Cutaneous Manifestations of Systemic Disease

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ABOIM Board Review
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Cutaneous Multisystem
Cutaneous Connective Tissue Conditions
Connective Tissue Disease

- Discoid Lupus Erythematosus
- Subacute Cutaneous LE
- Systemic Lupus Erythematosus
- Scleroderma
- CREST Syndrome
- Dermatomyositis
Lupus Erythematosus

- Spectrum from cutaneous to severe systemic involvement
  - Discoid LE (DLE) / Chronic Cutaneous LE
  - Subacute Cutaneous LE (SCLE)
  - Systemic LE (SLE)
- Cutaneous findings common in all forms
- Related to autoimmunity
Discoid LE (Chronic Cutaneous LE)

- Primarily cutaneous
- Scaly, erythematus, atrophic plaques with sharp margins, telangiectasias and follicular plugging
- Possible elevated ESR, anemia or leukopenia
- Progression to SLE only 1-2%
- Heals with scarring, atrophy and dyspigmentation
- 5% ANA positive
Discoid LE (Chronic Cutaneous LE)

Scaly, atrophic plaques with defined margins
Discoid LE (Chronic Cutaneous LE)

Scaly, erythematous plaques with scarring, atrophy, dyspigmentation
Subacute Cutaneous LE (SLCE)

- Cutaneous disease with internal involvement
  - 20% Leukopenia, 75% arthralgias
- Psoriasiform, polycyclic, annular lesions
- Sun exposed sites commonly
  - Shawl distribution: V neck, upper outer and inner arms
- 80% ANA positive
  - Anti-Ro
Subacute Cutaneous LE (SLCE)

Psoriasiform, scaly plaques

“Shawl” distribution
Systemic Lupus Erythematousus (SLE)

- Young to middle age women
- Skin involvement in 80% of the cases (often malar rash)
- American College of Rheumatology has 11 criteria for SLE diagnosis
  - If 4 or more of the criteria are satisfied, then the patient is said to have SLE
    - ANA + 99%

- Possible drug induced
  - Procainamide, Hydralazine, Isoniazid, etc
<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1. Malar rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds</td>
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<td>2. Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions</td>
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<td>3. Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation</td>
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<td>4. Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless, observed by physician</td>
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<td>5. Arthritis</td>
<td>Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion</td>
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<td>6. Serositis</td>
<td>a) Pleuritis – convincing history of pleuritic pain, rubbing heard by a physician, or evidence of pleural effusion OR</td>
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<td>b) Pericarditis – documented by ECG, rub or evidence of pericardial effusion</td>
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<td>7. Renal disorder</td>
<td>a) Persistent proteinuria greater than 0.5 g/day or greater than 3+ if quantitation not performed OR</td>
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<td>b) Cellular casts – may be red cell, hemoglobin, granular, tubular or mixed</td>
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<td>8. Neurologic</td>
<td>a) Seizures – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance OR</td>
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<tr>
<td>disorder</td>
<td>b) Psychosis – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance</td>
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<td>9. Hematologic</td>
<td>a) Hemolytic anemia with reticulocytosis OR</td>
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<td>disorder</td>
<td>b) Leukopenia – less than 4000/mm³ total WBC on two or more occasions OR</td>
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<td>c) Lymphopenia – less than 1500/mm³ on two or more occasions OR</td>
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<td></td>
<td>d) Thrombocytopenia – less than 100,000/mm³ in the absence of offending drugs</td>
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<tr>
<td>10. Immunologic</td>
<td>a) Anti-DNA antibody to native DNA in abnormal titer OR</td>
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<tr>
<td>disorder</td>
<td>b) Anti-Sm: presence of antibody to Sm nuclear antigen OR</td>
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<td>c) Positive finding of antiphospholipid antibodies based on: (1) an abnormal serum level of IgG or IgM anticardiolipin antibodies, (2) a</td>
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<td>positive test result for lupus anticoagulant using a standard methods, or (3) a false-positive serologic test for syphilis known to be</td>
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<td>positive for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test (FTA-ABS)</td>
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<td>11. Antinuclear</td>
<td>An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs</td>
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<tr>
<td>antibody</td>
<td>known to be associated with 'drug-induced lupus' syndrome</td>
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Systemic Lupus Erythematosus (SLE)

