

Scleroderma Soup



The tests you need and what they mean

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Types of Scleroderma

Localized (AKA Morphea)

Limited (AKA CREST)

Diffuse (AKA Progressive Systemic)



Localized lesions



The furrows of the mouth in systemic disease (usually limited)



Severely affected hands (usually diffuse)

Localized Disease

Usually starts with Raynaud

- Morphea
 - Single, few or many patches of thickened skin
 - Usually fades out after 3-5 years, but scarring or skin color change may persist
- Linear
 - More common in children
 - Bands or streaks of hardened skin on face or limbs

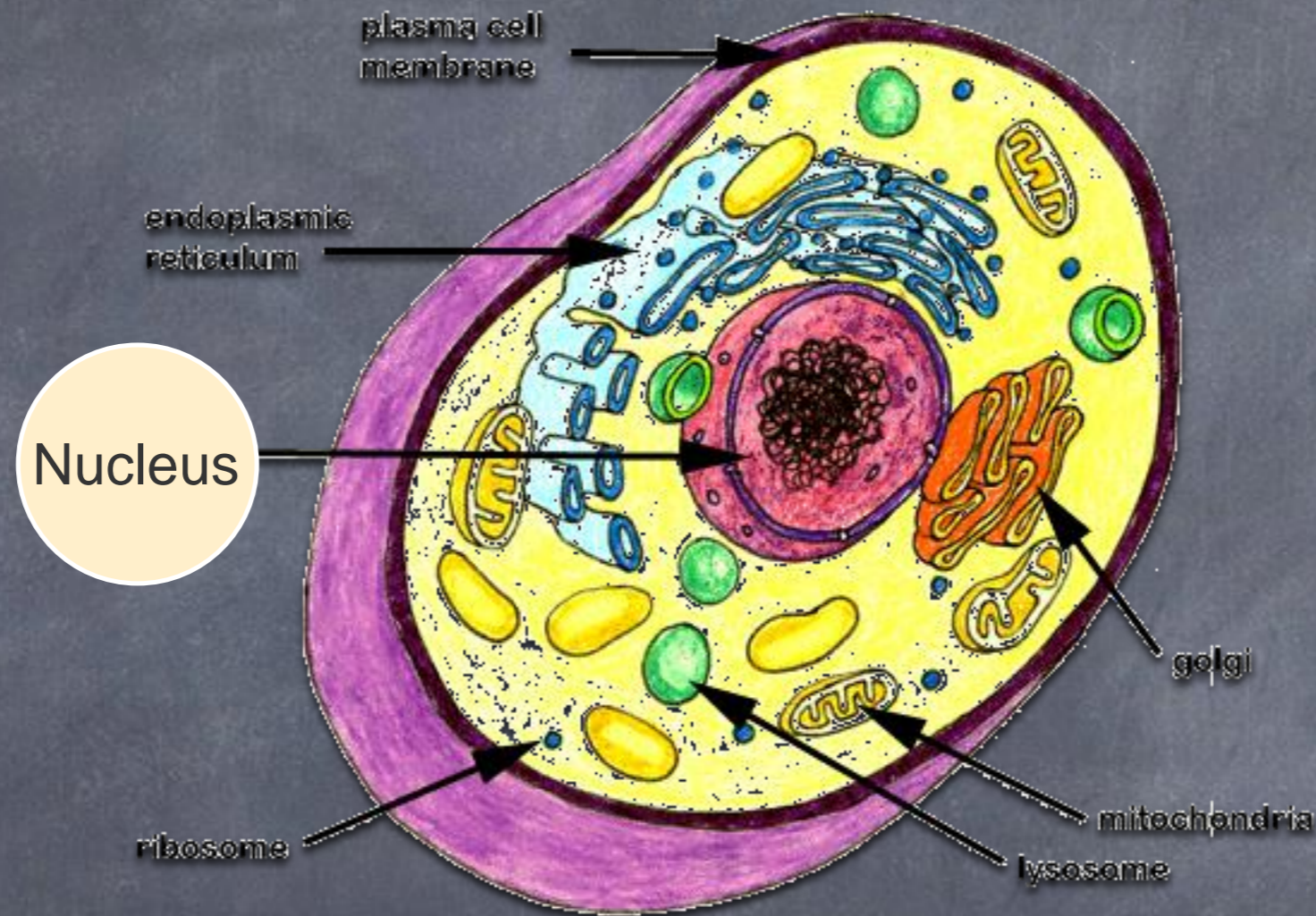
Localized Disease

- NOT Systemic Scleroderma
- At least annual dermatology examination
- Biopsy skin lesion, screening blood tests
- Evaluation of lesions for depth and stability or progression
- Increasingly aggressive treatments available if joint involvement or progression seen
- Physical therapy
- Do not have cosmetic procedures done until disease has stabilized

Limited and Diffuse

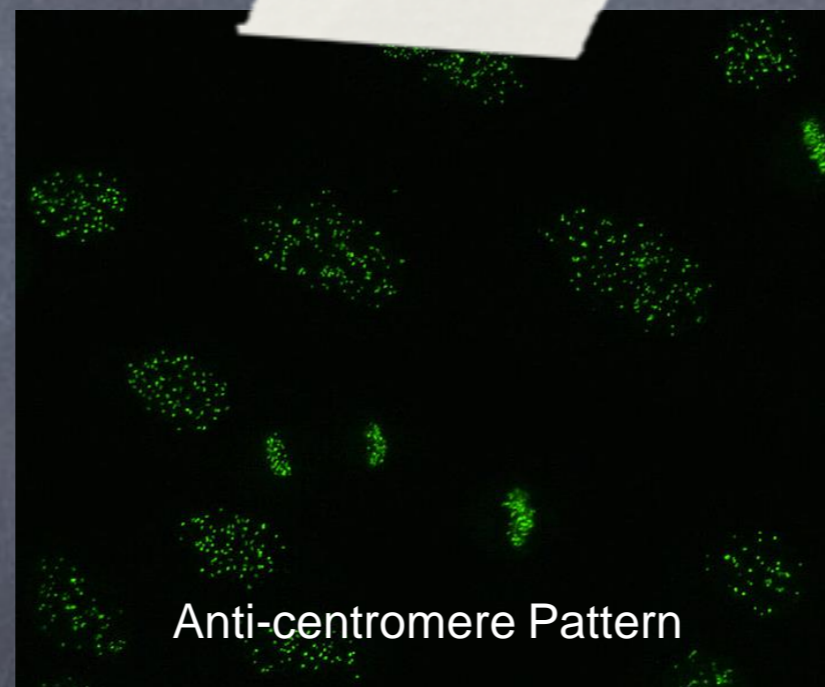
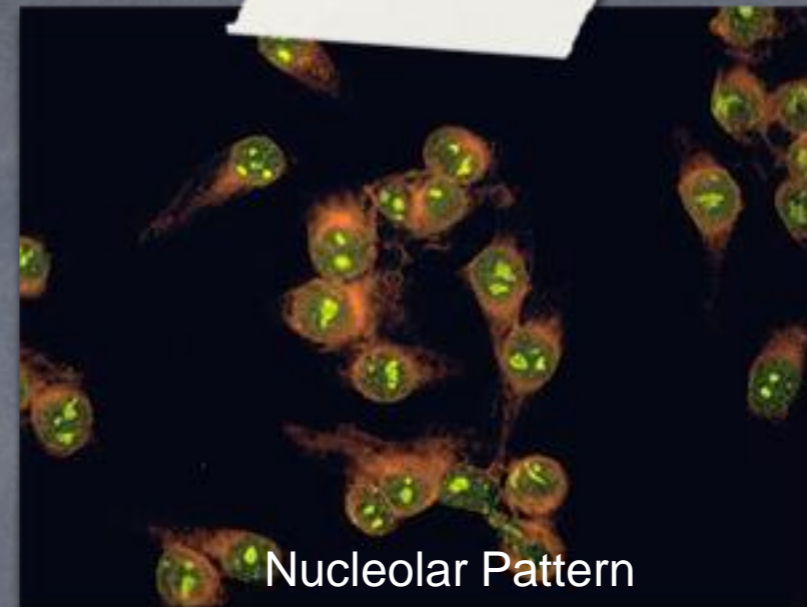
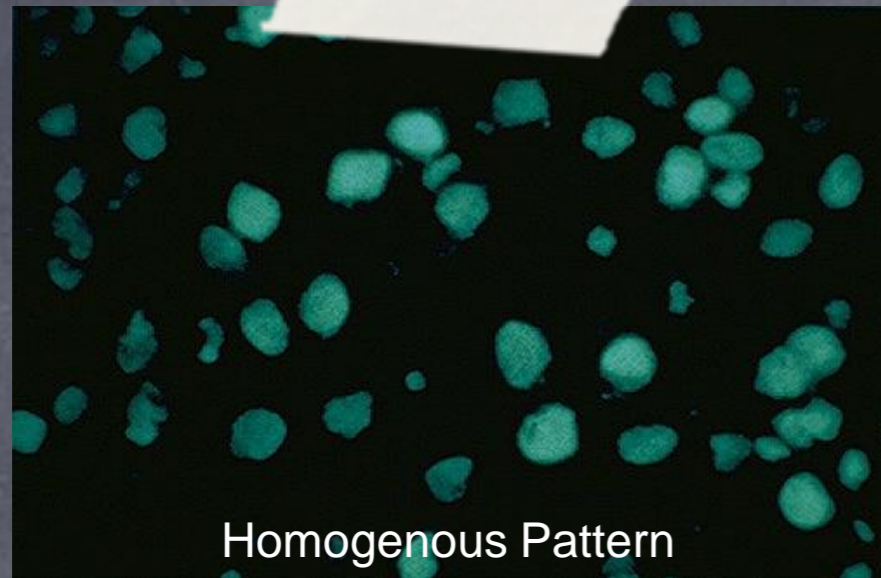
Systemic Disease

