Scleroderma Soup

The tests you need and what they mean

Holly Hauser, M.D.
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

The Central Dogma

DNA

Transcription: the synthesis of an RNA copy of a segment of DNA

RNA

Translation

Protein
Scleroderma Antibodies:
Anti-centromere Antibody (ACA)

- 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

Centromere: attaches the DNA strands together
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
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## Table I.

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|                     | - Right heart catheterisation  
|                     | - Laboratory markers (BNP, pro-BNP)  
|                     | - Measures of dyspnea  
|                     | - Electrocardiogram  
|                     | - Blood pressure  
|                     | - Treatment  
| II Pulmonary        | - Spirometry and diffusing capacity  
|                     | - Chest radiograph  
|                     | - High-resolution computed tomography (HRCT) of lungs  
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| III Gastrointestinal | - Weight and Body mass index (BMI)  
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|                     | - Test for esophageal dysmotility  
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| IV Renal            | - Blood pressure  
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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 $\geq 25$ (normal is 8-20)
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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 with PAH

- **DLCO**
  - Drops with both ILD and PAH
  - A greater RELATIVE drop with PAH

**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
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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

Symptoms: Often, no early symptoms. Swelling, headache, heart failure are late symptoms.
Why will Blood Pressure Rise with Kidney Involvement?

it’s complicated!

Problem: Tight arteries
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?

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