



School of Continuous  
Professional Development

31<sup>ST</sup> ANNUAL

# INTERNAL MEDICINE BOARD REVIEW

Date here (if needed)





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# RAYNAUD'S, SCLERODERMA, INFLAMMATORY MYOPATHIES, AND SJÖGREN'S SYNDROME

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# DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Nothing to disclose

# REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Yes – calcium channel blockers and sildenafil

*All relevant financial relationships have been mitigated.*

# LEARNING OBJECTIVES

At the end of this presentation, learners will be able to:

- Diagnose and manage secondary Raynaud's Phenomenon
- Understand the clinical presentation and initial evaluation of rheumatologic diseases including:
  - Scleroderma (localized, limited, and diffuse)
  - Sjogren's Syndrome
  - Inflammatory Myopathies
  - Mixed Connective Tissue Disease

# CASE #1

Ms. Jones is a 19 year-old woman who presents with a 3-month history of persistent bluish-purple discoloration of her fingers on both hands. The discoloration is constant but does worsen with cold exposure. Warming the hands does not improve symptoms. She denies numbness, tingling or pain.

PMH: None

FH: Primary Raynaud's phenomenon in a sister

SH: +Tobacco use

ROS: Hyperhidrosis of the palms, otherwise, negative

Meds: None

Vitals: BP 102/70, HR 86, RR 14, BMI 15kg/m<sup>2</sup>

Exam: Bluish-purple discoloration of 2<sup>nd</sup>-5<sup>th</sup> digits. No digital ulcers or pitting. Brachial & radial pulses 2+ bilaterally. Allen's test was normal. Nailfold capillary exam shows mildly enlarged, but not dilated, capillary loops. Which of the following is the mostly likely diagnosis?

1. Acrocyanosis
2. Raynaud's Phenomenon
3. Chilblain's lupus (Pernio)
4. Achenbach syndrome
5. Buerger Disease

# CASE #1 ANSWER

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1. **Acrocyanosis**
2. Raynaud's Phenomenon
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4. Achenbach syndrome
5. Buerger Disease

# CASE #1 EXPLANATION

Reference: Kurklinsky AK, Vascular Medicine, 2011

1. **Acrocyanosis:**
  - **Characterized by non-reversible cyanosis of the digits.**
  - **Patients may experience worsening with the cold, but there is a lack of resolution with rewarming.**
  - **Hyperhidrosis of the affected regions is often seen.**
  - **Non-specific nailfold capillary changes can be observed.**
  - **Seen in approximately 40% of patients with Anorexia Nervosa and is associated with abnormal thermoregulation (patient had a BMI of 15kg/m<sup>2</sup>).**
2. **Raynaud's Phenomenon:**
  - Characterized by cyanosis or pallor that is provoked with the cold, and reverses with rewarming and often associated with hyperemia upon rewarming. Non-reversibility suggests an alternative diagnosis.
  - Family history of primary Raynaud's phenomenon may raise suspicion, as it is common for other family members to have Raynaud's symptoms, but this was a distractor in this question.
3. **Chilblain's lupus (Pernio):**
  - Characterized by papules, plaques, and or nodular lesions which may be painful.
  - Acrocyanosis may co-exist with pernio lesions, but patient lacked cutaneous lesions.
4. **Achenbach syndrome:**
  - Characterized by painful, ecchymosis-like discoloration on the volar aspect of the finger usually sparing the distal segment. The presence of cyanosis of the entire fingers bilaterally is not consistent.
  - Spontaneous, and usually resolves in a few days, though cases lasting a few months are reported.
5. **Buerger Disease**
  - Classically presents with ischemic pain and nodules/digital ulcers in males < age 45 years old who smoke. She denies pain and has no lesions.

# Diagnosis and Management of Raynaud's Phenomenon



# RAYNAUD'S PHENOMENON

- Characterized by bi- or tri-phasic color changes in the distal extremities
  - Cyanosis, pallor, erythema
  - Nose, earlobes, tongue, and areolae may also be involved
- Provoked by exposure to the cold and reverses with rewarming
  - May also be provoked by stress
- May be primary (idiopathic) or secondary (many causes)



# RAYNAUD'S PHENOMENON

## DISTINGUISHING PRIMARY VS. SECONDARY

Characteristic	Primary (idiopathic)	Secondary to Autoimmune Disease
Age of Onset	Late teens to early 20s	> 40 years old red flag
Family Members with RP	Yes	Less common
Ischemic complications	None	Can be associated with digital ulcers, pitting, gangrene, digital loss
Nailfold Capillaries	Normal	Normal or Abnormal*
Autoimmune serologies	Absent	Often present

\*Higher sensitivity for systemic sclerosis than other autoimmune conditions<sup>1</sup>

# RAYNAUD'S PHENOMENON ASSOCIATED WITH SYSTEMIC AUTOIMMUNE DISEASES

- Frequency of Raynaud's Phenomenon
  - Scleroderma: >95%<sup>1</sup>
  - Systemic Lupus: 30%<sup>2</sup>
  - Sjogren's Syndrome: 11-33%<sup>3</sup>
  - Inflammatory myopathies: 10-40%<sup>4</sup>

1. Walker UA, et al., Ann Rheum Dis., 2007

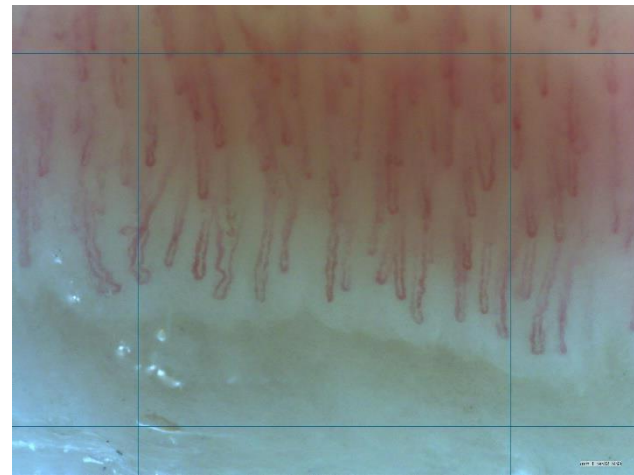
2. Barbacki A, et al., J Clin Rheumatol., 2022

3. Lin, W et al., Clinical Rheumatol., 2021

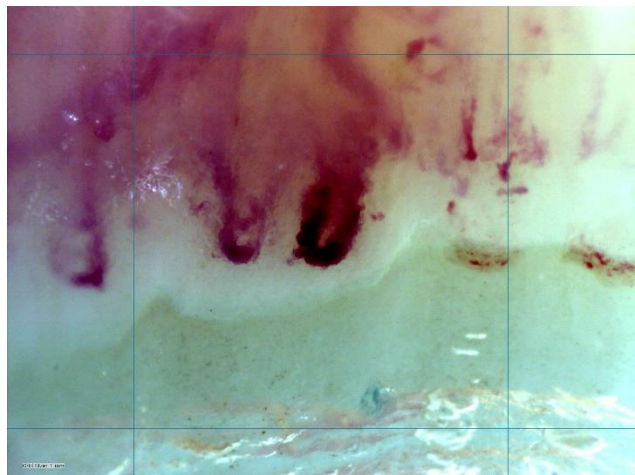
4. Pauling & Christopher-Stine, Rheumatology, 2021

# NAILFOLD CAPILLAROSCOPY

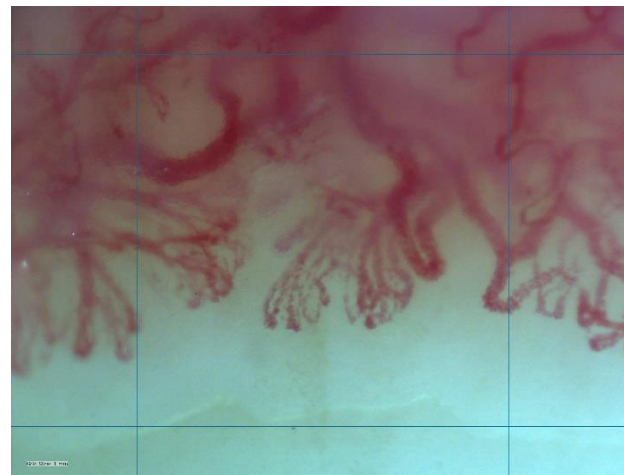
- Abnormal nailfold capillaries can be seen in systemic sclerosis, undifferentiated connective tissue disease, inflammatory myopathies, Sjogren's syndrome, systemic lupus erythematosus
- Bedside Exam:
  - Ophthalmoscope at 40 diopters with a drop of oil
  - Clip on microscope to phone
  - Dermatoscope at bedside
- Detailed Assessment:
  - Video Nailfold Capillaroscopy



