Immune-mediated Disorders

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Bullous Pemphigoid

What Not To Miss

- Drug induced
  - PEARL: PF ChaNGs—Penicillamine, PCN derivatives, PUVA, furosemide, captopril, NSAIDs, gold, sulfasalazine
- Early Disease
  - Urticarial plaques or pruritus alone can be early manifestation, especially in the elderly

Key DDx

- Diabetic bullae
- Bullous impetigo
- Bullous insect bite reaction
- Epidermolysis Bullosa Acquisita
- Pemphigus Vulgaris
- Cicatricial pemphigoid
- Allergic contact dermatitis
- Bullous drug eruption
- Porphyria cutanea tarda or pseudoporphyria

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Work Up Pearls

- Do two biopsies
  - One for H&E (lesional—edge of a blister)
  - Second for immunofluorescence (perilesional)
    - Ideally, a lesion less than 72 h old
    - PEARL: If only urticarial lesions, DIF should be lesional
- Serum tests used if biopsy is inconclusive
  - Some areas, such as scalp, that may have extensive excoriation, may show nonspecific biopsy and negative DIF so IIF can be diagnostic in these cases
  - IIF for circulating anti-BMZ IgG
  - ELISA to detect Ab to BP180 and BP230
    - ELISA can also be used to monitor disease activity

Treatment Ladder

- Mild-moderate disease
  - High potency topical steroids (Class I)
    - Can be used as monotherapy in severe disease [1]
  - Minocycline or doxycycline 100 mg twice daily [2] with or without niacinamide 0.5–2.0 g three times daily
- Moderate-severe disease
  - Prednisone taper (slow), consider starting steroid sparing agent at or shortly after starting oral prednisone [3]
    - 0.5–1.0 mg/kg daily controls disease over 1–3 weeks, slowly taper once disease is controlled over 3 months
  - Methotrexate 10–25 mg weekly
    - Need lower doses in elderly and CKD patients [4]
  - Mycophenolate mofetil 1–3 g per day, divided twice daily [5]
  - Dapsone for mucosal-predominant or neutrophil/eosinophil-rich BP [6]: 50–200 mg daily
  - Azathioprine [5] titrate up to dose of 2.5 mg/kg daily
- Severe or refractory disease
  - IVIG [7] 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months
  - Pulse solumedrol 2 gm IV total, divided over 3–5 days
  - Rituximab 1000 mg once and repeated in 2 weeks is 1 cycle [8, 9]
    - Patients often need more than 1 cycle
    - May need to continue second immunosuppressive until rituximab starts to work
    - Consider ordering CD20 lab after infusion to assess effect of medication
  - Omalizumab 150–300 mg every 4 weeks [10]

Dermatomyositis

What Not To Miss

- Drug induced
  - Hydroxyurea (MC), statins, D-penicillamine, cyclophosphamide, BCG vaccine, TNF-α inhibitors
- Occult malignancy
  - Up to 40% of adults may have an occult malignancy
  - Strong association with ovarian cancer in women
- Amyopathic DM
  - Must do pulmonary and malignancy work up
- DM associated with anti-MDA5 antibody
  - Can be fatal
  - Painful palmar papules, ulcerations in oral mucosa and overlying Gottron's papules on elbows/knees
  - Rapidly progressive interstitial lung disease, panniculitis, arthritis, less muscle involvement [11]
    - ILD diagnosed with PFTs with DLCO (diffusing capacity of the lungs for carbon monoxide) and high resolution chest CT if needed
- Children with DM can present with calcinosis cutis

Key DDx

- Systemic lupus erythematosus
- Mixed connective tissue disease
- Phototoxic/photoallergic drug eruption
- PMLE
- Contact dermatitis
- CTCL

Work Up Pearls [12–14]

- Clinical findings
  - Cutaneous findings: heliotrope rash, Gottron's papules overlying joints of hands, photosensitivity, poikiloderma, shawl and V sign, holster sign, calcinosis cutis, mechanic's hands, dilated capillary loops of nail folds, jagged cuticles, scalp erythema and scaling

