Connective Tissue Disease Module Outline

Introduction

Skin findings are common in patients with systemic diseases, including those with connective tissue disorders. In fact, cutaneous lesions are often the presenting sign. As such, clinicians need to be aware of various dermatologic conditions as their presence will frequently trigger an investigation, or aid in a more focused investigation, for the underlying systemic disease. This module will review 3 patient cases and emphasize significant cutaneous, clinical and laboratory findings associated with each disease to make the correct diagnosis. This module is not meant to be an exhaustive review of connective tissue disease (CTD), but to serve as an introduction to understanding CTD processes and how systemic CTD and skin findings interrelate.

Goals and Objectives

By the end of this module, the learner should be able to:

1. Recall common connective tissue diseases
2. Differentiate key clinical features of the various conditions discussed
3. Utilize various autoantibodies to help differentiate the diseases
4. Identify dermatologic findings, in a variety of skin tones, that are associated with the following rheumatic diseases:
    a. Systemic lupus erythematosus
    b. Cutaneous lupus erythematosus
    c. Dermatomyositis
    d. Systemic sclerosis (scleroderma)

Pre Test Questions

1. Approximately what percent of patients with discoid lupus erythematosus (DLE) have, or will develop, systemic lupus erythematosus?
    a. 5%
    b. 20%
    c. 50%
    d. 80%
2. Which of the following skin findings are pathognomonic for dermatomyositis?
    a. Malar rash
    b. Heliotrope rash
    c. Gottron papules
    d. Periungual telangiectasia
3. Which of the following conditions is LEAST likely to be associated with photosensitivity?
    a. Rheumatoid arthritis
    b. Systemic lupus erythematosus
    c. Systemic sclerosis
    d. Dermatomyositis
4. What is the leading cause of death in patients with systemic lupus erythematosus, after the first decade of disease?
    a. Renal failure
    b. Atherosclerosis
    c. Sepsis

    d. Pulmonary fibrosis
5. Which of the following forms of cutaneous lupus is most commonly associated with cutaneous scarring and dyspigmentation?
    a. Acute cutaneous lupus
    b. Discoid lupus
    c. Neonatal lupus
    d. Drug-induced lupus
6. Monitoring for malignancy, for up to 5 years after the initial diagnosis, is recommended for patients with which of the following conditions?
    a. Systemic sclerosis (scleroderma)
    b. Behcet syndrome
    c. Systemic lupus erythematosus
    d. Dermatomyositis
7. Presence of which of the following auto-antibodies is associated with an increased risk of cancer in patients with dermatomyositis?
    a. Anti-dsDNA
    b. Anti-TIF-1 gamma
    c. Anti-Scl 70
    d. Anti-MDA5
8. Vitiligo-like depigmentation, with maintenance of perifollicular pigmentation, is most commonly seen in which of the following conditions?
    a. Acute cutaneous lupus erythematosus
    b. Chronic cutaneous lupus
    c. Systemic sclerosis (scleroderma)
    d. Raynaud phenomenon
9. Digital autoamputation is more common in which of the following conditions?
    a. Systemic sclerosis (scleroderma)
    b. Rheumatoid arthritis
    c. Systemic lupus erythematosus
    d. Dermatomyositis
10. Which of the following antibodies is typically found in CREST syndrome (a form of limited systemic sclerosis)?
    a. Anti-centromere
    b. Anti-Jo1
    c. Anti-Scl 70
    d. Anti-SSB (La)

Morphologic and Histologic Terms

- Annular - ring shaped lesion, with clearing (normal skin) in the center
- Arcuate - half-moon shaped
- Bulla - fluid filled lesion, typically greater than 0.5-1cm in diameter (AKA: a larger blister - see vesicle below)
- Calcinosis cutis - deposition of calcium salts in the dermis and subcutaneous tissue
- Gottron papule - pink, violet, or red colored papules over the joints of the hands and fingers [metacarpophalangeal (MCP), proximal interphalangeal (PIP), distal Interphalangeal (DIP) joints]; pathognomonic for dermatomyositis
- Heliotrope sign - red-purple discoloration of the upper eyelids, may be accompanied by eyelid swelling. It is named for the purple heliotrope flower and can be seen in BOTH dermatomyositis and systemic lupus erythematosus
- Interface dermatitis - histologic term describing inflammation along the dermal-epidermal junction (the interface between the dermis and the epidermis). A common histologic finding in various connective tissue diseases
- Jacoud's arthropathy - chronic, deforming, non-erosive arthritis with ulnar deviation of the fingers with MCP joint subluxation
- Malar rash - erythema over the nose and cheeks, typically spares the nasolabial folds as it is a photosensitive rash
- Macule - flat, non-palpable, color change of the skin, typically less than 1cm in diameter
- Morbilliform - extensive number of small, flesh colored or pink-to-red, macules and/or papules; lesions vary size (1-3mm) and may coalesce into larger patches. This is the ONLY macular-papular rash.
- Panniculitis - inflammation of subcutaneous fat
- Papule - circumscribed, firm, raised skin lesion, less than 1cm in diameter
- Papulosquamous - skin conditions that affect the epidermis and consist of plaques or papules with scale
- Patch - flat, non-palpable color change of the skin, typically greater than 1cm in diameter
- Plaque - circumscribed, firm, plateau-like, raised skin lesion, greater than 1cm in diameter
- Periungual / nail fold telangiectasia - small, dilated, and sometimes tortuous, blood vessels within the proximal nailfold (cuticle) of finger and/or toes
- Photosensitivity - heightened reaction to sunlight
- Poikiloderma - skin changes that include both hypopigmentation and hyperpigmentation as well as erythema and variable atrophy, with dilation of the fine blood vessels (telangiectasia)
- Psoriasiform - psoriasis-like; resembling psoriasis or a psoriatic lesion, may be used as a morphologic or histologic term
- Raynaud phenomenon - classic triphasic color changes of digits upon cold exposure
- Scale - visible peeling or flaking of outer skin layers due to an epidermal process
- Serositis - inflammation of serous membranes (membranes lining closed internal body cavities: the pleura, pericardium and peritoneum)
- Shawl sign - a characteristic photosensitivity reaction demonstrating poikiloderma across the upper back, shoulders, and posterior neck
- V-sign - a characteristic photosensitivity reaction demonstrating poikiloderma across the mid upper chest (v-neck distribution)
- Vasculitis - inflammation of blood vessels

- Vesicle - small fluid filled lesion, typically less than 0.5cm in diameter; (AKA a small blister - see bulla above)

