

**Scleroderma: Digital ischemia, Scleroderma Renal Crisis, Cardiac Scleroderma and other manifestations**

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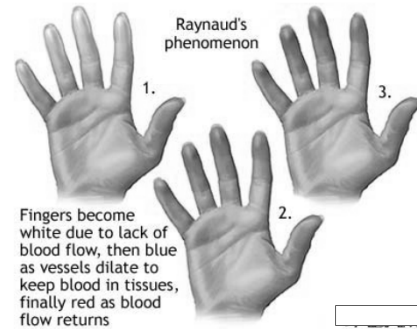
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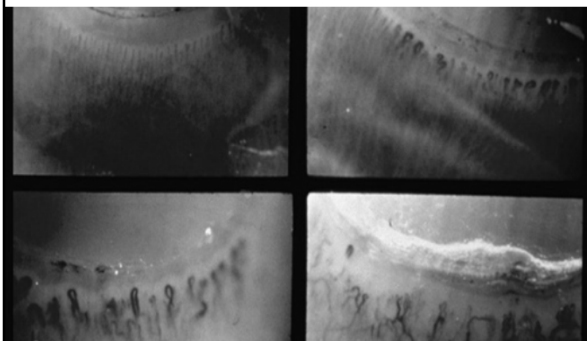
**Digital Ischemia**  
**(Raynaud's phenomenon, finger and toe ulceration / gangrene)**

**Raynaud's phenomenon**

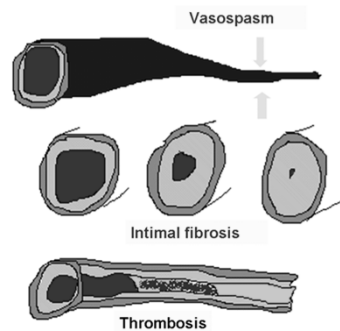
- **Primary Raynaud's** - 5% to 10% of the general population
- **Secondary Raynaud's** - 90-95% of cases of scleroderma
- Presenting sign of limited scleroderma, and may precede other signs of disease by years
- As a consequence of blood vessel injury, first as a **functional reversible process**
- With time, there is a **structural change in the vessel**, leading to blood vessel occlusion and lack of oxygen delivery to the tissues at the fingertip
- This can lead to skin ulceration and gangrene (seen only in secondary Raynaud's phenomenon, e.g. in Scleroderma)
- **Nail fold capillaroscopy**: capillary dilatation (limited disease), capillary dropouts (diffuse disease) can be helpful to differentiate primary from secondary Raynaud's phenomenon



**Nailfold Capillaroscopy**



**Microvascular narrowing in SSc**

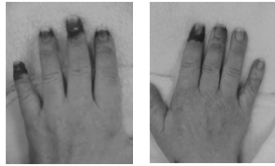


Adapted from CD-ROM: "Approaches to treatment of fibrotic & vascular disease in Scleroderma" (Boston Univ SOM)

**Treatment Strategies For Raynaud's And Digital Ulcers**

- Vasodilators: Ca channel blockers / ACE-I / ARBs / SSRIs
- Topical nitrates: patch or paste (ointment)
- Alpha- adrenergic blockers: Prazosin / Doxazosin
- PDE-5 inhibitors: Sildenafil, Tadalafil, Vardenafil
- Endothelin receptor antagonists: Bosentan
- Drugs affecting blood viscosity: Pentoxifylline / Cilostazol
- Antiplatelet drugs: Low dose Aspirin or Clopidogrel
- IV Prostaglandins: Epoprostanol / Alprostadil / Iloprost (Europe)
- Good local wound care
- Prolonged systemic antibiotics for infected ulcers or osteomyelitis
- Surgery: Cervical or digital sympathectomy / digital amputation / vascular grafts and reconstruction


**What is the appropriate treatment for the threatened digit?**



- Beginning of necrosis at the end of the digit
- Epoprostenol - IV infusion 2-6 ng/Kg/min continuously X 3-5 days \*
- Alprostadil - IV infusion 0.5-6 ng/Kg/min continuously X 3-5 days
- Most effective agent in the acute setting
- Intravenous antibiotics - if there is infection

