Brief overview of systemic sclerosis (scleroderma)

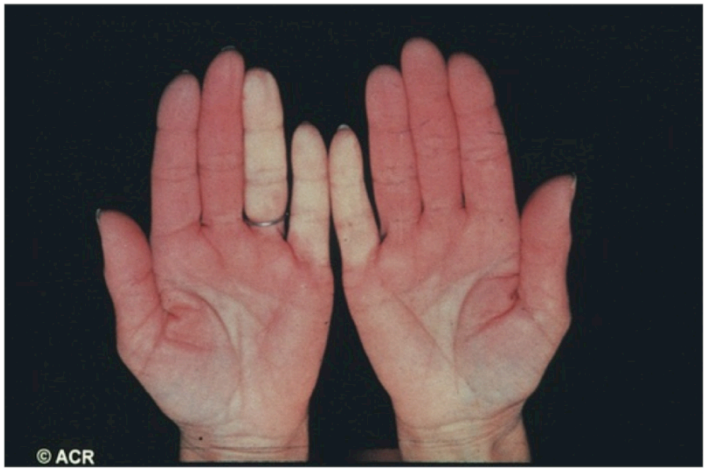
Dinesh Khanna, M.D., M.S.

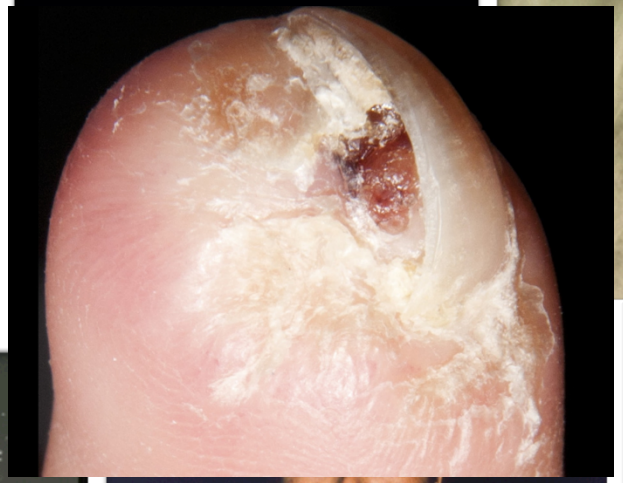
Frederick G. Huetwell Professor
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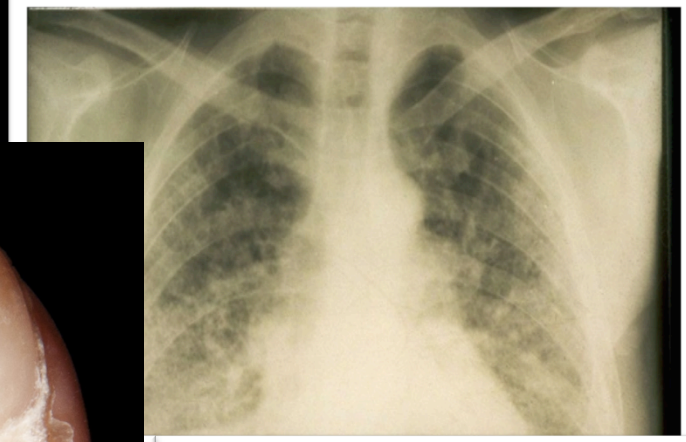
Cytori Meeting January 2015

