Systemic Sclerosis

- It is a systemic autoimmune disease characterized by vasculopathy and fibrosis of the skin and other organs
- It is more common in women and blacks
- Most common age to occur is 30-50
- First degree relatives have higher risk
- Pathogenesis :
    - Endothelial damage and chemokine production
    - Antibodies against nuclear antigens
    - Elevated levels of interleukins
    - Overproduction of ECM leading to fibrosis
- Environmental factors
    - CMV infection
    - rapeseed oil : toxic oil syndrome
    - L tryptophan : eosinophilia myalgia syndrome
    - silica
    - polyvinyl chloride
    - epoxy resins
    - aromatic hydrocarbons
    - Drugs : bleomycin, pentazocine and cocaine
- Raynaud phenomenon is the main symptom
    - It is a vasospastic attack triggered by cold or emotional stress
    - Can be primary or secondary to drugs, rheumatic and hematological diseases, vibrating tools, beta blockers, and chemotherapy like cisplatin
    - Triphasic presentation : ischemia - cyanosis- hyperemia
    - Rewarming is associated with transient numbness & pain
    - It normally subside within an hour (typically 15–20 mins)
    - The thumb is spared in the primary form
    - The primary form has no finger edema, periungual erythema nor arthritis unlike the secondary
    - Nailfold capillary changes support the diagnosis
- 2 Types
    - Localized Scleroderma : morphea / linear scleroderma / coup de sabre
    - Systemic sclerosis : limited and diffuse
- Morphea : solitary or multiple circular patches of thickened skin
- Linear scleroderma
    - Streaks of thickened skin in one or both lower limbs
    - Subcutaneous tissue may become fibrosed
    - Atrophy of supporting structures, muscle and bone
    - In children, the growth of affected long bones can be retarded
    - When linear scleroderma lesions cross joints, contractures develop

Systemic Sclerosis SSc

- Limited SSc involves distal extremities (below elbows & knees), face and neck while diffuse SSc involves also the trunk and proximal extremities
- Limited SSc has slow progression while diffuse SSc is rapid
- Raynaud phenomenon precedes the skin involvement in limited SSc while occurring concurrently with diffuse SSc
- CREST syndrome : occurs mostly in limited SSc but can also occur in diffuse SSc
    - Calcinosis Cutis : occurs on pressure points like knees, elbows & fingertips : much more common in limited SSc
    - Raynaud Phenomenon
    - Esophageal dysmotility : decreased lower esophageal sphincter pressure → dysplasia and GERD
    - Sclerodactyly : bilateral Skin thickening and loss of creases on the dorsum of the fingers causing limited range of motion
    - Telangiectasia : small dilated intradermal blood vessels
- Musculoskeletal symptoms
    - Puffy fingers
    - Digital ulceration due to peripheral vasculopathy and pitting
    - Nailfold abnormalities
    - Tendon friction rub in the bursa : in diffuse SSc
    - Joint flexion contractures
    - Arthritis with palpable synovitis
    - Acroosteolysis
    - Myositis
- Facial features
    - Loss of facial expression (mask-like facies)
    - Microstomia (fish mouth)
    - Beak nose
    - Shortened frenulum
- Pulmonary Symptoms (leading cause of death)
    - Interstitial Lung Disease
        - Presenting with dyspnea and dry cough
        - CT scan will show fibrotic changes (ground glass) and PFTs will show reduced FVC and DLCO but unaffected flow rates
        - Risk factors : males / african americans / those with diffuse skin involvement / positive ScL-70
        - Treated with cyclophosphamide
    - Pulmonary Hypertension
        - Occurs more prominently in limited SSc (in diffuse SSc occurs only secondary to fibrosis)
        - Risks : limited SSc / anticentromere antibodies / severe Raynaud / late

diagnosis
        - PFTs show isolated reduced DLCO
        - CXR will show enlarged pulmonary arteries
        - Right heart catheterization is required to confirm diagnosis but a pulmonary artery pressure > 40 mmHg on echo is diagnostic
        - May lead to heart failure
    - Pulmonary Fibrosis : occurs more frequently, severely and earlier in diffuse SSc
- Renal Crisis
    - Occurs mainly in diffuse SSc
    - Risks : men / blacks / diffuse skin involvement / anti-SCL70
    - Symptoms
        - Abrupt onset of malignant Hypertension with symptoms of HTN crisis like
            - Headache
            - Papilledema and impaired vision
            - Hypertensive encephalopathy
            - Congestive heart failure
        - Oliguria with AKI (high Cr)
        - Hematuria and Proteinuria
        - Microangiopathic hemolytic anemia
        - Thrombocytopenia
    - Major cause of death in SSc
    - Diagnosis : urinalysis and CBC
    - Treated by ACEi
- Cardiac Symptoms : pericarditis / Endomyocardial fibrosis / diastolic dysfunction
- Gastrointestinal symptoms : small bowel dysmotility causing constipation / malabsorption / incontinence / watermelon stomach (antral vascular ectasia) / primary biliary cholangitis / gastroparesis
- Typical presentation of limited SSc : CREST + symptoms of pulmonary HTN + Raynaud + anti centromere antibodies
- Serologic findings and diagnostics
    - ANA is positive in 90% of cases
    - anti centromere antibodies : limited SSc
    - anti RNA Polymerase 3 & anti topoisomerase 1 (anti SCL70) : diffuse SSc
        - anti centromere positive patients are more likely to develop raynaud
    - Cardiopulmonary assessment
    - Renal assessment
    - Normal ESR and CRP
- Treatment
    - For Raynaud : calcium channel blockers (avoid beta blockers as they induce vasospasm) / phosphodiesterase inhibitors PDEis / SSRIs / IV PGs
    - For calcinosis : CO2 laser or surgical excision
    - For cutaneous fibrosis : phototherapy / MTX / Cyclophosphamide

- For ILD : Cyclophosphamide
- For GERD : PPIs
- For pulmonary hypertension : PDEis / endothelin-1 antagonists (bosentan)