- Muscle disease: progressive symmetric proximal muscle weakness +/− esophageal muscles (dysphagia), cardiac disease (mostly subclinical EKG findings)
- Other: pulmonary (15–65% with interstitial lung disease), arthralgia/arthritis
- Remember DM can cause panniculitis and vasculitis in addition to the more common cutaneous manifestations
- Also consider dermatomyositis in the differential of intractable scalp pruritus/dysesthesia

- Labs
  - +ANA in 40%, CK, aldolase, CBC, CMP, TSH, UA
  - Antibodies to consider
    - Anti-Mi-2, anti-Jo-1, anti-SRP, anti-NXP-2, anti-PM-Scl, anti-Ku, anti-MDA5, anti-TIF-1-γ, anti-U1RNP

- Diagnostics
  - PFTs with diffusing capacity of the lungs for carbon monoxide (DLCO), EMG, MRI or muscle biopsy, ECG, barium swallow (if esophageal symptoms).
  - Cancer screenings (age appropriate): CT chest/abdomen/pelvis, transvaginal/testicular ultrasound, colonoscopy, pap smear and mammogram.

- Biopsy
  - PEARL: Can be identical to lupus erythematosus

Treatment Ladder

- Skin-limited disease
  - 1st line (will not treat muscle disease): photoprotection, topical CS/CNI +/− hydroxychloroquine 5 mg/kg daily up to 200 mg twice daily; Caution: 30% of patients will get cutaneous drug eruption
  - 2nd line: systemic steroids, methotrexate, mycophenolate mofetil, IVIG

- Skin + muscle disease
  - 1st line:
    - systemic steroids [15] (slow taper) 0.5–1.0 mg/kg daily controls disease over 1–3 weeks, slowly taper once disease is controlled over 3 months
    - Methotrexate [16] 10–25 mg weekly
    - Mycophenolate mofetil 1.0–3.0 g daily, divided into twice daily dosing [15]
    - Azathioprine [17] titrate up to dose of 2.5 mg/kg daily
  - 2nd line: IVIG [18] 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months

  - Other: rituximab, cyclophosphamide, cyclosporine, leflunomide, chlorambucil, tacrolimus
  - If interstitial lung disease: steroids, rituximab, cyclophosphamide

- Monitoring
  - Malignancy screens [13]
    - Most important within first 2 years, risk decreases 5 years after dx
  - Review of systems

Outside the Box Treatment Options

- Tofacitinib for refractory patients
- PEARL: TNF inhibitors are contraindicated as they can worsen myositis

Lupus Erythematosus

What Not To Miss

- Active systemic involvement
  - Malar rash can be a sign so need at least CBC, CMP and UA
- PEARL: Malar rash is persistent (vs. rosacea which waxes and wanes) and spares the nasolabial folds (vs. dermatomyositis and seborrhea, which involve NLF)
- Drug induced
  - Procainamide, hydralazine, isoniazid, d-penicillamine, minocycline, TNF-α inhibitors
- Rowell Syndrome [19]
  - EM-like lesions in a lupus patient
  - +ANA, Anti-Ro, RF

Work Up Pearls

2012 SLICC criteria: need 4, at least 1 clinical and 1 immunologic OR biopsy proven lupus nephritis and +ANA or dsDNA [20]	
Dermatologic	ACLE, CCLE, non-scarring alopecia, oral/nasal ulcers
Systemic	Synovitis, serositis, renal, neurologic
Hematologic	Hemolytic anemia, leukopenia/lymphopenia, thrombocytopenia
Immunologic	ANA, anti-dsDNA, anti-Sm, antiphospholipid, low complement (C3, C4 or CH50), direct Coombs' test