- Pleural effusions
- Heart problems
- Lupus nephritis
- Arthritis
- Butterfly rash
- Symptoms of systemic lupus erythematosus may vary widely with the individual
- Raynaud’s phenomenon

[Diagram showing various symptoms and areas affected]
Systemic Lupus Erythematosus (SLE) 
ACR Criteria*

1) D – Discoid Rash
2) O – Oral Ulcers
3) P – Photosensitivity
4) A – ANA + (99%)
5) M – Malar Rash
6) I – Immunologic DO
7) N – Neurologic DO
8) R – Renal Disorder
9) A – Arthritis
10) S – Serositis
11) H – Hematologic DO
Lupus Erythematosus Laboratory Findings

- Antinuclear Antibodies (ANA)
  - 5% DLE
  - 80% SCLE
  - 99% SLE

- Anti-dsDNA + in SLE
  - Correlates with renal disease and SLE activity
  - (anti-histone + in drug-induced)

- False + VDRL

- Anemia, leukopenia, thrombocytopenia, low complement, urinary findings
Lupus Erythematosus Laboratory Findings

- Lupus Band Test
  - direct immunofluorescence of skin biopsy
  - Linear IgG deposition at dermal-epidermal junction
Lupus Erythematosus Differential Diagnosis

- If DLE
  - Sarcoid – lacks atrophy & follicular plugging
  - Lymphocytic infiltrating dz – lack of atrophy

- If erythematous lesions
  - Rosacea – central face, pustules, no atrophy, “triggers”
  - Photosensitivities – history, clinical, labs
Lupus Erythematosus Treatment

- **DLE**
  - Sunscreen
  - Antimalarials - gold standard (hydroxychloroquine)
  - Topical/intraleisonal/systemic steroids
  - Most common morbidities – scarring, rare SCC

- **SLE**
  - PLUS:
  - Systemic steroids for renal, CNS, hematologic, rheumatologic findings
  - Treat secondary infections
  - Most common cause of death – renal & CNS
Raynaud’s Phenomenon

- Clinical
  - Episodic vascular insufficiency of digital arterioles
  - Related to cold and emotions
  - Pallor, cyanosis, hyperemia
  - Often painful
Raynaud’s Phenomenon
Etiology

- Less than half have connective tissue disease
  - Idiopathic (Raynaud’s Disease)
- Scleroderma (>50%), SLE, Dermatomyositis
- Pneumatic hammer operators
- Ergotism
- Vinyl chloride (industrial)
- Cryoglobulins/macroglobulins
Raynaud’s Phenomenon Treatment

- Avoidance of cold
- Vasodilators
  - Nifedipine (Ca+ channel blockers)
  - Prazosin (alpha blockers)
  - Nitroglycerin 2% topical
  - Sympathectomy in severe cases
Scleroderma

- Cutaneous to severe systemic
- Morphea
  - Localized scleroderma - atrophic scar with dyspigmentation
  - Smooth, hard, somewhat depressed, yellowish white, or ivory-colored lesions
  - Common on the trunk
Scleroderma

- **Acrosclerosis**
  - Sclerodactyly – tight skin over hands, digits
  - Sclerosis of skin
  - Poikiloderma (slight atrophy, telangiectasia, dyspigmentation)
  - Telangiectatic mats
  - Calcinosis cutis
Scleroderma

En coupe de sabre (linear morphea)
Scleroderma Systemic Findings

- Abnormal esophageal/intestinal motility
- Pulmonary fibrosis
- Renal disease
  - Possibly rapid, fatal
- Most often anti Scl-70
Scleroderma: CREST Syndrome*

- Calcinosis
- Raynaud’s
- Esophageal dysmotility
- Sclerodactyly
- Telangiectasias

- Mild form of progressive systemic sclerosis
- Most often anti-centromere
Scleroderma Etiology

