Systemic sclerosis

4th year MBBS

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Consultant Rheumatologist

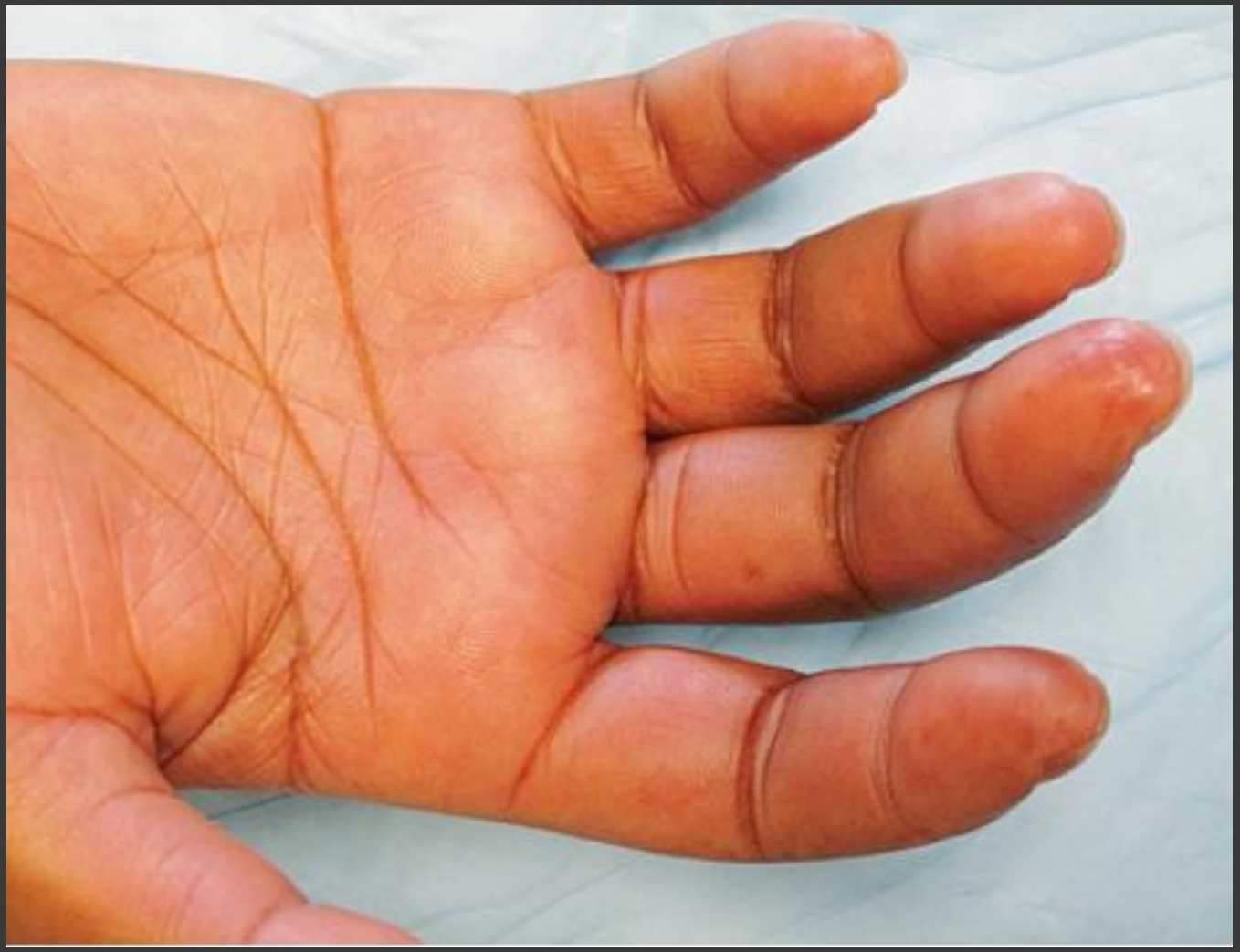
Case 1

- A 35-year-old woman presented with a 6-month history of bilateral hand stiffness and swelling
- She had a 15-year history of Raynaud's phenomenon with blanching and cyanosis of the fingertips on cold exposure
- developed painful sores on several fingerpads which were slow to heal, and at times white chalky material would extrude from the ulcers.

- She complained of dysphagia and heartburn and was found on barium swallow to have esophageal dysmotility with GER

Examination

- puffy fingers with loss of skin creases over dorsum of fingers
- digital pitted scars on several fingerpads, some with ulceration chalky white exudate
- periungual erythema and telangiectasias on fingers, hands and face
- normal skin texture of the proximal arms and legs, chest, and abdomen.
- mild flexion contractures of the fingers

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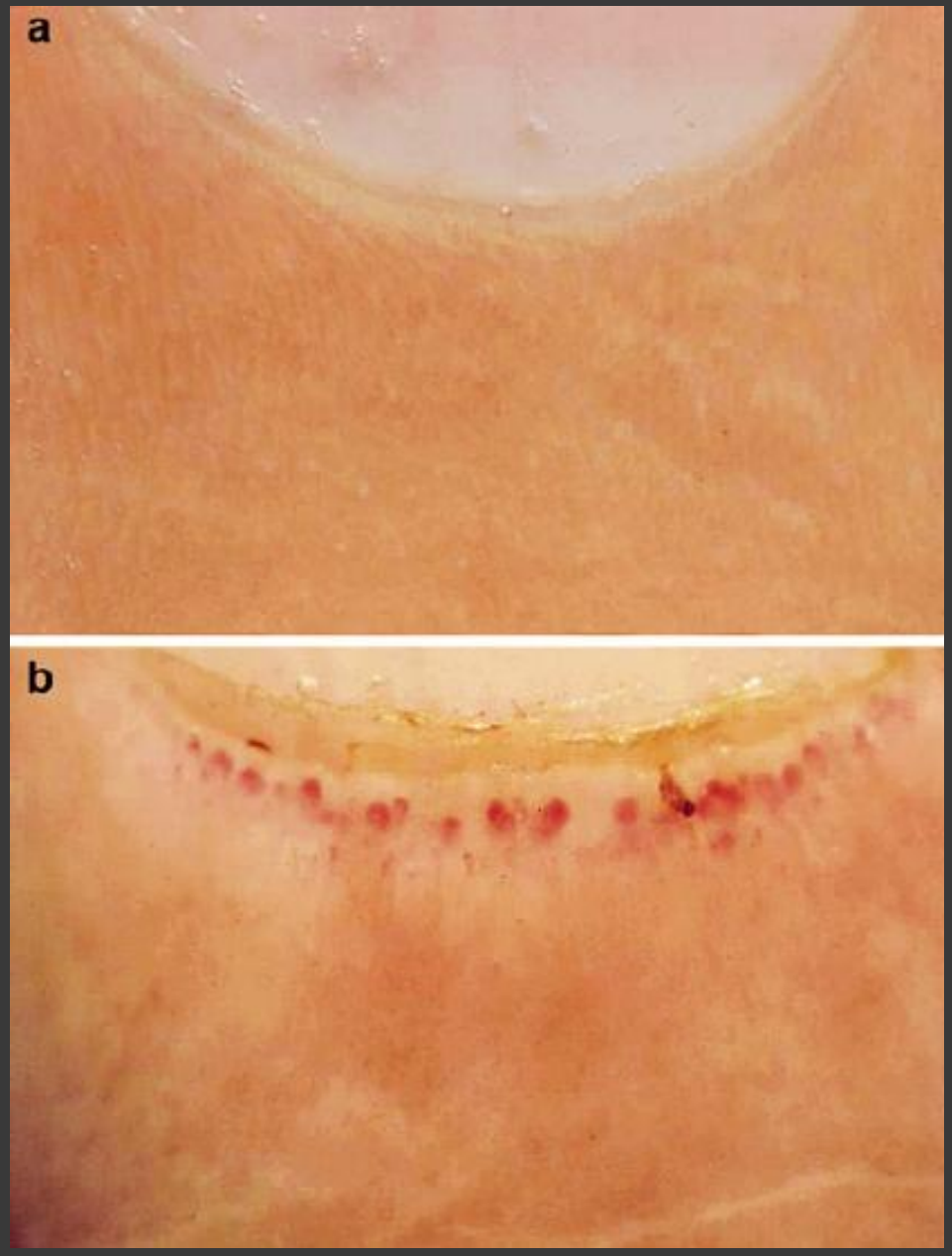
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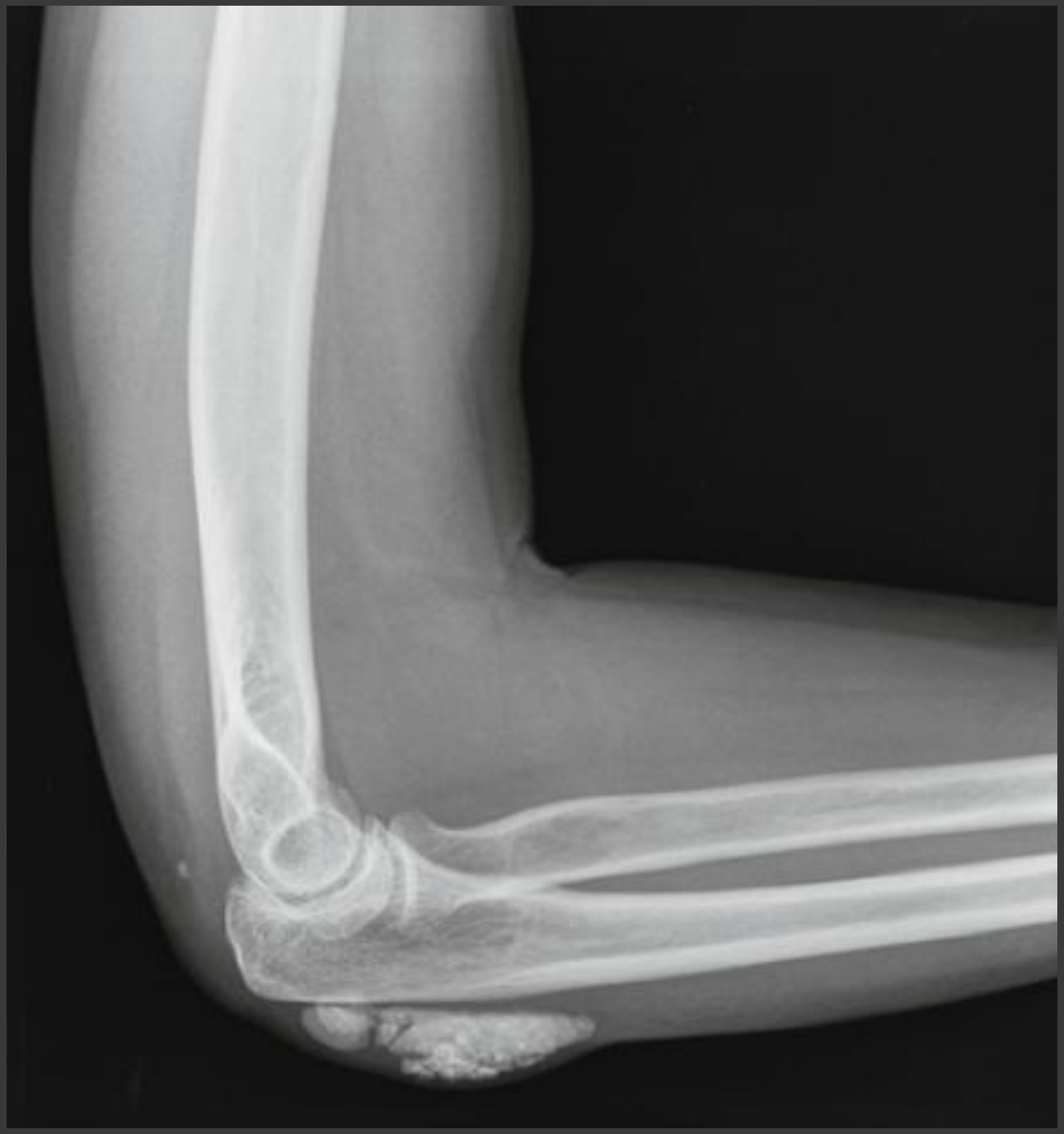
Investigations