- Labs including CBC with diff, CMP, UA with microscopy, ANA, dsDNA, Ro/La, Sm, RNP, anti-phospholipid Abs (anticardiolipin, b2-glycoprotein, lupus anticoagulant), C3/C4, CH50, ESR, CRP, +/− anti-histone (drug-induced), anti-U1RNP
  - Anti-dsDNA—nephritis, CNS
  - Anti-Smith—most specific for SLE
  - Ro and La—photosensitivity, Rowell's, SCLE
  - Ro—counsel females of child bearing potential risk of neonatal lupus
    - If positive, refer to maternal-fetal-medicine or high-risk OB
- Skin biopsy
- Multidisciplinary evaluation based on lab abnormalities
  - Particularly rheumatology and nephrology
  - Cardiology and pulmonary as needed based on review of symptoms

Treatment Pearls [21]

- Preventive interventions: smoking cessation, photoprotection
- Mild disease
  - Hydroxychloroquine 5 mg/kg daily actual body weight (max 400 mg daily)
  - Chloroquine <2.3 mg/kg daily
  - Quinacrine 100 mg once daily
  - NSAIDs
  - Prednisone 5–15 mg daily for mild-moderate disease
- Moderate-severe
  - Prednisone 1–2 mg/kg daily, can do IV pulse methylprednisolone 0.5–1.0 g daily for 3 days in acutely ill patients
  - Methotrexate 10–15 mg weekly
  - Azathioprine titrate up to dose of 2.5 mg/kg daily
- Severe disease with major organ involvement
  - High dose prednisone + cyclophosphamide
  - Mycophenolate mofetil 1–3 g per day, divided into twice daily dosing
  - Azathioprine titrate up to dose of 2.5 mg/kg daily
- Other
  - Thalidomide
    - PEARL: Thalidomide requires Thalomid REMS program
  - Lenalidomide
  - Dapsone

Out of the Box Treatment Options

- Recalcitrant disease
  - Rituximab or belimumab
  - Abatacept

- anti-IL-6 Ab
- anti-IL-10 Ab
- Ustekinumab
- JAK inhibitors such as tofacitinib 5 mg twice daily
- IVIG 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months
- Clinical trials

Discoid Lupus Erythematosus

What Not To Miss

- Progression to SLE
  - Widespread (above and below the neck) and childhood DLE have higher rates of progression [22]
- Squamous cell carcinomas
  - May form in chronic DLE scars

Key DDx

- Scalp: tinea capitis, CCCA, lichen planopilaris
- Face/body: seborrheic dermatitis, sarcoidosis, PMLE, granuloma faciale, Jessner's, burn scar, syphilis

Diagnostic Pearls

- Review of systems
- Rare to see DLE below the neck if there is not involvement above the neck
- ANA+ in 5–25%

Treatment Ladder [23, 24]

- Treat aggressively if active disease given risk for scarring
- Camouflage cosmetics
- Strict photoprotection
- Topical
  - Topical or intralesional steroids
- Systemic
  - Hydroxychloroquine 5 mg/kg daily up to 200 mg twice daily
  - Chloroquine < 2.3 mg/kg daily
  - +/− quinacrine 100 mg daily

- Refractory disease
  - Methotrexate 10–20 mg weekly
  - Retinoids: acitretin 10–50 mg daily, isotretinoin 0.5–1.0 mg/kg daily
  - Systemic steroids (not recommended long term): 20–40 mg daily
  - Mycophenolate mofetil 1–3 g per day, divided into twice daily dosing
  - Dapsone 25–2'00 mg daily

Out Of The Box Treatment Options

- Severe refractory disease: thalidomide, lenalidomide, IVIG

Subacute Cutaneous Lupus

What Not To Miss

- Progression to SLE
  - Up to 30–50% can progress
  - Often is mild disease
- Drug induced in up to 1/3 of cases [25]
  - Hydrochlorothiazide, terbinafine, griseofulvin, statins, NSAIDS, CCBs, antihistamines, PPIs, docetaxel, ACE-I, TNF-alpha inhibitors, many others

Key DDx

- Erythema annulare centrifugum
- Erythema multiforme
- Annular psoriasis
- Secondary syphilis
- Tinea corporis
- PMLE