- Unknown
- Autoimmune
  - Anti-centromere (limited/CREST)
  - Anti Scl-70 (systemic sclerosis)
- Overproduction of collagen
Scleroderma Differential

- If Morphea
  - Lichen sclerosus (often genital, can coexist)
- If Telangiectasias
  - Osler-Weber-Rendu (nasal bleeds, no sclerosis)
- If Sclerodactyly
  - Porphyria cutanea tarda (bulla, photosensitive, hypertrichosis)
Scleroderma Treatment

- Morphea – intralesional steroids
- Raynaud’s –
  - Primarily calcium channel blockers (nifedipine, verapamil)
- Progressive systemic sclerosis
  - No approved therapies
  - Symptomatic
  - Some uncontrolled studies with D-penicillamine
Dermatomyositis*

- Heliotrope – violaceous discoloration around eyes
- Gottron’s papules – erythematous, papules over interphalangeal joints
- Telangiectasias/poikiloderma
- Raynaud’s phenomenon
- Symmetrical proximal muscle weakness

- Children – calcinosis common, possible ulceration
Dermatomyositis

Poikiloderma

Gottron’s

Heliotrope rash
Dermatomyositis Labwork

- Elevated muscle enzymes
- EMG
- Muscle biopsy
- Ultrasound/MRI
Dermatomyositis Differential

- Almost always pathognomonic
  - Heliotrope rash
  - Gottron’s papules
- Exclude other causes of muscle disease
Dermatomyositis

- Associated with malignancy in 10-50% of adults (often lymphoma)
- Increased malignancy rate over general population
Dermatomyositis Treatment

- Physical Therapy
- Symptomatic Treatment
- Systemic Steroids
- Immunosuppressives
  - Ex. methotrexate

<table>
<thead>
<tr>
<th>THERAPEUTIC LADDER FOR DERMATOMYOSITIS</th>
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<tr>
<td><strong>Systemic therapy</strong></td>
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<tr>
<td>Oral prednisone: 1 mg/kg tapered to 50% over 6 months and to zero over 2-3 years ①</td>
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<tr>
<td>option to use pulse, split dose, or alternate day ①</td>
</tr>
<tr>
<td>Low-dose weekly methotrexate ②</td>
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<tr>
<td>Azathioprine: 2-3 mg/kg/day ③</td>
</tr>
<tr>
<td>Others: high dose intravenous γ-globulin ①</td>
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<tr>
<td>pulse cyclophosphamide ③</td>
</tr>
<tr>
<td>chlorambucil ③</td>
</tr>
<tr>
<td>cyclosporin ②</td>
</tr>
<tr>
<td>not plasmapheresis ③</td>
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<thead>
<tr>
<th>Cutaneous lesions</th>
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<tr>
<td>Sunscreens (high solar protection factor with some protection against UVA) ①</td>
</tr>
<tr>
<td>Topical corticosteroids ①</td>
</tr>
<tr>
<td>Hydroxychloroquine (increased frequency of drug eruptions in patients with dermatomyositis) ②</td>
</tr>
<tr>
<td>Hydroxychloroquine plus quinacrine ②</td>
</tr>
<tr>
<td>Low-dose weekly methotrexate ②</td>
</tr>
<tr>
<td>Retinoids ③</td>
</tr>
<tr>
<td>Others: dapsone ②</td>
</tr>
<tr>
<td>thalidomide ③</td>
</tr>
<tr>
<td>mycophenolate mofetil ②</td>
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Dermatomyositis Prognosis

- **Children**
  - Generally good
  - Possible residual from calcinosis or contractures

- **Adults**
  - Often progressive and fatal
  - Aspiration common
  - Cardiac involvement with failure
  - Possible malignancy
Sarcoidosis Clinical

- Systemic disorder
- Persistent with remissions and recurrences
- Common in blacks (10x higher)
- Cutaneous variation
  - Plaques, annular lesions, nodules, papules
  - Lupus pernio: violaceous, atrophic plaque on nose, cheeks or ears
- Erythema nodosum common early
- Diagnosis of exclusion
Sarcoidosis
Sarcoidosis – Lupus Pernio