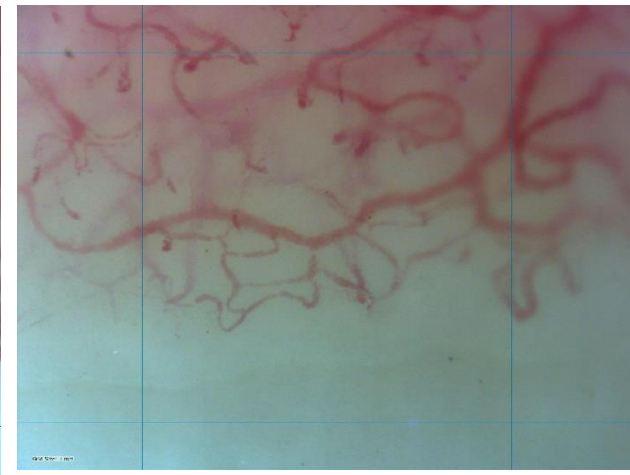
Normal



Dilated Capillary



Branched/Bushy Capillaries



Loss of capillary architecture

# SECONDARY RAYNAUD'S PHENOMENON OR MIMICS

Category	Underlying Etiology
Occupational	Hand-arm vibration syndrome (vibration white finger)
Environmental	Frostbite
Drugs	Chemotherapeutic agents (bleomycin, cisplatin), cyclosporine, sympathomimetics (e.g. amphetamines), beta-blockers interferons, cocaine, polyvinyl chloride
Vaso-occlusive	Cryoglobulinemia, cryofibrinogenemia, cold agglutinin disease, paraneoplastic (paraneoplastic acral vascular syndrome), paraproteinemia, post-embolic/thrombotic
Endocrine	Hypothyroidism
Large vessel	Thoracic outlet syndrome (neurogenic), crutch pressure (compressive)
Miscellaneous	POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal plasma cell disorder, Skin changes)
Associations/Mimics	complex regional pain syndrome (mimic), carpal tunnel or other neuropathies (cold sensitivity/mimic), nicotine (cold sensitivity/vasoconstriction)



# RAYNAUD'S MANAGEMENT

1. Maintain warm core body temperature and peripheral extremities
2. Discontinue smoking and vasoconstricting medications if possible
3. If conservative measures ineffective and symptoms are severe:
  - Calcium Channel Blockers
  - Sildenafil 20mg three times a day
  - IV Epoprostenol for critical digital ischemia
  - Bosentan for recurrent digital ulcer prevention (in scleroderma)
  - +/- Arterial Flow Pumps (digital occlusive disease in scleroderma with digital ulcers)

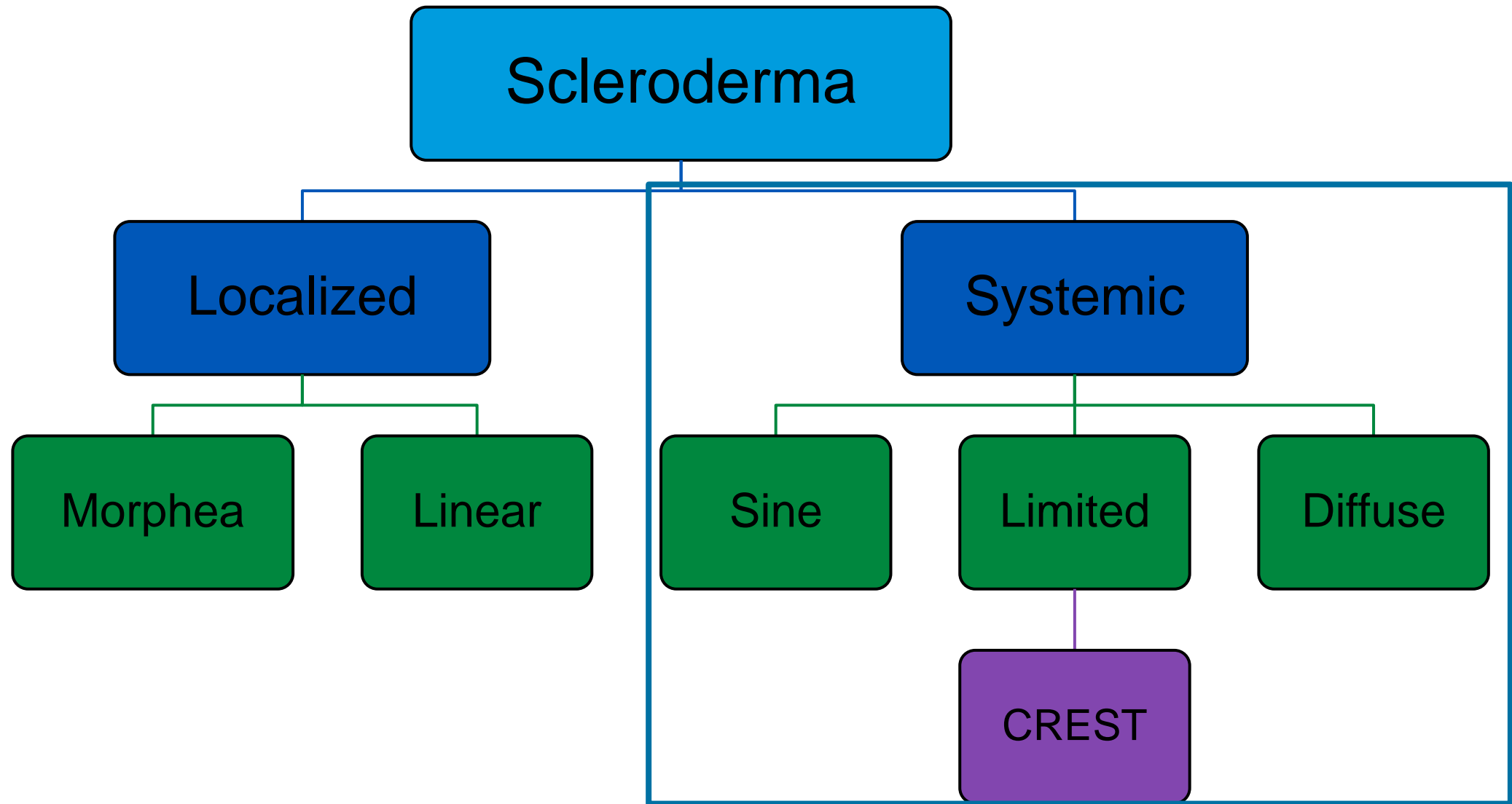
# Scleroderma and related conditions

Scleroderma (systemic sclerosis): sine, limited and diffuse

Scleroderma: localized (morphea)

Eosinophilic Fasciitis

Scleromyxedema



# SCLERODERMA A.K.A SYSTEMIC SCLEROSIS

- Multisystem disease manifested by fibrosis, vasculopathy, autoimmunity
- Epidemiology:
  - Prevalence: 305 per 1 million<sup>1</sup>
  - Age/Demographics: 30s to 50s, female predominance
- Subsets (sine, limited, diffuse) based on degree of skin involvement
  - Distal to elbows = limited
  - Proximal to elbows ± trunk = diffuse
  - No skin involvement = sine
- All subsets at risk for internal organ involvement
  - Autoantibodies can help with risk prediction

# ACR 2013/EULAR CLASSIFICATION CRITERIA FOR SYSTEMIC SCLEROSIS

Item	Sub-item(s)	Weight/Score
Skin thickening of the fingers of both hands extending proximal to the MCPs		9
Skin thickening of fingers ( <i>count only higher score</i> )	Puffy digits	2
	Sclerodactyly	4
Fingertip lesions ( <i>count only higher score</i> )	Digital ulcers	2
	Fingertip pitting scars	3
Telangiectasias		2
Abnormal Nailfold Capillaries		2
Pulmonary Arterial Hypertension and/or Interstitial Lung Disease ( <i>maximum score 2</i> )	Pulmonary Arterial Hypertension	2
	Interstitial Lung Disease	2
Raynaud's Phenomenon		3
SSc Antibody	Anti-centromere	3
	Anti-topoisomerase (Scl70)	
	Anti-RNA Polymerase III	

A patient with a score  $\geq 9$  is classified as definite scleroderma with 91% sensitivity and 92% specificity