Diagnostic Pearls [26]

- Anti-Ro/SS-A (75–90%), Anti-La (30–40%), ANA (60–80%, usually speckled)
  - More common in Caucasians (vs. DLE)

Treatment Ladder [23, 24]

- 1st line localized disease
  - Diligent photoprotection
  - Topical corticosteroid
  - Hydroxychloroquine 5 mg/kg daily up to 200 mg twice daily

- 1st line severe disease
  - Topical corticosteroid
  - Hydroxychloroquine 5 mg/kg daily up to 200 mg twice daily + systemic corticosteroids
- 2nd line—add
  - Quinacrine 100 mg daily
  - Methotrexate 10–25 mg weekly
  - Retinoids: acitretin 10–50 mg daily, isotretinoin 0.5–1.0 mg/kg daily
  - Dapsone 25–200 mg daily
  - Mycophenolate mofetil 1–3 g per day, divided twice daily

Out Of The Box Treatment Options

- Thalidomide for severe disease

Pemphigus Vulgaris

What Not To Miss [27]

- Drug induced
  - Thiol/sulfa containing drugs, penicillamine, captopril, cephalosporins, gold, rifampin, indocin, penicillin, piroxicam, pyritinol, pyrazolone derivatives, enalapril, aspirin
- Mucosal involvement
  - Ask about and examine ALL mucosal surface areas
  - Consider consultation with ophthalmology, dentistry/ENT, gynecology/urology

Key DDx

- Paraneoplastic pemphigus
- Pemphigus foliaceus
- Bullous pemphigoid
- Cicatricial pemphigoid
- Erythema multiforme
- Stevens-Johnson syndrome
- Mycoplasma-induced rash and mucositis
  - PEARL: More common in young males

Diagnostic Pearls

- Nikolsky sign and Asboe-Hansen sign
- Biopsy

- Lesional H&E
- Perilesional DIF

- Serum to support diagnosis and monitor disease activity
  - ELISA (Dsg 1 and 3)
  - IIF (monkey esophagus)

Treatment Ladder [28, 29]

- First line
  - Systemic steroids + steroid sparing agent
  - Glucocorticoids 1.0–1.5 mg/kg daily
    - When no new lesions form, taper very slowly over months
  - Rituximab 1000 mg once and repeated in 2 weeks is 1 cycle, repeat cycles every 6 months may be necessary
    - Emerging data supports this as first line with systemic steroids
  - Azathioprine titrate up to dose of 2.5 mg/kg daily
  - Mycophenolate mofetil 2–3 g daily
- Refractory disease
  - Methotrexate 10–25 mg weekly
  - Dapsone 50–200 mg daily
  - Cyclophosphamide 1–3 mg/kg daily
  - Cyclosporine 2.5–5.0 mg/kg daily
  - IVIG (may be combined with rituximab): 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months

Out Of The Box Treatment Options

- Plasmapheresis or plasma exchange
- Immunoadsorption

Psoriasis, Cutaneous

What Not To Miss

- HIV infection
  - Can precipitate or worsen existing psoriasis
- Associated disorders
  - Cardiovascular disease
  - Metabolic syndrome
  - NASH
  - Lymphoma
  - Mood disorders
  - May need multidisciplinary care

- Erythrodermic or pustular psoriasis
  - Make sure to ask about any systemic steroids from PCP or Urgent Care
- Psoriatic arthritis
  - Affects up to 30% of patients
  - Associated with morning stiffness, nail changes, tendon/ligament involvement
- Concurrent or antecedent perianal or body fold cutaneous group A strep infection, especially in a child presenting with sudden onset guttate psoriasis

Key DDx

- Atopic dermatitis
- Contact dermatitis
- Nummular dermatitis
- Seborrheic dermatitis
- Pityriasis rubra pilaris
- Lichen planus
- Subacute cutaneous lupus erythematosus
- Mycosis fungoides
- Tinea corporis
- Crusted scabies
- Secondary syphilis
- Bowen's—if few, smaller lesions