Abbreviations

- ACR - American College of Rheumatology
- AKA - “other wise known as”
- ALT - alanine aminotransferase - found in liver and muscles
- ANA - antinuclear antibody
- AST - aspartate aminotransferase - found in liver and muscles
- CBC - complete blood count
- CK - creatine kinase
- CNS - central nervous system
- Cr - creatinine
- CT - computerized tomography
- CTD - connective tissue disease
- DAT - direct antiglobulin test
- DIF - direct immunofluorescence
- DIP - distal Interphalangeal joints of the hands
- DEJ - dermal-epidermal junction
- DfDx - differential diagnoses
- ESR - erythrocyte sedimentation rate
- ESRD - end stage renal disease
- EULAR - European Alliance of Associations for Rheumatology
- GI - gastrointestinal
- H&E - hematoxylin and eosin - common stains for biopsies
- HTN - hypertension
- LDH - lactate dehydrogenase
- MCP - metacarpophalangeal joints of the hands
- PIP - proximal interphalangeal joints of the hands
- PTT - partial thromboplastin time (measure of clotting)
- RBC - red blood cell
- SLE - systemic lupus erythematosus
- SSA - anti-SSA autoantibodies (stands for anti–Sjögren's-syndrome-related antigen A autoantibodies, also called anti-Ro
- SSB - anti-SSB autoantibodies (anti–Sjögren's-syndrome-related antigen B autoantibodies, also called anti-La
- dsDNA ANA
- SSc - systemic sclerosis AKA scleroderma
- UA - urinalysis

Cases

This next section contains presentations of 3 patients with different CTDs. Cases include a clinical scenario, skin findings, other relevant physical findings, differential diagnoses, important laboratory tests and a discussion. The diagnoses are based on a combination of clinical and laboratory findings.

- Note on inclusive history taking

- In the following fictional patient encounters, it can be assumed that we have already asked the patient for identifying pronouns.
- If a patient is referred to as male/female, it refers to their sex assigned at birth.

CASE #1

- Case presentation
  - Clinical history
    - BY, a 32-year-old female (she/her/hers), presented with a 3 day history of this facial rash that developed after kayaking the previous weekend. She also reported a few weeks of knee pain and oral ulcers, which she thought might be due to spicy foods, as well as feeling a little more tired than usual.
  - Physical findings
    - Malar erythema is present on both cheeks
    - Several oral erosions are present on the hard palate
    - Proximal nail fold telangiectasia are present on all fingers
- Differential diagnosis (DfDx) for this case:
  - Systemic lupus erythematosus (SLE)
  - Mixed connective tissue disease (MCTD)
  - Systemic sclerosis (SSc)
  - Dermatomyositis (DM)
  - Drug-induced lupus (DIL)
  - Rheumatoid arthritis (RA)
  - Behcet disease (BD)
  - Rosacea

- Significant laboratory results for <u>this patient</u>:
  - Complete blood count
    - Leukopenia, mild anemia, and thrombocytopenia = pancytopenia (abnormal)
  - Complete metabolic panel
    - Elevated serum creatinine (Cr) and blood urea nitrogen (BUN) (abnormal)
  - Urinalysis
    - Hematuria and proteinuria (abnormal)
  - ANA titer
    - 1:640 (elevated - abnormal)
  - C3 and C4 complement levels
    - Decreased (abnormal)
  - Anti-dsDNA antibody
    - Positive (abnormal)
  - Anti-Smith antibody
    Positive (abnormal)
  - (+) Anti-SSA/Ro, anti-SSB/La antibodies
    - Positive (abnormal)
  - Anti-histone, anti-U1RNP, antiphospholipid antibodies
    - All negative (normal)
  - Coagulation studies
    - Normal

    - C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)
        - Elevated (abnormal)

- Skin biopsy:
    - Histologic findings from a skin biopsy, stained with H&E, demonstrated an interface dermatitis with disruption of the dermal-epidermal junction (abnormal).
    - Direct immunofluorescent staining (DIF) identified granular deposition of IgG at the dermal-epidermal junction (DEJ) (abnormal).

- **Analysis of present data that support, or refute, the various diagnoses in the DfDx to determine the most likely diagnosis in this case:**

    - Systemic lupus erythematosus (SLE)
        - <u>Supportive Data</u>:
            - Clinical
                - Malar rash with photosensitivity
                - Arthralgias
                - Oral ulcers (mucositis)
                - Fatigue/malaise
                - Proximal nail fold telangiectasia
            - Laboratory
                - (+) ANA
                - (+) Anti-Smith antibody
                - (+) Anti-dsDNA antibody
                - (+) Anti-SSA (Ro)/ Anti-SSB (La) antibodies
                - Pancytopenia (but only anemia specific to SLE is an autoimmune hemolytic anemia)
                - Low C3 and C4
                - Renal involvement (hematuria, proteinuria, elevated Cr/BUN)
                - Elevated inflammatory markers (CRP & ESR)
                - Skin biopsy with an interface dermatitis and (+) DIF
        - <u>Non Supportive Data:</u>
            - None of the data refute the possible diagnosis of SLE
    - Mixed Connective Tissue Disease (MCTD)
        - <u>Supportive Data:</u>
            - Clinical
                - Arthralgias
                - Photosensitivity
            - Laboratory
                - (+) ANA
                - Anemia and leukopenia
                - Renal involvement (hematuria, proteinuria, elevated Cr/BUN)
                - Elevated inflammatory markers (CRP & ESR)

            - Skin biopsy could show an interface dermatitis and (+) DIF
        - Non Supportive Data:
            - Clinical
                - Lack of the following:
                    - Shortness of breath
                    - Skin thickening / tightening
                    - Proximal muscle weakness / polymyositis
            - Laboratory
                - Lack of the following:
                    - High titer positive anti-U1RNP antibodies. Although Anti-U1RNP antibodies can be seen in SLE and other CTD, they are typically recognized as a serological marker for MCTD
                    - Presence of other lupus-specific antibodies makes SLE more likely than MCTD

- Systemic Sclerosis (SSc)
    - Supportive Data:
        - Clinical
            - Proximal nail fold telangiectasia
        - Laboratory
            - (+) ANA
            - Renal involvement with elevated Cr/BUN
    - Non Supportive Data:
        - Clinical
            - Lack of the following
                - Raynaud phenomenon
                - Skin thickening/tightening
                - Dysphagia
                - Shortness of breath
            - Photosensitivity is not a part of SSc
            - Skin tightness can affect joint mobility, but joint pain is not a typical feature of SSc
        - Laboratory
            - Lack of the following
                - Anti-centromere antibody
                - Anti-Scl 70 antibody
            - Pancytopenia is rare in SSc
            - Skin biopsy would show excessive dermis, not an interface dermatitis

