Cutaneous Lupus
History of SLE

- Historians have theorized, in combination with the porphyrias, that SLE could have been a contributor to the Vampires and Werewolf legend, due to the photosensitivity and scarring nature.

- Three periods:
  - **Classic**: First recognized in the Middle Ages. Lupus (Latin for Wolf) was used by the 12th century physician Rogerius to describe the butterfly Malar Rash of SLE. The word erythematous is derived from the Greek word ερυθρός, meaning “red.”
    - The word has multiple sources,
      - Some historians claim that the rash looked like the fur on a wolf’s face
      - Others claim the rash resembled wolf bites or scratches
      - Finally, some think the term comes from the French word for wolf (loup), related to a French style of mask women wore to conceal their faces.
  - **Neoclassic**: 1872 Móric Kaposi recognized systemic manifestations of disease
  - **Modern**: 1948 – the Lupus Erythematosus cell was described (PMN with ingestion of the nuclear material of another cell). While it was present in many other diseases, it defined the era of clinical-laboratory and pathophysiologic descriptions that have defined the Connective tissue diseases.
    - 1979 SCLE described by Gilliam, Sontheimer and Thomas
Etiology and pathogenesis of SLE

- Unfair and poorly written question #1 – What is the pathogenesis of SLE?
- A - As with any autoimmune condition, these are not understood completely
  - the pathogenesis of specific skin disease is intertwined with that of systemic lupus.

**Keys:** interplay of *internal patient environment* and *external environment* leading to:
- 1) genetic and environmental factors that predispose a person to
- 2) a break in immune tolerance against self
- 3) affecting various types of components in the immune system
  - Innate and adaptive (sensitized) cells
  - Cytokine profiles
  - Complement (amount, deposition, and processing)
- 4) leading to unregulated immune activation and tissue damage
SLE Etiology – Susceptibility Phase – Genetic predisposition

- Evidence for genetic predisposition in general:
  - While family history of any connective tissue disease is a strong risk factor for SLE, it is nonspecific and likely shows polygenic inheritance.
  - Increased sibling risk (up to 20 fold)
  - Skin lesions sometimes follow lines of Blashko (possible post-zygotic mutation, or loss of heterozygosity of a genetic locus)

- Mechanisms for predisposition: A Multi-step process, initiated by one gene, then exacerbated by additional genes or loci

- The players (that we know)
  - 1-TNF genes and other cytokines
  - 2-Complement genes
  - 3-HLA genes
  - 4-Hormones
Evidence for TNF Genes/cytokines predisposing towards lupus:

- In one study of patients with SLE, there was a substantial increase of a promoter polymorphism (genetic defect) in a TNFα gene (-308A).
- LIGHT (UVB) + artificially added IL-1α (photo induced cytokine) = increased amounts TNF-α -308A promoter.

Possible mechanisms for predisposition:

- At least this one gene defect (likely more) may contribute directly to the photosensitivity of patients with SCLE.
Evidence for HLA Genes predisposing towards lupus:

- They show strong hereditable component, especially MHC class II DR. For example in DLE alone:
  - Increase in DRE HLA-B7, -B8, -DR2, -DR3, DQA0102
  - Decrease in HLA-A2
  - Maximum risk for DLE: combination of HLA-DR3, HLA-DQA0102, and HLA-B7

Possible mechanisms for predisposition:

- Theoretically, MHC alleles may act by shaping the T-cell repertoire.
- Specifically, HLA class II antigens are closely associated with specific autoantibody genes
SLE Etiology – Susceptibility Phase - Complement Genes

- Evidence for Complement Genes predisposing towards lupus
  - Genetic deficiency of early complement components (esp. C1q, C4 and somewhat C2) predispose patients to developing lupus
  - Complete congenital deficiency of C1q is the strongest single risk factor for development of photosensitive SLE
- Possible mechanisms to be covered later
SLE Etiology – Susceptibility Phase - Hormones

- Evidence for hormones predisposing towards lupus
  - **Female:Male Ratio of 9:1 in SLE**
  - Lupus patients metabolize estrogens differently. Increased estrogens, decreased testosterone:
    - Can have up to a 20-fold increase in the fraction of high-potency to low-potency estrogens compared to normal,
    - Also have a decreased availability of testosterone and other androgens
- Possible mechanisms for predisposition
  - Sex hormone affect the immune system!!
  - Increased estrogen and progesterone levels promote humoral autoreactivity causing an increase in
    1) the number of self-reactive lymphocytes that bypass developmental deletion
    2) the CD4/CD8 ratio (favoring humoral response)
    3) the number of B cells that express high affinity recognition of self-DNA
  - Androgens, conversely, shift the overall cytokine profile to a TH1 cell-mediated response
SLE etiology – Induction/Triggering Phase – Important point