# SCLERODERMA SPECIFIC AND ASSOCIATED AUTOANTIBODIES

Autoantibody	Diffuse vs. Limited	Disease Associations
Centromere	Limited	Associated with PAH, subset of patients with CREST (calcinosis, Raynaud's, esophageal dysmotility, sclerodactyly, telangiectasias)
Anti-Scl70	Limited or diffuse	Associated with progressive ILD
RNA Polymerase III	Diffuse	Associated with rapidly progressing skin thickening, renal crisis and malignancy
PM-Scl	Limited or diffuse	Overlap disorder associated with ILD and myositis

Antibodies are usually mutually exclusive

# SCLERODERMA CUTANEOUS FEATURES



## Telangiectasias

- Matted
- Face, tongue, lips, hands



## Sclerotic Skin

- Shiny, taut skin
- Loss of “wrinkles/creases”
- Contractures

## Acro-osteolysis

- Resorption digital tufts
- Nails growth curves over distal finger



## Calcinosis

- Commonly found over areas of trauma such as extensor surfaces or tips of fingers

# SCLERODERMA – INTERSTITIAL LUNG DISEASE (ILD)

- 45-85% of patients with SSc will have evidence of ILD on high resolution CT.<sup>1</sup>
  - 25-40% will have progressive ILD<sup>2</sup>
- Risk factors for progressive ILD include:
  - Diffuse cutaneous disease
  - Anti-Scl70/Topoisomerase I positivity
  - African American Race
- Treatments
  - Mycophenolate mofetil or cyclophosphamide (equivalent efficacy)
  - Nintedanib (FDA approved for scleroderma-ILD)
  - Tocilizumab (FDA approved for scleroderma-ILD)



1. Schurawitzki, H. et al., Radiology, 1990  
2. McNearney, TA, et al., Arthritis Rheum, 2007

3. Tashkin, DP, et al., Lancet Respir Med., 2016

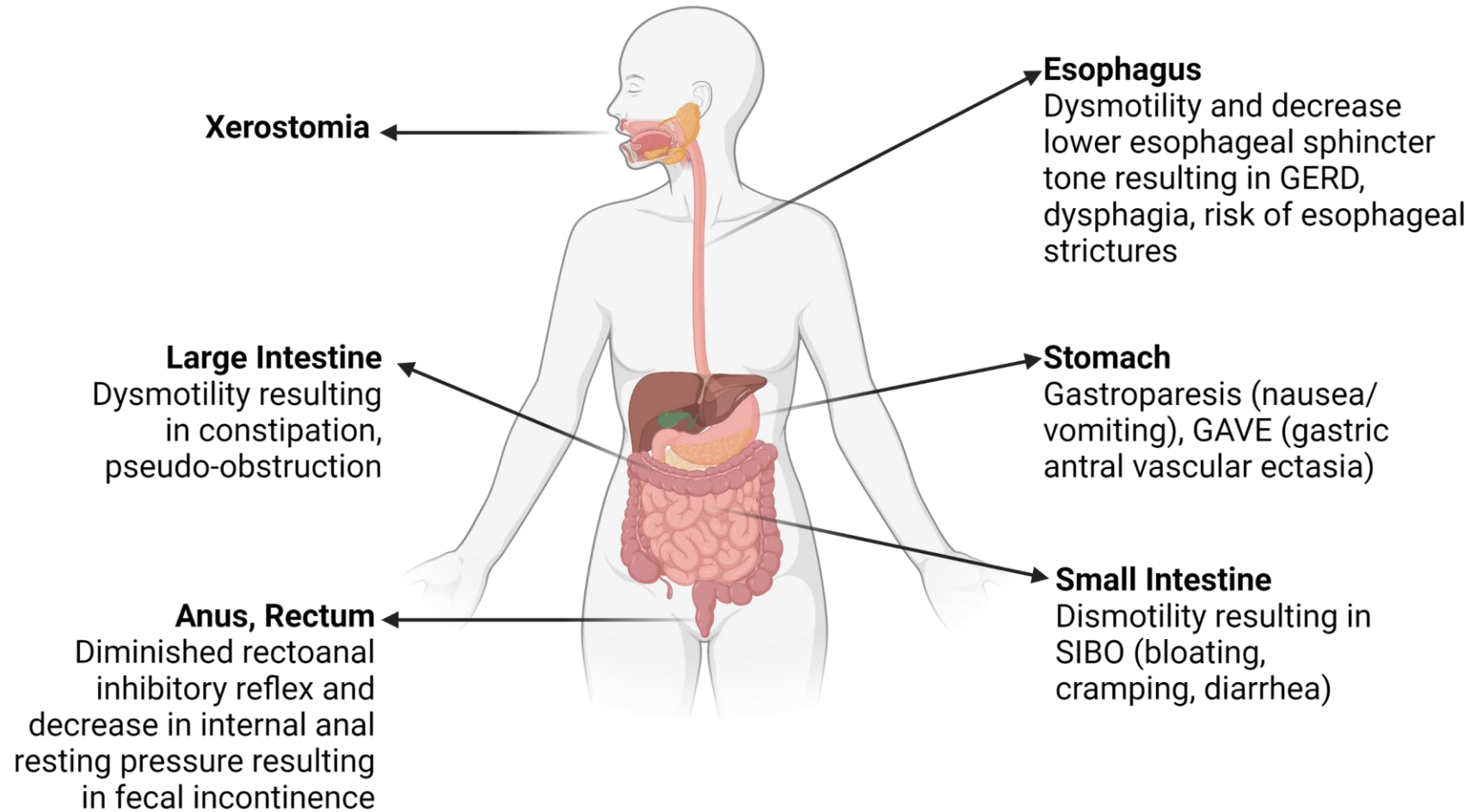
# SCLERODERMA – PULMONARY ARTERIAL HYPERTENSION

- Occurs in approximately 10% of patients<sup>1</sup>
- Usually occurs later in the course of disease
- DETECT algorithm<sup>2</sup>
  - Step 1: FVC%/DLCO%, telangiectasias, anti-centromere antibody, NT-proBNP, serum urate, right axis deviation
    - generates recommendation to obtain echocardiogram or not
  - Step 2: Echocardiogram measured right atrial area, TR velocity or RVSP
    - generates recommendations to proceed to right heart catheterization (RHC)
- In clinical practice, often utilize combination of annual echocardiogram screening, PFTs, and NT-proBNP to assess for evidence of pulmonary hypertension and need for RHC to confirm

1. Steen and Medsger, Ann Rheum Dis, 2007

2. Coghlan JG et al., Ann Rheum Dis., 2013

# SCLERODERMA – GASTROINTESTINAL MANIFESTATIONS



GAVE a.k.a  
“Watermelon Stomach”

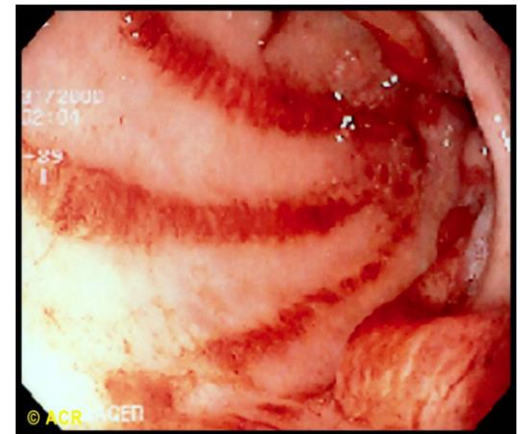
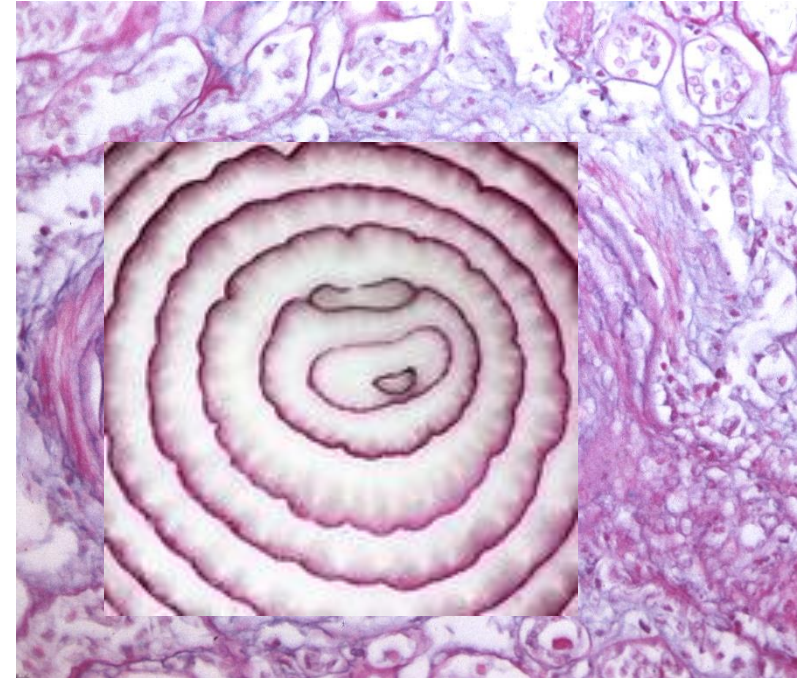