- Dermatomyositis (DM)
    - Supportive Data:
        - Clinical

        - Photosensitive rash on the face
        - Proximal nail fold telangiectasia
    - Laboratory
        - (+) ANA
        - Elevated inflammatory markers CRP/ESR
        - Skin biopsy would show an interface dermatitis (but DIF would be negative)
- <u>Non Supportive Data:</u>
    - Clinical
        - Lack of the following
            - Proximal muscle weakness
            - Photosensitive rash in other locations
            - Gottron papules
            - Pulmonary involvement
        - Arthritis is not a common feature of DM
        - Oral ulceration / mucositis is rare in DM
    - Laboratory
        - Lack of the following
            - (+) elevated creatine kinase (CK)
        - Renal involvement is rare in DM
        - Pancytopenia is not a hallmark of DM
        - Skin biopsy would show an interface dermatitis, but DIF would be negative

- Drug-Induced (Systemic) Lupus (DIL)
    - <u>Supportive Data:</u>
        - Clinical:
            - Skin findings are consistent with DIL
        - Laboratory
            - (+) ANA is seen in DIL
    - <u>Non Supportive Data:</u>
        - Clinical
            - No associated medication reported
                - Associated drugs are many and could include hydralazine, procainamide, tumor-necrosis factor inhibitors, alpha-interferon, penicillamine
        - Laboratory
            - (+) Anti-dsDNA antibody is very rare in DIL (unless due to tumor-necrosis factor inhibitors)
            - Low complement levels are very rare in DIL
            - Renal disease is rare in DIL
            - Anti-histone antibodies are most common in DIL, although they can be seen in SLE as well. They are negative in this case.

- Skin biopsy would not show an interface dermatitis with (+) DIF

- Rheumatoid Arthritis (RA)
  - Supportive Data:
    - Clinical
      - Arthritis/arthralgia
      - Sometimes nail fold telangiectasia are present
    - Laboratory
      - (+) ANA can can be seen in RA
      - Elevated CRP correlates to RA activity
  - Non Supportive Data:
    - Clinical
      - Lack of joint swelling
      - Lack of skin conditions seen in RA: vasculitis, rheumatoid nodules, pyoderma gangrenosum.
    - Laboratory
      - Renal involvement is rare in RA
      - Low complement levels are rare in RA
      - (+) Anti-dsDNA antibody is not a hallmark of RA
      - (+) Anti-Smith antibody is not a hallmark of RA
      - Skin biopsy would not show an interface dermatitis with (+) DIF

- Behcet Disease (BD)
  - Supportive Data:
    - Clinical
      - Oral ulcers
      - Arthralgias
    - Laboratory
      - Elevated CRP/ESR
      - (+) ANA can be seen in Behcet disease
  - Non Supportive Data:
    - Clinical
      - Lack the following
        - Eye symptoms (uveitis)
        - Genital ulcers
      - Photosensitivity is not seen in Behcet
    - Laboratory
      - Low complement levels are rare in Behcet
      - (+) Anti-dsDNA antibody not a hallmark of Behcet
      - (+) Anti-Smith antibody is not a hallmark of Behcet
      - Skin biopsy would not show an interface dermatitis with (+) DIF

- Rosacea
  - Supportive Data:
    - Clinical
      - Facial erythema; sometimes affects the scalp or chest
      - Photosensitivity of face
    - Laboratory
      - There are no lab abnormalities associated with rosacea
  - Non Supportive Data:
    - Clinical
      - In rosacea there is central facial erythema, often associated with facial telangiectasia, papules and pustules
      - Though patients are photosensitive, there are other triggers that cause a flush / blush reaction
      - The other skin signs described here are not seen in rosacea
      - There are no constitutional symptoms associated with rosacea
    - Laboratory
      - There are no lab abnormalities associated with rosacea
      - ANA would be negative
      - Skin biopsy would not show an interface dermatitis with (+) DIF

Considering all the clinical and laboratory findings that are present, the most likely diagnosis is:

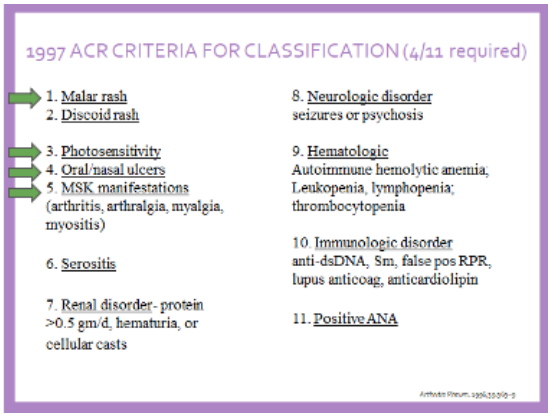
Systemic Lupus Erythematosus

Diagnosis / Discussion: Systemic Lupus Erythematosus (SLE)

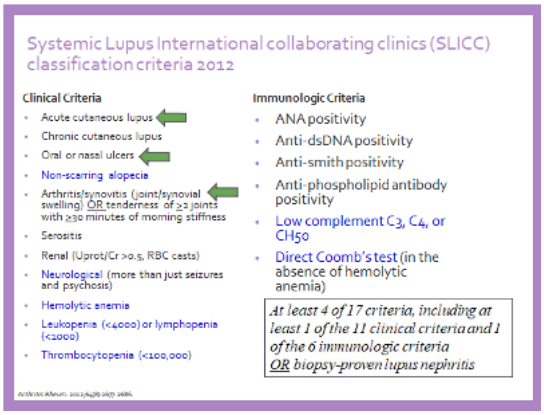
- Pathophysiology
  - Autoimmune, multisystem disease characterized by the presence of autoantibodies
  - Pathogenesis unknown, but follows the cumulative autoimmune hit hypothesis:
    - "The immune system can absorb a certain number of genetic polymorphisms/hits until reaching autoimmune dysfunction" in genetically predisposed individuals
  - Sun exposure can cause flares of SLE
- Epidemiology
  - Women are 10x more likely to have SLE than men
  - Most common in women 15-45 years of age
  - African American women are ~3x more likely to develop SLE
  - 20% of patients are children
- Social determinants of health/racial disparities
  - African American women are more likely to have more severe disease and greater morbidity
    - 3x higher risk of stroke (occurs earlier in disease)