- SLE induced by either of the following mechanisms (and likely more):
  - Dysregulated apoptosis
  - Cross reactivity to foreign antigens
  - Induction of SLE is characterized by increased antigen processing by **dendritic cells**
    - Affected by TNF-α and IFN-α
Dendritic cells

- Dendritic Cells, what do they do?:
- Immature dendritic cells sample their environment, and through use of toll like receptors, they recognize specific chemical signatures (as foreign), found on subsets of pathogens (bacteria and viruses)
- When they recognize foreign material, they become activated (mature), and present these foreign antigens via their MHC molecules, causing activation of B and T lymphocytes
- If they have defective MHC molecules (increased susceptibility), this may contribute to increased recognition of self as foreign and subsequent autoimmunity
SLE etiology – Induction/Triggering Phase – Dysregulated Apoptosis

- What normally happens: when cells undergo apoptosis, they are bound by complement, and quickly engulfed and disposed of by “housekeeping” macrophages,” and their intercellular contents are not available for immune surveillance.
- Dysregulation of this step can lead to induction of SLE in two ways
  - Increased apoptosis - If clearance of apoptotic material is not accomplished quickly, cells become necrotic and release previously “hidden” intracellular contents
  - Decreased apoptotic cell clearance - When levels of complement are low (increased susceptibility), this necrotic release of contents is increased, even if rate of apoptosis is stable
- Both of these mechanisms allow dendritic cells to process and present an increased number of self antigens that are normally “hidden”
SLE etiology – Induction/Trigger Phase UV Radiation

- Probably the most important factor in triggering disease in SLE
- Evidence: the photosensitivity of SLE
- Mechanisms:
  - Causes apoptosis of keratinocytes, making hidden proteins available for immune surveillance
  - UVB displaces autoantigens such as Ro/SS-A and La/SSB from internally to the cell surface
  - UV light upregulates chemokines that activate autoreactive-T-cells and IFN-α producing dendritic cells
- Evidence:
  - DLE has been provoked in normal skin of patients with lupus by delivery of high doses of UVB radiation
SLE etiology – Induction/Trigger Phase Drugs

- Evidence: Drug induced Lupus/SCLE
- Mechanisms:
  - Some drugs can cause T-cell DNA alteration which can increase the autoreactivity of the T-cells and trigger SLE
  - Also many drugs that induce Lupus have photosensitizing properties
SLE etiology – Induction/Trigger Phase Tobacco

- Evidence:
  - Smokers at a greater risk of developing SLE than nonsmokers and even former smokers
  - Also less responsive to antimalarial treatment
- Mechanisms:
  - ? May be related to lipogenic aromatic amines
SLE etiology – Induction/Triggering Phase - Foreign antigens/Viruses

- **Evidence:**
  - Viruses exacerbate SLE
  - Seroconversion to EBV is nearly universal in SLE patients
- **Mechanisms:**
  1. Increased apoptosis
  2. Induction of cell surface expression of Ro/SS-A and related autoantigens
  3. Immune Stimulation by related, foreign antigens
     - **IN CONTRAST TO INCREASED APOPTOSIS,** immune stimulation by a foreign antigen (viruses) can lead to epitope spreading and autoimmunization
  - Cross reactivity of EBV antigens and SLE autoantigens:
     - In one study, an epitope from EBV cross reacted with an epitope of Ro
     - Furthermore, rabbits immunized with this EBV epitope developed antibodies to Ro and other lupus antigens, and subsequently developed lupus
SLE etiology - Induction/Triggering Phase - IFN-α

- What is IFN-α?
  - It is made in Plasmacytoid Dendritic Cells (specifically induced by toll like receptors)
  - Causes monocytes to differentiate into Myeloid DCs
  - Myeloid DCs present self antigens to autoreactive CD4 T cells and support B-cell proliferation (as opposed to the “housekeeping macrophages which capture apoptotic cells)