Work Up Pearls

- Atypical appearing psoriasis can be psoriasiform drug eruption
  - Think of lithium, IFNs, B-blockers, ACE inhibitors, antimalarials, terbinafine, NSAIDs
- Biopsy
- Consider imaging for psoriatic arthritis
  - May need rheumatology consultation to help evaluate

Treatment Ladder: Cutaneous [30, 31]

- Topicals: for mild (as monotherapy) to severe disease
  - Topical corticosteroids
  - Calcipotriene
  - Coal tar
  - Anthralin
  - Calcineurin inhibitors
  - Calcitriol

- Tazarotene or salicylic acid for hyperkeratotic lesions
- Intralesional triamcinolone for treatment resistant plaques

- Phototherapy [32]
  - NBUVB two to three times weekly
  - Excimer laser (localized lesions)
  - PUVA is 2nd line

- Systemic
  - Methotrexate 10–25 mg weekly
  - Acitretin (erythrodermic, pustular) 25 mg every other day to 50 mg daily
  - Cyclosporine 3–5 mg/kg daily
  - Apremilast 30 mg twice daily (after starter pack)

- Biologics[33]: all given subcutaneously except infliximab which is given intravenously*
  - TNF-a inhibitors:
    - PEARL: Avoid in patients with CHF or multiple sclerosis
    - Adalimumab: 80 mg initial dose, followed by 40 mg one week later then every other week
    - Etanercept: 50 mg twice weekly for the initial 3 months, then 50 mg weekly
    - Infliximab: 5 mg/kg given at weeks 0, 2, 6, then every 8 weeks thereafter *
    - Certolizumab: 400 mg at weeks 0, 2 and 4, followed by 200 mg every other week
  - IL-12/23 inhibitor:
    - Ustekinumab: 45 mg at weeks 0, 4, and every 12 weeks thereafter; 90 mg for patients >100 kg (dosing is good for compliance concerns)
  - IL-23 inhibitors:
    - Guselkumab:100 mg at weeks 0, 4, and then every 8 weeks
    - Tildrakizumab: 100 mg at weeks 0, 4, and then every 12 weeks
  - IL-17 inhibitors:
    - PEARL: Avoid in patients with IBD. Look for mucocutaneous candidiasis
    - Secukinumab: 300 mg at weeks 0, 1, 2, 3, and 4 then every 4 weeks
    - Ixekizumab: 160 mg at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, 12 and then every 4 weeks
    - Brodalumab: 210 mg at weeks 0, 1, 2 and then every 2 weeks
    - PEARL: requires participation in a Risk Evaluation and Mitigation Strategy program due to concerns for suicidality.
- Other
  - Consider “day hospital” (steroid wraps and phototherapy) for severe disease—can be done in a clinic setting or with wraps alone at home

Treatment Ladder: Scalp [34]

- Topicals
  - 3 or 5% salicylic acid compounded with fluocinonide cream or ointment
  - Clobetasol or betamethasone dipropionate-calcipotriene foam/solution
  - Tar or salicylic based shampoos
  - Intralesional triamcinolone for localized thick plaques
- Excimer laser
  - PEARL: NB-UVB will not reach the scalp through hair
- Systemics as in cutaneous psoriasis section
  - Particularly apremilast and biologics

Treatment ladder, Nails [35]

- Gentle hand/foot care
  - Avoid trauma (manicures)
  - Apply emollients regularly
  - Keep nails trimmed
- High potency topical steroid under occlusion +/− vitamin D ointment to nail plate, hyponychium, proximal/lateral nail folds
- 2nd line: tazarotene or topical calcineurin inhibitors
- 1% 5FU solution or 5% 5FU cream without occlusion BID for 6 months
- Intralesional triamcinolone 2.5 mg/ml into proximal nail fold/matrix
- Systemic
  - Biologics
  - Acitretin
  - Apremilast
  - Methotrexate

Out Of The Box Treatment Options

- Tofacitinib 5 mg BID
- IVIG 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months

In The Context Of...