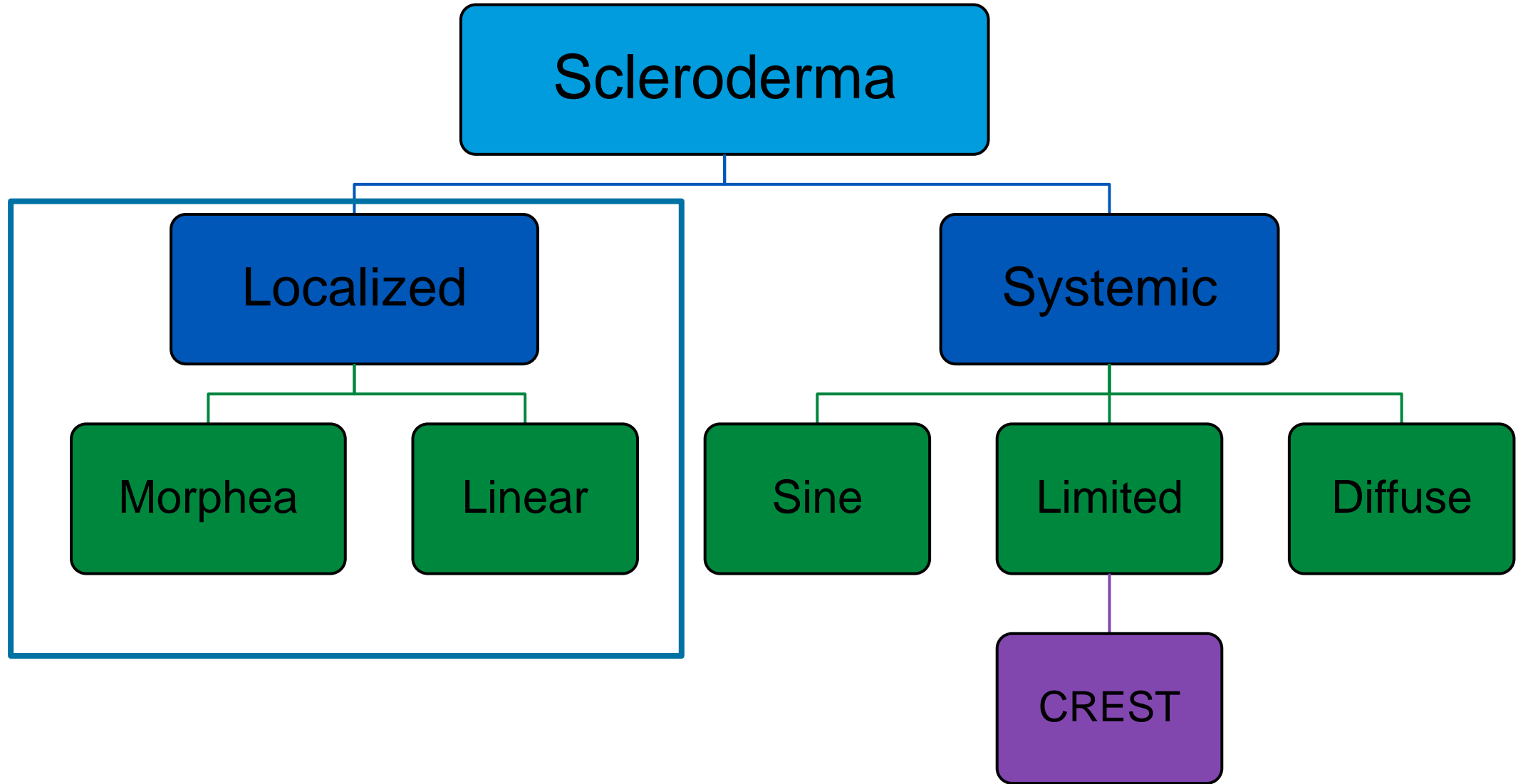
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# SCLERODERMA RENAL CRISIS

- Risk Factors:
  - Early disease (0-3 years)
  - Diffuse cutaneous disease
  - RNA Polymerase III positivity
  - Steroid exposure  $\geq 15\text{mg/day}$
- Associated with microangiopathic hemolytic anemia
- **Treatment: Early initiation of ACE inhibitors with aggressive titration!**
- Renal recovery can be seen 12-18 months post injury





# LOCALIZED SCLERODERMA

- Patients with localized scleroderma do NOT have systemic disease as seen in sine, limited, or diffuse scleroderma



En Coupe de Sabre / Linear



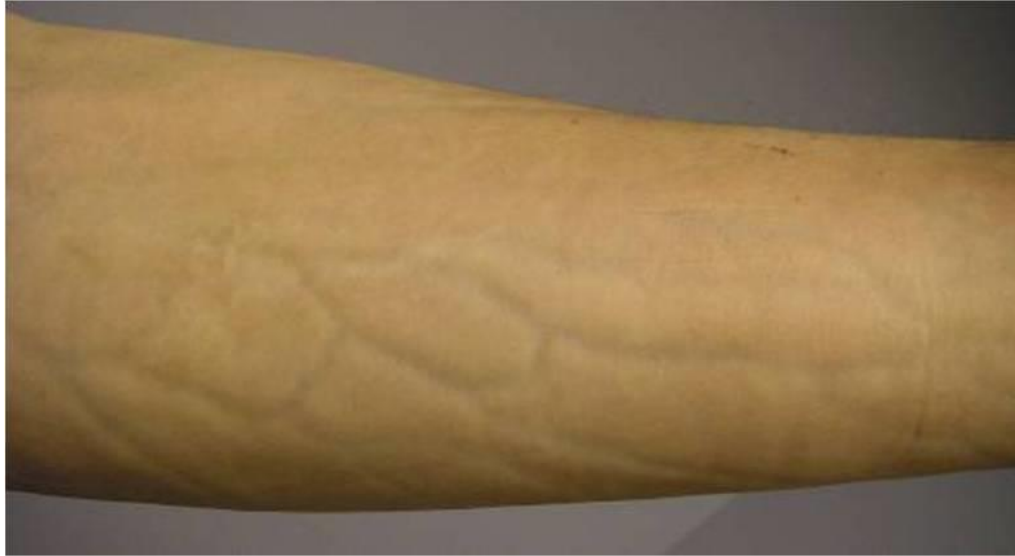
Morphea

# SCLERODERMA-LIKE CONDITIONS – A.K.A “MIMICS”

Condition	Manifestation	Comments
Eosinophilic Fasciitis	Orange peel induration (peau d'orange) of extremities, +/- peripheral eosinophilia, skin retraction over veins	Does NOT involve the hands Glucocorticoids mainstay of treatment
Scleredema	Indurated plaques/patches on back, shoulder girdle, neck	Associated with long-standing diabetes, MGUS, infection (usually strep URI)
Scleromyxedema	Waxy, papules over thickened skin of face, ears, trunk, neck arms, “donut sign”	Mucin deposition and stellate fibroblasts in dermis, associated with paraproteinemia (IgGλ)
Nephrogenic systemic fibrosis	Brawny, wood like induration of extremities, spares digits	Secondary to gadolinium exposure in renal disease; change in gadolinium formulation has decreased incidence
Drug/Toxin	Scleroderma-like tissue changes	Examples: bleomycin, organic solvents, docetaxel, L-tryptophan
Chronic Graft vs. Host disease	Localized or generalized skin thickening	Most commonly after a hematopoietic stem cell transplant



# EOSINOPHILIC FASCIITIS



Groove Sign



“Peau d’orange”



“cobblestoning”