- IFN-α is at the heart of SLE – evidence:
  - Levels increased at baseline in SLE patients
  - Recombinant IFN-α can induce SLE
  - IFN-α increases with disease flares

- Mechanisms:
  - IFN-α is made in an uncontrolled fashion due to either genetic alteration or a persistent stimulus (virus)
  - This turns on the adaptive immune response, leading to a break in tolerance to self antigens, and activation of T and B cells
SLE etiology - Induction/Triggering Phase – TNF-α

- Mechanism for triggering lupus:
- TNF-α induces even more apoptosis through the FAS-associated death domain
- It induces HLA-DR expression on keratinocytes and causes stimulation of an adaptive immune response
- Evidence against TNF triggering lupus:
- Lupus has been shown to worsen with anti-TNF therapy (etanercept and infliximab)
- Mechanism: TNF inhibits IFN-α (IFN-α causes lupus to flare)
- Therefore both too much TNF or too little TNF may induce lesions of cutaneous lupus
SLE etiology – Induction/Triggering Phase – Important point #1 (repeat)

- SLE thought to be induced by either*:
  - Dysregulated apoptosis
  - UV radiation
  - Drugs
  - Tobacco
  - Viruses
  - Complement deficiencies
  - Cross reactivity to foreign antigens
    - Viruses
- Induction of SLE is characterized by increased antigen processing by dendritic cells
  - Affected by TNF-α and IFN-α

* - in the susceptible person
SLE etiology - Expansion Phase T cells

- Involved in induction and expansion phases
- Dendritic Cells present self antigen to T-cells, causing T-cell activation
- T cells can cause tissue damage in end-organs, especially in DLE
SLE etiology - Expansion Phase B cells

- B-cells present antigens to autoreactive T-cells, and amplify T-cell activation.
- Hallmark of SLE is the production of autoantibodies by B-cells, some of which are directly pathogenic, leading to the Injury Phase.
- B-cells may not be as important in DLE.
SLE Etiology – Injury Phase

- What causes the injury to the tissue?
- Hallmark of SLE is the overproduction of autoantibodies by B-cells, some of which are directly pathogenic, including dsDNA, and Ro/SSA antibodies.
- Lupus patients have reduced clearance of immune complexes by the reticuloendothelial system
- Most of the tissue injury is due to B-cells due to immune complex and complement mediated damage through
  1. Direct cell death
  2. T-Cell activation
  3. Opsonization
  4. Blocking of target molecule function
- Cytotoxic T Cells – can also cause end organ damage, especially in CLE
Summary of SLE etiology

- Q - A patient asks: “How did I get this?”
- A - As with any autoimmune condition, these are not understood completely
  - Interplay of internal patient environment and external environment leading to:
    - 1) genetic and environmental factors that predispose a person to
    - 2) a break in immune tolerance against self
    - 3) affecting various types of components in the immune system
      - Innate and adaptive (sensitized) cells
      - Cytokine profiles
      - Complement (amount, deposition, and processing)
    - 4) leading to unregulated immune activation and tissue damage
Let’s take a step back:

- **What does this mean?**
  - The sheer number of different mechanisms for all of these phases is one of the main reasons for the highly variable nature of this disease and explains why it forms such a broad spectrum.

- **Lupus is a spectrum:**

  - This is why we classify lupus into different categories.
  - It is important to make these designations, as the type of skin involvement can reflect the underlying pattern of SLE activity.
Important Point #1

Q - Cutaneous presentations of Lupus should be divided into which 2 broad categories?

A – LE specific and LE non-specific (histologically)

- Cutaneous manifestations were traditionally divided into lesions showing characteristic histological changes of LE (LE-Specific Skin disease), or those not distinct, histopathologically, for LE (may be seen as a feature of another disease).
- The term “Cutaneous LE” has been often used interchangeably with the term LE-Specific skin disease.
Important Point #2

- Q - What are the three main lupus specific rashes?
- A - ACLE, SCLE, and DLE
- These terms do not reflect how long the individual lesions have been present, but refer to the pace and severity of SLE
How to approach the SLE patient
Case 1

- A 25 year old woman is sent with a 4 day history of a “bad rash.” She was out in the sun the prior weekend, and noticed the rash on her face, and upper chest. She says the rash started as small bumps that grew and now she’s “all red.” On physical exam, she has edema and erythema on her malar area and bridge of nose, but sparing her nasolabial folds. She has never had this rash before. Before walking into the room, you note that she smokes about 1ppd. You start to calculate her total pack years, then realize you don’t have any idea how that would be applicable and enter anyway.
What is your diagnosis?
Q – What is the most common clinical manifestation of Acute Cutaneous Lupus Erythematosus?