- Can be difficult to differentiate
- Current definition relates to degree of skin involvement, but this may not be related to prognosis in some cases
- Know your antibody type, as this may be more important than your degree of skin involvement
- Both cause systemic disease (affect the internal organs)
- Diffuse tends to be more aggressive, with early internal complications, while limited tends to be slowly progressive with late internal manifestations



Antibody Testing

Usually starts with looking at the Cell Nucleus
Antinuclear Antibody (ANA)



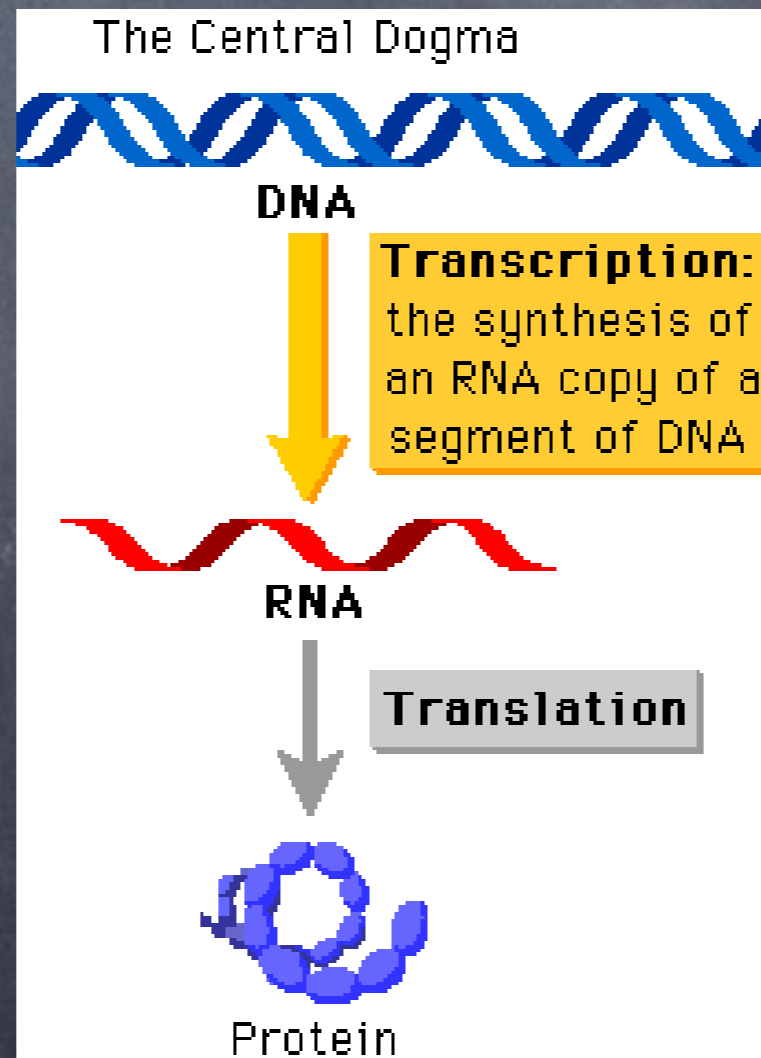
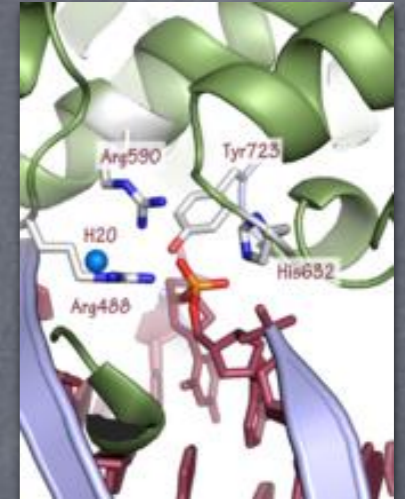
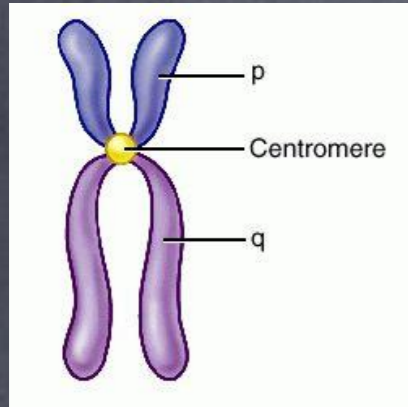
Positive ANAs come in patterns
Scleroderma Patients need to use this immunofluorescence method.
Newer, commercially available automated methods may miss up to 40% of scleroderma patients

What happens in the Cell Nucleus?