Violaceous, mildly atrophic plaques
Sarcoidosis Pulmonary Involvement

- Three stages
  - I – hilar adenopathy
  - II – hilar adenopathy with parenchymal disease
  - III – diffuse parenchymal disease
Sarcoidosis

- Lofgren’s syndrome
  - Early sarcoid
  - Erythema nodosum, hilar adenopathy, arthritis
    - uveitis, fever, fatigue
  - Prognosis – 80-90% resolution 6 months to 2 years
Sarcoidosis Systemic Involvement

- Hepatic granulomas
- Bone cysts
- Lymphadenopathy
- Muscle granulomas
- Cardiac granulomas
- CNS granulomas
- Hypercalcemia
- Hyperglobulinemia
Sarcoidosis Etiology*

- Unknown
- Abnormalities in immune response
- ACE (angiotensin converting enzyme) elevation 35-80%
Sarcoidosis Treatment*

- 30-70% need no treatment
- 10-20% severe
- 5-10% life-threatening
- Variable responses to treatment

Cutaneous lesions
- Corticosteroid injection
- Antimalarials
- Systemic corticosteroids
- Immunosuppressants

Pulmonary involvement
- Controversial benefit of systemic steroids

Hypercaldemia
- ? Medications
- Dietary modification
RENAL

- Renal Pruritis
- Perforating Dermatoses
- Nephrogenic Sclerosing Dermopathy
- Nail findings
Pruritus

- Generalized pruritus without a rash requires further workup
- Rule out ectoparasitic and cutaneous disease
- May demonstrate prurigo nodules, excoriations or no findings at all

- Differential?
Pruritus Differential

- Xerosis
- Medication
- Iron deficiency anemia
- Polycythemia
- Leukemia
- Lymphoma

- Multiple myeloma
- Uremia (most common cutaneous of ESRD)
- Cholestasis
- Hyperthyroidism
- Hypothyroidism
- Other
Pruritus workup

- Based on History and Physical findings
  Exclude primary disorder (eczema, scabies, xerosis)
- Conservative treatment depending on history and physical: mild soaps & detergents, moisturize, antihistamines, +/- topical anti-itch or steroids
- CBC +/- iron studies
- CMP
- TSH
- CXR
- HIV, Hepatitis Serology
- +/- SPEP
Internal Causes of Pruritus

- **CRF/Uremic Pruritus**
- **Liver Disease**
  - Obstructive disease
  - Hep C infection
  - Biliary Pruritus
  - Primary Biliary Cirrhosis
- **Infections**
  - AIDS
  - Parasites
- **Hematopoietic diseases:**
  - Polycythemia Vera
  - Iron-Deficiency Anemia
- **Malignancy**
  - Lymphoma (Hodgkin's)
    - Incidence of 10-25%
    - Presenting feature in 7%
  - Leukemia
  - Myeloma
  - Internal malignancies
  - Carcinoid
- **Hyper or hypothyroidism**
  - Diabetes +/-
- **Neuropsychiatric**
  - Anorexia nervosa
  - Multiple sclerosis
Biliary Pruritis

20-50% of pts w/ jaundice have pruritus

Chronic liver disease
- Primary biliary cirrhosis, primary sclerosing cholangitis, obstructive choledocholithiasis, carcinoma of the bile duct, cholestasis, HCV

Generalized, migratory, & not relieved w/ scratching

Serum level of conjugated bile acid does not correlate to degree of pruritus
- Likely a central mechanism
  - Have elevated opioid peptide levels

Treat underlying condition
- Naloxone, naltrexone, or nalmefene
- cholestyramine
RENAL DISEASE