- ANA 1:1280; centromere pattern.
- Radiographs: calcifications in the soft tissues
- PFTs normal
- Echocardiogram: normal



Diagnosis?

Objectives

- Definition & types
- Epidemiology
- Pathogenesis
- Genetics
- Clinical features
- Lab findings
- Treatment

Classification

- **Localized scleroderma**
  - morphea, diffuse morphea
  - Linear scleroderma, coup de sabre

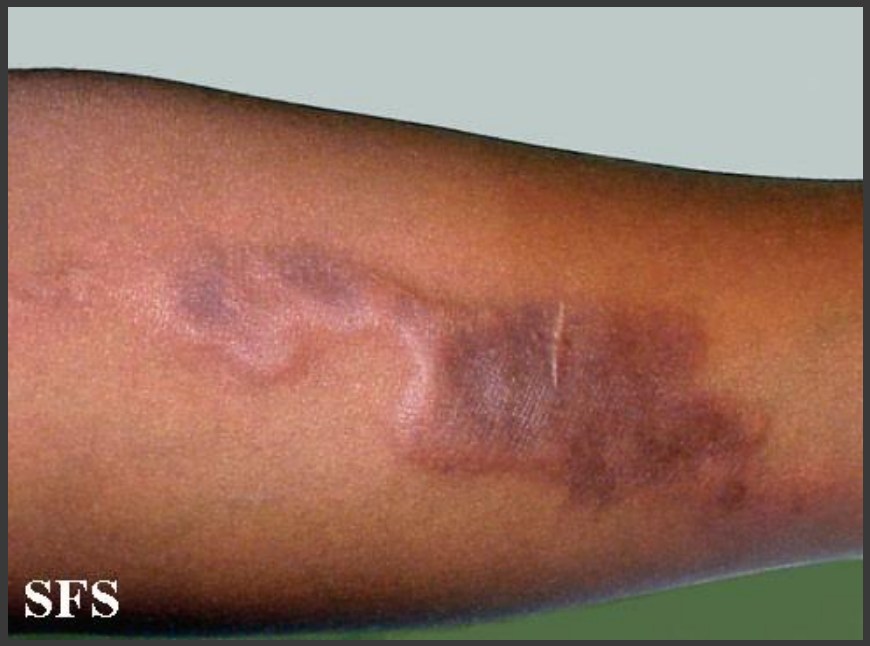
- **Systemic sclerosis**
  - Limited cutaneous SSc
  - Diffuse cutaneous SSc

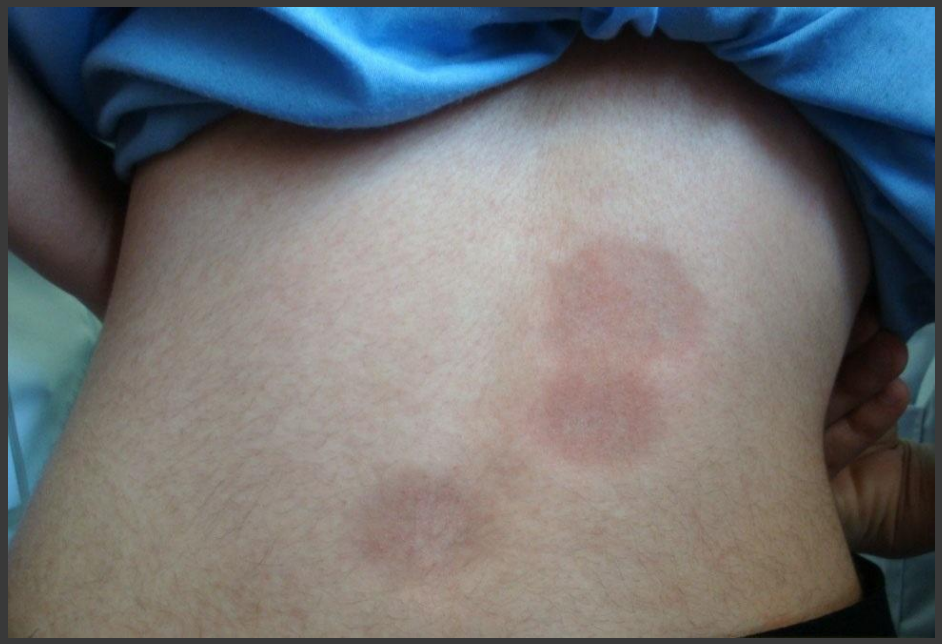
localized scleroderma

- A group of localized fibrosing skin disorders that primarily affect children

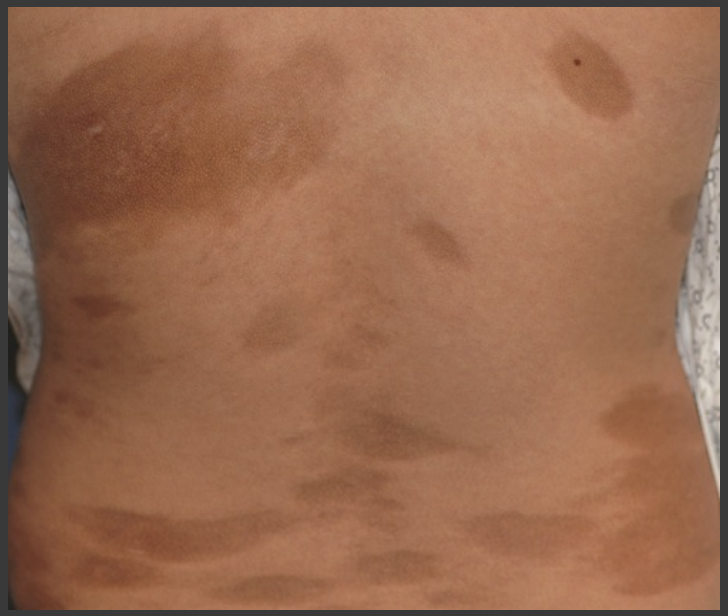
- Morphea: solitary or multiple circular patches of thickened skin and, less commonly, widespread induration (generalized morphea)