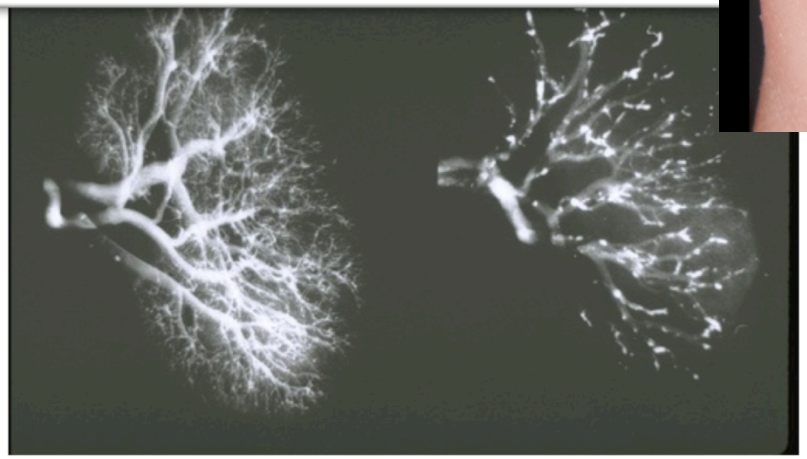
Scleroderma

- Autoimmune disease with no effective treatment or cure
- Affects approximately 300,000 patients in US
- Systemic form can affect heart, lungs, kidneys, and gut
- Mean age of onset is 50 years
- Female predominance of 3-5:1
- Prevalence of 60,000-70,000 patients

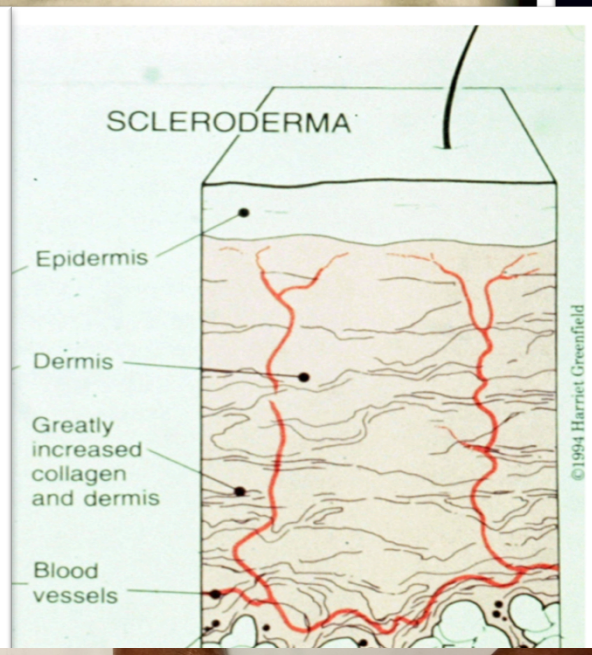

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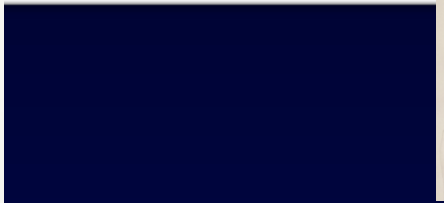







SCLERODERMA
Epidermis
Dermis
Greatly increased collagen and dermis
Blood vessels
©1994 Harriet Greenfield