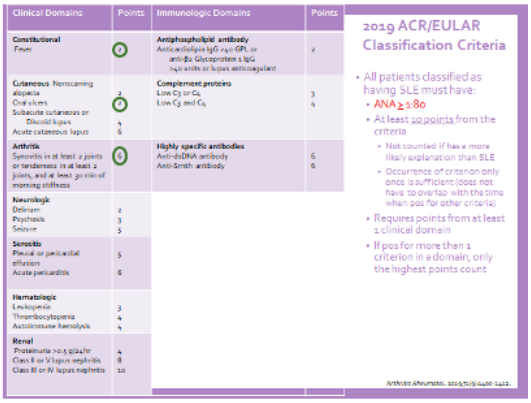
        - 24x higher risk of ischemic heart disease (accelerated course)
    - African Americans with SLE have a higher mortality than Caucasians with SLE
        - Mortality occurs 13 years (on avg) earlier in Blacks than White counterparts
- Systemic effects of SLE
    - In addition to affecting the skin and joints, SLE affects other organs systems, primarily the kidneys, the pleura of the lungs, pericardium, and central nervous system (CNS). Hematologic effects are also common.
        - Renal, cardiac, and CNS effects are typically the most serious manifestations
    - Many patients experience fatigue, weight loss, and fever
- Significant laboratory findings
    - Antinuclear antibody (ANA)
        - 99% sensitivity, but low specificity for SLE
            - ONLY order if clinical suspicion is present to avoid false positive results
            - Can be present in a variety of CTDs
            - Sometimes falsely positive in older individuals, and in those with autoimmune thyroid disease, chronic infections or malignancies
        - ANA levels do not correlate with disease activity
            - ANA does not become negative when the disease is quiescent and thus should typically not be repeated
    - Other serologic tests
        - Consider these if ANA is positive and clinical signs/symptoms of SLE are present
            - Anti-dsDNA and anti-Smith antibodies are most specific for SLE and support the diagnosis
                - Anti-dsDNA antibody may, or may not, fluctuate with disease activity
                - Anti-dsDNA antibodies may correlate with active lupus nephritis (renal disease)
            - Others that may help define subtypes of lupus or differentiate other diseases
                - Anti-SSA/Ro, anti-SSB/La antibodies are classically seen in SLE, SCLE, and Sjogren syndrome; sometimes in other CTDs
                - Antiphospholipid antibodies include lupus anticoagulant (LA) and anticardiolipin antibody and are markers of a hypercoagulable state
                - Anti-U1RNP antibody, though sometimes seen in SLE, is considered a marker for MCTD
    - Urinalysis is the most important and sensitive test for assessing renal involvement
        - Assesses presence of proteinuria, RBCs, active urinary sediment (blood cell casts or other casts)

        - Urinary protein-to-creatinine ratio can help quantify amount of proteinuria
    - Basic/comprehensive metabolic panel
        - Provides information about renal function, hepatic function, albumin, and electrolytes
    - ●CBC with differential
        - Necessary to look for hallmark hematologic effects of SLE
        - Leukopenia with lymphopenia, and sometimes neutropenia, are common
        - Autoimmune hemolytic anemia (DAT positive) and thrombocytopenia can be seen
    - Other lab findings:
        - Low complement (C3 and/or C4) levels in context of positive anti-dsDNA may suggest lupus nephritis
            - When C3 and/or C4 are low, SLE disease is active
        - Increased PTT may suggest the presence of a lupus anticoagulant and a hypercoagulable state
    - Skin biopsy
        - Commonly see an “interface dermatitis”
        - DIF commonly demonstrates IgA, IgG, or IgM deposits at the DEJ
    - Renal biopsy
        - Necessary if concerned about lupus nephritis (consider if >500mg proteinuria/day or if urinary sediment is “active” ie. shows cellular casts)
        - Can provide diagnostic and prognostic information depending on histologic findings

- Diagnostic criteria for SLE have been defined by various groups that require similar data with minor differences:
    - Criteria - by 1997 American College of Rheumatology (ACR) standards
        - Requires 4/11 findings from a variety of systems are shown below
        - 85% sensitive and 95% specific for correct diagnosis
        - Our patient meets the criteria with her clinical findings alone
        - 

    - Criteria - by 2012 Systemic Lupus International Collaborating Clinics standards

- Criteria combines clinical criteria with lab findings are shown below
- 95% sensitive and 90% specific for the diagnosis
- Our patient meets the criteria with combining her clinical and lab findings
- 

- Criteria - by 2019 ACR/European Alliance of Associations for Rheumatology (EULAR)
  - Criteria requires a positive ANA with titer of at least 1:80
  - Designed to allow earlier diagnosis
    - includes fever
    - Gives weight to more severe manifestations
  - Score of 10 or greater indicates SLE with 98% sensitivity and 97% specificity
  - Our patient meets these criteria as well
  - 

- Prognosis/natural history
  - SLE has a varied clinical course - from very mild to fulminate, fatal disease
  - Certain factors (i.e.: presence of renal disease, antiphospholipid antibodies, etc) affect the natural history
  - The mortality rate in patients with SLE are 2-5-fold greater than the general population
    - Current treatment strategies continue to lower the mortality rate
  - Mortality rates vary with respect to gender, age, socioeconomic factors and ethnicity
    - Men tend to have more fulminant disease and a higher mortality rate

        - Black patients have a higher mortality rate
    - Cardiovascular disease is the most common cause of death, followed by infection and fulminate SLE (affecting CNS / cardiac / renal systems)
        - Causes of death early in the disease are mostly from fulminate SLE, or infection from immune suppression
        - Causes of death later in the disease are more likely due to ESRD or cardiovascular disease
            - Leading cause of death 10 years after diagnosis is atherosclerosis/cardiovascular disease
    - Patients require serial monitoring of all organ systems to surveying for signs of organ damage

- **Major Types of Cutaneous Lupus Erythematosus**
- Acute cutaneous lupus
    - Acute cutaneous lupus is directly due to photosensitivity and is a sign of an acute flare of SLE
    - Photos
        - Photosensitivity on dorsal hands
        - Transient malar erythema

- Subacute cutaneous lupus erythematosus (SCLE)
    - SCLE has 2 major morphological presentations: 1) annular lesions; 2) papulosquamous plaques or papules that mimic psoriasis
    - Triggered by sun exposure, so sun exposed areas are mostly affected
        - Neck/extensor surface of the arms/back/chest)
    - Approximately 50% of patients have SLE, or will develop SLE
    - Most patients with SCLE will have anti-SSA/SSB (Ro/La) antibodies, even without a positive ANA or without SLE
    - Up to 30% of cases are drug-induced and not associated with SLE
    - Photos
        - Annular plaques
        - Hypopigmented plaques
        - Psoriasiform lesions

- Chronic cutaneous lupus erythematosus (discoid lupus erythematosus [DLE])
    - Only ~ 20% of patients with DLE have, or will develop, SLE
    - 80% will have skin only disease, which can be cosmetically devastating
    - DLE is more common in African American and Hispanic populations
    - Lesions are scarring
    - Both hypo- and hyperpigmentation can be seen
        - Lesional border is almost always hyperpigmented in people of color
    - Lesions are more common in photosensitive areas
    - Active lesions have erythema
    - Photos of:
        - Hypopigmented patch with hyperpigmented border

        - Conchal bowl
        - Plaques

- Neonatal lupus erythematosus
    - Neonatal lupus results from placental transfer of maternal antibodies anti-SSA (Ro), Anti-SSB (La), and possibly Anti-U1RNP, to the neonate
        - Has a 3% incidence in +Ro/La (SSA/SSB) pregnancies
    - Clinical manifestations in the neonate include
        - Erythematosus annular or arcuate macules, patches, or plaques on the skin
        - Congenital heart block (varies from 1st to 3rd degree)
    - Photos of
        - Annular plaques
        - Papules/plaques with scale