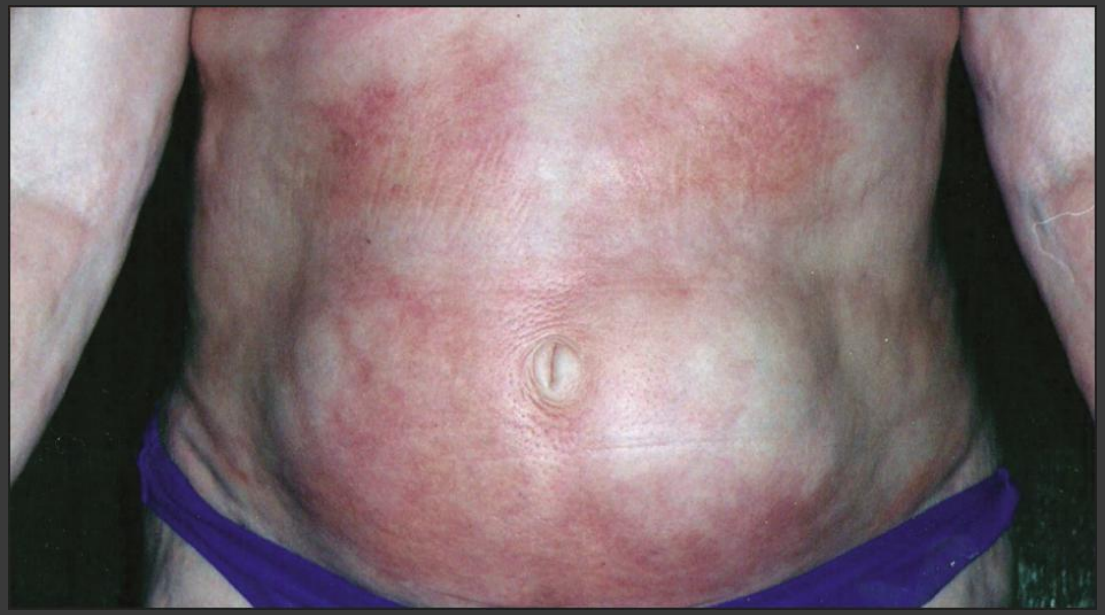
Morphea





Generalised morphea

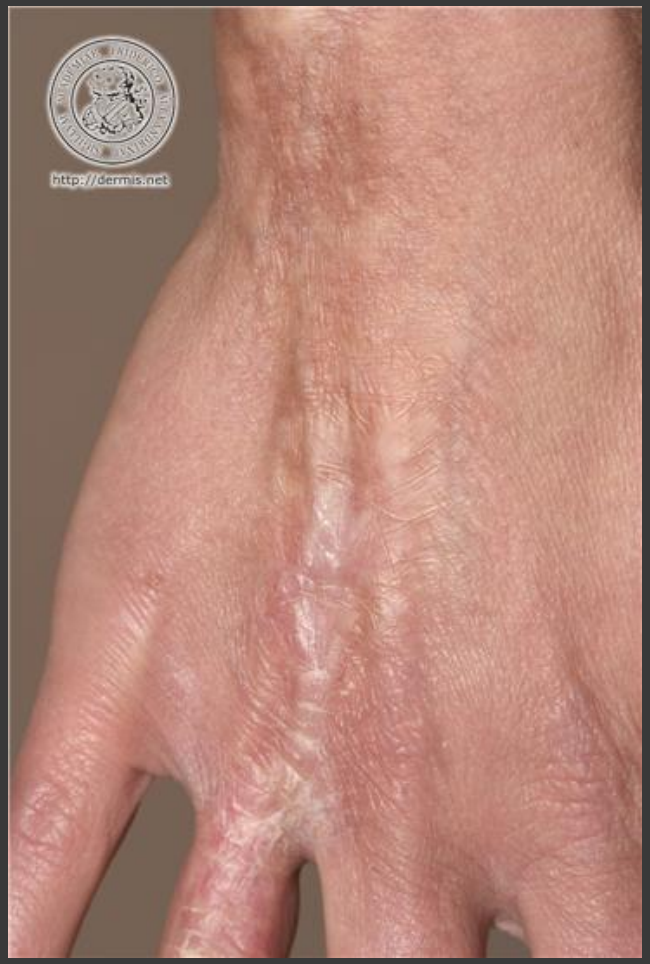




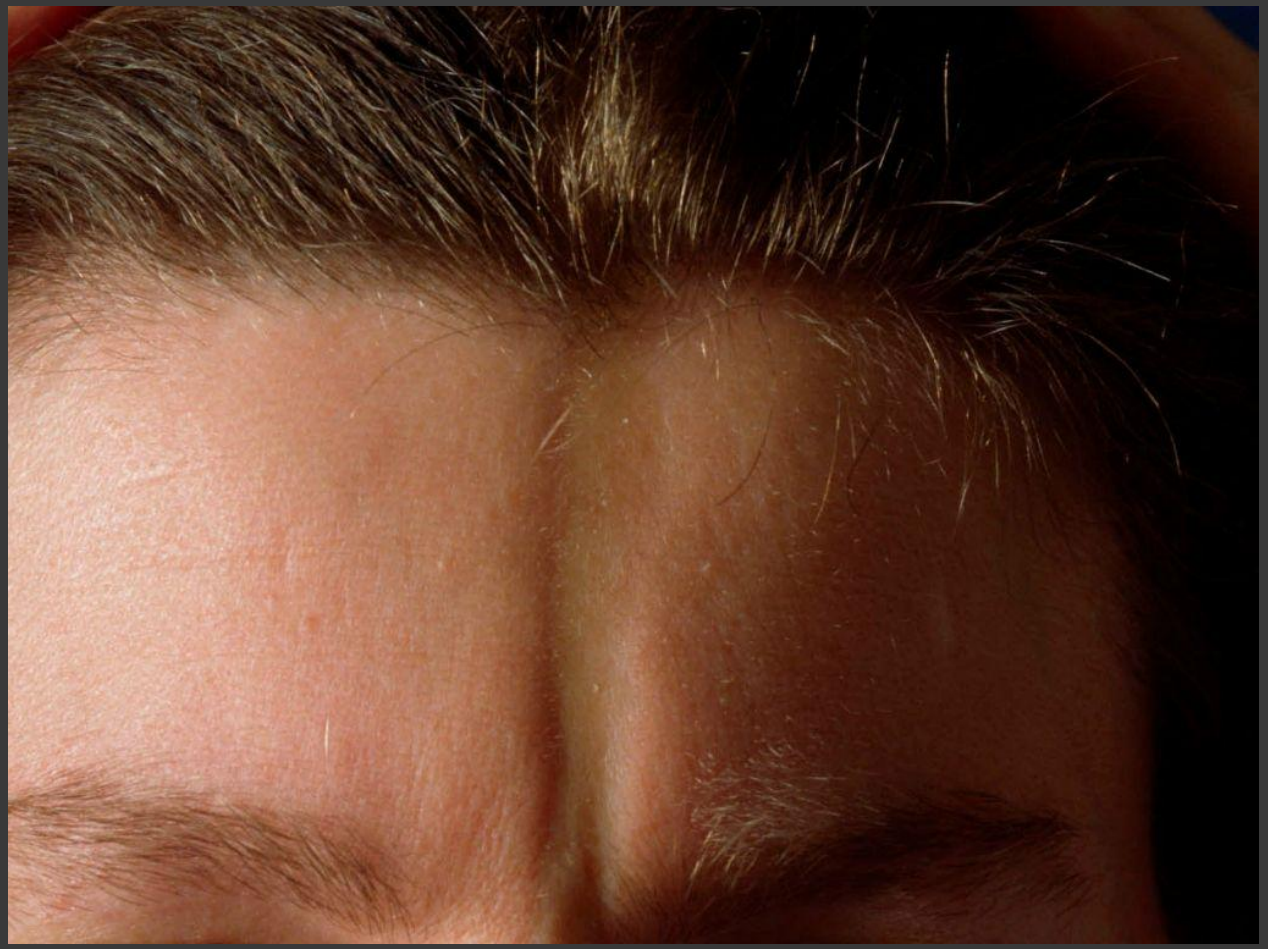
Linear scleroderma

- streaks of thickened skin, typically in one or both lower extremities
- may affect the subcutaneous tissues with fibrosis and 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 can develop.

Linear scleroderma



En coupe de sabre



Systemic sclerosis (SSc)

- A chronic systemic disorder of unknown etiology
- Characterized by thickening of the skin (scleroderma) and involvement of multiple internal organs, such as the lungs, GI tract, heart, and kidneys

2 subsets of SSc

1. Diffuse cutaneous SSc
2. Limited cutaneous SSc

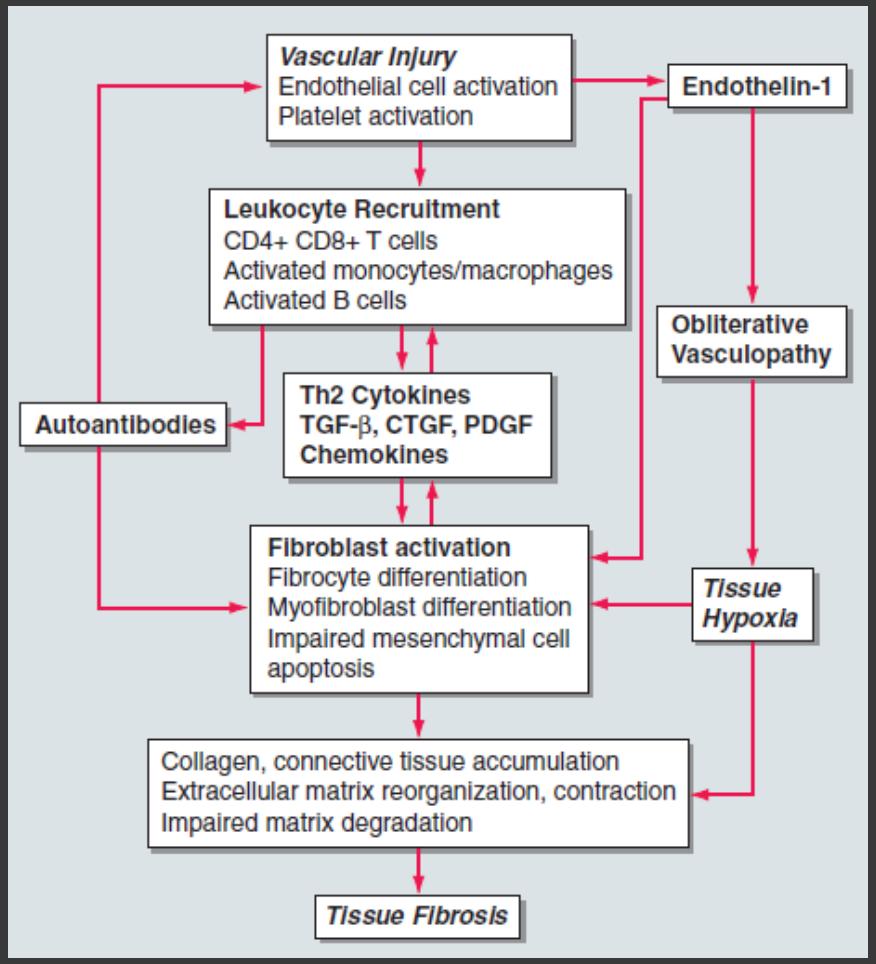
SUBSETS OF SYSTEMIC SCLEROSIS (SSc): LIMITED CUTANEOUS SSc VERSUS DIFFUSE CUTANEOUS SSc

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)

Epidemiology

- Affects all races.
- Incidence is 9–19 cases per million per year
- Prevalence of 286 cases per million population.
- More in females
- Most common age of onset is in the range of 30–50 years.
- More common in blacks & has worse prognosis
- Blacks more likely to have the diffuse form with ILD

Pathogenesis



Genetics

- non-Mendelian pattern of inheritance.
- concordance rate for SSc among twins is low (4.7%)
- 1.6% of SSc patients have a first-degree relative with SSc.
- risk of other autoimmune diseases, including SLE and RA is increased.

