Terminology

- **Macule**: flat, <1 cm
- **Patch**: flat, > 1 cm
- **Papule**: raised, <1 cm
- **Plaque**: raised, >1 cm
- **Vesicle**: fluid filled blister, <1 cm
- **Bulla**: fluid filled blister >1 cm
- **Pustule**: vesicle containing pus
- **Wheal**: transient, edematous papule/plaque
- **Scale**: flaking of corneal layer
- **Crust**: dry exudate
Terminology-Histopathology
• Hyperkeratosis: thickened stratum corneum
• Parakeratosis: retention of nuclei in stratum corneum
• Acanthosis: hyperplasia of the stratum spinosum
• Spongiosis: intraepidermal edema (from accumulation of fluid)
• Acantholysis: loss of connections between keratinocytes causing cells to become rounded
NEOPLASIA
Seborrheic keratoses

• Common benign epidermal tumor
• Present as verrucous, greasy stuck-on macules, papules or plaques
• Predilection for face, neck, and trunk
• Leser-Trélat: striking proliferation or increase in size and number of multiple seborrheic keratoses in conjunction with internal malignancy
  – Gastric adenocarcinoma most commonly detected
Basal Cell Carcinoma

- Most common form of cancer and skin cancer
- PTCH gene mutations most common
- 99% of cases in whites
- Most frequent site is on the face
- Slow growing
- Diagnose by biopsy
- Treatment is curative in early lesions
- Metastases are rare (0.0028-0.55%) – lymph node, lungs, bone, skin, liver
- Will cause regional destruction
Squamous Cell Carcinoma

• Etiology
  – UV light (most important), but X-irradiation, Chemicals (i.e. arsenic), Thermal injury

• Increased potential to metastasize compared to BCC

• P53 mutation most common

• Keratoacanthoma: rapidly growing over period of 4-6 weeks. Most are indolent. Most think of KA as well differentiated SCC (Controversial)

• Bowen’s disease=SCCis
  – Appears mainly on sun-exposed parts
  – Grows slowly by lateral extension
  – If left untreated, development of invasive carcinoma is possible
  – Full thickness epidermal atypia but no growth into dermis
SCC

• Metastases are rare
  – <2 cm = 1%
  – 2-5 cm = 5%
  – >5 cm = 15% (also with lower lip lesions)
• More common in scar SCC’s
• More common in renal transplant patients
SCC (Keratoacanthoma)

Fig. VIB1. e. Keratoacanthoma, medium power. The epidermis shows an abrupt transition from relatively normal to a proliferation of eosinophilic hyalized ground-glass–appearing atypical keratinocytes. At the dermal–epidermal junction, there is a brisk infiltrate of lymphocytes that are exocytotic to this proliferative atypical epithelium.
SCC
Actinic keratosis

• Precursor to squamous cell carcinoma
• Small percentage convert into SCC (<1% of lesions)
• Treatment
  – liquid nitrogen
  – 5-flourouracil topical
  – Imiquimod
Benign Proliferation of Melanocytes = Nevus

Junctional nevus

Compound nevus

Intradermal nevus
Malignant proliferation of melanocytes = Melanoma
Invasive Melanoma

• Melanoma which has grown into the dermis
• This happens quickly in some patients but slowly in others
• Prognosis based on depth of invasion and presence of ulceration
• Sentinel node biopsy is a newer prognostic test
• Most common mutation: BRAFv600e
Nodular melanoma
Melanoma (superficial spreading)
Amelanotic melanoma
Acral lentiginous melanoma

- Most common type of melanoma in darker skinned patients
Lentigo maligna melanoma

- Melanoma on sun damaged skin (face, forearms)
- Not great term
ABCDE’s of Melanoma

- A = Asymmetry
- B = Border
- C = Color
- D = Diameter > 6mm
- E = Evolution - our newest and perhaps most important criteria!
Pigmented Skin Disorders
Melasma

- “Mask of pregnancy”
- Associated with pregnancy or OCP use
- Most avoidable risk factor: sun
- If pregnancy associated, may fade few months after delivery
- Tx: sun avoidance, protection, tyrosinase inhibitors (hydroquinone), topical corticosteroids
Diagnosis?
Papulosquamous Diseases
Papulosquamous Diseases