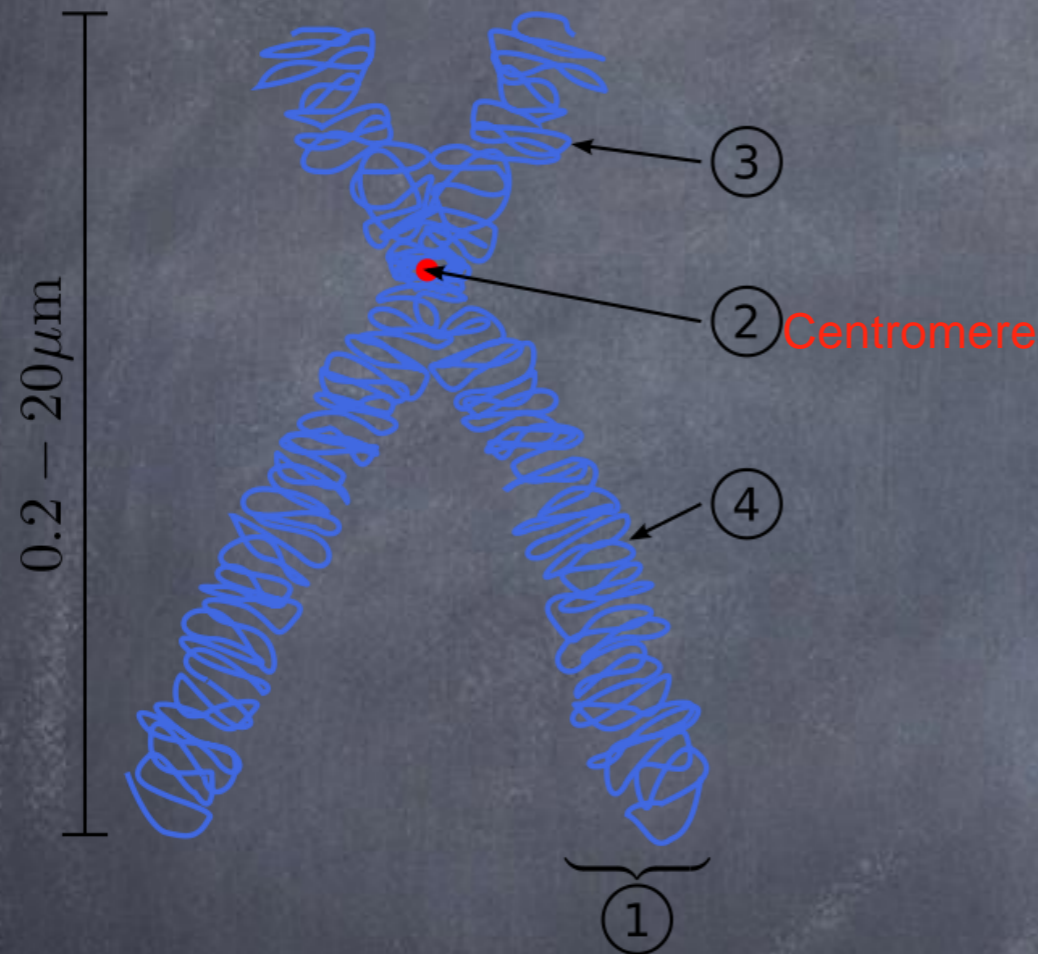
Genetics

Cell Division and Replication

Gene Expression



Scleroderma Antibodies: Anti-centromere Antibody (ACA)

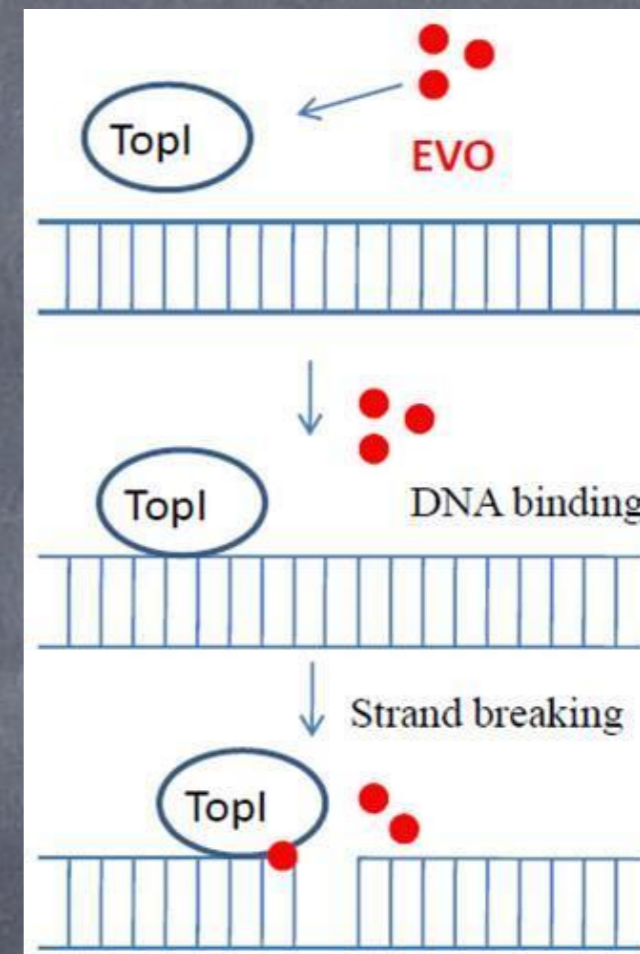


Centromere: attaches the DNA strands together

- Usually older, female patients
- Low percentage African American
- Long standing Raynaud, then puffy fingers
- GI symptoms, digital ulcers, calcinosis
- PAH in 20%, late onset possible
- Occasional cardiac involvement
- Severe interstitial fibrosis and renal crisis almost never occur

Scleroderma Antibodies: Anti-topoisomerase 1 (Scl-70 or ATA)

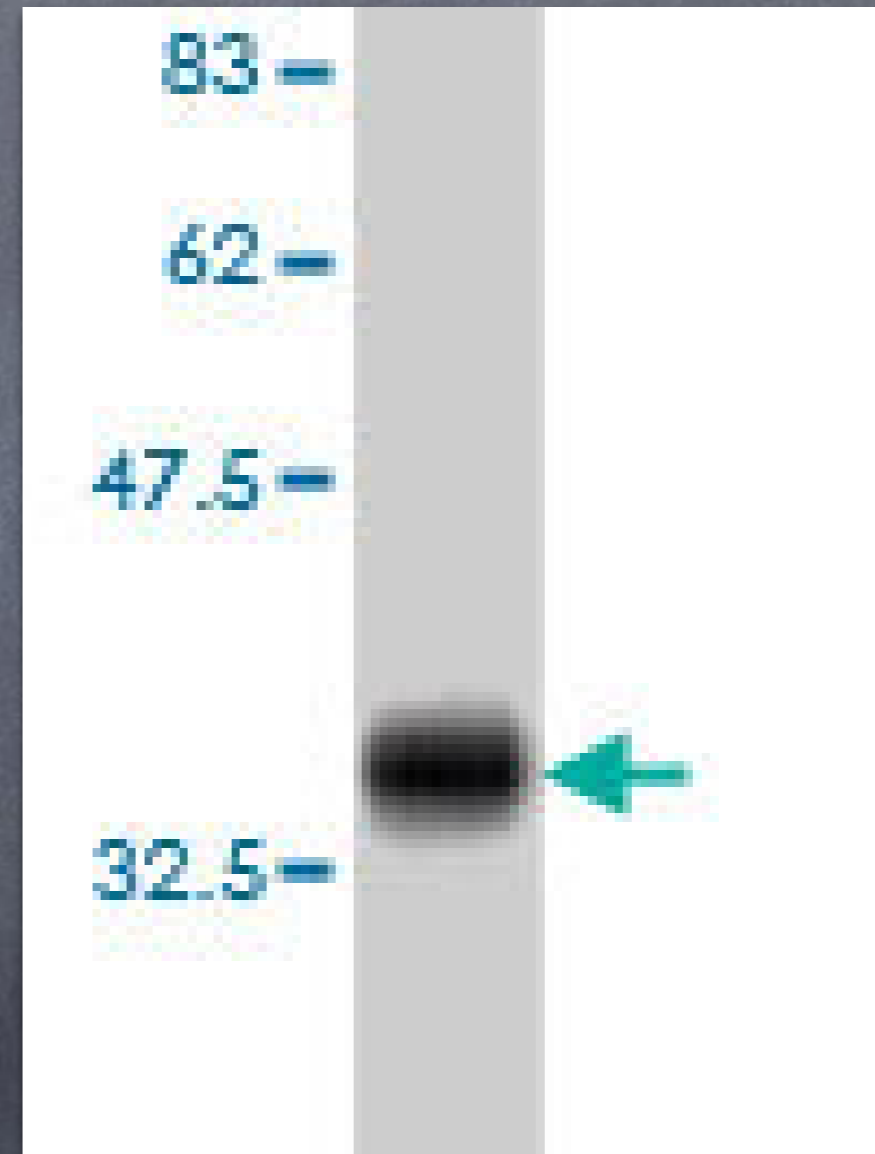
- Classic “diffuse” scleroderma (although not all will have diffuse skin changes)
- Common in African Americans
- Raynaud rapidly progresses to hand swelling
- Finger ulcers
- Joint and tendon involvement
- Cardiac and renal involvement
- Severe lung disease (more likely than other subtypes), early and aggressive
- Rare PAH



Topoisomerase I: involved in cutting and pasting DNA during cell division

Scleroderma Antibodies: anti-RNA polymerase III antibodies (ARA)

- RNA polymerase III is involved in gene transcription
- While ACA and ATA make up about half of the cases, ARA thought to be positive in 4-25% of the other cases
- Rapid onset of skin thickening after Raynaud
- Predominately diffuse cutaneous disease
- Strong association with hypertensive renal crisis