A - Arthritis (up to 45% of patients with CLE have arthritis)- Skin disease is the second most frequent clinical manifestation

Skin disease is seen in 35-60% of pt’s with SLE
- Typically precipitated or exacerbated by UV light
- May last hours, days, weeks or rarely more prolonged
- Post-inflammatory pigment change common
- Scarring does not occur unless complicated by bacterial infection

Q – How does flaring ACLE, most notably the malar rash, relate to underlying SLE?

A – ACLE occurs in the presence of flaring SLE and will wax and wane with underlying SLE disease (including nephritis)
Acute Cutaneous Lupus Erythematosus — LE Specific on Biopsy

- **Localized** or Butterfly malar rash
  - Common in acute cutaneous LE (occurs in 20-60% of patients with LE)
  - Begins on malar area and bridge of nose, classically associated with edema (can be severe)
  - Nasolabial folds are characteristically spared
  - May begin as macules and/or papules the may become confluent and hyperkeratotic
  - Ears and chest may also have early lesions with the localized butterfly rash
  - Eruption lasts days to several weeks, and resolves without scarring
Acute Cutaneous Lupus Erythematosus – LE Specific on Biopsy

Q- How does flaring ACLE relate to DLE?
A- It is rare for ACLE to occur with active DLE, but DLE lesions are seen in 25% of ACLE patients at some point in the disease course.
Acute Cutaneous Lupus Erythematosus – LE Specific on Biopsy

- **Generalized**: Maculopapular or SLE rash of generalized ACLE.
  - Morbilliform or exantheme eruption focuses over the extensor aspects of the arms and hangs, sparing the knuckles
  - Palms, soles, elbows, knees, or buttocks may be persistently erythematous or purplish, sometimes with overlying scale
Acute Cutaneous Lupus Erythematosus – LE Specific on Biopsy

- In severe cases, an extremely acute form can simulate TEN (not to be confused with Bullous LE).
  - Mucosa may not be involved.
  - Occurs predominately on sun exposed skin.
  - More insidious onset than TEN
Acute Cutaneous Lupus Erythematosus - Histology

- Less impressive than DLE or even SCLE
- Mainly shows a cell-poor interface dermatitis
- Mild focal vacuolar alteration of basal keratinocytes
- May see individually necrotic keratinocytes
- Upper dermis with pronounced mucinosis
- Uncommon to see basement membrane zone thickening, follicular plugging, or alteration of epidermal thickness
- DIF- 60-100 % display a lesional lupus band, but this can commonly be seen in sun damaged skin from healthy individuals.
Colloidal Iron Stain for Mucin
Acute Cutaneous Lupus Erythematosus - Treatment

- Specific Treatment (more later)
  - ACLE usually responds to systemic immunosuppression used to treat underlying SLE
  - Antimalarials can have a steroid sparing effect
Case 2

- A 40 year old Caucasian woman without insurance shows up 15 minutes late to your resident clinic on a Tuesday afternoon. Her chief complaint in her chart says “Rash x 6 days after a weekend at the beach.” You take a deep breath and enter.
Case 2 (cont)

- The woman is in her “thick” paper gown, opening in front. You immediately notice that she is covered in confluent, annular pink to faint violet, macules and patches located mostly on her face, arms, back and chest. Each lesion has fine scale diffusely covering it, and you notice slight dyspigmentation, especially in the center of the lesions. On her uninvolved skin, you notice annular areas of severe hypopigmentation (almost vitiligo-like). You gently poke her skin and notice it feels like skin-No induration whatsoever. You ask her if she has ever had this rash before, she says “Yes, several years ago, but I took a pill for a few months and it went away.” She does not know the name of the pill, or her prior diagnosis.
What is your diagnosis?
Subacute Cutaneous Lupus Erythematosus

- Described in 1979
- Also called symmetric erythema centrifugum, disseminated DLE, autoimmune annular erythema, subacute disseminated LE, superficial disseminated LE, psoriasiform LE, maculopapular photosensitive LE, and lupus erythematosus gyratum repens
- Subset of LE with specific clinical, serologic and genetic features
- May occur with an SLE flare or without
- Most common in women 15-40 (mean age of onset 5th decade)
- Makes up 7% to 27% of the LE population
Subacute Cutaneous Lupus Erythematosus