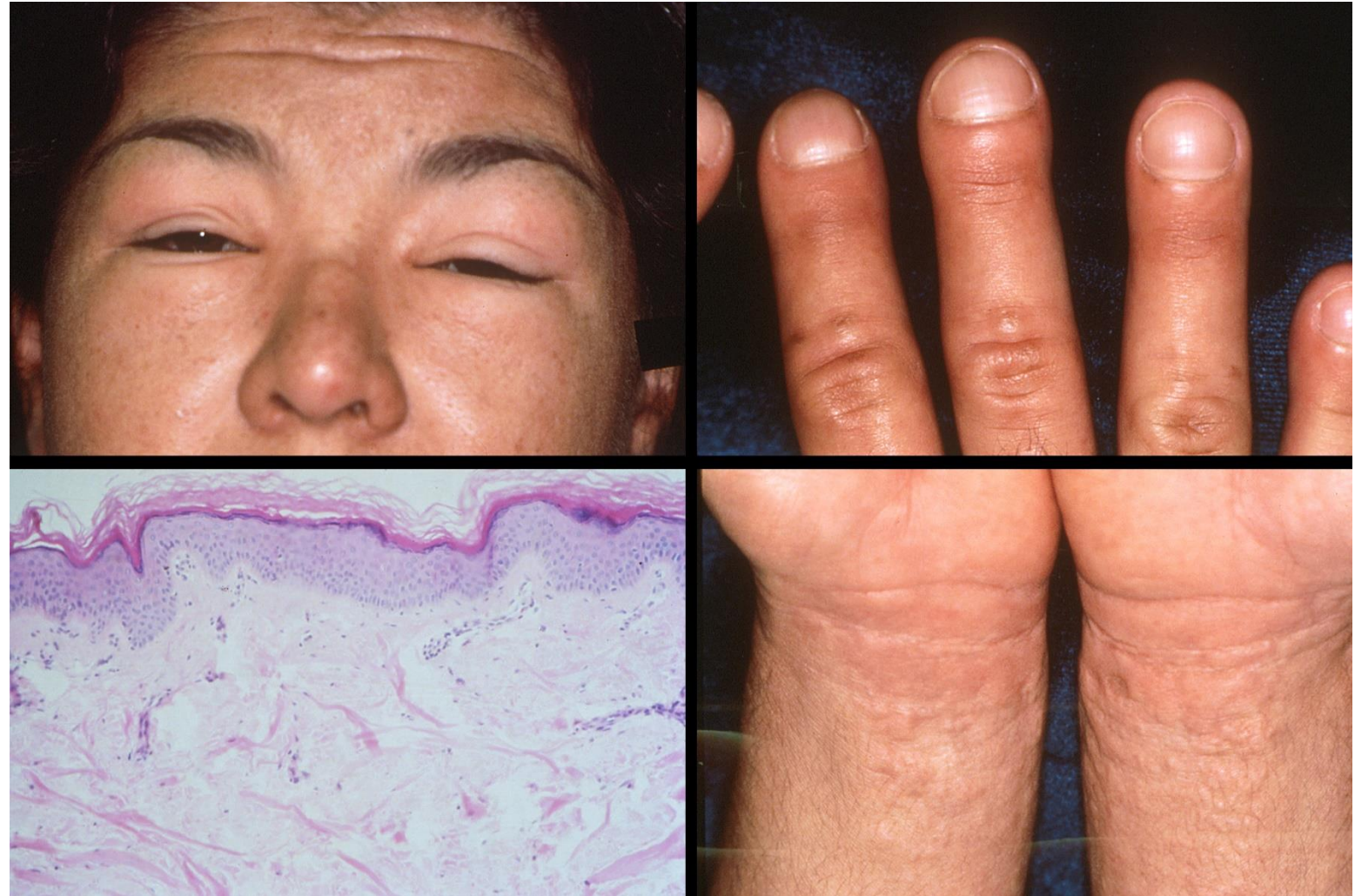
# SCLEROMYXEDEMA

Top Left: Leonine Facies

Top Right: "Donut Sign"

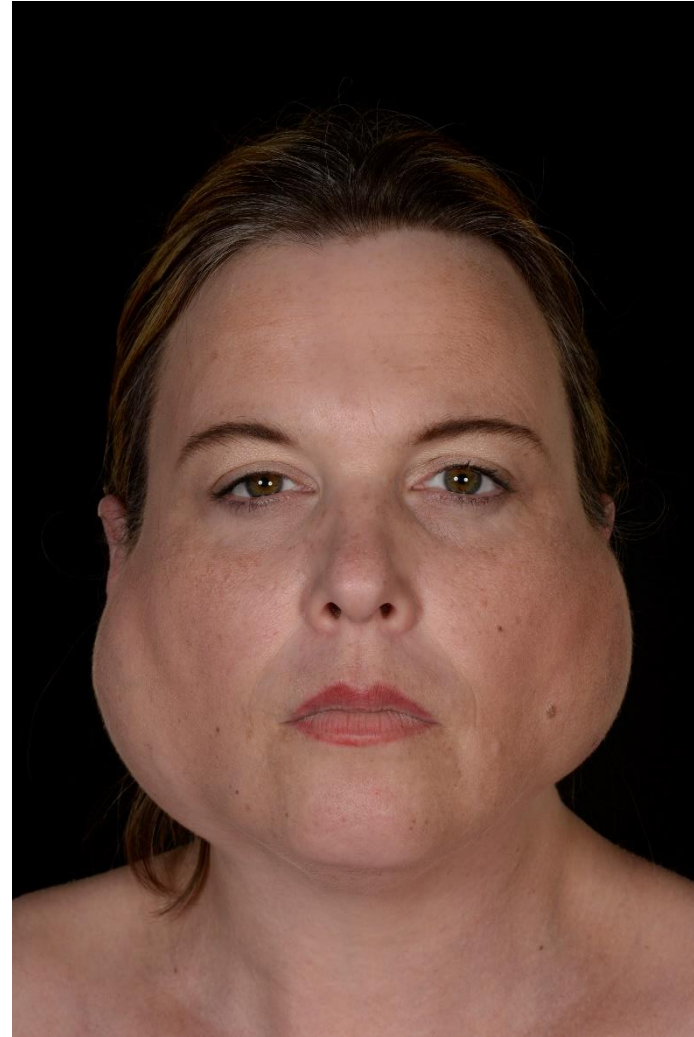
Bottom Left: collagen fibers spread apart by dense gray-pink mucopolysaccharide

Bottom Right: Papular skin changes





# Sjögren's Syndrome



# SJÖGREN'S SYNDROME

- Chronic autoimmune condition caused by lymphocytic infiltration of the exocrine glands
- Epidemiology
  - Prevalence: 92 per 100,000
  - Peak Age: 40 to 50
  - Female to male: from 9:1 to 20:1
- May be “primary” or co-expressed with another autoimmune disease (“secondary”)
- Classic Symptoms due to glandular dysfunction:
  - Xerophthalmia (47%)
  - Xerostomia (42%)
  - Parotid gland enlargement (24%)
  - Vaginal dryness

# SJÖGREN'S SYNDROME – EXTRAGLANDULAR ASSOCIATIONS

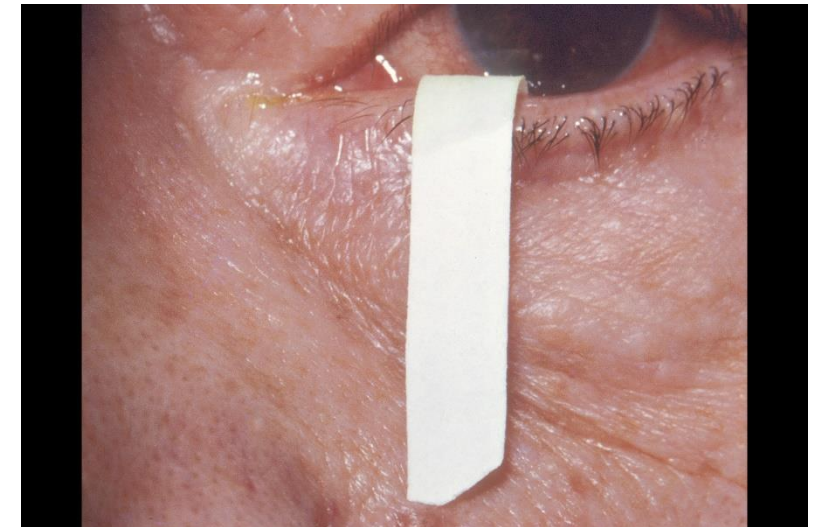
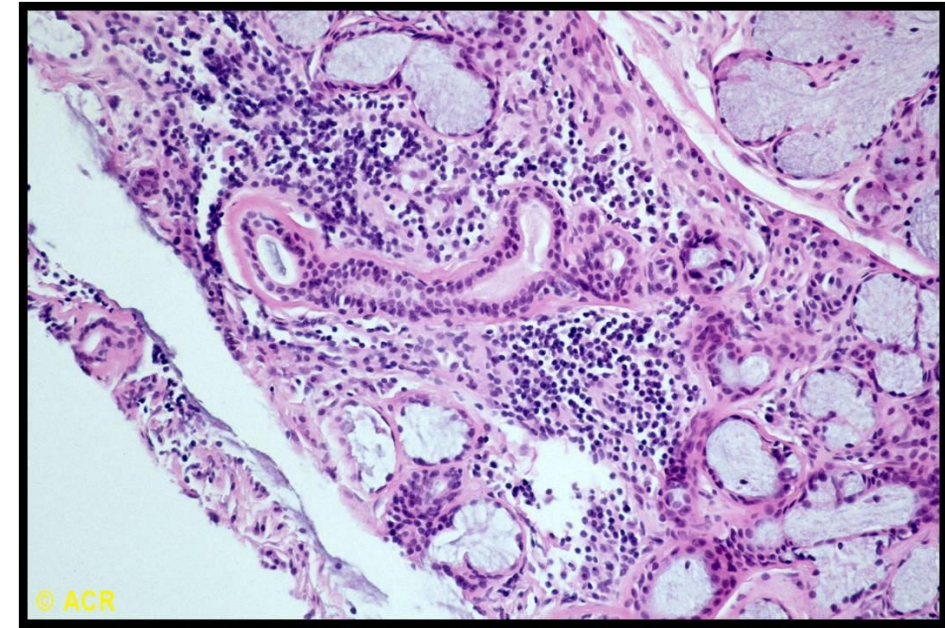
- Systemic manifestations/disease associations
  - Arthralgias/arthritis (28%)
  - Raynaud's phenomenon (21-33%)
  - Lung involvement (10-20%)
  - Renal involvement
    - Type I renal tubular acidosis (10%)
    - Tubular interstitial nephritis (<5%)
  - Liver involvement
    - Primary biliary cholangitis (3-8%)
    - Autoimmune hepatitis
  - Small fiber neuropathy
  - Vasculitis (small vessel) (5-10%)