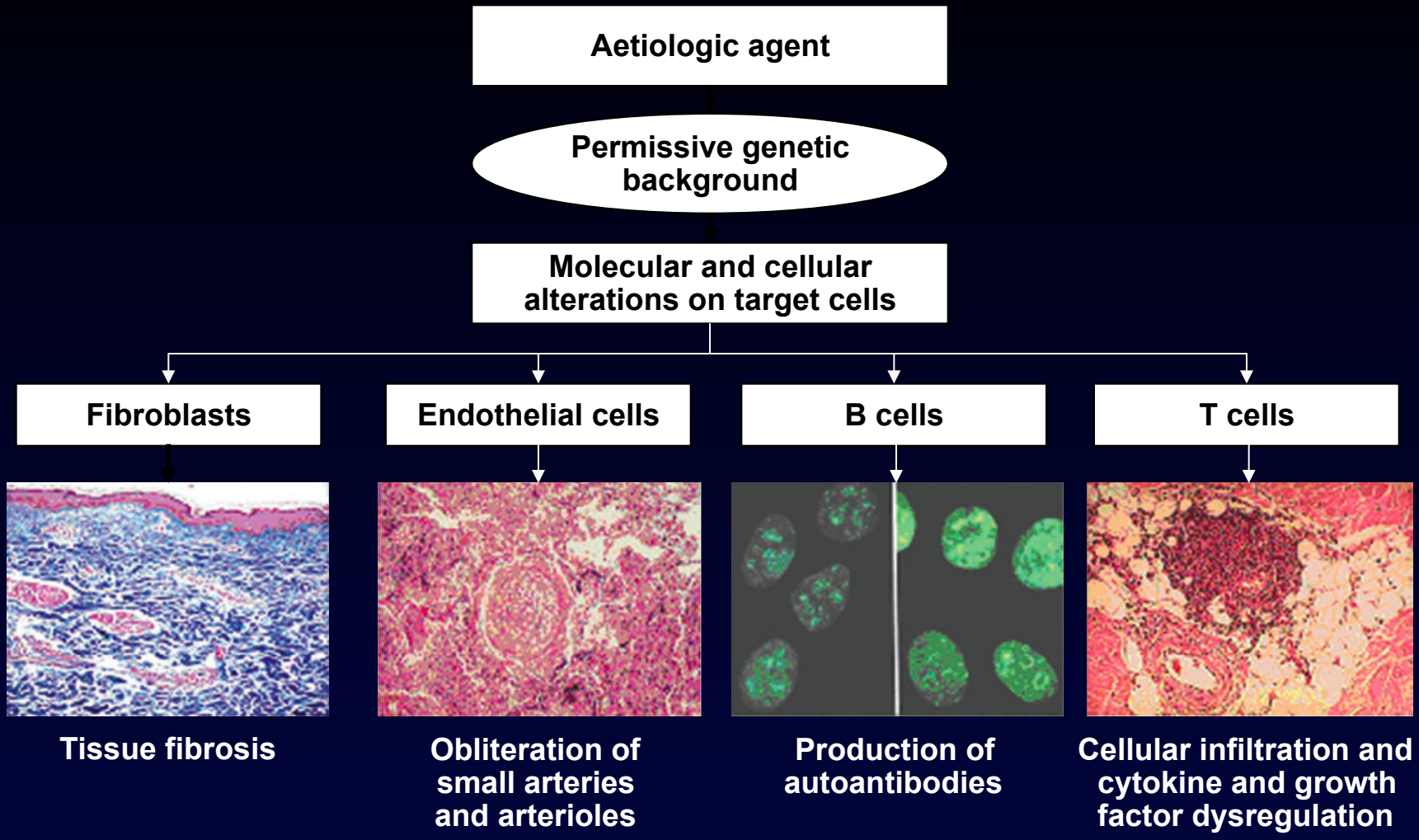


Systemic sclerosis—Mortality

- Highest case-specific mortality of any autoimmune rheumatic disease
- 6 fold increased risk of death for diffuse systemic sclerosis compared to general population
- Survival depends on severity of organ involvement
- 10 year survival for pts with diffuse systemic sclerosis ~70%

Steen V Ann Rheum Dis 2007

SSc— Pathogenesis



Jimenez S, *et al. Ann Intern Med* 2004;140:37–50.