- Other cutaneous disorders associated with SLE
    - Vasculitis
    - Calcinosis cutis
    - Raynaud
    - Lupus panniculitis
    - Bullous lupus erythematosus
    - Oral ulcers

- Non-cutaneous findings in SLE
    - Serositis
    - Jacoud's arthropathy
    - Nephritis
    - CNS disease
    - Cardiac disease

CASE #2

- Case presentation
    - Clinical history
        - JR is a 62-year-old female (she/her/hers) complaining of progressive muscle weakness for the past month; she is having a difficult time combing her hair and climbing stairs. Over this same time frame, she has noted an unintentional 8 pound weight loss and has developed a very itchy, reddish rash that affects her face, chest, hands, arms and back.
    - Physical findings
        -
        - Photodistributed erythema and poikiloderma over the scalp, neck, arms, "V" of the chest, and upper back across the shoulders
        - Erythema over the DIP, PIP, and some MCP joints of both hands
        - Flat-topped, violaceous, scaly 3-5 mm papules over the DIP, PIP, MCP joints of both hands

        - Nailfold telangiectasia of proximal nail folds of fingers of both hands
        - Violaceous discoloration of upper eyelids
        - Diffuse weakness of proximal muscles

- Differential diagnosis
    - Dermatomyositis (DM)
    - Polymyalgia Rheumatica (PMR)
    - Systemic Lupus Erythematosus (SLE)
    - Systemic Sclerosis (SSc)
    - Fibromyalgia Syndrome (FMS)
    - Drug Eruptions (DE)
    - Seborrheic Dermatitis (SD)
    - Contact Dermatitis (CD)
    - Rosacea

- Significant laboratory results for this patient:
    - CBC and platelet count
        - Normal
    - CMP
        - Elevated AST and ALT (abnormal)
    - Urinalysis
        - Normal
    - ANA
        - (+) 1:80 (abnormal, but low titer)
    - Creatine kinase (CK) and aldolase
        - Both elevated (abnormal)
    - C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)
        - Both elevated (abnormal)
    - Anti-Mi-2
        - Positive (abnormal)
    - Anti-MDA5 and anti TIF1-gamma
        - Both negative (normal)
    - Anti-Jo-1 antibody
        - Negative (normal)
    - Anti-centromere antibody (ACA)
        - Negative
    - Anti-dsDNA, anti-Smith, histone, antiphospholipid antibodies
        - All negative (normal)
    - Coagulation studies (PTT)
        - Normal

- Skin biopsy:
    - Histologic findings of a skin biopsy, stained with H&E, demonstrated an interface dermatitis (abnormal)
        - DIF was negative (normal)

- Muscle biopsy

- Histologic findings demonstrated muscle fiber necrosis, a inflammatory cell infiltrate, and perimysial inflammation with CD4 T cells and perifascicular atrophy (abnormal)

- **Analysis of present data that support, or refute, the various diagnoses in the DfDx to determine the most likely diagnosis in this case:**

    - Dermatomyositis
        - <u>Supportive Data:</u>
            - Clinical
                - Photodistributed erythema and poikiloderma of shoulders and chest
                    - Shawl sign
                    - V-sign
                - Erythema of eyelids
                    - Heliotrope rash
                - Violaceous papules over the knuckles
                    - Gottron papules
                - Muscle weakness
                - Itch
                - Constitutional symptoms of malaise, weight loss
            - Laboratory
                - Elevated muscle enzymes
                    - CK, aldolase, AST, ALT
                - Elevated ESR / CRP
                - Elevated myositis antibody
                    - Anti-Mi-2
                - ACA will be negative in DM
            - Pathology
                - Skin biopsy showing interface dermatitis with negative DIF
                - Muscle biopsy showing inflammation and atrophy

        - <u>Non Supportive Data:</u>
            - None of the data refute the possible diagnosis of DM
            - Anti-Jo-1; anti-MDA5 or anti-TIF 1-gamma can be present or absent in DM. IF present in DM, each would identify a specific subset of DM

    - Polymyalgia Rheumatica (PMR)
        - <u>Supportive Data:</u>
            - Clinical
                - Constitutional symptoms
            - Laboratory
                - Elevated ESR / CRP - this are typically VERY high in PMR
                - ACA will be negative in PMR

        - Non Supportive Data:
            - Clinical
                - Muscles are more stiff and painful than weak in PMR
                - There is no photosensitive rash associated with PMR
            - Laboratory
                - There are no specific lab tests to diagnose PMR
                - ANA is typically negative in PMR
                - Anti-Jo-1 antibody is variably present in PMR
                - Muscle enzymes are not usually elevated in PMR
                - Skin biopsy would not show an interface dermatitis

- Systemic Lupus Erythematosus (SLE)
    - Supportive Data:
        - Clinical
            - Photosensitivity - including heliotrope rash
            - Nail fold telangiectasia
            - Muscle weakness
            - Constitutional symptoms
        - Laboratory
            - (+) ANA - but often higher titer in SLE
            - ACA will be negative in SLE
            - Skin biopsy would show an interface dermatitis
    - Non Supportive Data:
        - Clinical
            - Erythema on hands is usually BETWEEN the joints in SLE, not over the joints as in this case
            - Poikiloderma, present here, is rare in SLE
            - Gottron papules are not seen in SLE
        - Laboratory
            - (+) ANA
            - Likely to have other antibodies present in SLE (for example, anti-dsDNA antibody and anti-Smith antibody)
            - Other organ system involvement is often present in SLE
            - Skin biopsy would show an interface dermatitis with (+) DIF

- Systemic Sclerosis (SSc / Scleroderma)
    - Supportive Data:
        - Clinical
            - Constitutional symptoms
            - Nail fold telangiectasia
            - (+) Itch
        - Laboratory
            - (+) ANA can be seen in SSc

            - Sometimes ESR/ CRP are elevated in SSc
        - Non Supportive Data:
            - Clinical
                - Photosensitivity is not seen in SSc
                - Gottron papules and heliotrope rash are not seen in SSc
                - Lack of skin findings associated with SSc: skin tightening/sclerodactyly; Raynaud phenomenon
                - Lack of visceral symptoms often associated with SSc: dyspnea, difficulty swallowing, hypertension, etc
            - Laboratory
                - Elevated muscle enzymes are not often seen in SSc
                - Lack of (+) anti-Jo-1 antibody that can be seen in SSc and defines a subset of SSc
                - Lack of (+) ACA antibody that is commonly present in SSc and defines a subset of SSc
                - Skin biopsy would not show an interface dermatitis with (+) DIF