- Erythroderma
  - Cyclosporine usually has fastest onset of action
  - If erythroderma and impaired kidney function, consider guselkumab, which may be faster acting [36]

- Co-morbid metabolic syndrome
  - Consider metformin
- Pregnancy
  - Topical steroids
  - NBUVB
  - Biologics (anti-TNFs, IL17, IL23) are mostly category B
    - Discuss if risks outweigh benefits, consider enrolling in pregnancy registry
    - Try to stop anti-TNFs at 30 weeks gestation and postpone live vaccinations in newborn babies
    - Certolizumab showed low transfer of the drug through placenta and minimal mother-to-infant transfer from breast milk in pharmacokinetic data.
  - Cyclosporine (Category C) for severe disease
  - PEARL: Impetigo herpetiformis is treated with systemic corticosteroids

Pyoderma Gangrenosum

What Not To Miss

- Unusual sites
  - Rarely PG can involve the eyes, lungs, heart, liver, gastrointestinal tract, CNS and lymphatics
- Other PG variations
  - Pustular, bullous, vegetative and suppurative panniculitis
- PEARL: Avoid unnecessary elective surgical procedures and debridement—if absolutely necessary, perform while on immunosuppressive therapy.

Key DDx

- Infection
  - PG is a diagnosis of exclusion and infection must be ruled out with tissue culture
- Consider underlying genetic causes including PAPA, PASH and PAPASH syndromes

Work Up Pearls [37]

- Biopsy at edge of ulcer for H&E + tissue culture to rule out infection
- Work-up (search for underlying disease)—CBC, ESR, LFTs, BUN/Cr, ANA, SPEP (IgA gammopathy), UA, hepatitis panel, ANCAs, RF, anti-phospholipid antibodies; +/− CXR, colonoscopy

Treatment Ladder [38]

- Local wound care with non-adherent dressing, avoiding pathergy, pain management (important to keep it moist)
- Topical
  - Intralesional triamcinolone 10–20 mg/ml
  - Topical corticosteroids/calcineurin inhibitors to periphery of ulcer and antimicrobial (i/e metronidazole gel) to the center of the ulcer
- Antibiotics
  - Doxycycline 100 mg twice daily
  - Minocycline 100 mg twice daily
  - Dapsone 50–200 mg daily
- Systemic
  - Glucocorticoid starting dose at 1 mg/kg
  - Cyclosporine 4–5 mg/kg daily and taper as tolerated
  - Azathioprine titrate up to dose of 2.5 mg/kg daily
  - Methotrexate 10–30 mg per week
  - Mycophenolate mofetil 2–3 g per day, divided twice daily
  - IVIG 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months
- Biologics: TNF-a inhibitors

Outside the Box Treatment Options

- Thalidomide
- Sulfasalazine
- Clofazimine
- Anakinra
- Canakinumab

Morphea

What Not To Miss

- Genital lichen sclerosus et atrophicus
  - Can occur in patients with plaque-type morphea
- Limb contractures or limb-length discrepancies
  - This can result from linear morphea

- Linear morphea of the head (En coup de sabre and Parry-Romberg syndrome) can result in alopecia, ocular, neurologic and dental abnormalities
  - Both must be treated aggressively

Key DDx

- Systemic sclerosis
- Nephrogenic fibrosing dermopathy
- Eosinophilic fasciitis
- Lipodermatosclerosis
- Drug or chemical induced sclerodermoid reaction (PEARL: Think taxanes or PVC)

Work Up Pearls

- Skin biopsy is confirmatory
  - PEARL: Biopsy containing fascia and muscle is needed if eosinophilic fasciitis is on the differential
- X-rays for linear morphea
  - MRI can evaluate for deeper involvement
- Testing for auto-Abs only indicated if signs of another autoimmune disease [39]

Treatment Ladder [40]