Western Blot Antibody Detection of ARA

ACA

PAH

ECHO/ right heart
cath

ATA

ILD

PFT/ CT

ARA

Hypertensive
Renal Crisis

BP

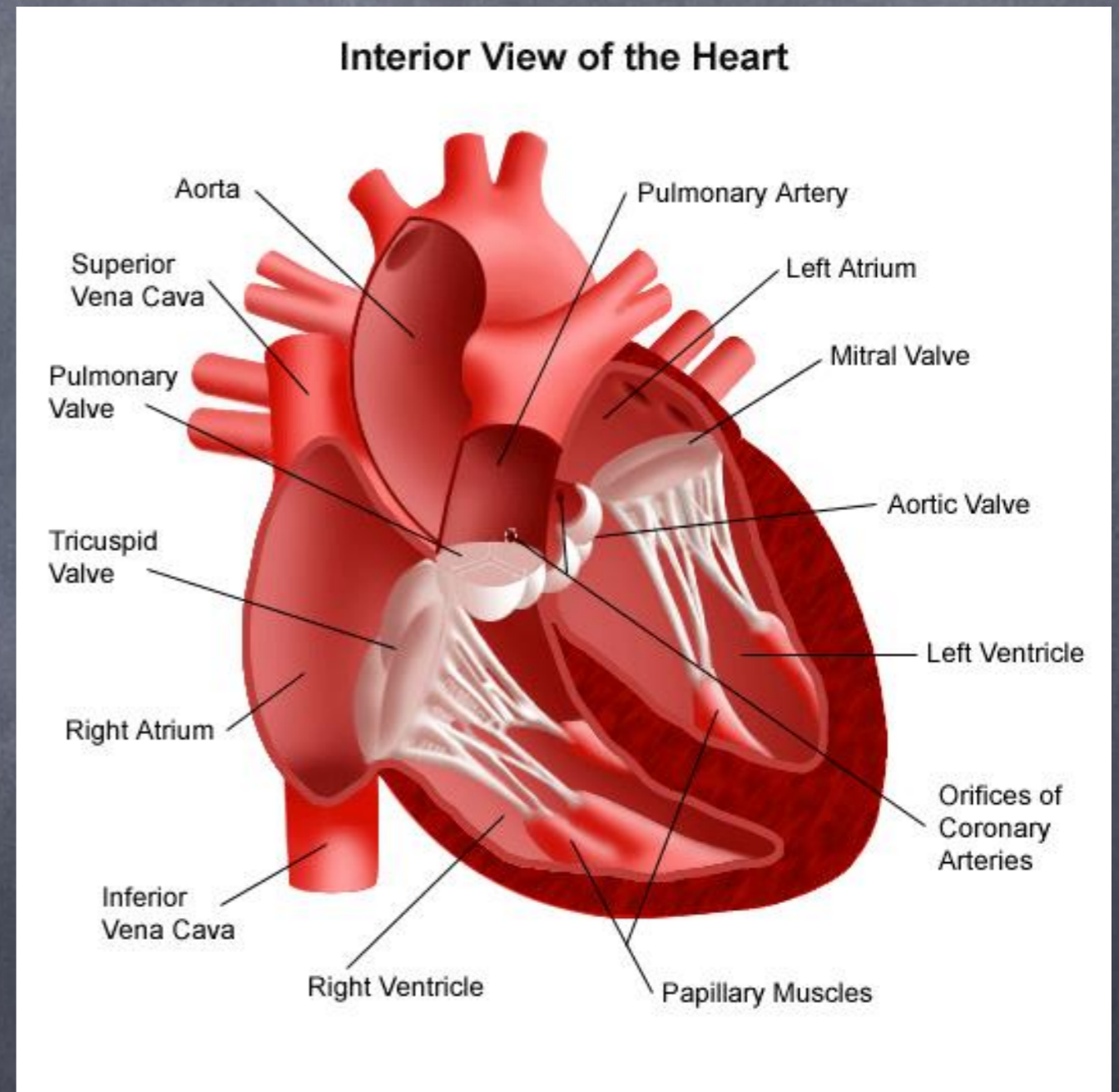
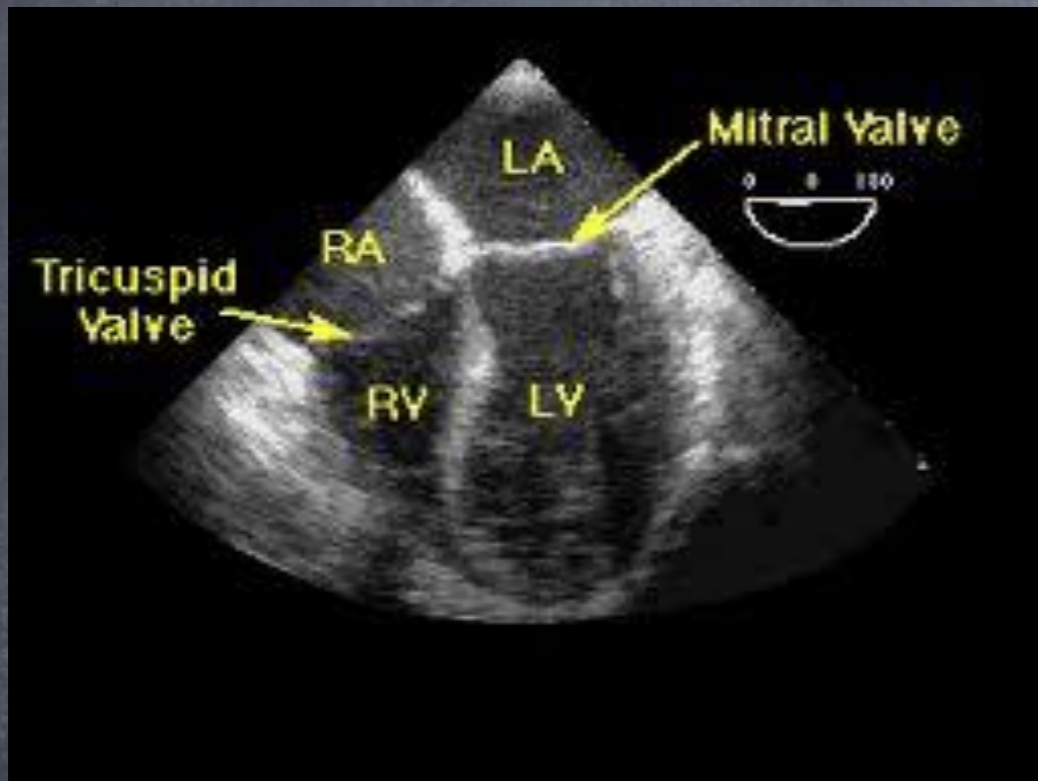
Quality Indicator set for Systemic Sclerosis

Table I.

Domain/Organ System	Tools/procedures
I Cardiopulmonary	<ul style="list-style-type: none"> - Echocardiography with Doppler - Six minute walk test - Right heart catheterisation - Laboratory markers (BNP, pro-BNP) - Measures of dyspnea - Electrocardiogram - Blood pressure - Treatment
II Pulmonary	<ul style="list-style-type: none"> - Spirometry and diffusing capacity - Chest radiograph - High-resolution computed tomography (HRCT) of lungs - Treatment
III Gastrointestinal	<ul style="list-style-type: none"> - Weight and Body mass index (BMI) - Laboratory markers (serum albumin, etc.) - Test for gastroparesis - Test for esophageal dysmotility - Test for malabsorption - Treatment
IV Renal	<ul style="list-style-type: none"> - Blood pressure - Laboratory markers (serum creatinine, creatinine clearance, urine protein, etc.) - Treatment
V Musculoskeletal	<ul style="list-style-type: none"> - Assessment of muscle weakness on physical exam - Measure of joint involvement (<i>e.g.</i> number of tender joints) - Laboratory markers (serum creatine phosphokinase) - Treatment
VI Cutaneous	<ul style="list-style-type: none"> - Physical exam to determine skin involvement - Treatment
VII Health-Related Quality of Life	<ul style="list-style-type: none"> - Measure of function
VIII Serologies	<ul style="list-style-type: none"> - Test for anti-topoisomerase I, anti centromere and anti-RNA polymerase III antibodies
IX Prevention and Drug Monitoring	

ACA	PAH	ECHO/ right heart cath
ATA	ILD	PFT/ CT
ARA	Hypertensive Renal Crisis	BP

Echocardiogram (ECHO)