# SJÖGREN'S SYNDROME

- When assessing a patient with sicca symptoms, rule out:
  - Anti-cholinergic, anti-histamine, diuretic medication effect
  - Hepatitis C
  - HIV
  - Hemochromatosis
  - IgG4 related disease
  - Sarcoidosis
  - Lymphoma
  - Amyloidosis
  - Prior radiation to the neck

# SJÖGREN'S SYNDROME

- Objective Testing:
  - Minor salivary gland biopsy
    - Focal lymphocytic sialadenitis and a focus score of  $\geq 1$  foci/4mm<sup>2</sup>
  - Anti-SSA/Ro positive
  - Schirmer's test
    - $\leq 5$ mm/5 min in at least one eye
  - Ocular Staining Score
    - $\geq 5$  in at least one eye
  - Unstimulated whole saliva flow rate  $\leq 0.1$ mL/min



# SJÖGREN'S SYNDROME

- Treatment of sicca symptoms is symptomatic
  - Xerophthalmia
    - Preservative free lubricating eye drops, punctal plugs, cyclosporine A 0.05% eye drops (Restasis)
  - Xerostomia
    - Over the counter dry mouth products, salivary substitutes, sugar free lozenges to stimulate saliva, cholinergic agents (pilocarpine, civemeline)
    - Dental visits every 6 months due to increased risk of caries
  - Immunosuppression is not beneficial for xerostomia/xerophthalmia but may be used for extra-glandular features
- Routine clinical assessment for lymphoma
  - Elevated risk (13-44 fold) of lymphoma
  - Risk factors: loss of previously positive rheumatoid factor, low C4, cryoglobulinemia, monoclonal gammopathy



## CASE #2

A 40-year-old woman with no significant past medical history presents to clinic with a 6-month history of sicca symptoms, rash, arthralgias, new onset Raynaud's and increasing difficulty going up a flight of stairs.

Physical Exam: decreased salivary pooling; raised erythematous rash over malar region, hips, and knees; dusky fingers and toes; MCP and PIP swelling and tenderness; and 4/5 proximal muscle weakness.

Laboratory:

ANA 1:320, speckled pattern

Positive SSA/Ro

Negative dsDNA, SSB/La, RNP, Smith, Jo-1, Rf, and anti-CCP antibodies

CK 800 (ULN 250)

Which of the following rheumatologic diagnoses best accounts for her presentation?

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2. Sjogren's Syndrome
3. Dermatomyositis
4. Scleroderma
5. Mixed Connective Tissue Disease

# CASE #2 – ANSWER

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# CASE 2 – ANSWER

REFERENCE: Lundberg, Ingrid E et al.,  
*Nature reviews. Disease primers*, 2021

## A. Systemic Lupus Erythematosus

- Malar rash, however, also with evidence of holster sign and several other features not specific to lupus

## B. Sjogren's Syndrome

- Sicca symptoms, but several other clinical features described and sicca symptoms common in other autoimmune diseases as an overlapping feature

## C. Dermatomyositis

- Proximal weakness, location of rash, elevated CK all key in diagnosis as well as recognizing the Raynaud's and sicca symptoms very common across autoimmune diseases

## D. Scleroderma

- Raynaud's present, however, recall Raynaud's can be seen in any autoimmune disease; dysphagia, but this may not be from dysmotility but rather oropharyngeal weakness