- Q - Lesions begin as scaly erythematous macules and/or papules, and evolve in what two presenting forms?
- A - Annular or psoriasiform plaques (the 2 subtypes of SCLE, usually a pt is one or the other, but may develop elements of both)
- Sun exposed surfaces and face and neck, v portion of chest and back, and sun exposed areas of arms
- Photosensitivity is prominent in ½ of patients
- Vary from red to pink with faint violet tones
- Thin scale, easily detached
- Follicles are not involved
- No scarring, but can leave permanent or long lasting leukoderma (vitiligo like) and telangiectasias
- Lesion are transient and migratory
Subacute Cutaneous Lupus Erythematosus – Workup

- Concomitant ACLE or DLE in 15-20% of cases at some point in the course.
- Q - How would one differentiate SCLE from ACLE and DLE:
  - A-
    - ACLE lesions more transient usually, and heal with less pigmentedary change
    - ACLE usually malar, SCLE usually neck shoulders UE and trunk, or lateral face
    - DLE with SCLE more severe (greater hyper or hypo pigmentation, scarring, follicular plugging and scale)
    - To differentiate DLE and ACLE, DLE is indurated, ACLE is not
- Most have antibodies to Ro/SSA antigen (70-90%), but not necessary to make a diagnosis of SCLE
- Q-what percent of SCLE patients are (+) for anti-La/SSB?
  - A- 30-50%, and overlap with Sjogren syndrome, and other autoimmune disease as well as possibly with PCT and with internal malignancy
- Most are positive for HLA-DR3
- 50% of patients meet criteria for SLE
- 75% of patients have arthralgia or arthritis, 20% have leukopenia, 80% have a (+) ANA test (usually in a particulate pattern)
Subacute Cutaneous Lupus Erythematosus – rare presentations

- TEN/Stevens Johnson’s-like rash
  - Intense injury to epidermal basal cells can cause active edge of annular lesions to undergo a vesiculobullous change that can look crusted or like (may look like the ACLE TEN-like rash)
  - Not to be confused with Bullous LE (which is a LE non-specific rash)

- Rarely presents as:
  - An exfoliative erythroderma
  - Acral distribution of annular lesions (do not confuse with ACLE),
  - Pityriasiform lesions
  - Exanthematous variants

- Q - What is Rowell syndrome
  - A - Erythema multiforme-like lesions occurring in patients with SLE with La/SSB antibodies
Subacute Cutaneous Lupus Erythematosus – Prognosis and Treatment

- Generally runs a mild course-renal, cns, vascular complications are rare (10-15% of pts)
- Progression often, but with many pts having long-term if not permanent remissions
- Risk factors for SLE in SCLE –
  - Papulosquamous variant
  - Leukopenia
  - High ANA titers (>1:640)
  - Anti-dsDNA antibodies
- Most patients respond to sun protection and antimalarials
- Most pts have intermittent recurrences of skin disease activity
- Neonatal lupus shares many features with SCLE (to be covered later)
Subacute Cutaneous Lupus Erythematosus - Histology

- Mild interface dermatitis, universal finding in active lesions, alternating with areas of lichenoid dermatitis.
- Pronounced epidermal atrophy.
- Mild hyperkeratosis
- **PARAKERATOSIS MAY BE PRESENT** (compare to DLE).
- **CHRONIC CHANGES SUCH AS FOLLICULAR PLUGGING, BASEMENT MEMBRANE ZONE THICKENING AND HEAVY LYMPHOID AGGREGATES ARE LACKING.**
- Mucin usually prominent, but may not be.
- Can not distinguish annular from psoriasiform SCLE on histology alone
- **DIF (+) in 30-60% cases.**
  - Dustlike particulate (represents in vivo bound Ro/SSA) deposition of IgG in epidermal nuclei (if Ro (+))
Case 3

“A 48-year-old white man developed a papulosquamous and annular eruption in sun-exposed areas during the summer. The patient was taking nifedipine for essential hypertension for four years. Serology showed the presence of antinuclear and anti-Ro/SSA as well as antihistone antibodies.
What is your diagnosis?
Subacute Cutaneous Lupus Erythematosus – Drug Induced