Pulmonary Hypertension on ECHO

Can identify many cardiac problems,
but is used in scleroderma to assess
for **Pulmonary Hypertension**

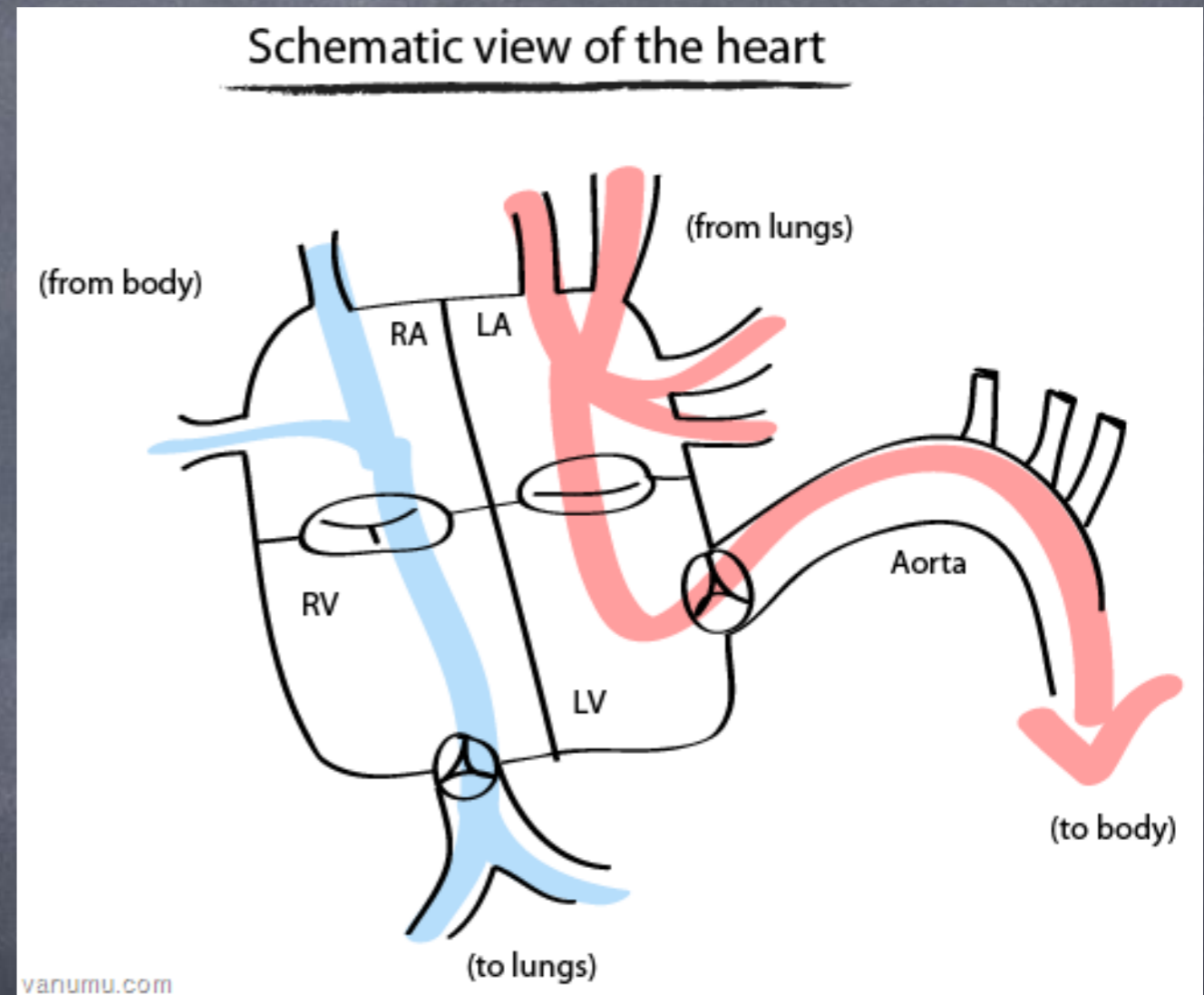
Screening Test!

PH = estimated pulmonary artery
systolic pressure above 30

Other PH findings:
RA and RV enlargement

Paradoxical movement of the
interventricular septum

Tricuspid regurgitation (velocity ≥ 3)



PAH

Pulmonary Arterial Hypertension



Normal Artery/ PH

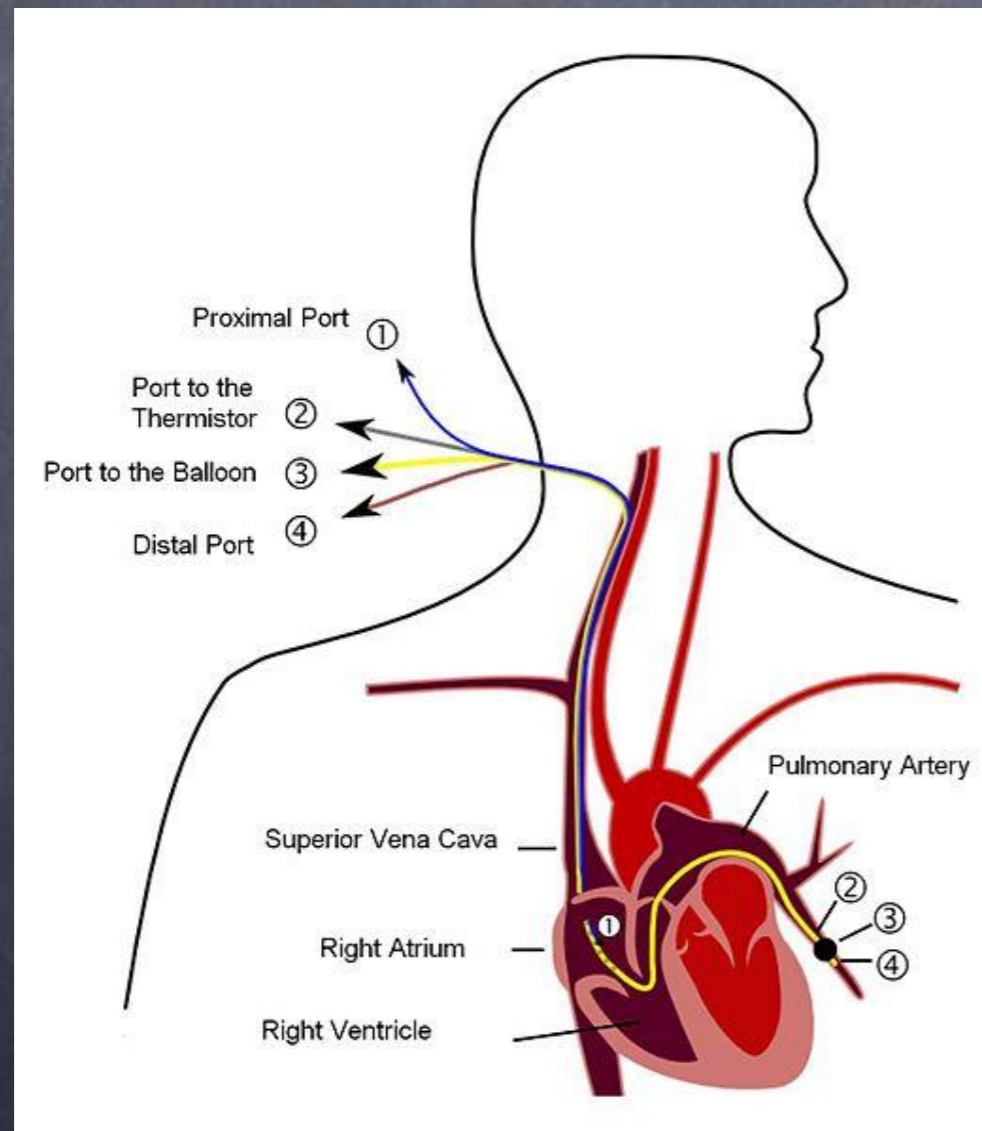


Affected Artery/ PAH

Symptoms: Range from nothing (early) to very short of breath (late)