Environmental factors

- CMV infection: molecular mimicry with Scl-70 antigen
- rapeseed oil: *toxic oil syndrome*
- L-tryptophan: *eosinophilia-myalgia syndrome*
- miners exposed to silica
- polyvinyl chloride
- epoxy resins
- aromatic hydrocarbons
- Drugs: bleomycin, pentazocine and cocaine

Clinical features

Raynaud's phenomenon:

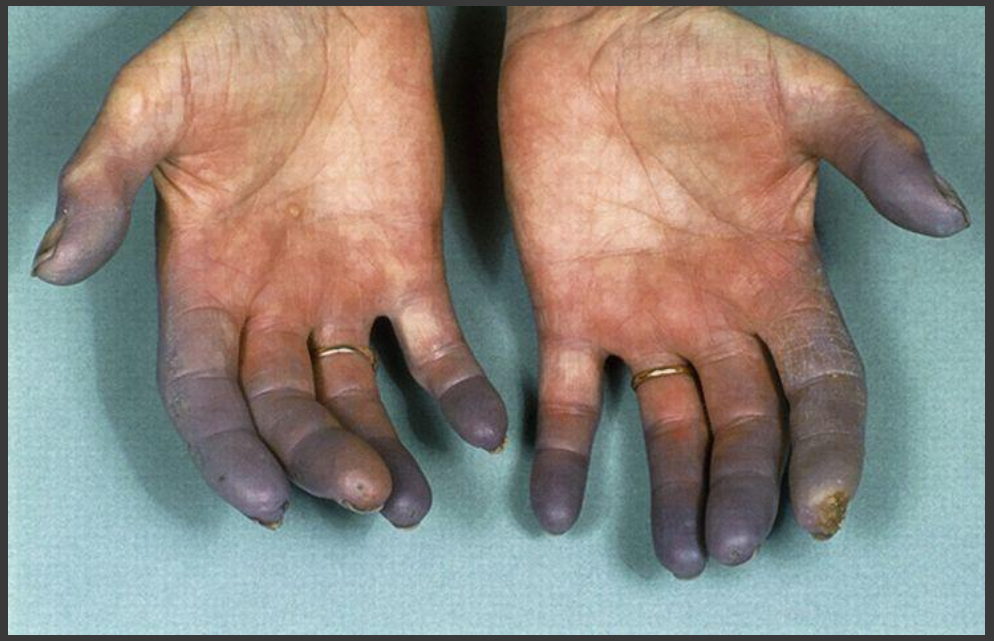
- Episodic vasoconstriction in the fingers and toes
- Attacks are triggered by exposure to cold, stress, and vibration.
- Attacks start with pallor, followed by cyanosis. Eventually erythema develops with rewarming
- Underlying pathogenic mechanisms:
    - Vasoconstriction
    - Ischemia
    - reperfusion.
- 3–5% of the general population have Raynaud's phenomenon

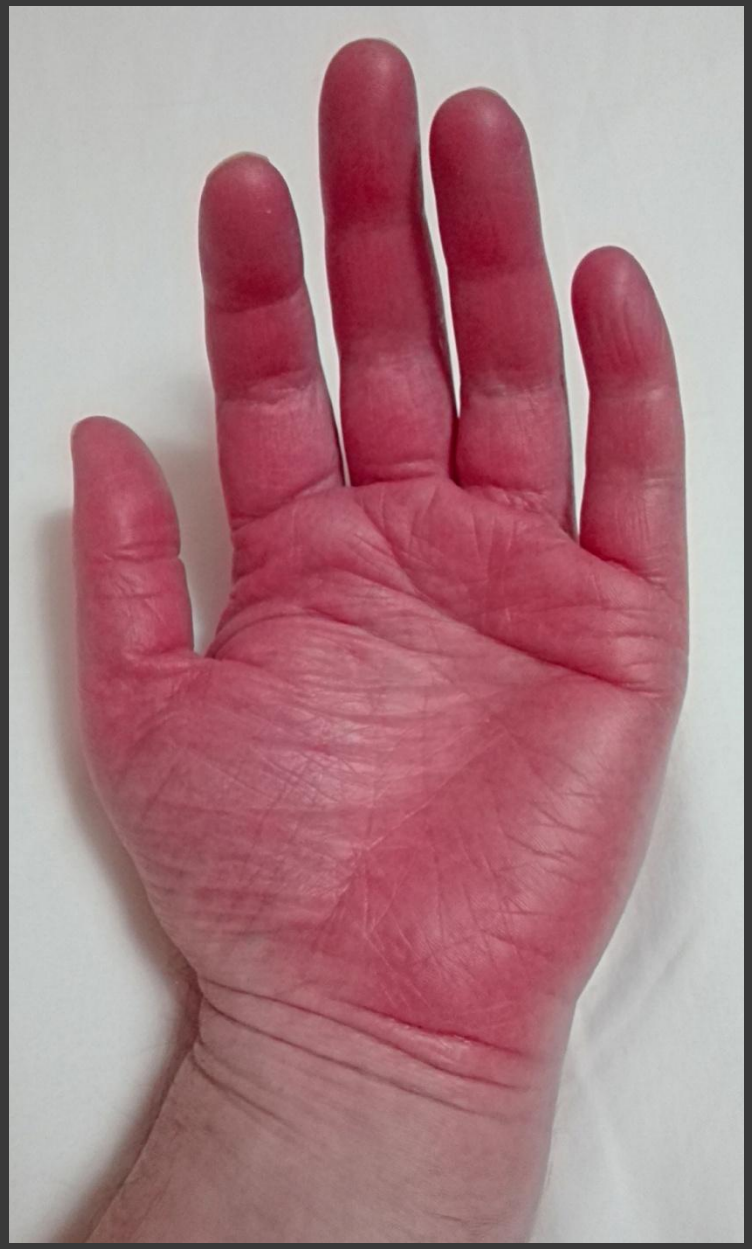
Raynaud's

- **Primary**
- **Secondary:**
  - CTDs: SSc, SLE, Sjogren, Cryoglobulinaemia
  - hematological disorders
  - endocrine conditions
  - Occupational: vibrating tools
  - beta blockers
  - anticancer drugs such as cisplatin and bleomycin

Raynaud's Phenomenon

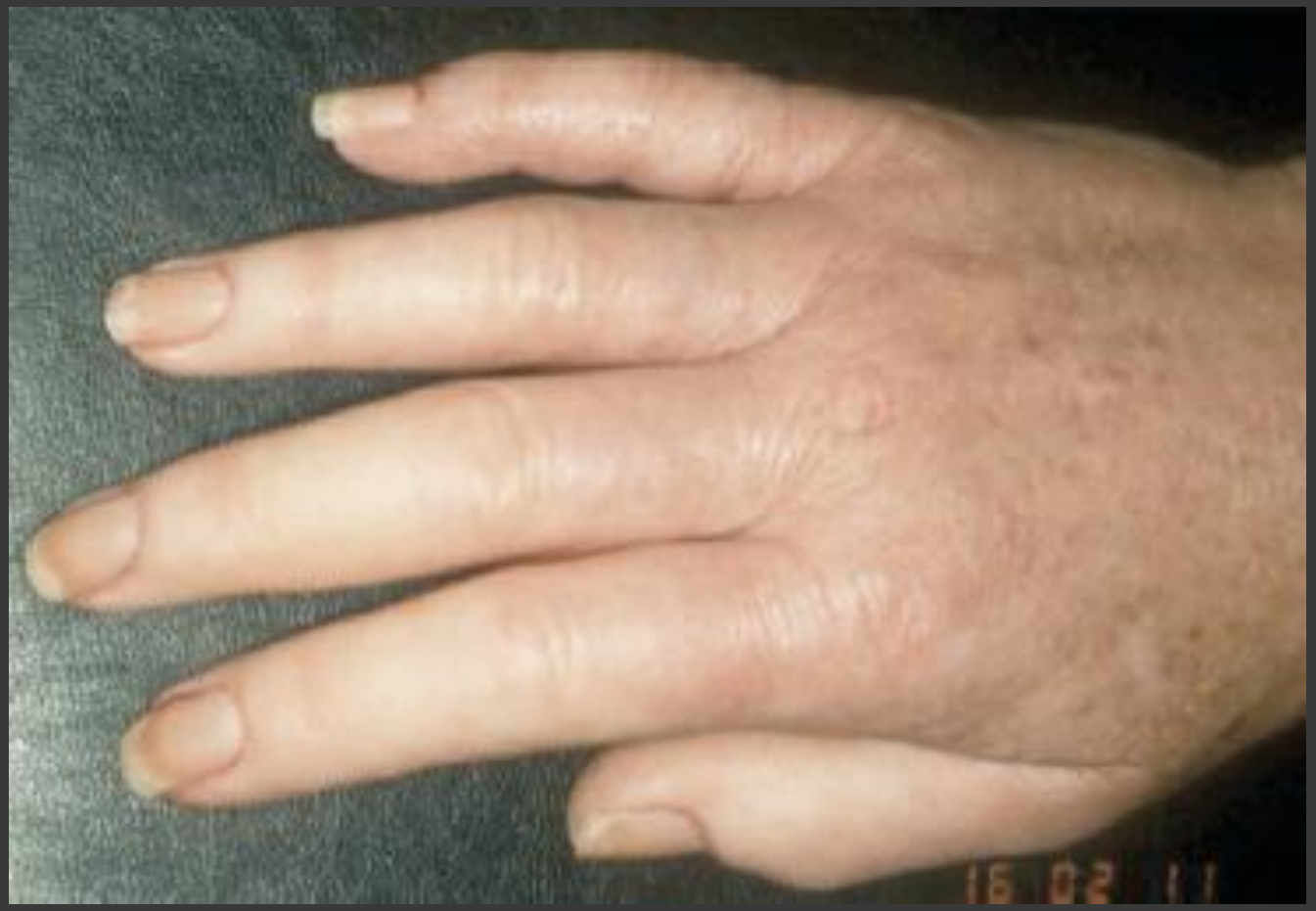
	Primary	**Secondary**
Sex	Female	Male and Female
Age of Onset	Menarche	Mid 20's or later
Finger Edema	No	Frequent
Periungual erythema	Rare	Frequent
Arthritis	No	Frequent
Nail fold capillaroscopy	Normal	Dilated tortuous capillaries
Autoantibodies	Absent	Present