## E. Mixed Connective Tissue Disease

- Several overlapping features present, however, RNP negative

# Inflammatory Myopathies

Dermatomyositis

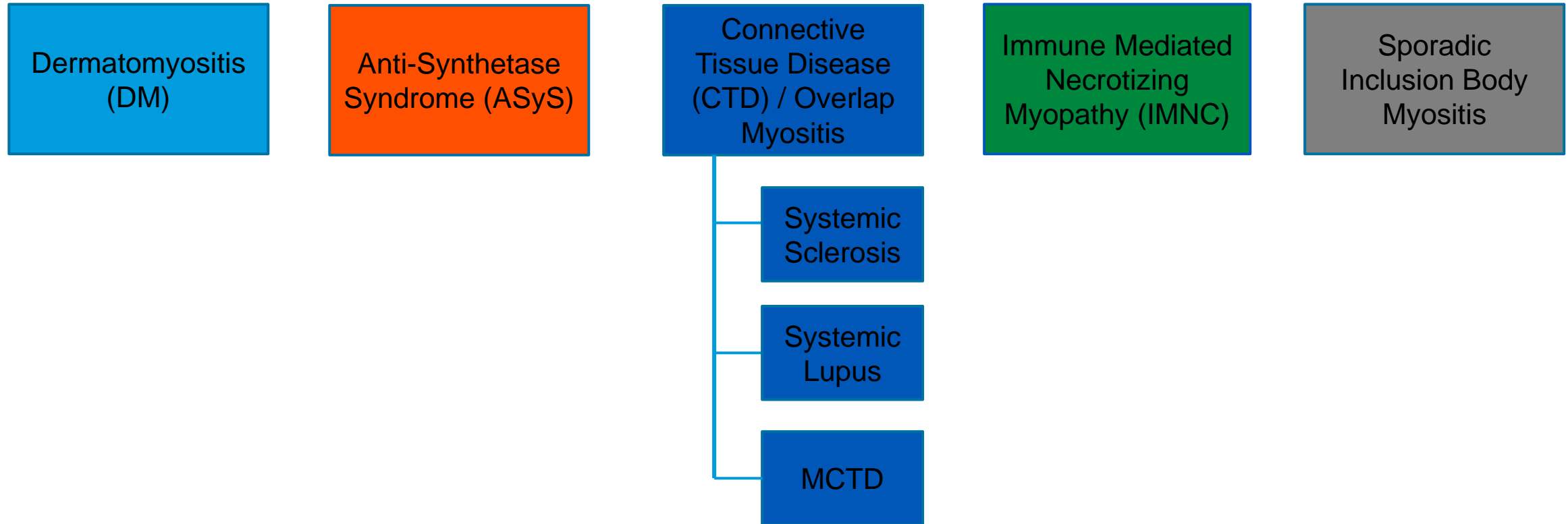
Anti-Synthetase Syndrome

Necrotizing Autoimmune Myopathy

Inclusion Body Myositis

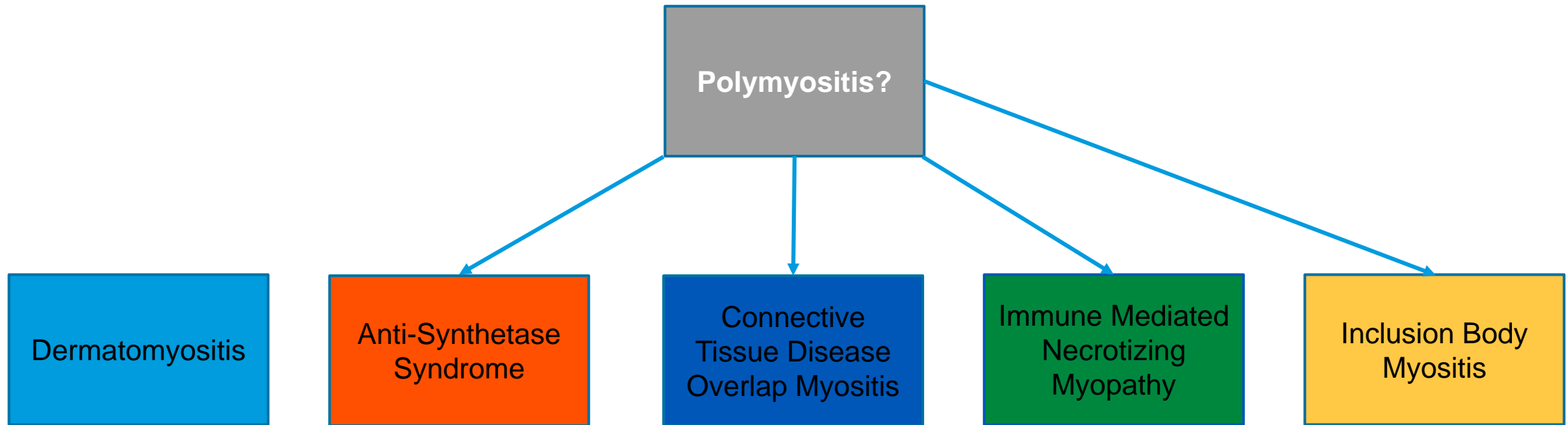
~~Polymyositis?~~ → CTD associated myopathies?

# IDIOPATHIC INFLAMMATORY MYOPATHIES





# IDIOPATHIC INFLAMMATORY MYOPATHIES (SYSTEMIC AUTOIMMUNE MYOPATHIES/IMMUNE MEDIATED MYOPATHIES)



# Immune Mediated Myopathies

- Epidemiology<sup>1</sup>
  - Incidence: ~4 per 100,000 person-years
  - Prevalence: ~22 per 100,000 persons
- Age<sup>1</sup>
  - Juvenile DM
  - Median age 45-64
- Female to Male ratio<sup>1</sup> → 3:2
  - Anti-SRP+:<sup>2</sup> ~5:1
  - Anti-HMGCR+ (statin-exposed):<sup>3</sup> ~1:1

- Extra-Muscular Manifestations
  - Rash
  - Calcinosis
  - Raynaud's Phenomenon
  - Inflammatory Arthritis
  - Interstitial Lung Disease
  - Sclerodermatous skin changes
  - Sicca symptoms
  - Esophageal/small bowel dysmotility
  - Fevers

1. Smoyer-Tomic et al., BMC Musculoskelet Disord., 2012

2. Pinal-Fernandez, I et al., Arthritis Care Res., 2017

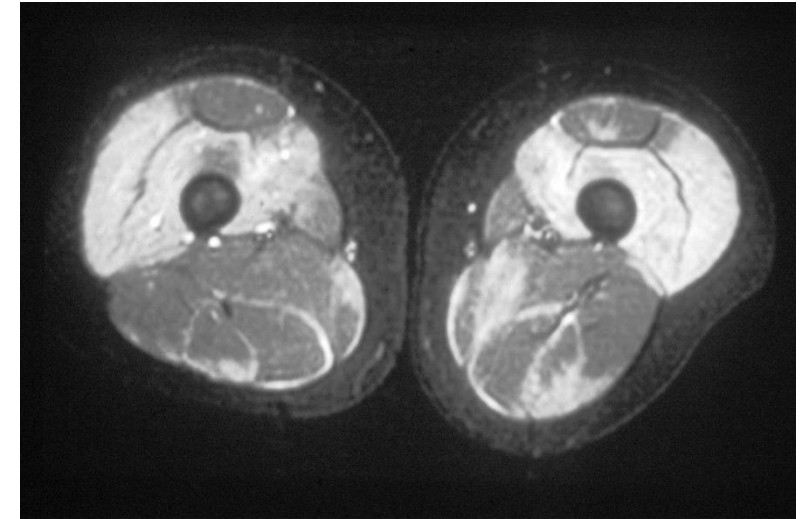
3. Mohassel, P., et al., Neurol Neuroimmunol Neuroinflamm, 2019

# INFLAMMATORY MYOPATHY: CLINICAL CHARACTERISTICS & INITIAL EVALUATIONS

- Clinical:
  - Proximal, symmetric muscle weakness
    - Exception: distal finger flexor weakness and asymmetry in IBM
  - Dysphagia in some patients (oropharynx is a skeletal muscle)
  - Muscle pain is less common
    - Exception: necrotizing myopathies
- Laboratory:
  - Elevated muscle enzymes (90% of the time)
    - Muscle enzymes: CK, aldolase, AST, ALT, LDH
  - Myositis specific and associated autoantibodies

# INFLAMMATORY MYOPATHY: ADDITIONAL DIAGNOSTIC WORK-UP

- EMG
  - Irritability of myofibrils on needle insertion, **Short duration, low amplitude motor unit potentials** on muscle contraction
- MRI of proximal muscles with STIR
  - Shows “edema” seen in inflammation; non-specific
  - May increase diagnostic yield of muscle biopsy
- Muscle Biopsy (guided by EMG (opposite side) or MRI)
  - Biopsy weak muscle, but not atrophied, muscle



T2 weighted image of the thighs with STIR which enhances edema (white) and suppresses fat signal to improve detection of muscle inflammation.

# DERMATOMYOSITIS: CUTANEOUS FEATURES



Heliotrope rash



V-neck sign



Holster Sign



Gottron's



Gottron's over knees



Periungual hyperemia

# DERMATOMYOSITIS: MYOSITIS SPECIFIC ANTIBODIES & CLINICAL PHENOTYPE

MSA	Cutaneous Features	Other Differentiating Features	Malignancy Risk
Mi-2	Classic DM rash	<ul style="list-style-type: none"> <li>Prominent Myositis</li> <li>Responds well to therapy</li> <li>ILD rare</li> </ul>	+
SAE	Classic DM rash	<ul style="list-style-type: none"> <li>Skin may precede myositis</li> <li>+/- mild ILD</li> </ul>	+
TIF-1 gamma (P155/140)	Severe DM rash	<ul style="list-style-type: none"> <li>May experience blistering, severe pruritis, subcutaneous edema</li> </ul>	+++
NXP2	May have minimal cutaneous DM	<ul style="list-style-type: none"> <li>Prominent Myositis</li> <li>Peripheral Edema</li> <li>Calcinosis</li> </ul>	+
MDA5	Deep skin ulcerations	<ul style="list-style-type: none"> <li>Rapidly progressive ILD</li> </ul>	+
	Palmar papules Mechanics hands	<ul style="list-style-type: none"> <li>Arthritis</li> <li>May be amyopathic</li> </ul>	



# MALIGNANCY RISK IN INFLAMMATORY MYOPATHIES

- Malignancy risk is increased within 3 years of onset of myositis<sup>1</sup>
  - SIR 4.7 for dermatomyositis
  - SIR 1.8 for other myopathies
  - Anti-synthetase syndrome not associated with increased risk (strongest data for anti-Jo1 antibody positive patients)
- Screening annually for 3 years in dermatomyositis
  - CT chest, abdomen, pelvis
  - Mammogram and pelvic ultrasound for women
  - Testicular ultrasound for men?
  - Update age-appropriate screening (e.g. colonoscopy)

# ANTI-SYNTHETASE SYNDROME

- Classic Triad:
  1. Interstitial Lung Disease (ILD),
  2. Myositis
  3. Inflammatory Arthritis
- Only ~20% have full triad at onset<sup>1</sup>
  - Isolated ILD, myositis, or inflammatory arthritis at presentation common, with the second and third feature developing in first year
- Other features: Raynaud's Phenomenon, Mechanic's Hands, Fever
- ILD: high prevalence
  - Screen all patients with high resolution CT scan
- Myositis Specific Antibodies
  - Jo1, PL7, PL12, EJ, OJ, KS, Zo, Ha