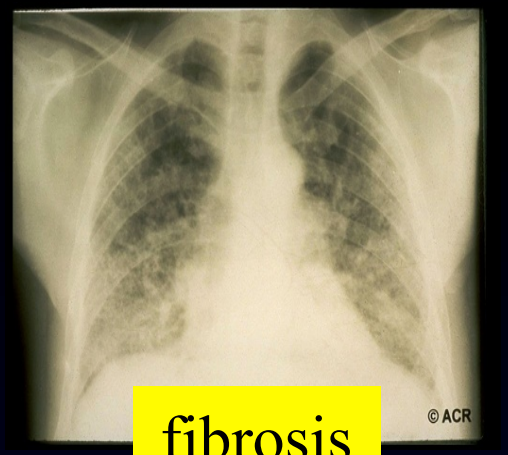
Underlying organ pathology

Skin



fibrosis
immune

ILD



fibrosis
immune

GI



fibrosis
vascular

Heart



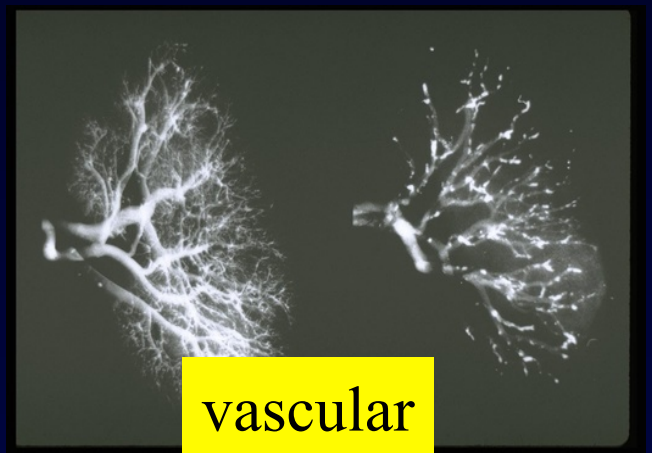
fibrosis
vascular

Raynauds



vascular

Renal



vascular

PAH



vascular

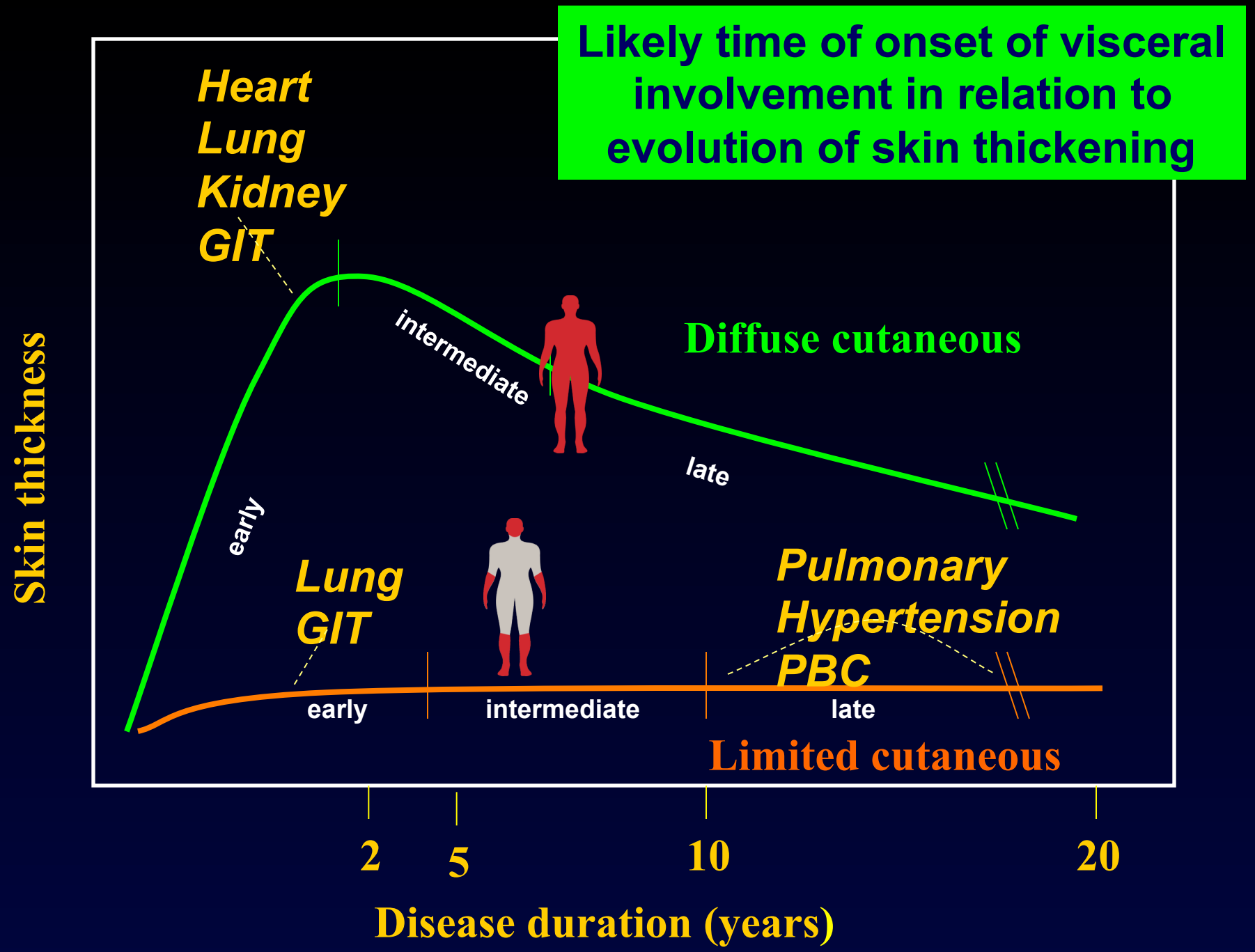
Cost of illness in scleroderma

- Annual direct and indirect costs of SSc are ~1.9 billion US dollars/yr in North America
- Morbidity costs represent 56%(includes SSc-related disability 30-50%)
  - UCLA cohort—40% early disability
  - Per patient cost due to loss of productivity-- $11,000/yr
  - Direct costs represent 32% (spread over the long disease duration)
- Per patient costs for SSc are 3 fold higher than non-SSc patients

Bernatsky. Arth Rheum 2009