Skin

- skin thickening: symmetrical and bilateral
- Loss of creases on the dorsum of the fingers
- fixed flexion contractures
- Face: taut and shiny skin, loss of wrinkles
- Microstomia
- Beaked nose
- Telangiectasia: face, hands, lips, and oral cavity.
- slow-healing ulcers, may become infected
- Calcinosis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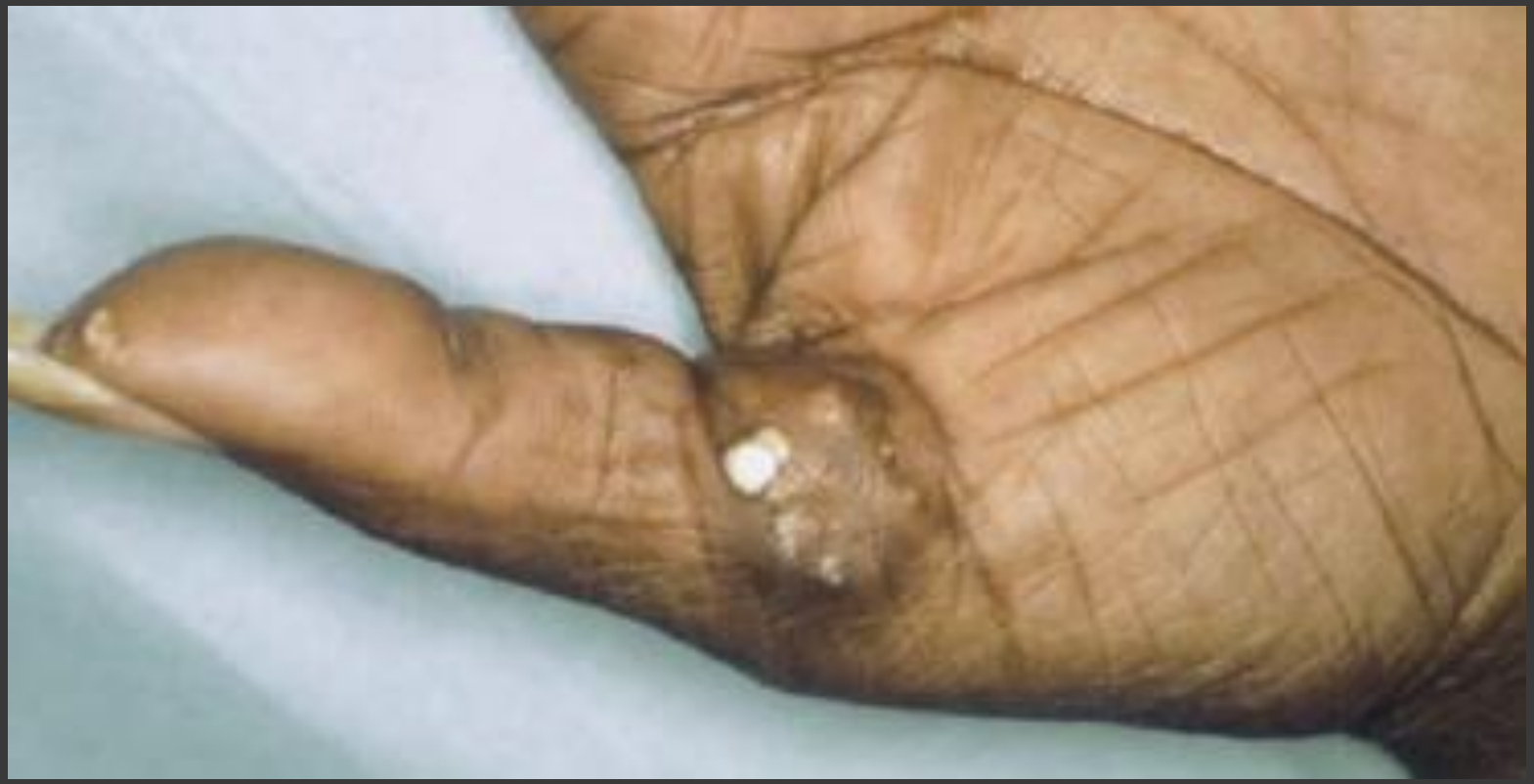
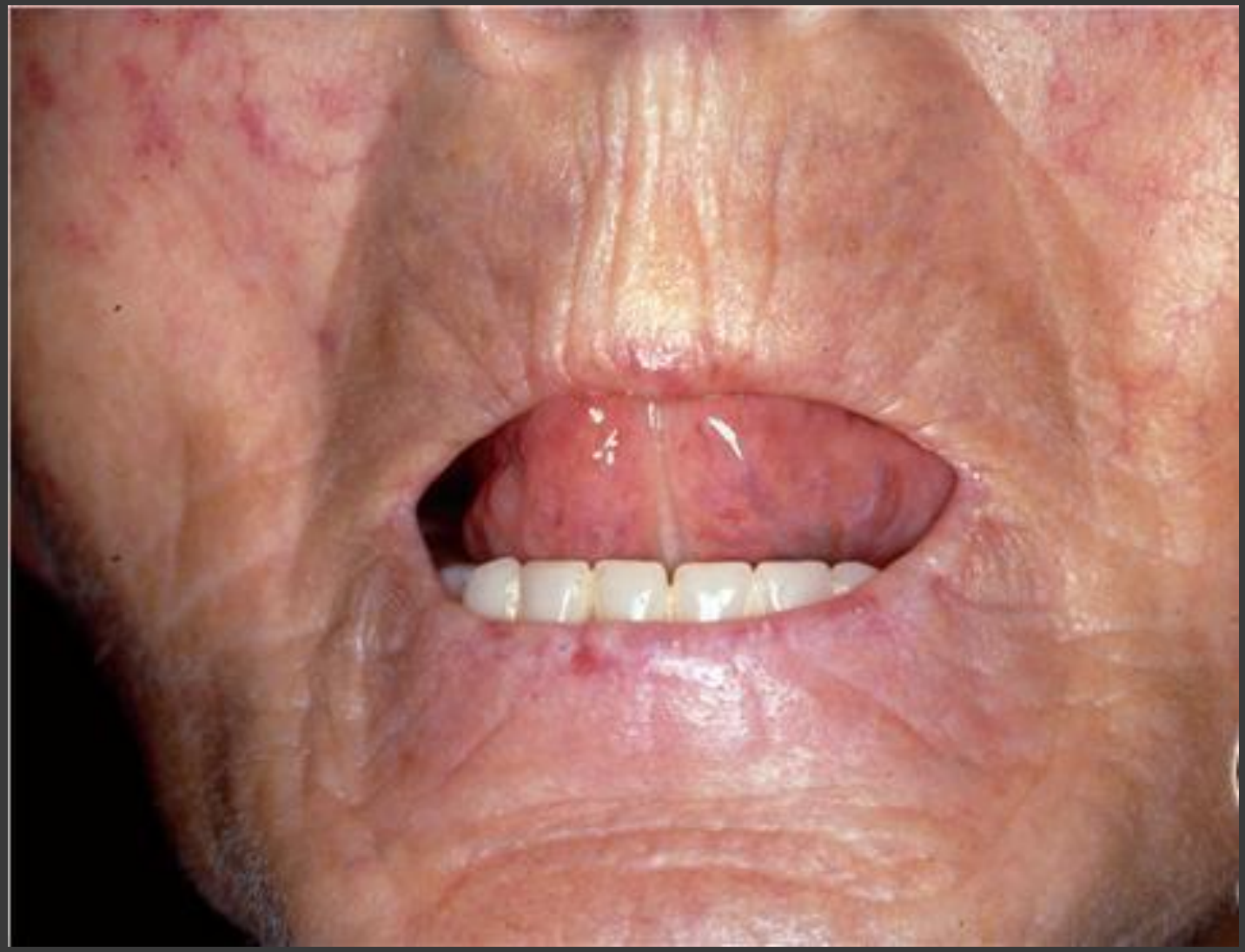
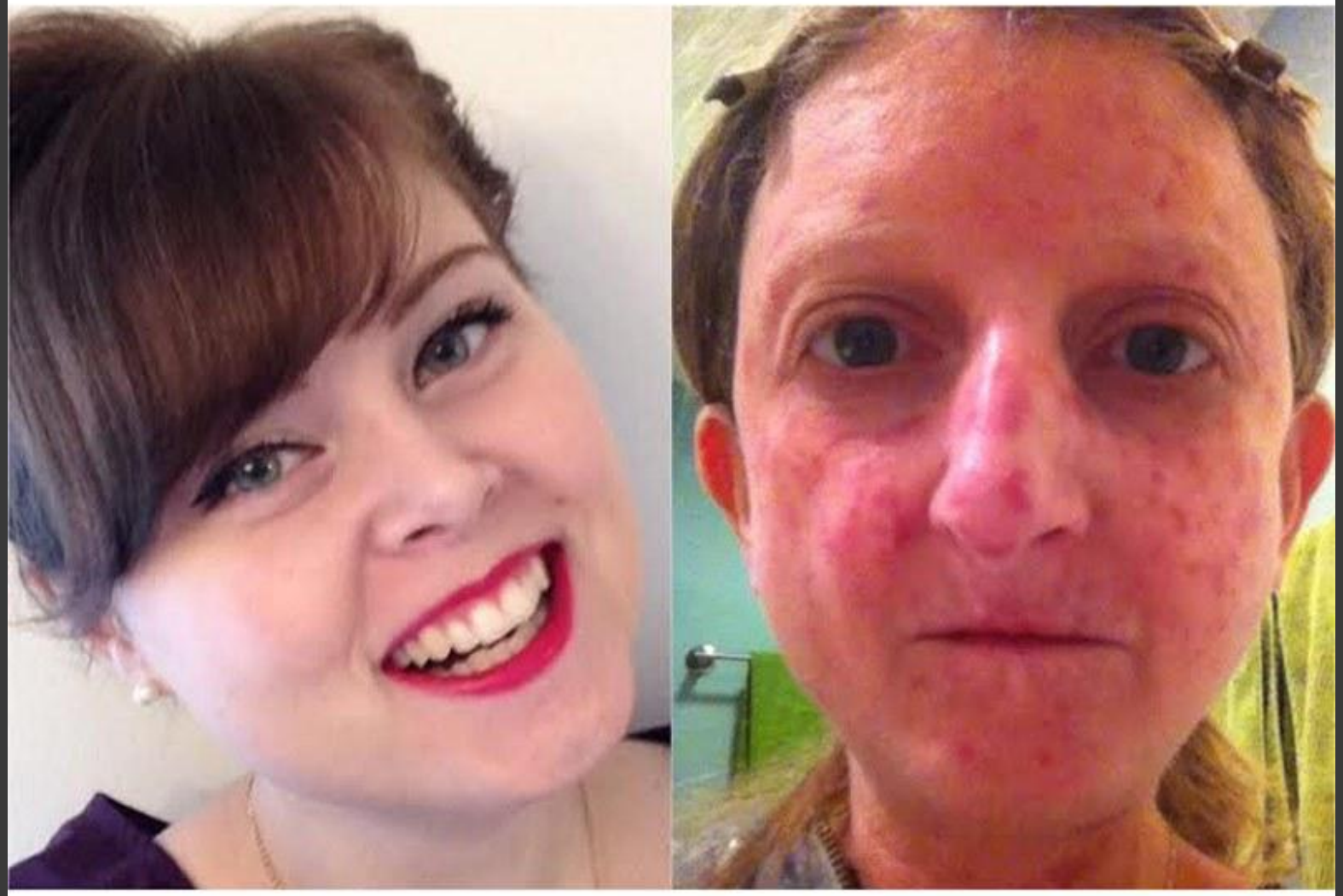
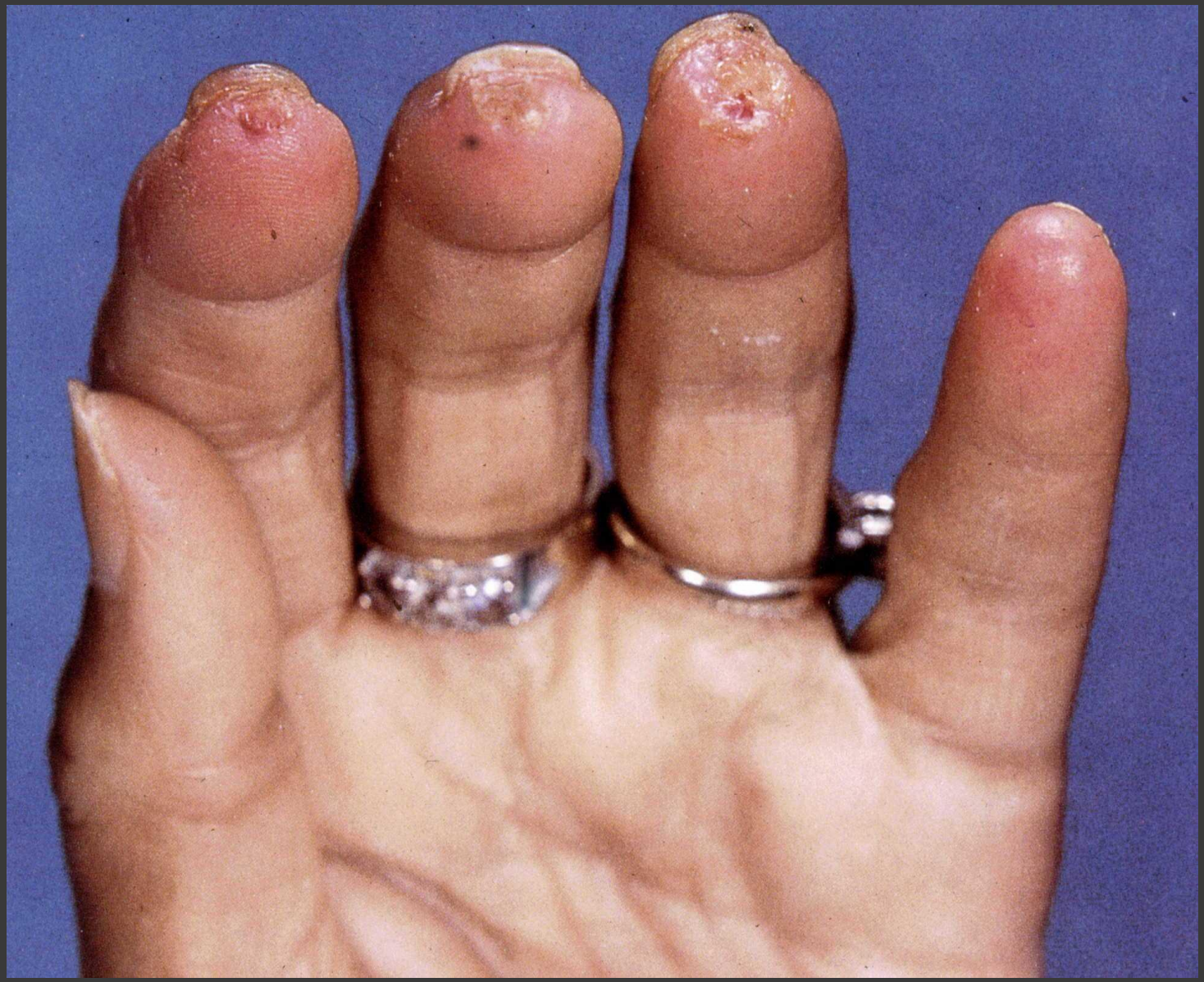