RENAL PRURITIS

- “Uremic pruritus” = used synonymously
  - However not secondary to elevated levels of serum urea
- **Chronic renal failure is the MC internal cause of systemic pruritus**
  - 20-80% of patients with CRF
- Typically **generalized, severe, and intractable**
- Multifactorial mechanism:
  - **Xerosis**, secondary hyperparathyroidism, inc. serum histamine, hypervitaminosis A, iron-deficiency anemia, neuropathy, **inc. levels of poorly dialyzed compounds**
  - Complications = Lichen simplex chronicus, prurigo nodularis may result
Treatment Renal Pruritis

- **Responds well to NB/UVB**
  - Recurs after discontinuation

- **Aggressive emollients for xerosis**

- **Gabapentin**
  - 3x weekly w/ hemodialysis

- **Nalfurafine (TRK-820)**
  - IV 3x weekly
  - k-opioid agonist

- **Thalidomide**
  - Pruritus lowest during day after HD
  - Pruritus peaks 2\textsuperscript{nd} night after HD
  - Pruritus is HIGH during HD
Perforating disease

- Arising in adults
- “Kyrle’s disease”
- Associated with renal failure, DM, and rarely liver disease and internal malignancy

Clinical:

- Pruritic keratotic papules
  - Result of collagen extrusion from dermis to epidermis
  - Likely secondary to trauma
- Legs are MC location

Treatment:

- UV light, emollients
Nephrogenic Fibrosing Dermopathy

- Patient with renal insufficiency & hemodialysis
- Exposure to gadolinium based contrast medium
- Clinical:
  - Thickened, sclerotic, edematous, hyperpigmented papules or plaques
    - “Woody induration”
  - MC on the Extremities
    - face is spared (unlike scleroderma)
- Treatment:
  - Ineffective- optimize renal function via transplantation
  - Phototherapy, rapamycin
Half and Half Nails

Nail changes are common in renal patients:

- Hemodialysis: 76%
  - Half & half (MC)
  - Splinter hemorrhages
  - Absent lunula
- Renal transplant: 56%
  - Leukonychia (MC)

**Half & half nails**
- Proximal nail is white
- Distal ½ is red/pink/brown
- Sharp demarcation line
Cutaneous and Gastrointestinal
These patients have an increased risk of:

A. Melena and intussusception.
B. Adenomatous polyps.
C. Epistaxis.
D. Halitosis.
E. Oral ulcers.

Increased chance of cancer of colon, pancreatic cancer in men; and ovary, breast and endometrial in women.
LIVER DISEASE

- Gardner syndrome
- Hemochromatosis
- Porphyria Cutanea Tarda
- Associated nail findings
Gardner’s Syndrome

- Epidermal cysts, osteomas, lipomas, fibromas
- Colon or rectal polyps (adenomas)
- High malignant potential by age 40
  - Half with carcinoma by age 30, most die before age 50
- Autosomal dominant
- Tx: total colectomy
Hemochromatosis

*Bronze Diabetes*

- **AR → HFE-gene**
- **MC white European population; 5th decade**
- **M>F (2 ° female iron loss w/ menses)**
- **Inc. intestinal Iron absorption → iron overload → organ deposition**

**Clinical Features:**

- **Skin** = metallic-grey hyperpigmentation
  - Sun-exposed areas w/ mm involvement in 20%
  - Nails = koilonychia (50%)
  - Hair = sparse to absent
- **GI** = hepatomegaly, hepatocellular CA, abd. pain, wt. loss
- **CVS** = arrhythmias, heart failure
- **Endocrine** = IDDM; hypogonadism; loss of libido
- **MSK** = polyarthritis (20-70%)
Hemochromatosis

Bronze Diabetes

Many with genetic mutations do not develop disease
- Increased risk: alcohol, smoking and Hep C

Dx:
- Elevated plasma iron & serum ferritin
- Transferrin saturation (TS) >45
- Liver bx: if ferritin >1000, Inc. LFTs or >40yrs
- Gene studies

Once cirrhosis is present → HCC risk is 30%

Tx:
- Phlebotomy (can prevent cirrhosis)
- Deferoxamine (chelator)
- Supportive care (insulin, testosterone, anti-arrhythmics)
- Restrict Vit. C
Porphyria Cutanea Tarda