Singh M. AC&R 2012

High unmet medical need

- High cost of disease burden, co-morbidities, and mortality associated with internal organ involvement


Likely time of onset of visceral involvement in relation to evolution of skin thickening
Heart
Lung
Kidney
GIT
Diffuse cutaneous
intermediate
late
early
Lung
GIT
Pulmonary
Hypertension
PBC
early
intermediate
late
Limited cutaneous
Skin thickness
2
5
10
20
Disease duration (years)

Hand dysfunction in scleroderma

- Almost universal in patients with SSc
- Has impact on quality of life and work productivity
- Leads to early disability
- Treatment is largely supportive

Guillevin L. Clin Exp Rheumatol. 2013
Granel B. Ann Rheum Dis 2014

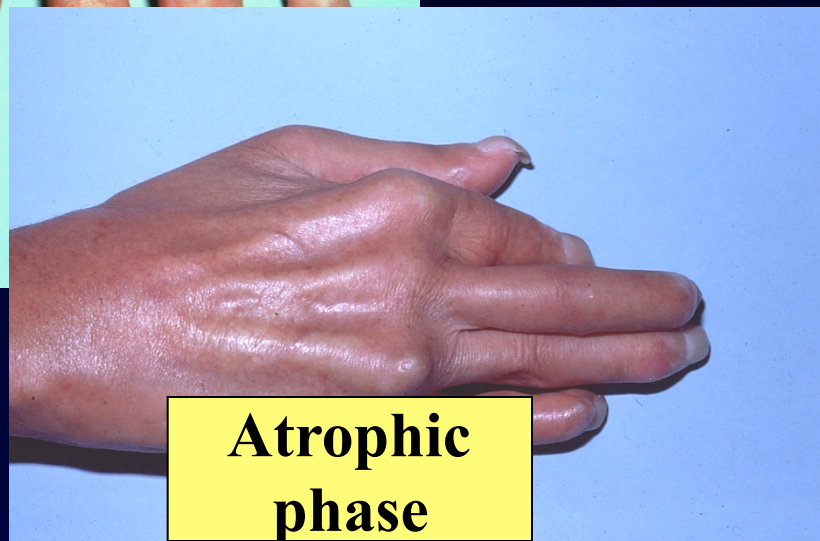
Different phases of skin involvement in scleroderma