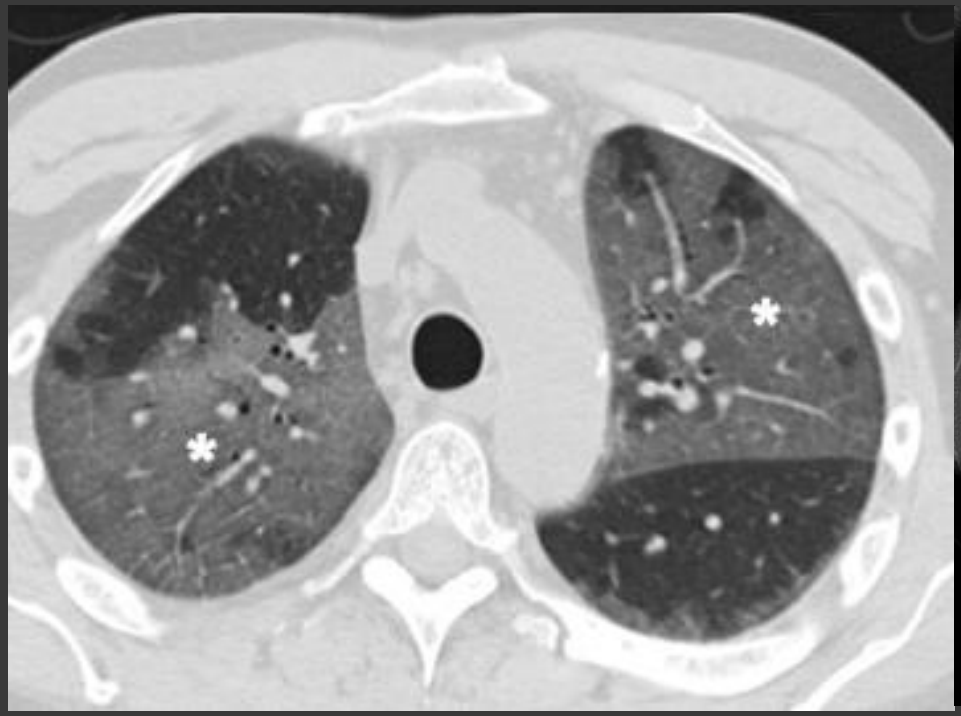
Lung

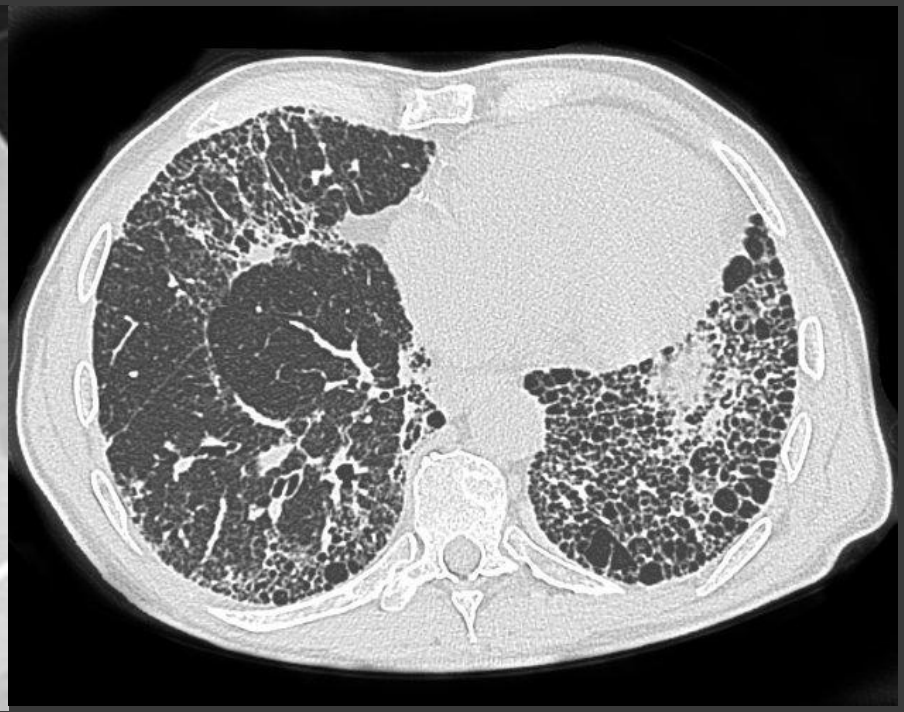
- The leading cause of death
- two main types of pulmonary involvement:
  - ILD
  - PAH
- Other:
  - aspiration pneumonitis complicating GER
  - restrictive ventilatory defect due to chest wall fibrosis

ILD

- cause restrictive lung disease with impaired gas exchange
- PFT show decreased FVC and DLCO but unaffected flow rates
- Risk factors:
  - male gender
  - African-American race
  - diffuse skin involvement
  - Severe GER
  - SCl-70
  - low FVC or DLCO at initial presentation.

ILD



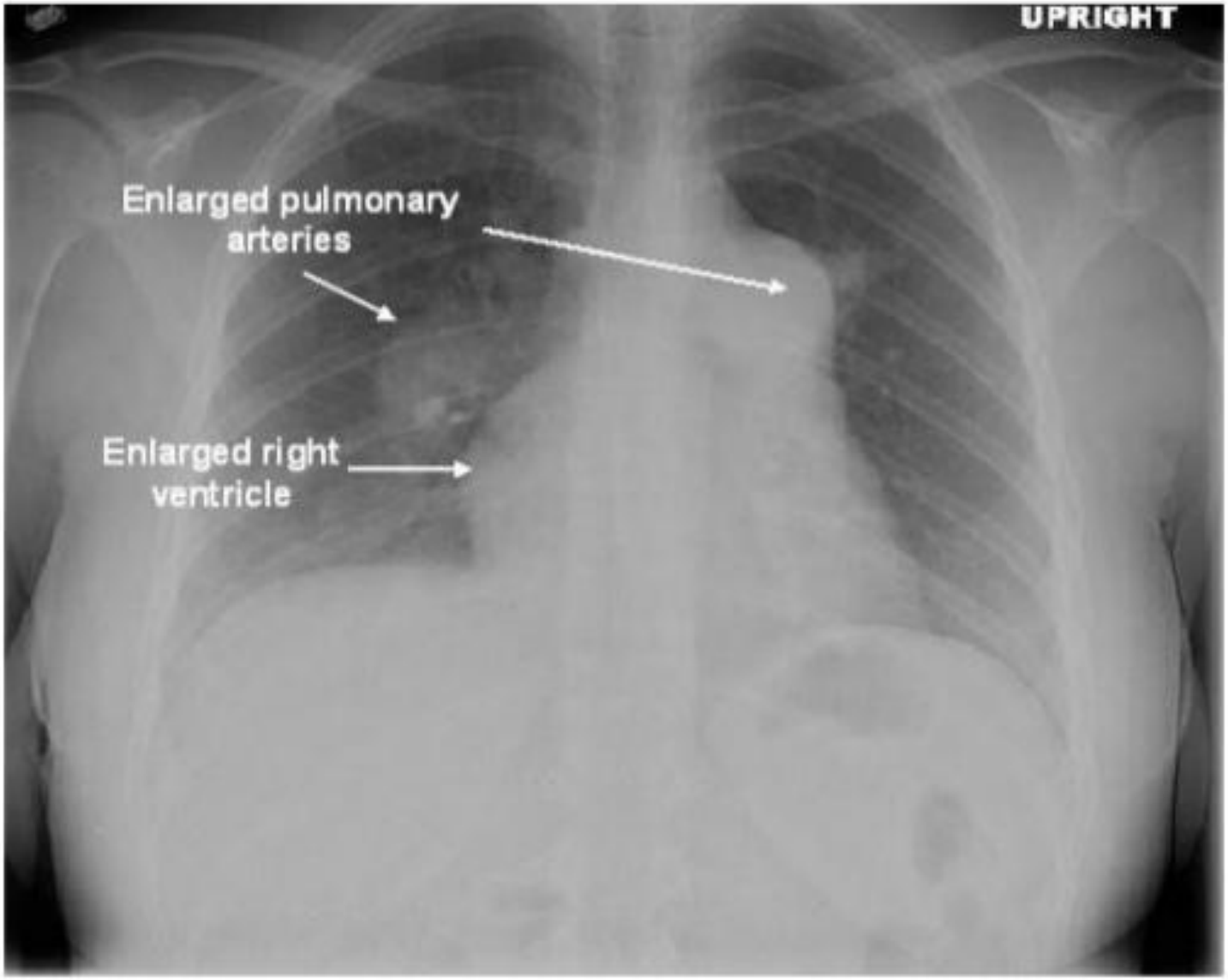


Pulmonary arterial hypertension (PAH)