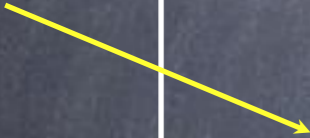
Right Heart Catheterization

- The best test to check for PAH



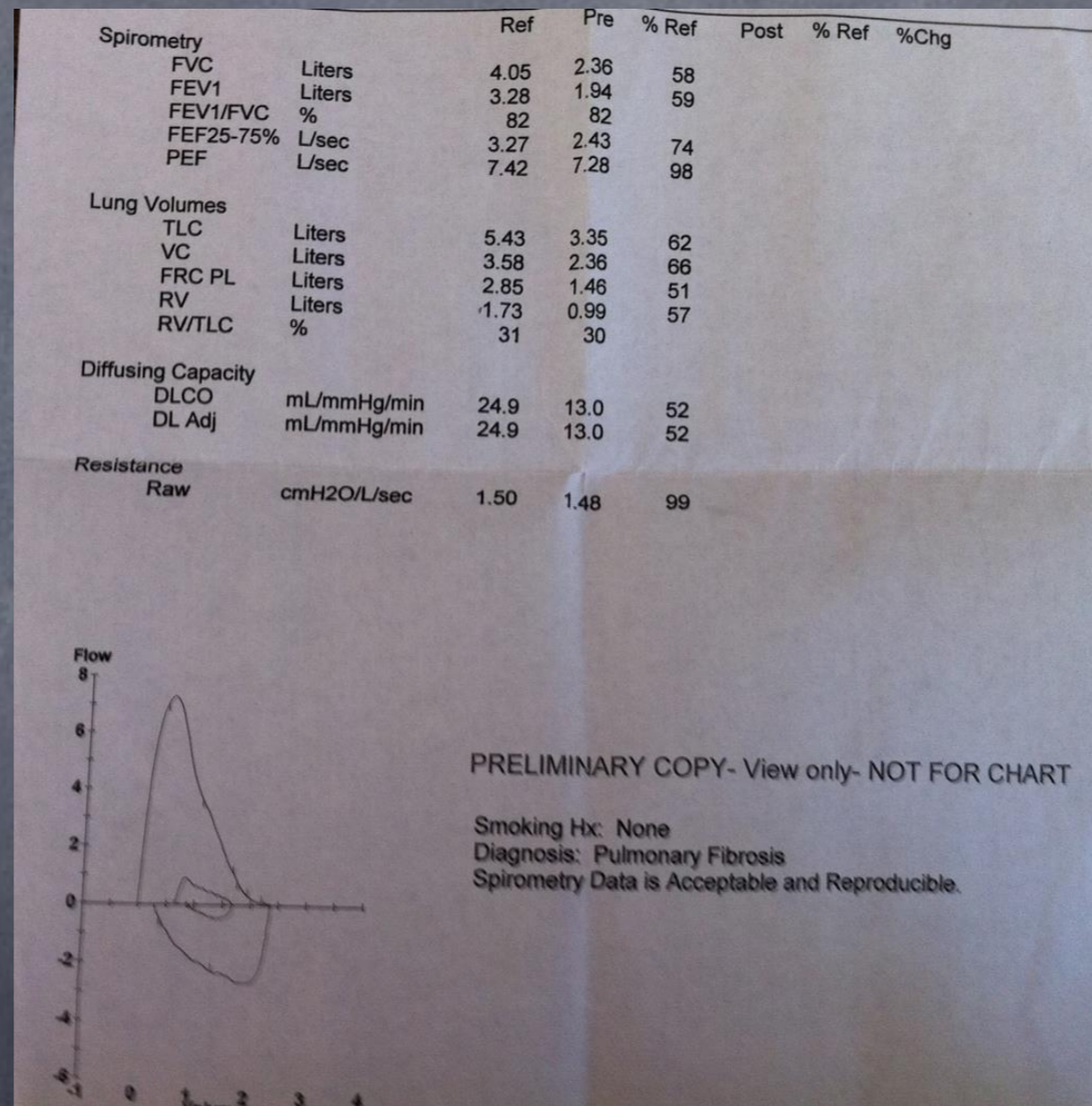
- **MEAN** pulmonary artery pressure ≥ 25 (normal is 8-20)

ACA	PAH	ECHO/ right heart cath
ATA	ILD	PFT/ CT
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PFTs

(Pulmonary Function Tests)



On the hunt for interstitial lung disease

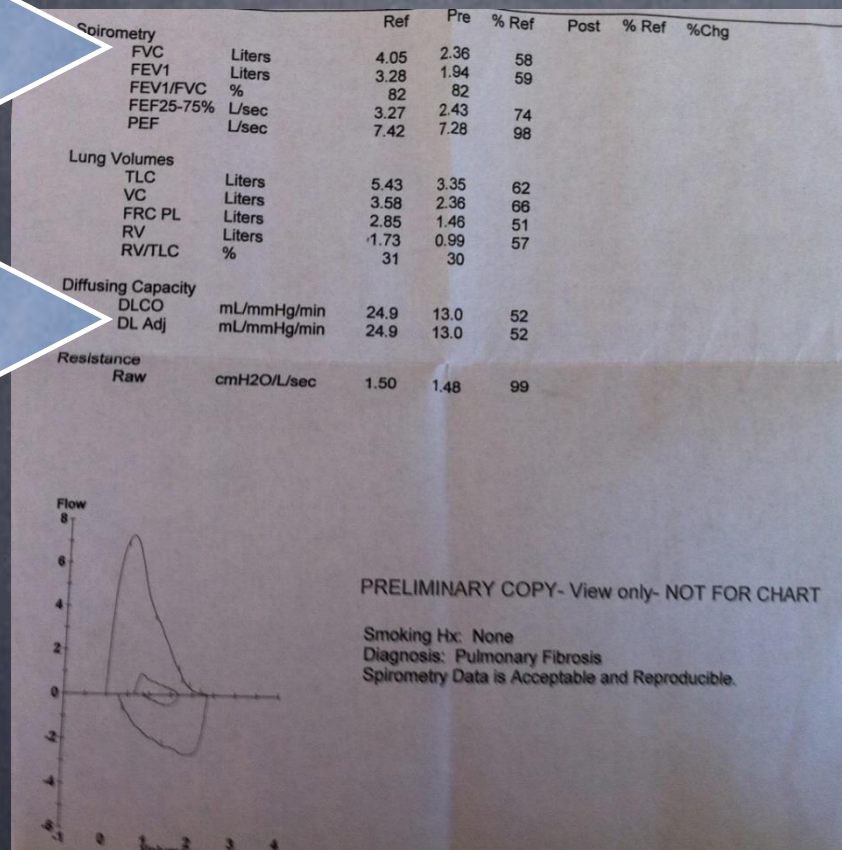
FVC and DLCO Adj

- FVC = Forced Vital Capacity

- big breath in, then forced breath out for at least 6 seconds
- measures the volume of air you blow out
- effort dependent

- DLCO = Diffusion Capacity

- breathe in CO mixture and hold for 10 seconds
- breathe out and measure how much CO was absorbed
- be sure to monitor the number that is adjusted for anemia and altitude



