjogren even without Rheumatoid Arthritis.

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## Auto Antibodies in Sjogren:

- ANA (Anti Nuclear Ab.)
- Anti – Ribo Nuclear - protein

~~Ribo~~ Ribo Nuclear protein → Ribosomes

eg: Anti SSA & Anti SSB.

↓

(S)jog (S)ynd.

## Significance of Anti SSA & Anti SSB

* Anti SSA & Anti SSB can cross the placenta & cause Neonatal lupus. — Rash, CONGENITAL HEART BLOCK *, Anemia

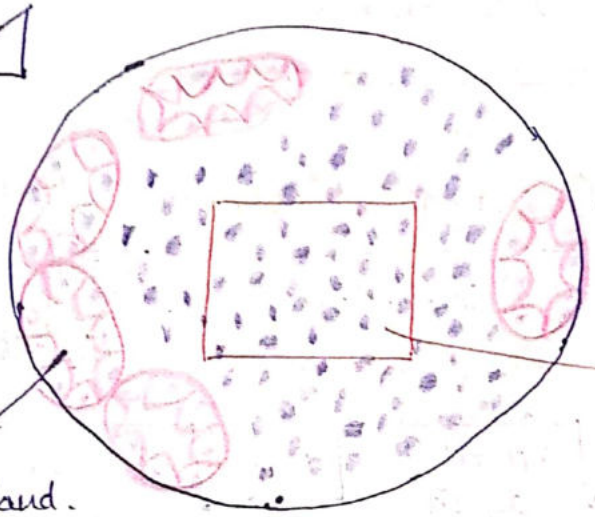
* Anti SSA & Anti SSB are also seen in SLE pts. so pregnant women * with SLE should be screened for * Anti SSA & Anti SSB boaz these Auto Ab can cause Neonatal lupus. in fetus.

* Anti SSA & Anti SSB is assoc. with extraglandular manifest. (joints, skin, CNS).

Biopsy of Minor Salivary gl. of Lip.

Lymphocytic Sialadenitis. → inflammn of minor salivary gland.

indicates presence of Sjogren synd.



(i) lymphocyte infiltratn.

Healthy salivary gland.

To rule out Amyloidosis (ii) & To rule out Sarcoidosis (iii) (Non caseating Gr.)

Significance of biopsy: Dry eyes & Dry mouth are present in other ds. also. Thats why To rule out other causes .....

③ Criteria for $\Delta^{sis}$.

(i) Dry eyes (↓ tear prodn)

(ii) ANA (or) Anti SSA & Anti SSA (or) Rheumatoid factor

(iii) Lymphocytic Sialadenitis

② out of ③ criteria needed for $\Delta^{sis}$..

Sjogren syndrome have ↑ risk of B-cell lymphoma.

* Initially pt with Sjogren syndrome have B/L enlargement of parotid
* But after about (10)-(15)yrs, one parotid enlarges more indicating B-cell lymphoma. ⇒ U/L enlargement of parotid in late Sjogren

III) SYSTEMIC SCLEROSIS (Scleroderma).
- (i) Limited Type
- (2 types)
- (ii) Diffuse Type

Autoimmune disease. → in which → ~~(activated)~~ Fibroblast deposit COLLAGEN → leads to → sclerosis (Hardening) of skin & Visceral org.

Pathogenesis:

* Autoimmune rxn against Unknown mesenchymal Ag. present either in Blood V/s (or) Conn. Tissue

↓

Damage of endothelium (or) Conn. Tissue leads to ↑ expression of adhesion molecules in endothelium

↓

Neutrophils arrive & inflammn starts.

↓

Also there is ↑ expressn of endothelin & ↓ NO. both of which lead to Vaso constricn → ischemia

↓

Produc$^n$ of PDGF & TGF-β by endothelium activates fibroblasts → collagen → systemic sclerosis

## Limited Type

* limited skin (only hands) with late visceral involvement

* Anti-centromere Ab's.

Mnemonic CREST.

C → Calcinosis.

R ⇒ Raynaud phenomenon. (early Δsis)

E → Esophageal dysmotility
* difficulty in swallowing (def. peristalsis)
* GERD

S → Sclerodactyly. (Hardening of fingers alone)

T ⇒ Telangiectasis of skin.
↓
dilated capillaries. (blood marks on skin)

* Prognosis is good.

## Diffuse Type

* Diffusely involves skin with EARLY visceral involvement. (Hands, chest limbs...)

* DNA topoisomerase I Ab's

Any organ can involved

(i) Vessels —#→ Raynaud phenomenon.

(ii) GIT
* Esophagus —#→ GERD, dysphagia
* Stomach —#→ late emptying
* small bowel —#→ malabsorpn.

(iii) Lungs: involvement m/c cause of death..
—#→
* interstitial fibrosis
* pulmonary HTN.

(iv) Kidneys.
2nd m/c cause of death
→ Scleroderma Renal crisis. (ARF & severe HTN).
Rx: ACE inhibitors.

(v) Heart:
due to pulm. HTN (or) sclerosis of cardiac tissue,
⇒ Heart failure.

* Prognosis is bad

## IV) Mixed Connective Tissue Disease (MCTD)

↳ SLE ⊕ Systemic sclerosis ⊕ polymyositis.

* Mixed overlapping features.

* This ds. initially manifests Non specifically as Arthritis (SLE), GERD (systemic sclerosis), myalgia (polymyositis), Raynaud ph.

↓ After some Time.

overlapping features of SLE, Systemic sclerosis, polym...

### Hallmarks of MCTD:

(i) Raynaud phenomenon
(ii) Lack severe CNS, Renal involvement.
(iii) But severe Arthritis & pulm. HTN present.

### ANA:

* ANA with serum Abs. against "$U_1$ RNP" (Ribo Nucl... - protein