Edematous phase



Indurative phase



Atrophic phase



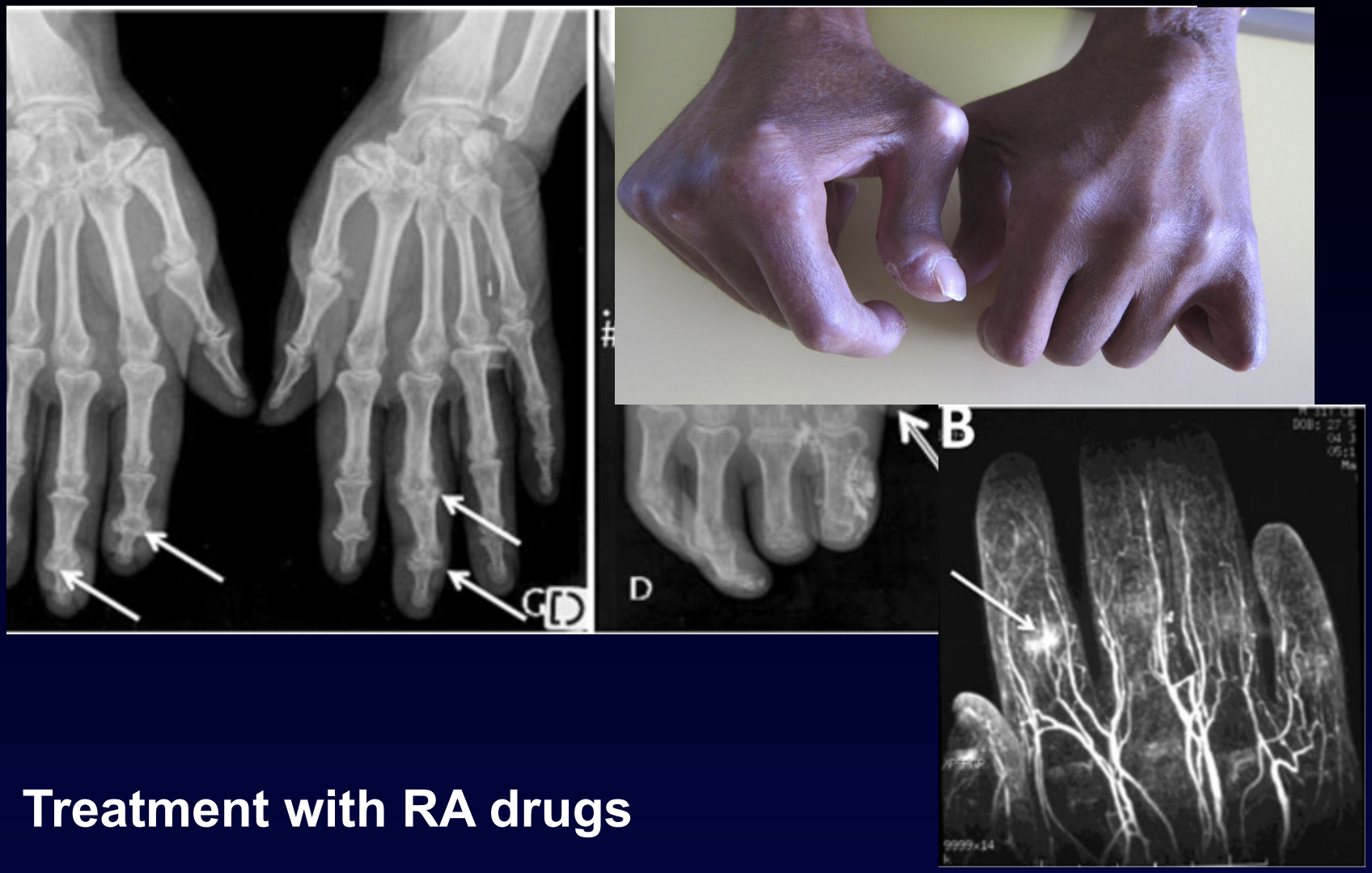
Fixed hand contractures with ulcers in a patient

Treatment

- Immunosuppressives in early disease
- Hand therapy and massage in early and ? Late disease
- Surgery with artificial joints