PFTs

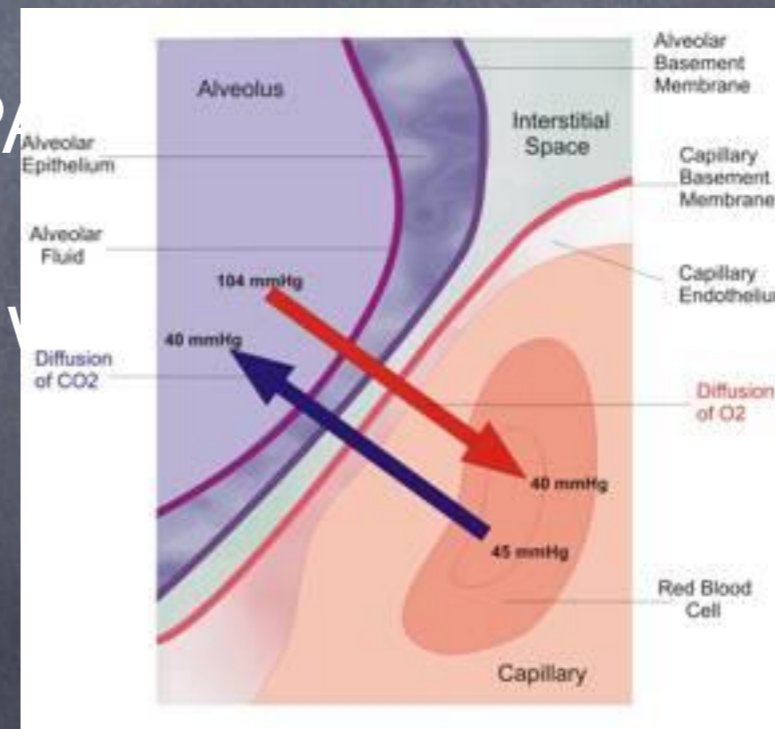
- FVC

- Drops with ILD
- Small drop may be seen w



- DLCO

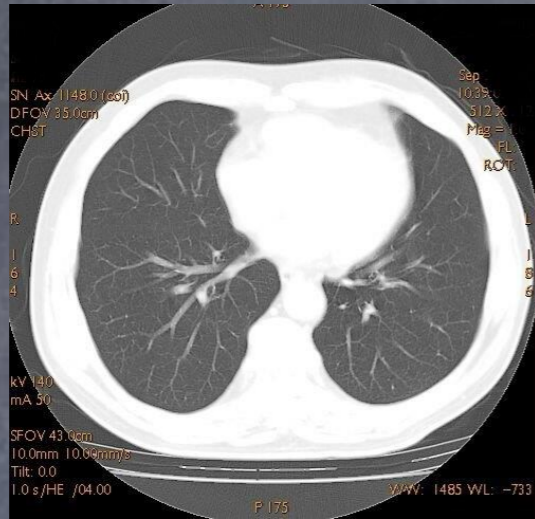
- Drops with both ILD and PA
- A greater RELATIVE drop v



Symptoms: Range from nothing (early) to very short of breath (late)

Chest CT Scan

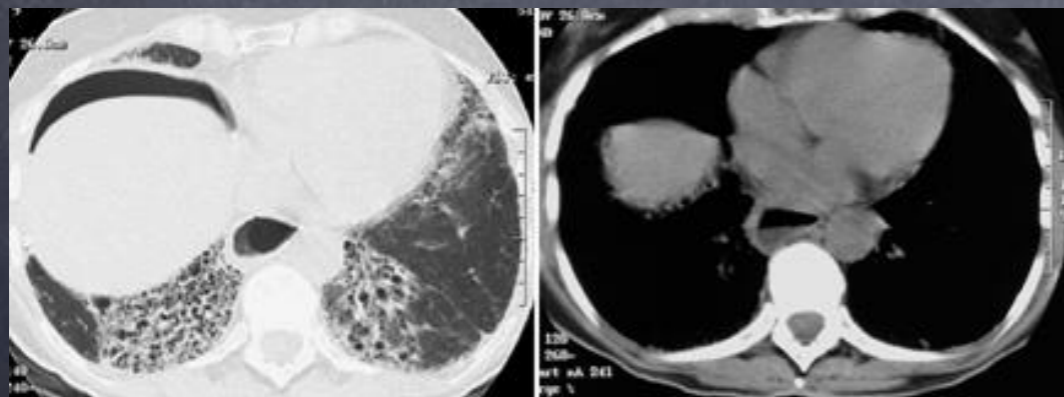
Scleroderma Findings



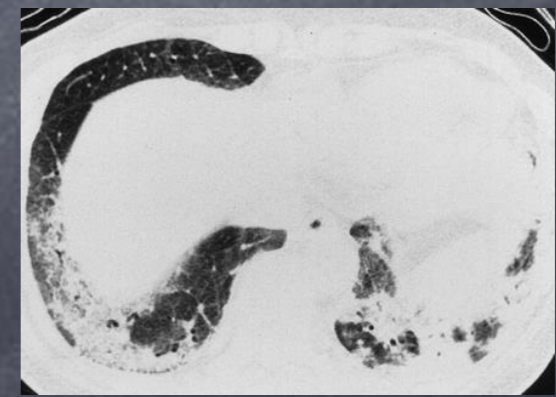
Normal Lung



Ground glass opacities



Honeycombing



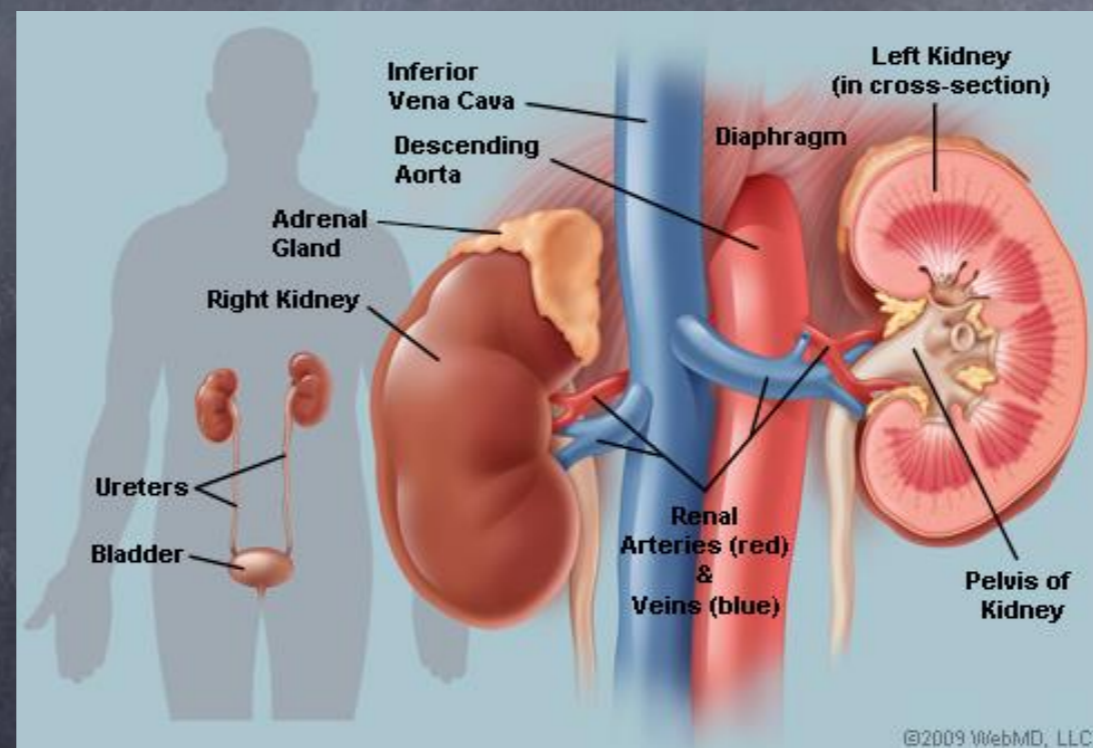
Nonspecific interstitial pneumonitis

ACA	PAH	ECHO/ right heart cath
ATA	ILD	PFT/ CT
ARA	Hypertensive Renal Crisis	BP



Renal Monitoring

- Blood pressure checks monthly for those with diffuse disease, which can increase to home checks several times a week if needed
- Laboratory blood and urine testing of kidney function



