Scleroderma

- An AUD which results from vascular injury (thus, tissue hypoxia), and collagen (not lymphocytes vs. Sjögren's) replacing smooth muscle cells. It has two types: (1) systemic sclerosis, and (2) **localized** scleroderma (**morphea**) which spares internal organs and only affects the skin. It's more common in females and blacks. Age of onset is between 30-50 y/o. Patients have ↑ risk for other AUDs like RA & SLE.

- **Morphea** is more common in **women** and diagnosed before the age of 18 (usually **children**). It has various manifestations, which include **circumscribed plaques**, **generalized** (or diffuse) coalescing **plaques** w/ widespread induration, and **linear (band-like) plaques** which, when invade the face, is called *En Coup de Sabre.*
- **Linear morphea** is invasive and can cause **atrophy** of supporting structures, muscle, and bone. Also, if these bands cross joints, contractures can develop, and bone growth can get affected.

- Now systemic sclerosis characterized by the involvement of **multiple internal organs**, such as the lungs, GI tract (GERD, gastroparesis, **gastric antral vascular ectasia**, malabsorption, intestinal pseudo-obstruction or diarrhea), heart (restrictive cardiomyopathy), and kidneys (renal HTN, called renal crisis, occurs within 4 yrs., ↑risk to occur in males, African Americans, patients w/ massive skin manifestations, or **anti-RNA polymerase III antibodies**). In addition to skin involvement which includes taut and shiny skin, loss of wrinkles, microstomia, beaked nose, slow-healing ulcers, telangiectasias in the face, hands, lips, and oral cavity.

- Renal crisis: abrupt onset of malignant hypertension accompanied by rapidly progressive renal failure (hematuria, proteinuria), hypertensive encephalopathy, congestive heart failure, and/or microangiopathic hemolytic anemia (thrombocytopenia and schistocytes). Tx. ACEIs.
- **Gastric antral vascular ectasia** (**watermelon stomach**): the blood vessels in the lining of the stomach become fragile and recurrently bleed (unexplained anemia).
- Systemic scleroderma can sometimes have musculoskeletal manifestations, which include arthralgia, contractures, tendon friction rubs, erosive asymmetrical polyarthritis, inflammatory myositis, and **acro-osteolysis** (lysis of distal phalanges).
- Scleroderma symptoms may be triggered by exposure to certain viruses (e.g., CMV), medications (bleomycin), or drugs (e.g., cocaine).

- It has two types, limited cutaneous systemic sclerosis (previously CREST syndrome, standing for **calcinosis**, **Raynaud's** phenomenon, **esophageal dysmotility**, **sclerodactyly**, **telangiectasias**) and diffuse cutaneous systemic sclerosis. CREST is "limited" because it spares the kidney and the heart.

SUBSETS OF SYSTEMIC SCLEROSIS (SSc): LIMITED CUTANEOUS SSc VERSUS DIFFUSE CUTANEOUS SSc

FEATURES	LIMITED CUTANEOUS SSc	DIFFUSE CUTANEOUS SSc
Skin involvement	Limited to fingers, distal to elbows, face; slow progression	Diffuse: fingers, extremities, face, trunk; rapid progression
Raynaud's phenomenon	Precedes skin involvement; associated with critical ischemia	Onset contemporaneous with skin involvement
Pulmonary fibrosis	May occur, moderate	Frequent, early and severe
Pulmonary arterial hypertension	Frequent, late, may be isolated	May occur, associated with pulmonary fibrosis
Scleroderma renal crisis	Very rare	Occurs in 15%; early
Calcinosis cutis	Frequent, prominent	May occur, mild
Characteristic autoantibodies	Anticentromere	Antitopoisomerase I (Scl-70)

- Raynaud phenomenon: ↓blood flow to skin (fingers and toes) in response to cold or stress: color change from white (ischemia) to blue (hypoxia) to red (reperfusion). Called Raynaud disease when 1° (idiopathic), Raynaud syndrome when 2° to a connective tissue disorders (e.g., MCTD, SLE, CREST syndrome), hematological disorders (e.g., cryoglobulinaemia), endocrine conditions, vibrating tools, drugs (e.g., BBs, anticancer drugs like bleomycin and cisplatin).

	Primary	Secondary
Sex	Female	Male and Female
Age of Onset	Menarche	Mid 20's or later
Finger Edema	No	Frequent
Periungual erythema	Rare	Frequent
Arthritis	No	Frequent
Nail fold capillaroscopy	Normal	Dilated tortuous capillaries
Autoantibodies	Absent	Present

- Tx. includes CCB (e.g., nifedipine), IV PG, topical NG, SSRI, PDE-5 inhibitors (e.g., sildenafil).

- The most frequent cause of death is pulmonary involvement, either (1) interstitial lung disease ILD (where PFT shows restrictive pattern w/ NL flow rates; ↑risk to occur in males, African Americans, patients w/ est. restrictive lung disease, severe GERD, massive skin manifestations, or anti-Scl-70 antibodies) or (2) pulmonary arterial hypertension PAH (resting pulmonary arterial pressure >25 mmHg which can cause **Rt. HF**; **PFT** shows ↓DLCO **only;** pulmonary artery enlargement on **CXR**, ↑risk to occur in CREST, and in pts. w/ anticentromere or RNP antibodies, late age at onset, or severe Raynaud's phenomenon).
- Right heart catheterization (to measure PAP) is required to confirm PAH.
- PAH tx. include:
  1) PDE-5 inhibitors (e.g., sildenafil)
  2) ERAs (e.g., bosentan)
  3) Prostacyclin analogs (e.g., epoprostenol, treprostinil)
  4) O2 therapy
  5) Lung transplantation

- Systemic scleroderma is a clinical dx. assisted by the presence of ANA, **anti-centromere** (limited- SSC (CREST) >> diffuse- SSC), and/or **anti-Scl-70** (limited- SSC (CREST) << diffuse- SSC) antibodies.
- Note that lab results often show normocytic anemia, and normal ESR.