- Psoriasis
- Lichen Planus
- Pityriasis Rosea
- Cutaneous T cell lymphoma
- Tinea versicolor
- Dermatophyte infections
- Seborrheic Dermatitis
Papulosquamous vs Eczematous

- Redness and scale
- Papules and plaques
- Little to no crust, erosion, vesicles
- Sharply marginated edges of lesions

- Redness and scale
- Plaques
- Erosions, crust, vesicles, excoriation
- Ill-defined edges of lesions
PSORIASIS

• Sharply marginated erythematous papules that coalesce into plaques; pruritic
• Large white to silvery scales
• Auspitz sign
• Koebner phenomenon
• Symmetric, extensor involvement
• Nail involvement
WHAT CONDITION IS ASSOCIATED WITH “GRID-LIKE” nail pitting?
Histology of Psoriasis

• Marked epidermal hyperplasia and lymphocytic dermal inflammation
• Genetic and environmental factors play a role in initiating and modulating disease
• Immunologic component
Pityriasis Rosea

• Pathogenesis: viral etiology (HHV7, HHV6)
  – Other rash caused by these viruses?
• Diagnosis: clinical, biopsy, KOH
• Begins as herald patch, followed in next 1-2 weeks with disseminated rash in “Christmas tree” configuration (lasts 6-8 weeks)
• Therapy is not necessary (self resolves in 6-8 weeks)
• Treat symptomatically for itching: antihistamines, UVB, topical steroids
Lichen Planus

- 5 P’s: Pruritic Purple Polygonal Planar Papules
- Wickham striae (typically buccal mucosa)
- Koebnerizes
- Trunk, extremities: flexural wrists, ankles
- Oral and genital
- Scarring alopecia, destructive nail changes
- Association with Hepatitis C
Saw tooth appearance of rete-ridges

A band-like lymphocytic infiltrate fills the papillary dermis. The infiltrate press against the undersurface of the epidermis

Dr. Sampurna Roy
Mycosis Fungoides

- Type of cutaneous T cell lymphoma
- Sharply margined red brown plaques—may resemble psoriasis
- Evolution from patch to plaque and nodules
- Often on trunk, buttocks, thighs
- Pruritic—variable intensity
- Sezary syndrome: erythroderma, LAD, atypical lymphocytes in skin and blood
Mycosis Fungoides

• Diagnosis: pathology (Pautrier’s microabcess-atypical lymphs in epidermis), immunohistochemistry, T cell gene rearrangements.
DIAGNOSIS?
Tinea versicolor

- Mainly disease in young adults
- Exacerbations and remissions
- Malassesia furfur, normal skin flora
- Treat with selenium sulfide shampoo, topical imidazole antifungals, systemic fluconazole (rarely needed)
- Prophylactic treatment to avoid recurrence
Tinea Corporus/Manum/Pedis

• Infection due to dermatophyte fungus (*capitis*: *Trichophyton tonsurans*, *Corporis*, *T. rubrum*, *Pedis*: *T. rubrum*)

• Erythematous annular, arciform plaques with leading edge of scale, post inflammatory hyperpigmentation

• Tx with topical azoles, terbinafine (if in hair follicle (i.e. *capitis*) need systemic treatment)
Diagnosis?
Impetigo

• Caused by?
  – Staph > Group A Beta hemolytic Strep or Strep pyogenes

• In bullous form, what causes the bullae?
  – Staph aureus exfoliative exotoxins A&B

• Exotoxin binds to:
  – Desmoglein 1 acantholysis at level of granular layer (subcorneal)

• Treatment:
  – mupirocin, fusidic acid 2% cream
  – oral Dicloxacillin, cephalexin
Diagnosis?
Erysipelas

• Cause?
  – group A strep

• How different than cellulitis?