- Fibromyalgia Syndrome (FMS)
    - Supportive Data:
        - Clinical
            - Generalized weakness
        - Laboratory
            - There are no specific lab tests to diagnose FMS
            - Labs are mostly normal in FMS
    - Non Supportive Data:
        - Clinical
            - No objective muscle weakness noted in FMS
            - No true constitutional signs/symptoms (ie. weight loss) in FMS
            - There are no characteristic skin findings for FMS
            - Muscles are often tender to palpation in FMS
            - Sleep disturbances are usually described in FMS
        - Laboratory
            - Muscle enzymes are normal in FMS
            - ESR/ CRP are typically normal in FM
            - Skin biopsy would not show an interface dermatitis with (+) DIF

- Drug Eruptions (DE)
    - Supportive Data:
        - Clinical
            - Many drugs can cause a photosensitizing rash
            - Itch is common a morbilliform drug reaction

- Laboratory
    - Most labs would be normal
- Non Supportive Data:
    - Clinical
        - One would not see the skin findings described here: poikiloderma, heliotrope rash, Gottron papules
        - This patient is on no medications
    - Laboratory
        - The only lab abnormality that would be expected would be an elevated eosinophil count - not described here.
        - Would not see any of the laboratory abnormalities described here
        - Skin biopsy would not show an interface dermatitis with (+) DIF

- Seborrheic Dermatitis (SD)
    - Supportive Data:
        - Clinical
            - Erythematous rash that can affect the scalp, face and mid chest
            - Sometimes there is significant itch of the scalp
        - Laboratory
            - All labs would be normal - there are no lab abnormalities associated with SD
    - Non Supportive Data:
        - Clinical
            - SD would not have any constitutional symptoms
            - Weakness is not associated with SD
            - One would not see the other skin findings described here: photosensitivity, heliotrope rash, Gottron papules
        - Laboratory
            - There are no lab abnormalities associated with SD
            - Skin biopsy would not show an interface dermatitis with (+) DIF

- Contact Dermatitis (CD)
    - Supportive Data:
        - Clinical
            - Erythema
            - Itch
        - Laboratory
            - None - There are no lab abnormalities associated with CD
    - Non Supportive Data:
        - Clinical

- The rash of CD is typically more localized than generalized as described here
- One would not see the other skin findings described here: photosensitivity, heliotrope rash, nail fold telangiectasia, Gottron papules, etc
- Other constitutional symptoms would not be seen
- There is no history of exposure to a contactant
- One often see vesicles in contact dermatitis; not described here

- Laboratory
  - There are no lab abnormalities associated with CD
  - Skin biopsy would not show an interface dermatitis with (+) DIF

- Rosacea
  - Supportive Data:
    - Clinical
      - Facial erythema; sometimes affects the scalp or chest
      - Photosensitivity of face
    - Laboratory
      - None - There are no lab abnormalities associated with rosacea
  - Non Supportive Data:
    - Clinical
      - In rosacea one sees central facial erythema, often associated with facial telangiectasia, papules and pustules
      - Though patients are photosensitive, there are other triggers that cause a flush / blush reaction
      - One would not see the other skin signs described here
      - There are no constitutional symptoms associated with rosacea
    - Laboratory
      - There are no lab abnormalities associated with rosacea
      - Skin biopsy would not show an interface dermatitis with (+) DIF

Considering all the clinical and laboratory findings that are present, the most likely diagnosis is:

Dermatomyositis

Diagnosis / Discussion: Dermatomyositis

- Pathophysiology

    - A multisystem autoimmune disorder characterized by photosensitivity, poikiloderma, heliotrope rash, nailfold telangiectasia and proximal muscle weakness
    - Some subsets have an increased risk of malignancy of up to 40%
    - Other subsets have an increased risk for severe interstitial lung disease
- Epidemiology
    - Higher prevalence in females, with a female:male ratio of 2:1
- Characteristic laboratory abnormalities
    - CK and aldolase - typically elevated with active myositis
    - AST, ALT, LDH - are often elevated; markers of muscle inflammation (as well as liver)
    - ESR - elevated, nonspecific marker of inflammation
    - Electromyography (EMG)
        - Documents the presence of an inflammatory myopathy with increased membrane irritability
- Skin biopsy
    - Demonstrates an interface dermatitis. DIF is usually negative.
- Muscle biopsy
    - Muscle fiber necrosis, degeneration, regeneration, inflammatory cell infiltrate; perimysial inflammation with CD4 T cells, perifascicular atrophy is classic
- Characteristic autoantibodies
    - Table: Specific vs associated antibodies
    -

Antibody	Association	Prevalence
Anti-tRNA synthetase (Jo-1)	Dermatomyositis, interstitial lung disease, "mechanic's hands"	20%
Anti-SRP (signal recognition protein)	African American women, poor prognosis	Rare
Anti-Mi-2	Older women, "shawl sign", good prognosis	5%
PM/SCL	Polymyositis/scleroderma overlap	rare
Anti-MDA-5	Clinically amyopathic DM (CADM), strongly associated with interstitial lung disease (rapidly progressive), arthritis and skin ulcerations	
Anti-TIF-1 gamma	Associated with extensive skin disease and increased risk of cancer	
Anti-HMGCR	Similar phenotype to anti-SRP (necrotizing myositis with little inflammatory infiltrate); associated with statin use in ~50%	

- Summary of autoantibodies
    - Anti-Mi-2
        - First DM-specific autoantibody recognized
        - Most common in the classic forms of DM, commonly with markedly elevated muscle enzymes and classic skin findings
        - Associated with a positive prognosis and a good response to corticosteroids

    - Anti-MDA5
        - Associated with rapidly progressive interstitial lung disease
        - Skin disease usually includes cutaneous ulceration, rare in other forms of DM
        - Is more common in Causasian and Asian females (genetic females)
        - Curiously, muscle disease is minor in this subset
    - Anti-TIF-1 gamma
        - Associated with malignancy
    - Anti-Jo-1
        - Its presence suggests a condition called “antisynthetase syndrome” manifested by:
            - Inflammatory myositis
            - Interstitial lung disease
            - Arthritis
            - Sometimes with DM; skin findings include “mechanic’s hands”
- Prognosis / natural history
    - Highly variable from skin-only changes to fulminate disease
    - Factors such as older age, delay in diagnosis, underlying malignancy are associated with a worse prognosis
    - Specific antibodies may identify subsets at risk for associated conditions
        - (see above)
    - Some antibodies may predict treatment responses
    - Patients at risk for malignancy require extensive monitoring for malignancy every 6 months for up to 5 years, including (some serially, some less often) including:
        - Colonoscopy
        - Chest x-ray
        - Pelvic CT or ultrasound in genetically female patients
        - Possible chest / abdomen / pelvic CTs
        - Mammograms
    - Patients at risk of interstitial lung disease require serial monitoring as well; consider:
        - Chest x-rays or CTs
        - Pulmonary function tests with diffusion capacity, etc
- Characteristic dermatologic findings in dermatomyositis:
    - Gottron papules
    - Heliotrope rash
    - Shawl sign
    - V sign
    - Mechanic’s hand
    - Holster sign
    - Facial erythema
    - Calcinosis cutis
    - Nail fold telangiectasia