- PAH: a mean pulmonary arterial pressure >25 mmHg at rest, as determined by right heart catheterization
- may occur in association with ILD or alone
- May lead to right heart failure and significant mortality.
- **Risk factors for PAH:**
  - limited cutaneous disease
  - anticentromere and RNP antibodies
  - late age at disease onset
  - severe Raynaud's phenomenon

PAH

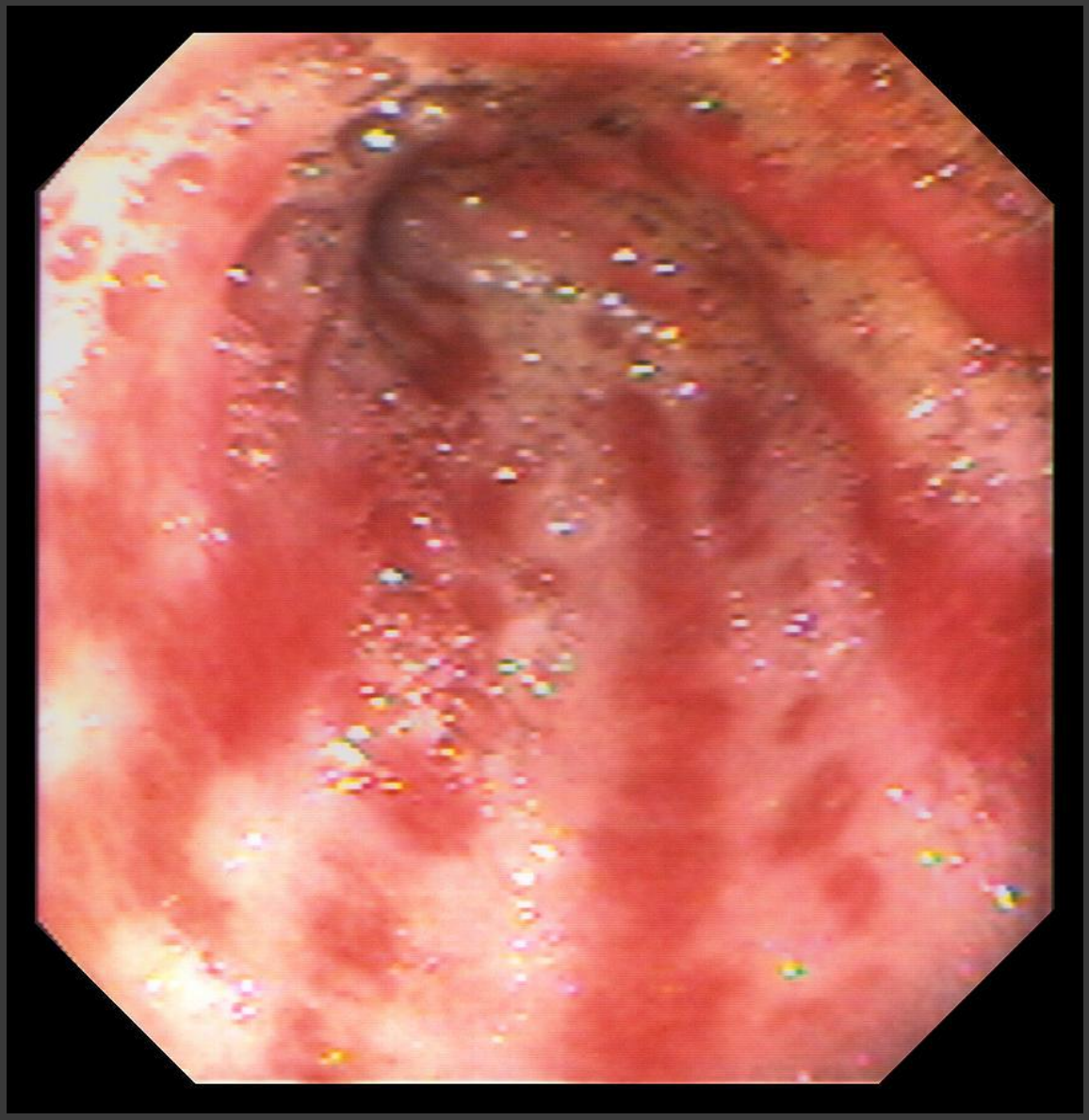
- PFT shows isolated reduction in DLCO
- CXR show PA enlargement
- PAP on Echocardiogram > 40 mmHg suggest diagnosis
- Right heart catheterization is required to confirm PAH


UPRIGHT
Enlarged pulmonary arteries
Enlarged right ventricle

Gastrointestinal tract

- Due to abnormal motility of the esophagus, stomach, and small and large intestines
- atrophy and fibrosis of smooth muscle, intact mucosa, and small-vessel vasculopathy.

- Gastroesophageal reflux disease (GERD) ➔ heartburn, regurgitation, and dysphagia
- Gastroparesis ➔ early satiety, abdominal pain and distension
- Gastric antral vascular ectasia gives a watermelon appearance on endoscopy ➔ recurrent episodes of occult gastrointestinal bleeding ➔ unexplained anemia.
- malabsorption and chronic diarrhea secondary to bacterial overgrowth.
- intestinal pseudoobstruction.



Renal

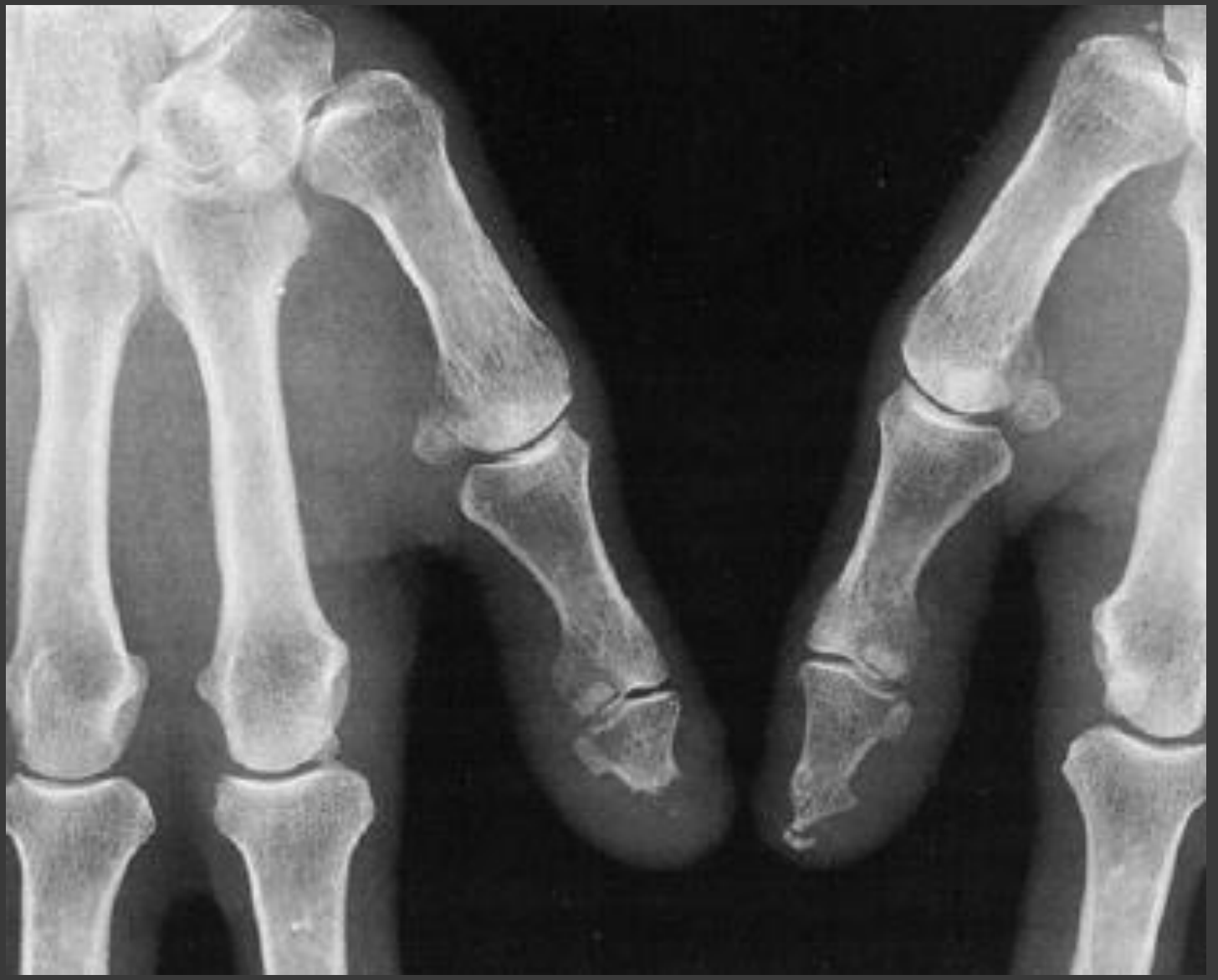
- Scleroderma renal crisis
  - occurs within 4 years of the onset of the disease.
  - Risk factors:
    - African-American race
    - male gender
    - diffuse skin involvement
    - autoantibodies to RNA polymerase III.
  - presents with abrupt onset of malignant hypertension.
  - In 10% of patients, blood pressure is normal