Mechanic's Hands

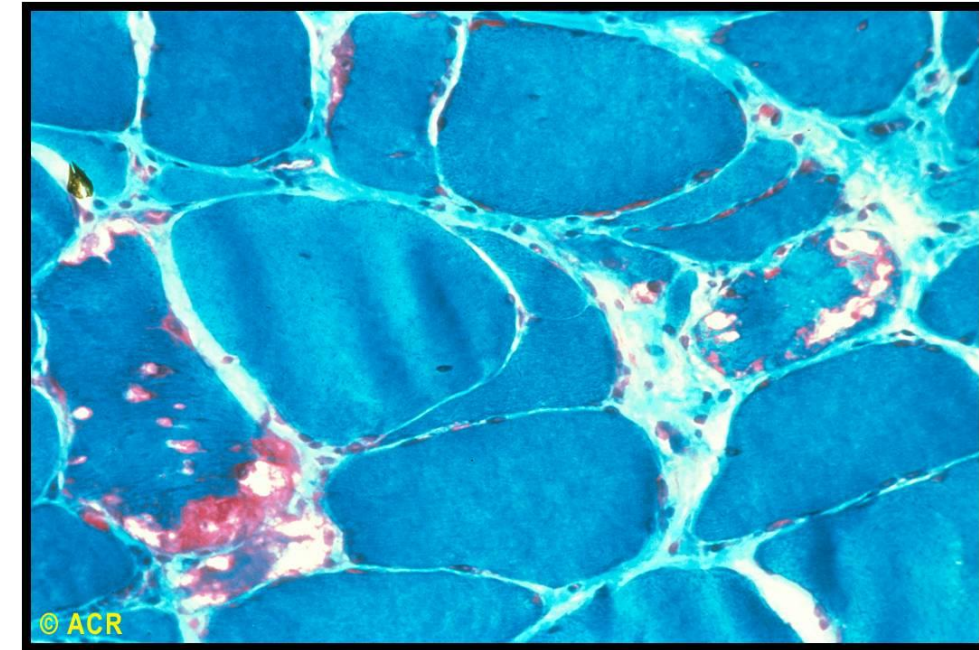
# IMMUNE-MEDIATED NECROTIZING MYOPATHY (NECROTIZING AUTOIMMUNE MYOPATHY)

- Characterized by significant elevation in CK (median peak around 4,700 IU/L) and often profound weakness
- Three Major Subtypes:
  - Anti-SRP
  - Anti-HMGCR
    - Associated with statin use
  - Antibody negative IMNC
    - Evaluate for malignancy
- Muscle biopsy
  - Muscle cell necrosis and regeneration
  - Upregulation of class 1 MHC
  - Lack of lymphocyte invasion

Pearl: Statins are present in oyster mushrooms and red yeast rice

# INCLUSION BODY MYOSITIS

- Predominately affects white males over age 50
- Distal forearm finger flexors affected, in addition to proximal muscle weakness; bilateral, but asymmetry common
- CK less than 800mg/dL, may be normal
- Anti-CN1A (Cytosolic 5'-NucleoTidase 1A) antibody in about 50%
- Muscle biopsy shows **red rimmed vacuoles** containing beta amyloid
- Slowly progressive, responds poorly to immunosuppression



# MIXED CONNECTIVE TISSUE DISEASE

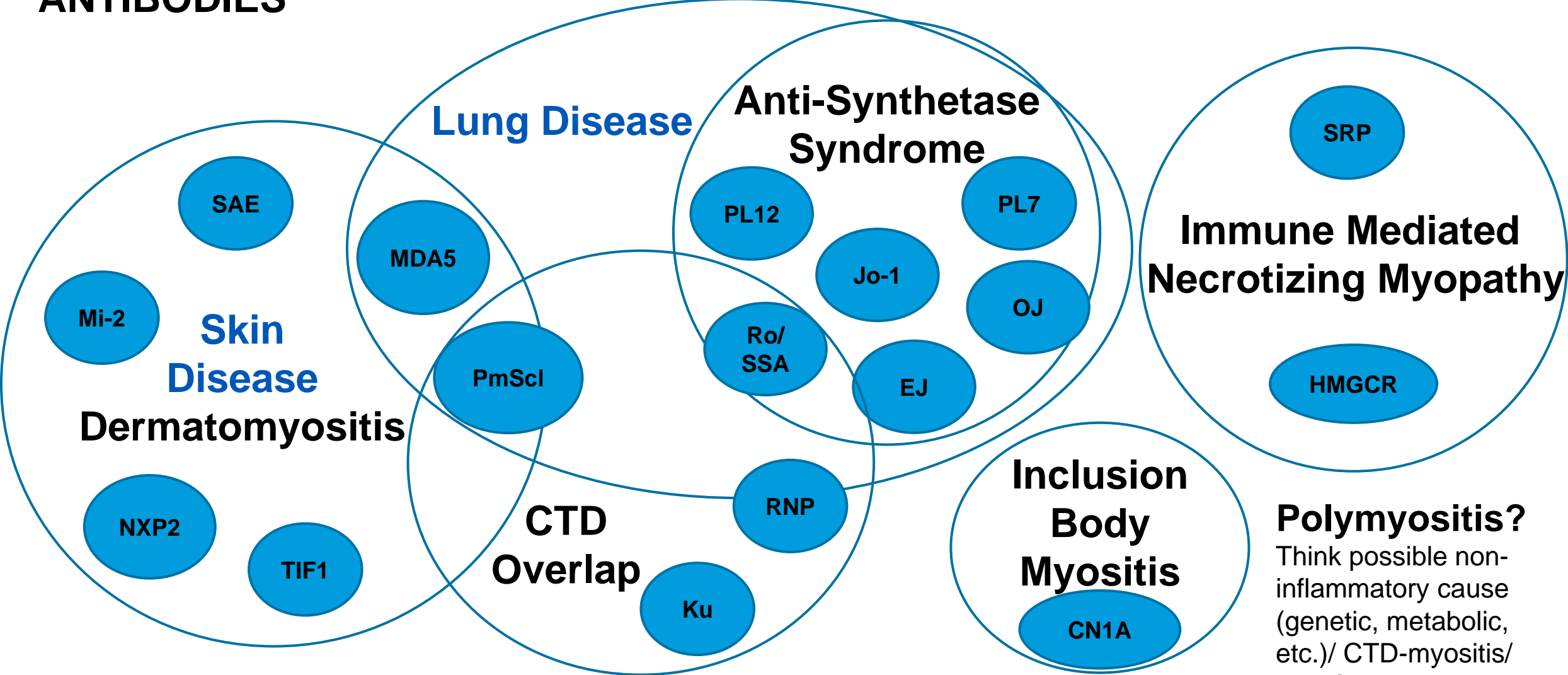
- Patients have clinical features of SLE, scleroderma, myositis
  - Generally do not meet full classification criteria of a single disease subset
- If patients with MCTD are followed for 10 years, 30-50% evolve into a defined connective tissue disease<sup>1</sup>
- Widely accepted that a patient must have a **high titer** anti-RNP antibody

# AUTOANTIBODIES SUMMARY

SLE	Scleroderma	Sjogren's	Myopathies
ANA dsDNA Smith SSA/Ro SSB/La RNP Histone Ribosomal P Antiphospholipids RNP	ANA (nucleolar) Centromere Topoisomerase (Scl70) RNA Polymerase III RNP	ANA SSA/Ro SSB/La (centromere) RNP	ANA tRNA synthetase (Jo1, PL-7, others) Mi-2 SRP P155/140 (TIF1gamma) MDA5 SSA/Ro RNP



# INFLAMMATORY MYOPATHIES: SUBTYPES, MANIFESTATIONS, AND ANTIBODIES



**Polymyositis?**  
 Think possible non-inflammatory cause (genetic, metabolic, etc.)/ CTD-myositis/ Anti-Synthetase Syndrome

# SUMMARY – RP, SSC, SJÖGREN, MYOPATHIES

## ***Diagnose and manage secondary Raynaud's Phenomenon***

- Triphasic color changes provoked by cold
- Onset over 40 years old highly suspicious for secondary cause
- Conservative and pharmacologic management

## ***Understand the clinical and laboratory evaluation of scleroderma (localized, limited, and diffuse)***

- Localized has no systemic disease
- Limited: skin thickening distal to elbows, often centromere+
- Diffuse: skin thickening proximal to elbows, often RNA Pol III+

# SUMMARY – RP, SSC, SJÖGREN, MYOPATHIES

## ***Understand the clinical and laboratory evaluation of Sjögren's Syndrome***

- Sicca symptoms
- Extra-glandular manifestations common
- Symptomatic management for glandular features

## ***Understand the clinical and laboratory evaluation of MCTD***

- Overlap of SLE, Scleroderma, Myositis
- Must be RNP positive

# SUMMARY – RP, SSC, SJÖGREN, MYOPATHIES

## *Understand the clinical and laboratory evaluation of Inflammatory Myopathies*

- Symmetric, proximal weakness
- Myositis specific antibodies have associated phenotypes and risks for extra-muscle clinical features
- Necrotizing myopathies: anti-SRP and anti-HMGCR
- IBM has distal flexor weakness, does not respond to immune suppression



# QUESTIONS & DISCUSSION

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