CASE #3

- Case presentation
    - Clinical history

        - Y is a 35-year-old nonbinary individual (they/them/theirs) who presents with fatigue, dyspnea and the inability to completely extend their fingers because of “tightness.” They also report cold-induced changes of the fingers and toes for the past few years during which the digits turn white, blue, and then red. More recently, the patient has noted a dry cough and significant shortness of breath when going up a flight of stairs. Further questioning revealed a mild, but progressive, dysphagia over the same time frame.
    - Physical findings
        - Elevated blood pressure of 158/90 mmHg with a pulse of 72 bpm
        - Tightness of the skin of the face and forearms
        - Sclerotic changes of the fingers and hands (sclerodactyly)
        - Contractures of both hands (Inability to make a fist as well as inability to fully extend fingers)
        - Nail fold telangiectasia
        - Dyspigmentation
- Differential diagnoses
    - Systemic sclerosis / Scleroderma (SSc)
    - Mixed Connective Tissue Disease (MCTD)
    - Stiff Skin Syndrome (SSS)
    - Systemic Lupus Erythematosus (SLE)
    - Dermatomyositis (DM)
    - Morphea

- Significant laboratory results for <u>this patient</u>:
    - CBC and platelet count
        - Mild anemia (abnormal)
    - CMP
        - Elevated serum creatinine (abnormal)
    - Urinalysis
        - Mild proteinuria (abnormal)
    - ANA
        - (+) 1:80 (abnormal, but low titer)
    - Anti-centromere antibody
        - Negative (normal)
    - Anti-Scl-70 antibody
        - Positive (abnormal)
    - dsDNA, SSA/SSB, and antiphospholipid antibodies
        - All negative (normal)
    - Coagulation studies
        - All normal

- Skin biopsy:
    - Histologic findings of a skin biopsy stained with H&E demonstrated expansion of the dermis (excessive collagen) with associated dermal edema and some perivascular mononuclear inflammatory cell infiltration and fibrosis (abnormal). DIF will be negative (normal).

- **Analysis of present data that support, or refute, the various diagnoses in the DfDx to determine the most likely diagnosis in this case:**

    - Systemic Sclerosis / Scleroderma (SSc)
        - Supportive Data:
            - Clinical
                - Raynaud phenomenon
                - Tight skin of face and forearms
                - Sclerodactyly
                - Nail fold telangiectasia
                - Dyspigmentation
                - Hypertension (HTN)
                - Dyspnea
                - Fatigue
            - Laboratory
                - Mild anemia
                - Mild proteinuria (not within the nephrotic range)
                - (+) ANA
                - (+) Anti-Scl-70
                - Skin biopsy demonstrates excessive collagen
        - Non supportive Data:
            - Clinical
                - None of the data refute the possible diagnosis of SSc
            - Laboratory
                - None of the data refute the possible diagnosis of SSc

    - Mixed Connective Tissue Disease (MCTD)
        - Supportive Data:
            - Clinical
                - Dyspnea
                - Dysphagia
                - Nail fold telangiectasia
                - Fatigue
            - Laboratory
                - Mild proteinuria
                - Mild anemia
                - (+) ANA
        - Non Supportive Data:
            - Clinical
                - Dyspigmentation
                - Contractures
            - Laboratory
                - ACA and anti-Scl-70 would be rare in MCTD
                - Would see a strongly (+) anti-U1RNP
                - Skin biopsy would not demonstrate excessive collagen

- Stiff Skin Syndrome (SSS)
  - Supportive Data:
    - Clinical
      - Tight skin
      - Joint immobility
    - Laboratory
      - None -There are no lab abnormalities associated with SSS
  - Non Supportive Data:
    - Clinical
      - SSS presents in infancy or early childhood
      - Affects the entire skin surface
    - Laboratory
      - Genetic testing for SSS is lacking
      - There are no other lab abnormalities associated with SSS

- Systemic Lupus Erythematosus (SLE)
  - Supportive Data:
    - Clinical
      - Raynaud phenomenon
      - Nail fold telangiectasia
      - Fatigue
    - Laboratory
      - (+) ANA
      - Anemia
  - Non Supportive Data:
    - Clinical
      - Lack of photosensitivity and other skin findings of SLE
    - Laboratory
      - Anti-Scl-70 antibodies would be rare in SLE
      - Lack of other laboratory markers for SLE
      - Skin biopsy would not demonstrate excessive collagen

- Dermatomyositis (DM)
  - Supportive Data:
    - Clinical
      - Constitutional symptoms
      - Nail fold telangiectasia
    - Laboratory
      - (+) ANA
  - Non Supportive Data:
    - Clinical
      - Lack of photosensitivity and other skin signs of DM
      - Lack of muscle weakness

- Laboratory
    - Anti-Scl-70 antibodies would be rare in DM
    - Lack of laboratory markers for myositis
    - Skin biopsy would not demonstrate excessive collagen
- Morphea
    - Supportive Data:
        - Clinical
            - Skin thickening
        - Laboratory
            - Skin biopsy would demonstrate excessive collagen
    - Non Supportive Data:
        - Clinical
            - Lack of systemic involvement
            - Skin changes in morphea are localized plaques, typically isolated plaques, not more generalized as described here
        - Laboratory
            - There are no lab abnormalities associated with morphea

Considering all the clinical and laboratory findings that are present, the most likely diagnosis is:

Systemic sclerosis

Diagnosis / Discussion: Systemic Sclerosis (SSc)

- Pathophysiology
    - Autoimmune, multisystem disease characterized by various autoantibodies, excessive collagen deposition, vascular abnormalities, and visceral involvement
    - Associated with excessive fibrosis of skin and internal organs
- Epidemiology
    - Higher prevalence in females with a female:male ratio of 3:1
    - Most commonly occurs between 30-50 years of age
    - Patients of African descent can present at an earlier age
- 2 Major subsets of SSc (termed limited and diffuse), defined primarily by skin involvement:
    - Both forms have the following:
        - Sclerosis of skin in a stocking/glove (acral) distribution
            - Contractures of hands
            - Loss of range of motion of wrists / ankles
        - Facial tightness
            - Reduction of oral commissure
            - Reduction of wrinkles
        - Salt and pepper depigmentation of any skin surface
            - “Vitiligo- like” color loss; with retention of color around the hair follicles