- **Uroporphyrinogen decarboxylase deficiency**
- Most common type of porphyria
- Clinical Manifestations:
  - Bullae, erosions on **sun-exposed skin**
    - heal with scars, milia and dyspigmentation
  - Hypertrichosis on face
  - Sclerodermoid changes of skin
  - Wine/tea colored urine
DRUGS & CHEMICALS

- Ethanol
- Estrogens
- Iron
- Hexachlorobenzene (fungicide)
- Chloroquine (high dose)

PREDISPOSITIONS

- Diabetes mellitus (25%)
- Hepatitis
  - HCV (94% in US)
  - HAV, HBV
- HIV infection
- Hemochromatosis genes
PCT Diagnosis & Treatment

**Diagnosis**
- Plasma porphyrin level
- 24 hour URINE PORPHYRINS
- WOOD’S LIGHT on urine specimen in office
  - Orange-red fluorescence (*high false negative rate*)

**Treatment**
- **Sunlight Avoidance**
- Avoid drugs/chemicals/ETOH that precipitate attacks
- Decrease consumption of iron-rich foods
- **Therapeutic phlebotomy** (TOC)
- Low dose Chloroquine
Peutz-Jeghers Syndrome

- Perioral melanotic freckles (often infancy)
  - Also gingiva, buccal and genital mucosa
- GI polyps
- 10-18x cancer risk (1/2 develop by age 40)
  - Colon, duodenum, pancreas, breast, thyroid, lung
- Abdominal: pain, bleeding, intussusception
- Autosomal dominant
- Regular, frequent gastrointestinal screening
Cutaneous and Gastrointestinal

Peutz-Jeghers Syndrome

Melanotic macules
Cutaneous and Gastrointestinal* (Intestine)

- Osler-Weber-Rendu (hereditary hemorrhagic telangiectasias)
  - Autosomal dominant
  - Mat-like telangiectasias on any body area
    - Mucous membranes, acral common
    - Earliest location under tongue
  - GI bleeding, epistaxis (first symptom), ulcers, A-V fistulas, hematuria
  - Treatment: blood replacement, address vessels
Cutaneous and Gastrointestinal

- Osler-Weber-Rendu (hereditary hemorrhagic telangiectasias)

Figure 1—Multiple small telangiectases of the tongue and buccal mucosa.

Figure 2—Arteriovenous malformation along the descending colon.

telangiectasias  A-V malformation
Cutaneous and Gastrointestinal (Intestine)

- Inflammatory Bowel Disease
  - Manifestations of ulcerative colitis and regional enteritis (Crohn’s) identical
  - Apthous ulcerations during exacerbations
  - Erythema nodosum in 5% of exacerbations
- Treatment
  - Therapy for bowel disease
Cutaneous and Gastrointestinal (Intestine)

- **Inflammatory Bowel Disease**
  - **Pyoderma Gangrenosum**
    - 1-10% of IBD
    - Undermined necrotic violaceous ulcer
    - Pustular onset
    - More common in UC
    - Frequent precipitation by trauma
    - Treatment: steroids and immunosuppressives
Pyoderma Gangrenosum

- Uncommon, recurrent, ulcerative neutrophilic disease
- Tender papulopustule → undergoes necrosis and ulceration with an irregular, undermined border
  - Heals with atrophic, cribiform, pigmented scars

50-70% have associated disease

- **MC Ulcerative colitis, Crohn's (20-30%)**
  - 1.5-5% of pts. with IBD develop PG
- Arthritis (20%)
  - Seronegative arthritis, RA, spondylitis of inflammatory bowel dz
- **Hematologic disease (15-25%)**
  - Leukemia (AML, CML), IgA gammopathy, myeloma,
- 25-50% of cases are idiopathic
Early lesion: papule with erythematous base
Cutaneous and Gastrointestinal (Intestine)

- Muir-Torre Syndrome
  - Autosomal dominant
    - Sebaceous neoplasms
    - Multiple keratoacanthomas
    - Internal malignancy
  - Cutaneous 10-20 years prior (preventative medicine!)
  - Colon cancer most common
Dermatitis Herpetiformis