Scleroderma renal crisis

- Urinalysis shows proteinuria and microscopic hematuria
- thrombocytopenia
- evidence of MAHA with fragmented red blood cells
- Rx: ACE inhibitors

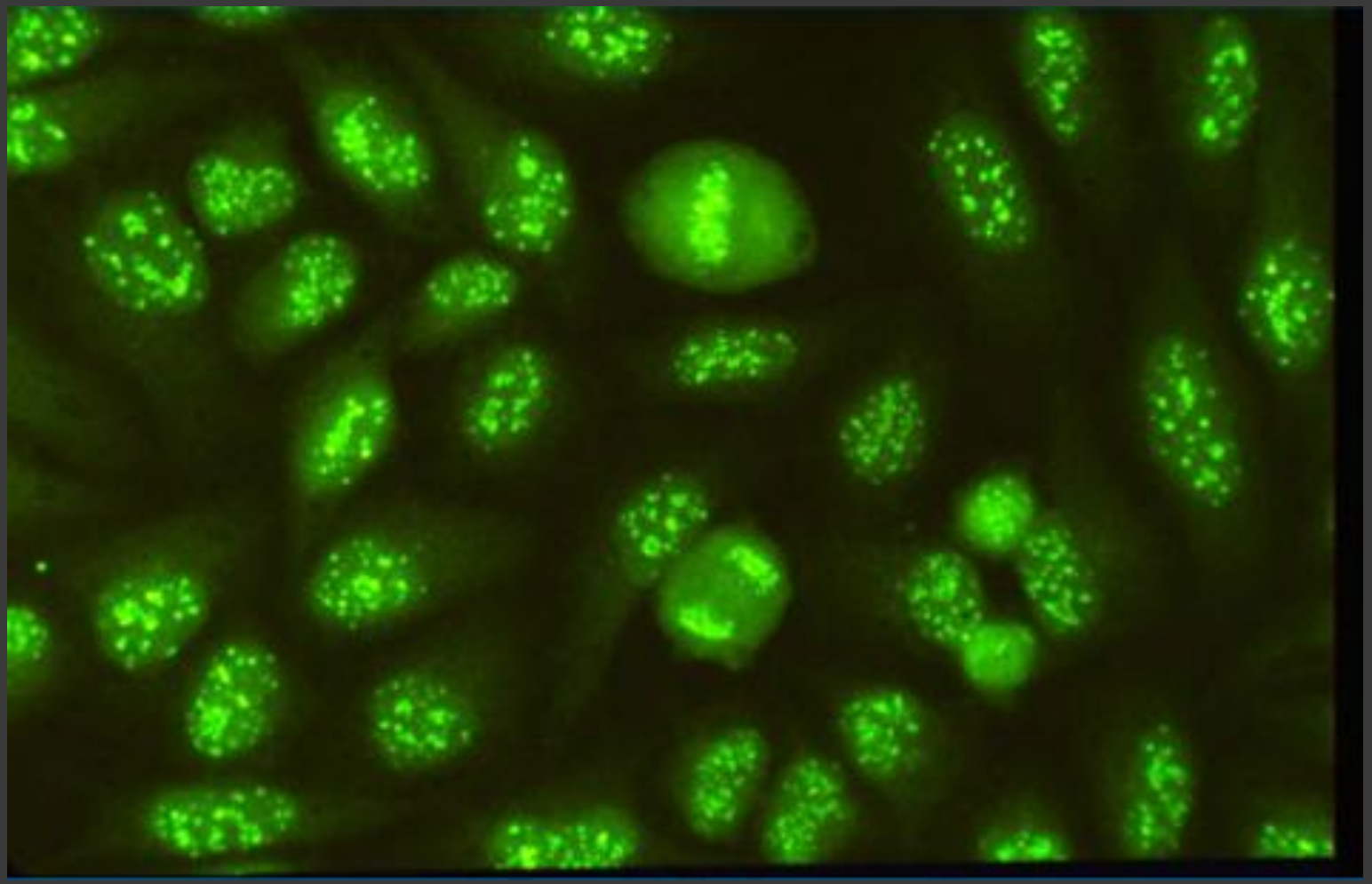
Musculoskeletal

- Arthralgia
- Joint contractures
- Tendon friction rubs
- Severe erosive asymmetrical polyarthritis (rare)
- inflammatory myositis
- Acro-osteolysis: Bone resorption in the terminal phalanges



Lab findings

- Normocytic anaemia
- ESR normal
- ANA
- Anti-Centromere (more common in l-SSC
- anti-SCl-70 (more common in d-SSC)



Treatment

- no therapy can alter the natural history of SSc
- Treatment aimed at alleviating the symptoms and in slowing the progression of the cumulative organ damage
- Glucocorticoids may decrease stiffness and aching but do not influence the progression of skin or internal organ involvement.

Treatment

- cyclophosphamide reduced the progression of ILD in patients with early symptomatic disease
- Mycophenolate mofetil treatment may improve skin induration

Treatment of Raynaud's

- dress warmly
- minimize cold exposure and stress
- Gloves
- Avoid drugs that could precipitate vasospasm
- Calcium channel blockers such as nifedepine
- phosphodiesterase inhibitors (e.g.sildenafil)
- serotonin reuptake inhibitors (e.g., fluoxetine),
- topical nitroglycerine
- intravenous prostaglandins.

Treatment of PAH

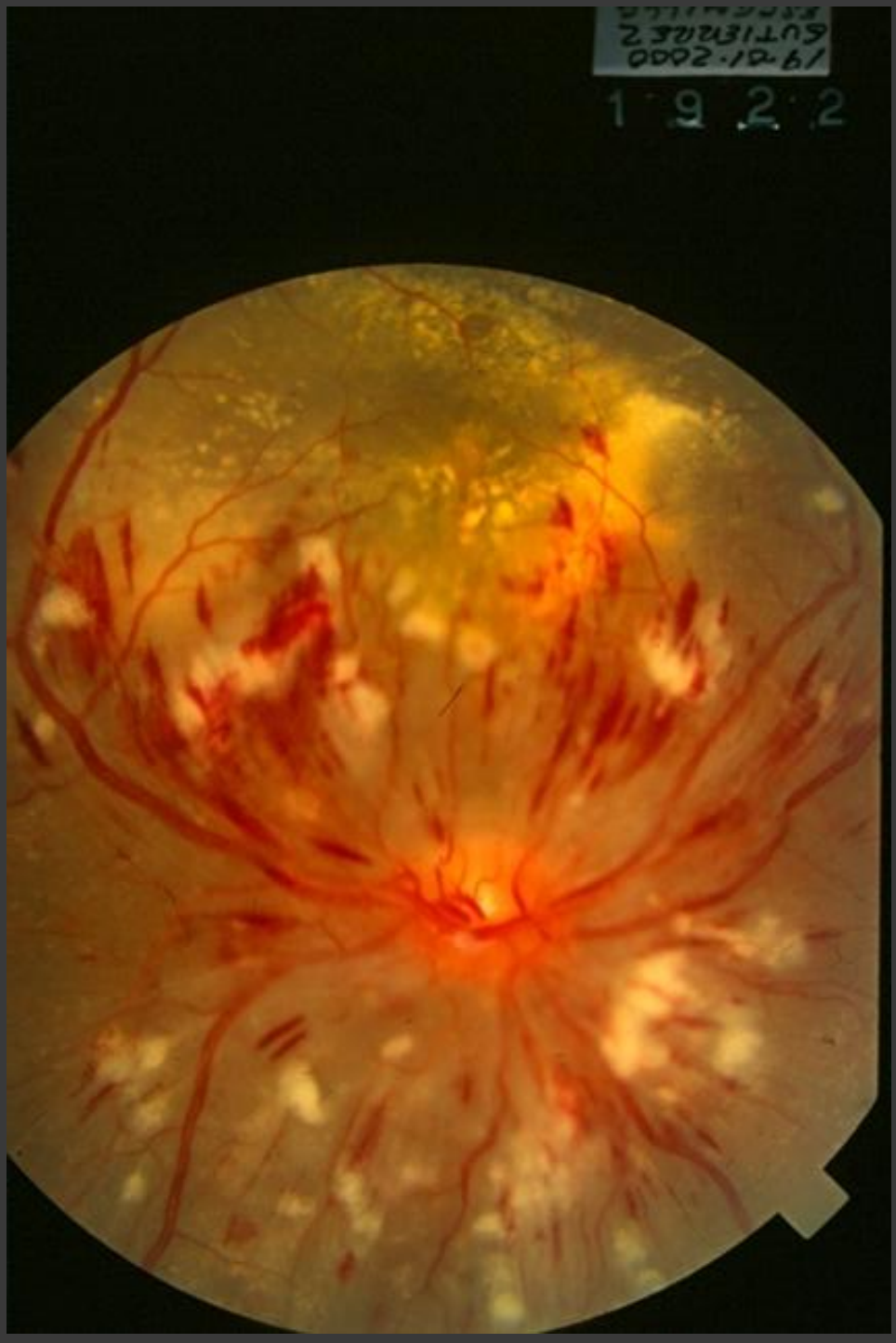
- Phosphodiesterase type 5 inhibitors (sildenafil)
- Endothelin-1 receptor antagonists (bosentan)
- Prostacyclin analogues (Epoprostenol, treprostinil)
- Oxygen therapy
- Lung transplantation

Case 2

- A 50-year-old woman was admitted to hospital with a 48-hour history of generalized headache and dyspnoea at rest.
- She had Raynaud’s disease that was controlled with nifedipine and had recently been referred to a gastroenterologist for investigation of difficulty in swallowing.

On examination

- The blood pressure was 220/130 mmHg
- Auscultation of the lungs revealed bibasal inspiratory crackles
- The ankles were mildly swollen
- Neurological examination was normal with the exception of the fundi, which revealed hard exudates, cotton wool spots and flame-shaped haemorrhages.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Investigations

Hb	11 g/dl
WCC	11 × 109/l
Platelets	100 × 109/l
Blood film	Shistocytes
	Microspherocytes
Sodium	138 mmol/l
Potassium	4.8 mmol/l
Urea	28 mmol/l
Creatinine	490 μmol/l
ECG	Left ventricular hypertrophy
Chest X-ray	Bilateral basal alveolar shadows and small pleural effusions
Urinalysis	Protein ++
	Blood 0

Diagnosis?

Any Questions?