        - Nail fold telangiectasia
        - Pulmonary disease and pulmonary hypertension
        - Raynaud phenomenon
            - Seen in various CTDs
            - Most common, and usually more severe in SSc
            - Classically has a triphasic color change due to the vascular response to cold: white, blue, red
            - May progress to painful crises with ulceration and necrosis, leading to autoamputation
            - It can also be seen in the absence of systemic disease
                - Then termed Raynaud disease
            - There is a strong association with smoking

    - Limited SSc - defined by skin disease that is limited to the acral presentation (arms / hands/ legs / feet / face)
        - Pulmonary HTN is more common than interstitial lung disease
        - Includes the CREST syndrome
            - **C**alcinosis cutis, anti-centromere antibody
            - **R**aynaud phenomenon
            - **E**sophageal dysmotility
            - **S**clerodactyly
            - **T**elangiectasia (which can be widespread)

    - Diffuse SSc - defined by the same changes described above but with a more generalized involvement, often has rapidly progressive skin changes
        - Widespread cutaneous sclerosis, affecting the torso, as well as the acral areas
        - Generally a more extensive disease with respect to, not only the skin, but also widespread vascular involvement affecting the lungs, heart, kidneys, gastrointestinal and musculoskeletal systems
        - May be associated with “scleroderma renal crisis” consisting of:
            - Rapidly progressive skin changes
            - Malignant hypertension
            - Rapidly progressive renal failure

- Localized scleroderma (AKA morphea)
    - Totally different disease than SSc, but has a very similar name which allows for the confusion.
    - A form of skin-only scleroderma that can cause localized and isolated sclerotic plaques on the skin
    - There are no systemic consequences
    - This does NOT evolve into SSc, so it is critical to understand and explain the differences, despite the highly similar names

- Characteristic laboratory abnormalities of SSc
    - CBC
        - Mild anemia is common due to various organ effects
    - CMP
        - Elevated BUN/ Cr - depending on degree of renal dysfunction
    - Urinalysis - mild proteinuria (not nephrotic range)

- Characteristic skin biopsy in SSC
    - Typically demonstrates excessive dermal collagen as well as intimal proliferation of vessels. Sometimes calcium deposits are present.

- Characteristic autoantibodies of SSc
    - ANA
        - (+) low titer common
    - Anti-centromere antibody (ACA)
        - Occurs in only 20-30% of patients with SSc
            - Considered specific for the diagnosis of SSc
        - Frequency varies with ethnicity of patient
            - Highest in Caucasians
            - Lower in Hispanics, African Americans
        - Most commonly associated with limited SSc
            - Most commonly CREST syndrome
        - Marker for a better prognosis overall
        - Does not fluctuate with disease activity
    - Anti-Scl 70 (AKA: anti-topoisomerase I)
        - Occurs in only 15-20% of all patients with SSc
            - Never seen in healthy patients
            - Rarely seen in other CTDs
        - Present in 40% of patients with diffuse SSc and only 10% of patients with limited SSc
            - It is extremely rare for a patient to have both ACA and anti-Scl 70 antibodies
        - Frequency unrelated to ethnicity
        - Associated with more severe pulmonary fibrosis / interstitial lung disease
        - Patients have a higher SSc-associated mortality rate

- Characteristic studies can evaluate organ involvement in SSc, or other CTDs affecting the same organ systems:
    - Pulmonary
        - Chest x-ray or CT can detect changes of interstitial lung disease
        - Pulmonary function tests including diffusion capacity can define lung function
    - Cardiac

        - Echocardiogram can evaluate cardiac function and pulmonary pressures (pulmonary HTN)
        - Right heart catheterization might be needed to evaluate cardiac effects or pulmonary HTN
    - Gastrointestinal (GI)
        - Barium swallow with manometry to evaluate dysphagia
        - Upper and lower endoscopies can evaluate for malignancy
    - Renal
        - BP monitoring
        - Serial metabolic profiles and urinalysis

- Prognosis / natural history of SSc
    - Highly variable and depends upon the form of SSc, as well as the severity of organ involvement
    - Limited SSc
        - Slower disease progression
        - Skin manifestations limited to face, hands, and fingers
        - Extracutaneous organ manifestations may occur - mainly as CREST syndrome; includes pulmonary fibrosis and pulmonary HTN
    - Diffuse SSc
        - Rapid disease progression is more common
        - Systemic organ involvement - fibrosis of internal organs is common
            - Lung - interstitial lung disease, pulmonary hypertension
            - Renal - scleroderma renal crisis
            - Microangiopathic hemolytic anemia
            - Cardiac - fibrosis, pericarditis, myocarditis
            - GI - esophageal and small bowel dysmotility
    - Leading cause of death is pulmonary fibrosis

- Cutaneous manifestations of SSc
    - Salt and pepper (vitiligo-like) depigmentation
    - Decreased oral aperture
    - Sclerodactyly
    - Calcinosis cutis
    - Telangiectasias - nail fold and facial

Review of Dermatologic Findings

Photosensitivity is seen in DM and SLE, but manifests differently

Malar rash = SLE

Heliotrope rash = both DM and SLE

Shawl sign, holster sign – DM

Erythema over the joints – DM

Erythema between the joints - SLE

DLE is the most common skin finding of lupus; but only ~ 20% of patients have SLE

The presence of cutaneous ulcers in DM is more common with the presence of anti-MDA5

Nail fold telangiectasia are seen in: SLE, MCTD, DM, SSc *RA- sometimes

Gottron papules are pathognomonic for DM

Vitiligo-like depigmentation is seen in SSc

Review of Auto-Antibodies

ANA can be seen in all CTD, but high titers more common in SLE
Anti-dsDNA and anti-smith are most specific for SLE
    Anti-dsDNA may be a marker for lupus nephritis
Anti-U1-RNP can be seen in several CTD but is most specific for MCTD
Anti-Mi-2; anti-MDA5 and anti TIF1-gamma are significant auto-antibodies for DM
    Anti-Mi-2 is most common in classic DM
    Anti-MDA5 is a marker for severe interstitial lung disease
    Anti-TIF1-gamma is a marker for malignancy
Anti-Jo-1 can be seen in various CTD and is a marker for lung disease
    Associated with antisynthetase syndrome, especially with DM
ACA and anti-Scl 70 are most specific for SSc
    ACA is associated with limited SSc and pulmonary HTN more than interstitial lung disease
    Anti-Scl 70 is associated with diffuse SSC, lung disease and a worse prognosis

Summary

Having completed this module the learner can do the following:

- Identify characteristic skin findings associated with different CTDs in various skin types
- Identify what labs to order and how to interpret results to help make the diagnosis
- Recognize when and how to evaluate for associated conditions such as lung disease, malignancy, etc
- Outline several social determinants of health that influence morbidity and mortality of different patient populations