- Chronic, relapsing/remitting, severely pruritic dz
- Symmetrical, polymorphous (often extensor)
- Itching and burning are intense (often only excoriations)
- Associated with gluten-sensitive-enteropathy
- Treatment: medication plus gluten-free diet
Dermatitis Herpetiformis

- Cutaneous manifestation of gluten sensitivity (Celiac Dz)
- Relapsing, severely pruritic grouped vesicles
  - May also be papules, urticaria, tense bullae
  - *May only see crusts* → *scratching!!*
  - Intense itching and burning
- Symmetrically on extensor surfaces, scalp, nuchal area, buttocks
Dermatitis Herpetiformis

- Male=female
- 2nd-5th decade (20-40)
- Related to celiac disease
  - 70-100% of DH pts. have abnormalities of jejunal mucosa (often asymptomatic)
  - 25% of celiac pts. have DH
Dermatitis Herpetiformis

**Diagnosis**
- Skin biopsy → characteristic histology!
- **Antiendomysial antibodies** (endomysial Ag is TTG)
  - Sensitive and specific (>80%)
  - Reflect severity of enteropathy and compliance of diet
- **Antigliadin antibodies** (>66%)
- Endoscopy: blunting and flattening of villi (80-90%)

**Treatment**
- Gluten free diet
- Dapsone
Cutaneous and Gastrointestinal (Intestine)

- Sign of Lesser-Trelat
  - Rapid increase in size/number of seborrheic keratoses
  - Occ also AN
  - Assoc Colon (or gastric) carcinoma
Cutaneous and Gastrointestinal (Liver)

- Hemochromatosis
  - Hyperpigmentation
  - Cirrhosis
  - Diabetes
  - Koilonychia
  - Elevated iron

Iron stain of liver
Cutaneous and Gastrointestinal (Liver)

- Porphyrias
  - Each associated with deficiency of enzyme in heme synthesis
  - Hepatic or Erythropoietic
  - Some forms with photosensitivity
  - Frequent alcoholism and Hep C

Vampire legend
Cutaneous and Gastrointestinal (Liver)

- **Porphyrias**
  - Vesicles and bullae (subepidermal) on sun-exposed areas
  - Atropic scarring
  - Milia
  - Facial hypertrichochisis
Cutaneous and Gastrointestinal* (Liver)

- Cirrhosis
- Spider angiomas
  - Palmar erythema
  - Clubbing
  - Terry’s nails (white)
- Jaundice
- Gynecomastia
Cutaneous and Gastrointestinal (Renal)

**Birt-Hogg-Dube**

- Autosomal dominant
- Trichodiscomas, fibrofolliculomas, acrochordons
- Numerous firm, flesh-color papules of head, neck, trunk
- Assoc bilateral renal tumors (pulmonary cysts, pneumothorax)
Cutaneous and Gastrointestinal (Renal)

- Nephrogenic Systemic Fibrosis
  - Gadolinium MRI contrast associated
  - Renal failure patients
  - Woody nodules/plaques, usually extremities
  - Variable course
  - <5% fatal (respiratory muscle fibrosis)
Cutaneous and Gastrointestinal (Renal)

Pseudoxanthoma Elasticum

- **Clinical**
  - Autosomal recessive more common
  - Yellow-tan papules ("plucked chicken skin") in flexural areas
  - Lax skin

- **Internal**
  - HTN frequent (renal vasculature)
  - Claudication
  - Angina
  - Recurrent GI bleed, epistaxis, rare GU
  - Angioid streaks (blindness possible)

Angioid streaks
Cutaneous and Gastrointestinal (Renal)