Nagaraja, Denton, and Khanna. Rheumatology (Oxford) 2014

RA-like disease—joint damage



Treatment with RA drugs

Subcutaneous calcinosis







Digital ulcers

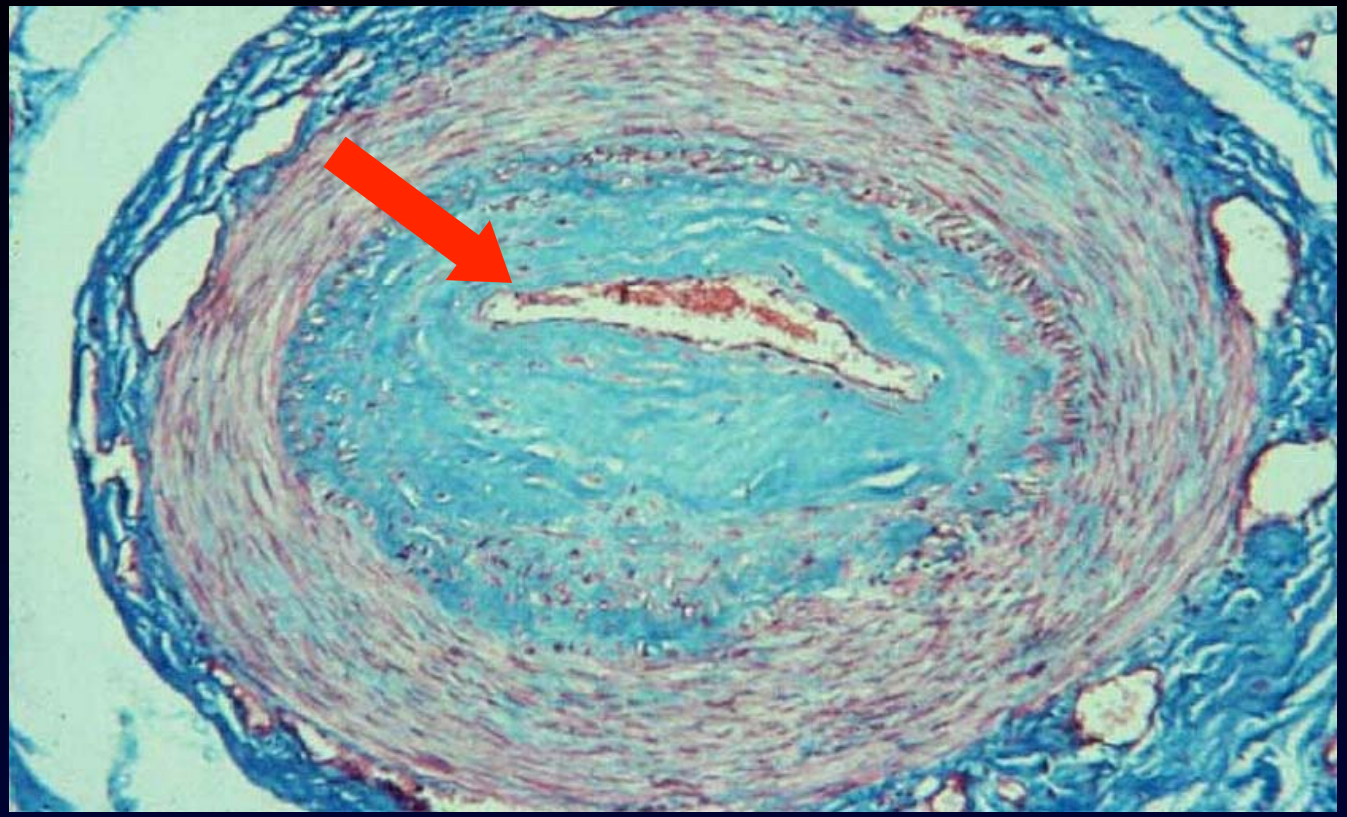








Digital vascular injury in SSc



•Masson-Trichrome stain of digital artery from patient with SSc. Striking fibrotic intimal hyperplasia and adventitial fibrosis. The arterial lumen is severely compromised.

Treatment

- Medications
  - Vasodilators such as calcium channel blockers, sildenafil, prostacyclin (medications used for PAH)
- Digital sympethectomy
- Amputation

Conclusion

- Hand dysfunction is almost universal in patients with SSc
- High morbidity
- No preventive management
- Treatment largely supportive and based on manifestation(s)
- Autologous stem/progenitor cells delivery can potentially fulfill this unmet need