Renal Crisis: Scleroderma Renal Arterial Involvement



Normal Artery



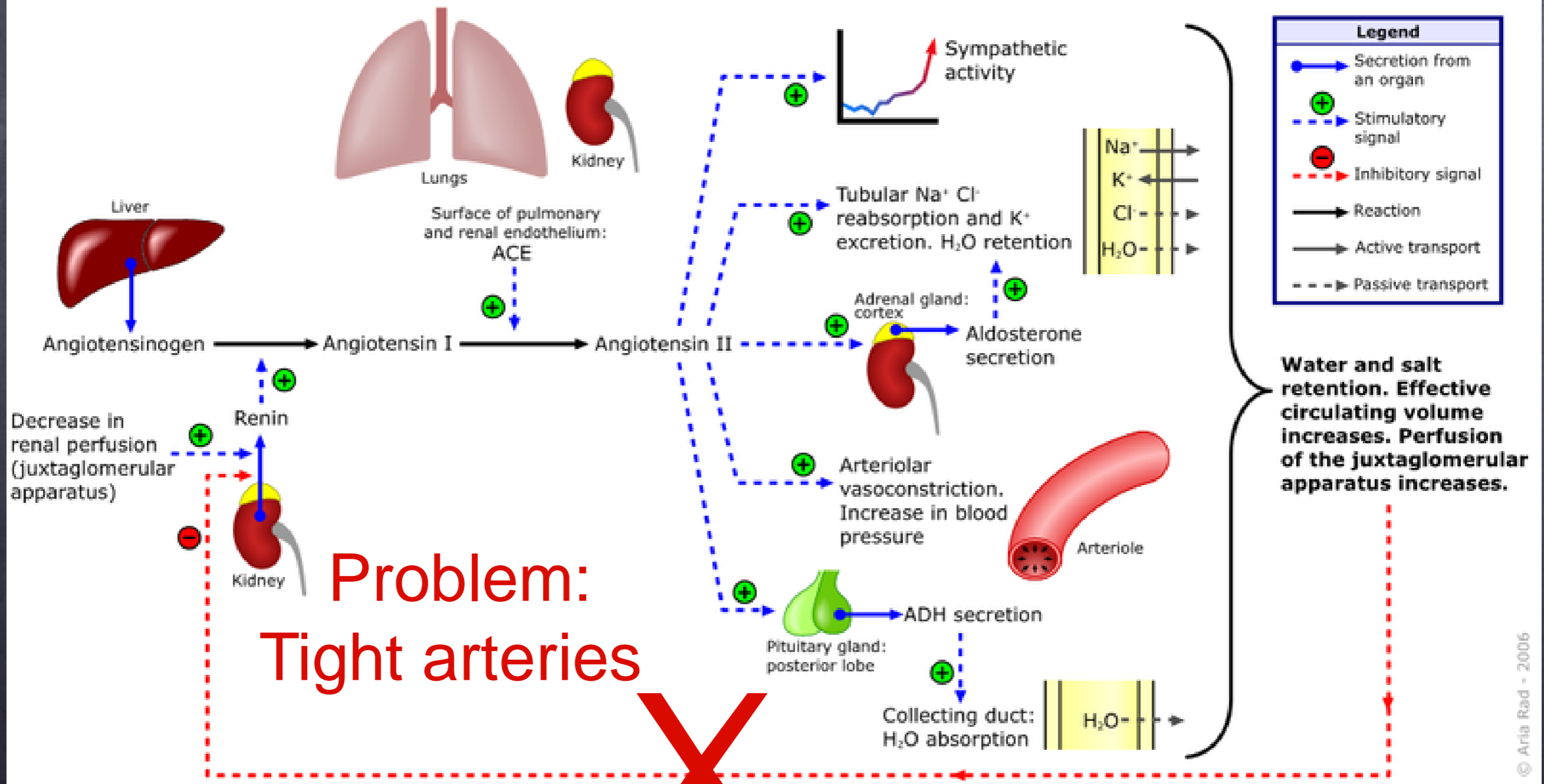
Affected Artery

Symptoms: Often, no early symptoms. Swelling, headache, heart failure are late symptoms.

Why will Blood Pressure Rise with Kidney Involvement?

it's complicated!

Renin-angiotensin-aldosterone system



Blood Pressure



- Normal: Systolic lower than 120, Diastolic lower than 80
- Prehypertension: Systolic 120-139, Diastolic 80-90
- Hypertension: Systolic above 140, Diastolic above 90

*Check your own blood pressure routinely at home or at your local pharmacy

What have we learned?

Localized
Disease

ATA

?

25-46%

ACA

ARA

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Quality Indicators

Do not indicate quality care

Provide clear and measurable way to
assess doctors who are not within
standards of care

Define the minimum standard

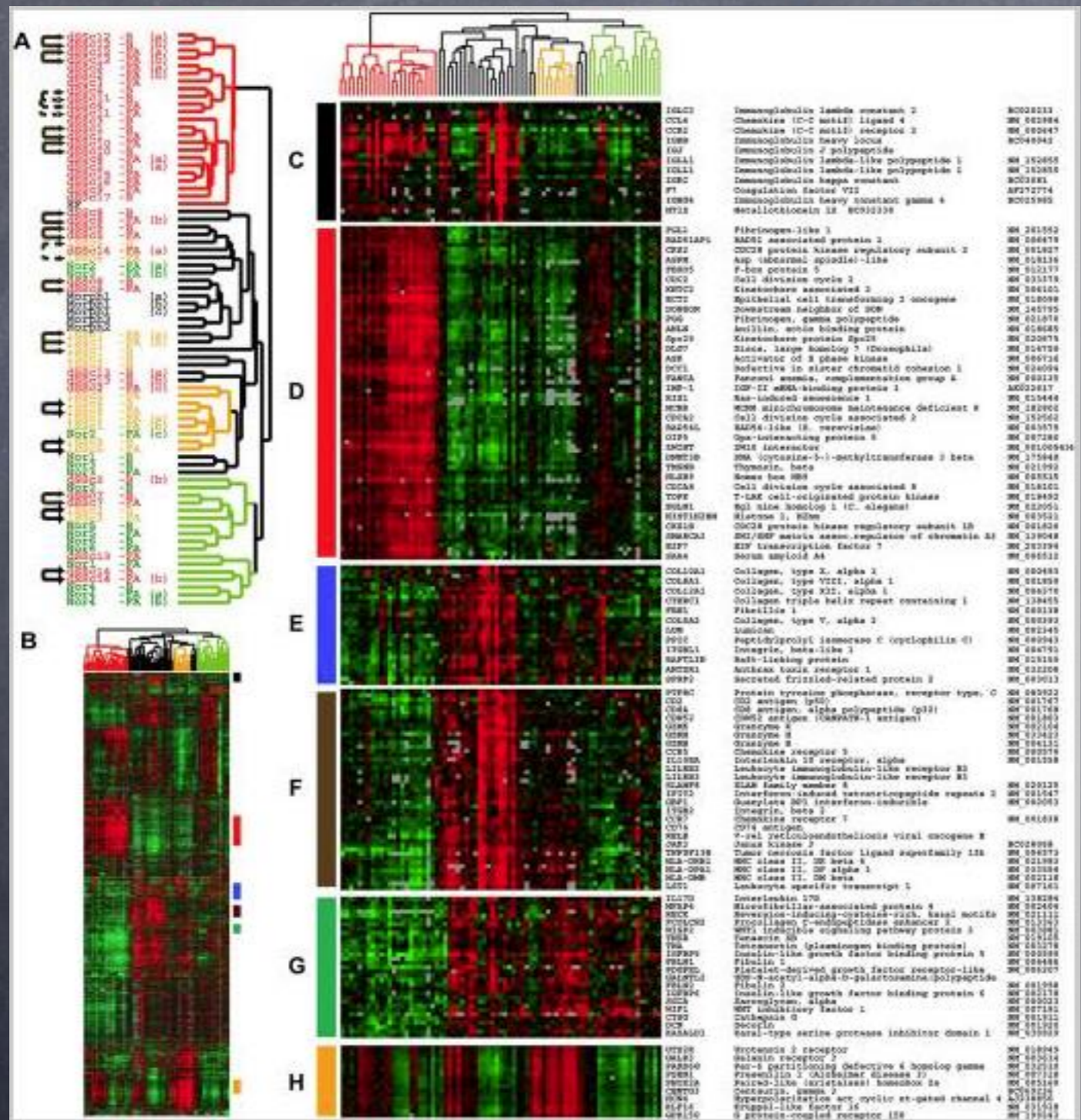
What's next in our understanding of the various types of scleroderma?

Genetic studies may redefine the subtypes of scleroderma

Molecular subsets in the gene expression signatures of scleroderma skin.

Milano A, Pendergrass SA, Sargent JL, George LK, McCalmont TH, Connolly MK, Whitfield ML.

Published 2008, PLoS ONE



Red - diffuse
 Black - morphea (+ 1 EF)
 Orange - limited
 Green - normal

See a Scleroderma Specialist

- Caring for Scleroderma is COMPLICATED
- You often need treatment BEFORE you get symptoms for the most serious complications
- Get the right tests, and someone who understands what the results mean
- Stay up-to-date as advances come along, and as recommendations change
- Be in the right place when a new treatment is available

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And suddenly there it was, the perfect opening for Tommy's novel, lying at the bottom of his bowl of Alphabet Soup.