Pseudoxanthoma Elasticum

- Treatment
  - None distinctive
  - Possibly limit calcium and phosphorus intake
Cutaneous and Endocrine
Hypo- and hyperthyroidism
- Addison’s Disease
- Acanthosis Nigricans
- Necrobiosis Lipoidica Diabeticorum
- Diabetic Dermopathy
- Diabetic Bullae
- Xanthomatoses
# Hypothyroidism

| Skin changes                                      | Dry, rough, or coarse; cold and pale, boggy and edematous (myxedema)  
|                                                 | Yellow discoloration as a result of carotenemia  
|                                                 | Easy bruising (capillary fragility)  
| Cutaneous diseases                                | Ichthyosis and palmoplantar keratoderma  
|                                                 | Eruptive and/or tuberous xanthomomas  
| Hair changes                                      | Dull, coarse, and brittle  
|                                                 | Slow growth (increase in telogen hair phase)  
|                                                 | Alopecia of the lateral third of the eyebrows  
| Nail changes                                      | Thin, brittle, striated  
|                                                 | Slow growth  
|                                                 | Onycholysis (rare)  

Hypothyroidism
Myxedema

- Systemic mucinosis
- Severe lack of thyroid hormone

**Clinical:**
- Skin becomes rough & dry
- **Facial skin is puffy**
  - dull, flat expression
- Macroglossia, broad nose
- **Chronic periorbital infiltration**
- Carotenemia $\rightarrow$ palms & soles
- Diffuse hair loss
  - lateral 3rd eyebrow hair
- Onycholysis
Table 53.5 Dermatologic manifestations of hyperthyroidism.

<table>
<thead>
<tr>
<th>DERMATOLOGIC MANIFESTATIONS OF HYPERTHYROIDISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous changes</td>
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<tr>
<td>Fine, velvety, or smooth skin</td>
</tr>
<tr>
<td>Warm, moist skin due to increased sweating</td>
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<tr>
<td>Hyperpigmentation – localized or generalized</td>
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<tr>
<td>Cutaneous diseases</td>
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<tr>
<td>Vitiligo</td>
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<td>Urticaria, dermatographism</td>
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<tr>
<td>Pretibial myxedema and thyroid acropachy</td>
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<tr>
<td>Hair changes</td>
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<tr>
<td>Fine, thin</td>
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<tr>
<td>Mild, diffuse alopecia</td>
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<tr>
<td>Hair disease</td>
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<tr>
<td>Alopecia areata</td>
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<td>Nail changes</td>
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<tr>
<td>Onycholysis</td>
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<tr>
<td>Koilonychia</td>
</tr>
<tr>
<td>Clubbing from thyroid acropachy</td>
</tr>
</tbody>
</table>

Pretibial myxedema

- Pretibial plaque with dry scaly epidermis
- Often hyperthyroidism
- Possible euthyroid
- Frequent exopthalmos
- Accumulation of glycosaminoglycans associated with thyroid stimulating antibodies
- Tx: intralesional or topical steroids
Endocrine Disorders*

- Hypothyroidism
  - Cold, thick, dry skin
  - Coarse hair
  - Loss of lateral eyebrows
  - Brittle nails
  - Xanthomas
  - Purpura
Endocrine Disorders*

- Hyperthyroidism
  - Fine, moist skin
  - Diffuse hair loss
  - Possible association with
    - Alopecia areata
    - Vitiligo
Hyperthyroidism

Grave’s Disease
Pretibial Myxedema
Exophthalmos
Endocrine Disorders

- Diabetes
  - Necrobiosis lipoidica (dibeticorum) (NLD)
    - Red-yellow atrophic plaques
    - Usually lower legs
    - Control of diabetes does not influence
    - Treatment not satisfactory
Necrobiosis Lipoidica Diabeticorum

- 20% of patients have diabetes or glucose intolerance
  - 0.3-3% of diabetics have NLD
  - F>M
- Clinical:
  - Red-brown papules that progress to yellow-brown atrophic, telangiectatic plaques with violaceous, irregular border
  - Common sites include shins, ankles, calves, thighs and feet
  - Ulceration occurs in 35% lesions
Endocrine Disorders

- Diabetes
  - Recurrent candidiasis

- Eruptive xanthomas
  (also manifestations of lipid abnormalities)
Endocrine Disorders

- Diabetes
  - Ulcers secondary to vascular impairment or neuropathy
  - Fat necrosis secondary to insulin injections