- Circumscribed lesions
  - Topical or intralesional corticosteroids
  - Topical calcineurin inhibitor
  - Topical calcipotriene
  - Topical imiquimod
  - UVA1 or NBUVB (if UVA not available)
    - PEARL: UVA-1 preferred because it penetrates deeper
- Generalized or localized with functional/cosmetic threat (face, over joints)
  - Methotrexate 15–25 mg weekly +/− systemic prednisone 1 mg/kg daily for 2–3 months
  - Mycophenolate mofetil 2–3 g daily, divided twice daily
- Consultation with PT/OT, Orthopedics/Plastic surgery/OMSF
- Other options
  - Cyclosporine 2–5 mg/kg daily in 2 divided doses
  - Hydroxychloroquine 5 mg/kg daily up to 200 mg twice daily
  - Acitretin 12.5–50 mg daily + PUVA
  - Extracorporeal photopheresis
  - Bosentan 31.25–62.5 mg twice daily

Outside Of The Box Treatment Options

- Fillers for improved cosmesis once morphea stabilizes
- CO2 laser to decrease contractures and increase mobility over joints
- Infliximab, rituximab, imatinib, JAK inhibitors, thalidomide

Systemic Sclerosis

What Not To Miss

- PEARL: African American patients have a more severe course and increased mortality
- Extracutaneous findings
  - Pulmonary disease is the leading cause of mortality.
  - GI is the most common site of visceral disease and associated with increased morbidity but not mortality
  - Scleroderma renal crisis risk can be decreased with ACE-I
  - Scleroderma renal crisis has been associated with use of systemic corticosteroids in retrospective studies

Key DDx

- Generalized morphea
- Scleredema
- Scleromyxedema
- Eosinophilic fasciitis
- Nephrogenic systemic fibrosis
- Chronic GVHD
- Exogeneous: polyvinyl chloride (PVC) exposure, bleomycin toxicity, radiation effects

Workup Pearls

- CBC with diff, BUN, Cr, CK, U/A,
- Auto-antibodies
  - ANA (95% +), anti-Scl-70
  - anti-centromere Ab (associated with CREST)
  - anti-RNA pol III Ab (associated with rapidly progressive skin involvement, renal disease and cancer)
- At time of diagnosis and for monitoring: high resolution CT of lungs, PFTs with DLCO, ECG, ECHO (to assess pulmonary arterial HTN), GI consultation as appropriate
- Diagnosis [41]

ACR/EULAR 2013 Criteria. ≥ 9 = definite SSc.	
Cutaneous findings:	**Systemic findings:**
Skin thickening of fingers proximal to MCP joint (9)	Pulm art. HTN (2) or ILD (2)
Skin thickening of the fingers: puffy fingers (2) or sclerodactyly (4)	Raynaud's phenomenon (3)
Fingertip lesions: ulcers (2), pitting scars (3)	Ab's (ANA, anti-Scl-70, anti-RNA pol III) (3 max)
Telangiectasia (2)	
Abnormal nail fold capillaries (2)	

Treatment Ladder (cutaneous) [42]

- Multidisciplinary approach
  - Rheumatology +/− nephrology, pulmonology, gastroenterology
- 1st line
  - Oral corticosteroids
  - Methotrexate 10–25 mg weekly
  - Mycophenolate mofetil 2–3 g per day, divided twice daily
  - PUVA or UVA1
  - Rituximab 1000 mg once and repeated in 2 weeks is 1 cycle, repeat cycles may be necessary
- 2nd line
  - Azathioprine titrate up to dose of 2.5 mg/kg daily
  - Cyclophosphamide 1–3 mg/kg daily
  - IVIG 1–2 g/kg per cycle divided into 3–5 consecutive days per month for 3–6 months
  - Bosentan
  - Sildenafil

Outside Of The Box Treatment Options

- Myeloablative autologous hematopoietic stem-cell transplantation
- Low-energy extracorporeal shock-wave therapy
- Clinical trials for refractory or progressive disease

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