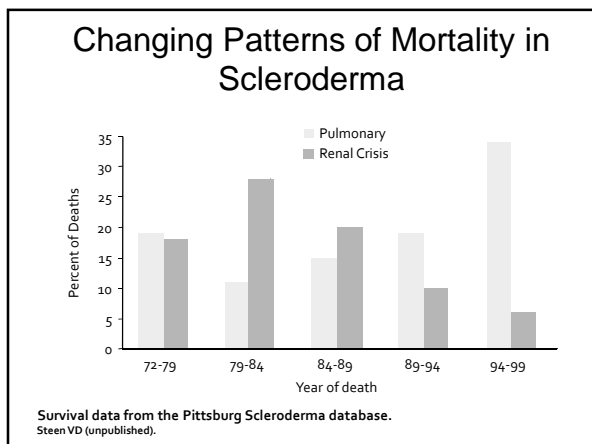
\* Hummers LK, Wigley FM. *Rheum Dis Clin N Am.* 29 (2003): 293-312  
\* Wigley FM et al. *Ann Intern Med.* 1994, Feb 1;120(3):299-206

**What is the appropriate treatment for the threatened digit?**



- Sympathectomy - cervical or digital
- Micro-ETS (Endoscopic Thoracic Sympathectomy)
- Revascularization procedures
- Auto-amputation is preferred to surgical amputation

**Scleroderma Renal Crisis**



**Factors Occurring Prior to Onset of Renal Crisis**

<u>Predictive of SRC</u>	<u>Not Predictive of SRC</u>
✓ Early diffuse SSc (<4 yrs)	✓ Previous HTN
✓ Rapid progression of skin thickening	✓ Abnormal urinalysis
✓ New cardiac events – CHF, Pericardial effusion	✓ Previous increase in serum creatinine
✓ High dose steroids (?)	✓ Plasma renin
✓ RNA Polymerase III antibody	✓ Pathologic abnormalities in renal blood vessels
✓ New anemia	✓ Anti-Scl-70 or anti-centromere antibody

Steen VD. *Rheum Dis Clin North Am.* 2003; 29: 315-333

**Kidney involvement in Scleroderma**

- Early diffuse disease (2-5 years after onset)
- Rapid onset malignant phase hypertension with renal failure (abrupt rise in BP more important than absolute numbers, normotensive RC -10%)
- MAHA (drop in Hb, rising LDH, schistocytes)
- Thrombocytopenia
- Proteinuria
- Slower onset of gradually progressive loss of renal function sometimes
- NOT an inflammatory glomerulonephritis

**Management of Renal involvement**

- Monitor BP 2-3 times weekly in early diffuse disease and alert physician if DBP > 90 mmHg for two days in a row
- Follow serum creatinine, urine protein (dipstick)
- **Scleroderma Renal Crisis** – ACE inhibitors in maximal doses, may add other anti-hypertensives, creatinine may go up, but still continue ACE-I
- ARBs may not be as effective
- Aim: to control blood pressures to diastolic < 85 mmHg, and < 80 mmHg if possible
- 30-40% recover sufficient renal function to d/c dialysis
- Renal transplant - viable option

**Heart involvement:**

- Subclinical myocardial involvement – in ~100% Clinical expression ~25% - Perfusion abnormalities on Thallium-201 scintigraphy: SPECT / MRI
- Myocardial fibrosis leading to cardiomyopathy (systolic and diastolic dysfunction) – CHF
- Conduction defects (Septal infarction pattern and ventricular conduction abnormalities)
- Pericarditis / Pericardial effusion (renal crisis?)

Follansbee et al: Am J Med. 1985 Aug;79(2):183-92.

**Management of scleroderma heart disease**

- At present, treatment of cardiac scleroderma is essentially symptomatic and empiric. CHF - ACE-I, vasodilators
- No benefit from steroids or immunosuppressive drugs have been demonstrated
- Perfusion abnormalities improve with Nifedipine, Nicardipine, Captopril
- Nifedipine improves myocardial metabolism – PET scan
- Nifedipine / Nicardipine improve LV and RV function – Echo, Radionuclide ventriculography
- Pacemaker / AICD
- Cardiac transplant

Follansbee et al: Am J Med. 1985 Aug;79(2):183-92.

**Other manifestations:**

- Joint pain / inflammatory arthritis / tendon friction rubs
- Serositis (Pericarditis / pleurisy)
- Myopathy (muscle disease)
- Sjögren's Syndrome (secondary)
- Primary Biliary Cirrhosis (liver disease)
- Autoimmune thyroid disease
- Vasculitic leg ulcers
- Erectile dysfunction in men

**PROGNOSIS**

- ❖ **Diffuse disease:**
  - ✓ Variable disease course, but overall prognosis is worse than that in limited scleroderma
  - ✓ Survival is 40 - 60% at 10 years
  - ✓ Progressive pulmonary fibrosis, Pulmonary hypertension, Severe GI involvement, and Scleroderma heart disease are the main causes of death
- ❖ **Limited disease:**
  - ✓ Relatively better prognosis
  - ✓ Survival is ≥ 70% at 10 years