• Superficial variant, cellulitis is in deep dermis and subcutaneous tissue

• Well-demarcated and raised, tender erythema

• Most commonly on leg; used to be on face

• Treat with Penicillin
Seborrheic Dermatitis

- Inflammatory reaction against metabolites from *Malessezia sp.*
- Patterned in sebum rich areas of body (scalp, nasolabial folds, eyebrows, chest, axilla)
- Tx with selenium sulfide, zinc, ketoconazole and topical steroid solution/foam/cream. Pimecrolimus cream (Elidel)
- What diseases are seborrheic dermatitis associated with or worsened by?
  - Parkinson’s disease
  - AIDS, HIV
Acanthosis Nigracans

- Associated with DM, obesity, metabolic syndrome
- Rare association with internal malignancy
  - Can be found in combination with Sign of Lesser Trelat (eruptive sebhorric keratoses)
Eczema

- Flexural, ill defined pink scaled plaques
- Scale not micaceous like psoriasis
- Face involvement more common vs. psoriasis
- Infection (staph, molluscum, HSV) more common
- Pruritic
- +FH history of atopy: eczema, hayfever, asthma
Case 1

Describe the lesions...
Case 1

• 75 year old man
• Itchy lesions over legs and arms
• No oral lesions
Diagnosis?
Bullous Pemphigoid

- Onset usually after age 60
- Can start as pruritic urticarial plaques without blister formation
- Blisters are often intact and do not spread with pressure
- Mucosal involvement in 10%
Bullous Pemphigoid

• Antibodies develop against two proteins associated with the upper portion of the hemi-desmosome
  – BPAG1 = 230kD
  – BPAG2 = 180kD (collagen XVII)
Keratinocyte

Desmosome

Hemi-desmosome

Basement membrane
Linear deposits of IgG and C3 on blister roof
Case 2

- 55 year old woman
- Mouth sores over past several months
- Now with skin lesions
Case 2

Describe the lesions
Diagnosis?
Pemphigus Vulgaris

- Mean age 50-60 although range is broad
- Almost all develop painful erosions of the oral mucosa
- Develop thin, flaccid blisters that can appear anywhere
- Develop crusts that are resistant to healing
- Prior to immunosuppressants, higher mortality that BP
Pemphigus Vulgaris

• IgG autoantibodies to desmosomal structural proteins called desmogleins
  – Desmoglein 1 and 3
  – Desmoglein 3 (mucosal dominant)
Case 5

Describe the lesions
Case 5

• 34 year old woman
• Recent “canker sore” on lip
Diagnosis?

Erythema Multiforme
Erythema Multiforme

- Relatively common, often recurrent
- Often associated with HSV, but 50% of cases without known cause
- Target lesions are most classic
- Center can vesiculate
Erythema Multiforme

• Clinically, of the blistering eruptions, most commonly in the differential of bullous pemphigoid
Case 4

Describe the lesions
Case 4

- 45 year old man with HIV
- Started on Bactrim prophylaxis 2 weeks prior
Diagnosis?

Toxic Epidermal Necrosis
Toxic Epidermal Necrolysis

- 80% of cases are caused by drug exposure
  - Antibiotics (sulfa, penicillins)
  - Anticonvulsants
  - NSAIDs
  - Allopurinol
Toxic Epidermal Necrolysis

- Skin tenderness and erythema
- Background of a morbilliform eruption
- Usually lesions have dusky appearance at center
- Skin “shears” off in large sheets
- Biopsy shows epidermal necrosis
- Can often resemble pemphigus vulgaris
Background rash
Sheets of denudation
• EM $\rightarrow$ SJS $\rightarrow$ TEN spectrum
  – Controversial, but not for Step 1 😊

• SJS <10-30% BSA

• TEN >30% BSA
Describe the lesions
Dermatitis Herpetiformis

- Grouped, clustered pink-red crusted to hemorrhagic papules
- Usually will just see excoriations b/c so pruritic
- Common on elbows, knees, and buttocks
- Anti-transglutaminase (TTG)
- Associated with celiac disease
SSc: skin findings

- Other findings:
  - Early: pitting digital edema
  - Mid: indurated phase with taut, shiny appearance
  - Late: gradual softening of the skin
  - Mat-like telangiectasias (squared off)
  - Dyspigmentation “salt and pepper leukoderma” or diffuse bronzing
  - Proximal nail fold capillary dilated loops alternating with capillary loss
  - Calcinosis cutis
  - Hyper or hypo-trichosis in affected areas of skin
  - Facial disfigurement: microstomia, lip retraction, “beaked” nose, perioral furrows
  - Raynaud’s phenomenon (secondary Raynaud’s)
  - Cutaneous ulcers – painful and debilitating
  - Pterygium inversum unguis – distal bed adheres to ventral nailplate (also seen in LE or as an idiopathic change)
  - Radiographs show diffuse calcification of skin
Definitions...

- Systemic sclerosis (SSc) = scleroderma = progressive systemic sclerosis
  - Name conveys that there is both skin and internal organ involvement
  - “progressive” fell out of favor because not necessarily progressive

- SSc has 2 subtypes: limited and diffuse (both with internal involvement)
  - Limited SSc: Fibrosis of skin on fingers, hands, face (includes CREST)
  - Diffuse SSc: Generalized fibrosis usually beginning on hands but then extending to forearms, arms, face, tru and LE
SSc/Scleroderma - Epidemiology

Female predominance of 3-4 to 1
Usual onset 30-50yrs old; can affect children and elderly
Significant M&M with 10yr survival rate of <70%
SSc pathogenesis

• Immune dysregulation
  • Autoantibody production

• Fibrosis
  • Final common pathway
  • Excessive deposition of collagens, proteoglycans, fibronectin, fibrillins, adhesion molecules, growth factors
SSc diagnostic criteria (thanks, ACR!)

- One major OR two minor required
- Major criterion
  - Systemic cutaneous sclerosis proximal to the MCP or MTP joints
- Minor criteria:
  - Sclerodactyly
  - Digital pitting scars/loss of substance from finger pad
  - Bibasilar pulmonary fibrosis
Limited SSc: Fibrosis of skin on fingers, hands, face (includes CREST)
Diffuse SSc: Generalized fibrosis usually beginning on the hands but then extending to forearms, arms, face, trunk and LE

<table>
<thead>
<tr>
<th></th>
<th>Diffuse</th>
<th>Limited*</th>
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</thead>
<tbody>
<tr>
<td>Skin involvement</td>
<td>Distal and proximal extremities, face, trunk</td>
<td>Distal to elbows, face</td>
</tr>
<tr>
<td>Raynaud’s phenomenon</td>
<td>Onset within 1 year or at time of skin changes</td>
<td>May precede skin disease by years</td>
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<tr>
<td>Organ involvement</td>
<td>Pulmonary (interstitial fibrosis); renal</td>
<td>Gastrointestinal; pulmonary arterial hypertension after 10-15 years of disease in &lt;10% of patients; biliary cirrhosis</td>
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<td></td>
<td>(renovascular hypertensive crisis); gastrointestinal; cardiac</td>
<td></td>
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<tr>
<td>Nail fold capillaries</td>
<td>Dilatation and dropout</td>
<td>Dilatation without significant dropout (avascular areas)</td>
</tr>
<tr>
<td>Antinuclear antibodies</td>
<td>Anti-topoisomerase 1/SCL-70</td>
<td>Anticentromere</td>
</tr>
</tbody>
</table>

* Also referred to as CREST (calcinosis, Raynaud’s, esophageal dysmotility, sclerodactyly, telangiectasia).
SLE cutaneous manifestations

- Butterfly facial erythema
- Associated edema
- Ears and chest may also be involved
- Oral ulcers
SLE Diagnostic Criteria (ACR)

1. Discoid rash
2. Oral ulcers (present in 21%)
3. Photosensitivity
4. Arthritis
5. Malar rash
6. Immunologic disorders (anti-dsDNA, anti-Sm, antiphospholipid antibodies)
7. Neurologic disorders (seizures or psychosis in the absence of other known causes)
8. Proteinuria (>0.5g/day or casts)
9. + ANA test
10. Pleuritis/pericarditis
11. Blood abnormalities (hemolytic anemia, leukopenia, thrombocytopenia)

How many criteria must be met?
SLE is diagnosed if 4 of 11 criteria are present serially or simultaneously.
DOPAMINE RASH

D: Discoid rash
O: Oral Ulcers
P: Photosensitivity
A: Arthritis
M: Malar
I: Immuno markers (anti Sm, dsDNA, ro, la, histone for drug induced, etc)
N: Neuro changes (psychosis, personality changes, seizures)
e: - nothing (Elevated ESR doesn’t count)

R: Renal
A: +ANA
S: Serositis (Pleurisy, pericarditis)
H: Hematologic (Hemolytic anemia, thrombocytopenia, leukopenia)
SLE Cutaneous Manifestations

- Periungual telangiectasia and slow wandering glomeruloid loops
- Purplish or erythematous palms, soles, elbows, knees
- Non scarring hair loss or lupus hairs (short hairs anterior hairline)
- Livedo
- Multiple eruptive DFs
- Calcinosis cutis
What is this?

- Interknuckular involvement
Classifications of LE

• **Acute Cutaneous LE**
  – Involves primarily the epi and upper
  – Usually systemic disease

• **Subacute Cutaneous LE**
  – Associated with anti-Ro/SSA aAbs, photosensitivity
  – Majority do not have significant systemic disease

• **Chronic Cutaneous LE**
  – Majority do not have significant systemic disease

• **Discoid LE**
  • Epi upper and lower dermis, and adnexal structures, and they can scar

• **Hypertrophic LE**

• **Chillblain LE**

• **Tumid Lupus**
  • Dermis but there is no prominent epidermal or adnexal involvement

• **Lupus Panniculitis**
  • Involves the subcutaneous tissue and may result in disfiguring depressed scars

• **Other**
  – Bullous SLE
Your patient has:

- Proteinurea, hemolytic anemia, anti-Sm, and antiphospholipid antibodies
- Does she have SLE?
  - NO, only has 3 criteria (anti-Sm and APL are same)
- Malar rash, proteinuria, anti-Sm, + ANA
- Does she have SLE?
  - YES, has 4 of the ACR criteria (ANA is own point)
Systemic Manifestations of LE

- Arthralgias (95%, early symptom)
- Constitutional sx (fever, wt loss)
- Adenopathy
- Pleuritis/ILD/pleural effusions
- Deforming arthropathy
- Thrombosis of vessels
- Nephritic or nephrotic syndromes
- Myocarditis or pericarditis
- Raynauds
- CNS involvement
- Idiopathic thrombocytopenic purpura
- Myopathy

- Most due to immune complex disease, esp vasculitis
Lab Findings of SLE

- Hemolytic anemia
- Thrombocytopenia
- Decreased C3, C4
- Leukopenia
- ESR
- Coombs positive (sometimes)
- RF may be present
- False positive serologies for syphilis
- IgG may be high
- Serum globulin increased
- Albumin to globulin ratio reversed
- UA: albumin, RBCs and casts in urine
Drug-induced SLE Syndrome

- What key systemic findings does drug-induced lupus LACK?
  - CNS and renal involvement
- What are the predominant symptoms?
  - Musculoskeletal sx and serositis (arthralgias, myalgias, pleuritis)
- Less often have signs of cutaneous lupus (5-25%)
- What is the autoantibody *usually* associated with drug induced LE?
  - Anti-histone (95%)
Drug Induced SLE

- Hydralazine
- Isoniazid
- Procainamide
Drug-induced LE

• A different set of drugs has been reported as capable of triggering anti-Ro aAb production and cutaneous lesions of SCLE

• Name them:
  – Hydrochlorothiazide, diltiazem, griseofulvin, terbinafine

• These usually don’t have anti-histone aAb (as seen in classic drug induced SLE!)
What’s the diagnosis?

DLE
Who gets it?

- Largest risk factor?
- Gender (F:M 6:1)
- Other strong risk factor?
- Race (AA: caucasian 4:1)
  - Earlier age and higher mortality
Clinical features of DLE

- Dull red macules or indurated plaques
- Develop adherent scale
- Evolve with atrophy, scarring and pigment changes
- In darker skinned individuals, can get hyper and de-pigmentation
- Perifollicular erythema
- Extractable anagen hairs
• Common sites
• Above the neck – scalp, bridge of the nose, malar cheeks, lower lip, ears (conchal bowl and external canal)
• Unusual to see lesions below the neck without lesions above
What’s the diagnosis?

- **SCLE**
  - Presentation?
  - Sun-exposed areas (face, trunk)
  - Polycyclic annular or psoriasiform plaques
  - Telangiectasia and depigmentation may be present
  - Follicles not involved
  - scale is loose
  - **NO SCARRING**
What antibody should you associate with SCLE?

- Anti-Ro (seen in 60-100%, probably about 70%)
- What other disease should you think about with anti-Ro Ab’s?
- Sjogren’s
Diagnosis?

Neonatal Lupus

• Presentation?
  – annular erythematous macules and plaques
• Are they present at birth?
  – NO - appear in the first few weeks of life
• Most common location?
  – head (periocular/ periorbital) involvement is more common than extremities, trunk
• Associated with which Antibody?
  – Anti Ro
• Serious complication?
  – >50% have congenital heart block
• Prognosis for skin lesions?
  – Skin lesions resolve by 6 months
What other complications can babies with anti-Ro+ mothers get?

- 3\textsuperscript{rd} degree heart block
- SCLE
- Hepatobiliary disease
- thrombocytopenia

Based on information from the Research Registry for Neonatal Lupus (USA), there is an approximately 20% mortality, and approximately two-thirds of children require pacemakers.
What’s the diagnosis?

Dermatomyositis

- Heliotrope rash—pink/violet discoloration are signs of inflammation of underlying orbicularis oculi muscle
- Erythema, scaling and swelling of upper face
- Telangiectatic vessels become prominent in nail folds
- Sausage shaped loops with adjacent avascular regions
Cutaneous manifestations of DM

Upper back and neck “Shawl sign”

Periungual telangiectasias:
Sausage shaped loops with adjacent avascular regions
Cutaneous manifestations of DM

Gottron’s Sign: pink to reddish purpule atrophic or scaling eruption of knees, knuckles or elbows
Gottrons papules: flat topped polygonal violaceous papules over knuckles
Mechanics hands: HK, scaling, fissuring and hyperpigmentation of fingertips and sides of thumb
Criteria for DM (ACR)

1. Skin lesions
2. Heliotrope rash
3. Gottron’s papules or sign
4. Proximal muscle weakness
5. Elevated CK or aldolase
6. Muscle pain on grasping or spontaneous pain
7. Myogenic changes on EMG
8. Anti Jo-1 Ab
9. Non-destructive arthritis or arthralgias
10. Systemic inflammatory signs (fever, elevated CRP or ESR)
11. Path c/w myositis

Must have first criterion + 4 others for DM
Lab findings of DM

- Elevated serum CK
- Elevated aldolase, LDH, transaminases
- Leukocytosis
- Anemia
- Elevated ESR
- + DIF with granular staining of IgA, IgM, IgG
- EMG changes
- Check for malignancy!!!
Muscle changes

• Symmetric or asymmetric?
  – Symmetric
  – Involves shoulder girdle and pelvic girdle

• May progress to involve swallowing, talking and breathing

• T or F? It can have cardiac involvement
  – TRUE

• T or F? The majority of the time, skin involvement precedes muscle involvement
  – True

• Name 4 ways to evaluate for muscle disease?
  – CK, aldolase, EMG or MRI
More DM matching

- Interstitial lung disease
- Sclerodermatomyositis
- Acute, shawl, cuticle + good prognosis
- Mixed connective tissue disease + DM

- Anti-RNP
- Anti-Ku Ab
- Anti-Mi-2 Ab
- Anti-Jo-1 Ab
- Anti-PM/scl

“Mi shawl is a good prognosis”
“Jo can’t blow 1 b/c he has ILD”

Jo-1 is also known as: Histidyl tRNA synthetase