- Name 3 drugs that can cause SCLE?
- hydrochlorothiazide, ace inhibitors, calcium channel blockers, cinnarizine, interferons, anticonvulsants, griseofulvin, glyburide, piroxicam, D-penicillamine, spironolactone, statins, terbinifine, sulfonylureas, oxpranolol, gold therapy, naproxen, ranitidine, efalizumab, propylthiouracil, systemic 5-fu, lansoprazole, bupropion, acebutolol, tiotropium inhaled
- Anti TNF therapy has induced both SCLE and DLE lesions
Case 4

- A 55 year old African American man presents to your clinic with multiple dull red indurated painless plaques with slight scale and central atrophy located on his malar cheeks, neck, central face, sparing his nasolabial folds. He states the plaques begin as similar colored “bumps.” He also says he’s been losing hair on his scalp.
What is your diagnosis?
Discoid Lupus Erythematosus – epidemiology

- Often presents in young adults
- Q- Are men more likely to have SLE or DLE?
  - A – DLE. Women:men in DLE is 3:2-3:1 (much lower than that of SLE-more common in men than SLE
- Likely more common in African Americans
- Age of onset usually between 20-40 years of age
- Often occurs in the absence of SLE, or smoldering SLE
- Q- Is SLE or DLE more common?
  - A - SLE in general is 7x more common than DLE
- Most common form of CCLE, present in 15-30% of SLE population in various ways
Discoid Lupus Erythematosus – clinical

- Q-Is DLE photoexacerbated?
- A-Yes, it is potentiated by sunlight, but not as much as with ACLE or SCLE

- Begins as dull red macules or indurated plaques that develop adherent scale, extending into the follicle.
  - Classically coin shaped “discoid” lesions
  - Lesions begin as painless erythematous patches that can be confused with lp
  - Itching, rarely are severe
  - Scale/hyperkeratosis extends into patulous (widespread) follicles making “carpet tack” like spines under the scale “langue au chat” or “cat’s tongue”
Discoid Lupus Erythematosus – clinical

- Evolve with atrophy, scarring and pigment changes (usually both hyper and depigmentation), as well as telangiectasia
- Sharply marginated, white borders with white striae, central depression in older lesions.
- Can also have a symmetric, hyperkeratotic butterfly shaped DLE plaque over the malar areas of the face and bridge of nose which also spares the nasolabial folds like ACLE
  - May be present initially with only periorbital edema and erythema
  - DLE is indurated, ACLE and SCLE should not be indurated
Discoid Lupus Erythematosus – Clinical - Hair

- Lesions may be erythematous or urticarial, but erythema may be minimal, especially on the scalp
- When the lesions extend into the follicle, they cause scarring alopecia
  - The scalp is involved in 60% of DLE patients with 1/3 reporting irreversible scarring alopecia
  - On the scalp, lesions begin hairless depressed patches-
    - Look for perifollicular erythema and easily extractable hairs
    - Easily extractable hairs shows active disease-good for monitoring response to therapy
  - Scarred areas may be smooth or have dilated follicular openings in the few remaining follicles
  - BUT the alopecia may look like a noninflammatory alopecia (may need to biopsy to differentiate)
Discoid Lupus Erythematosus – clinical – Mucous Membranes

- Mucosal involvement in 24-25% of DLE patients
  - Mouth, nose, eye or vulva
  - When the lesions occur periorally, they resolve with a striking acneiform pattern of pitted scarring
  - Lips – lesions are gray or red and hyperkeratotic, possible eroded and surrounded by a narrow, inflammatory zone
  - Perforation of the nasal septum happens, and is more common with SLE than DLE
  - DLE more often affects the lower lid and patients can develop ectropion
Discoid Lupus Erythematosus – clinical – SCC

- Rarely-aggressive SCC arises in longstanding DLE lesions
  - More often in mucosal lesions
  - Therefore, check for nodular asymmetry of mucosal DLE lesions to assess risk of cancer
Discoid Lupus Erythematosus – Localized

- Usually DLE lesions occur only **above the neck**-scalp, bridge of nose, malar areas, lower lip, ears (concha and external canal frequently).
- This is termed localized DLE, and has a slightly different overall picture than generalized.
- Like generalized, only 5% progress to SLE, likely even less.
Discoid Lupus Erythematosus – Generalized

- In order to classify lesions as generalized, they have to involve the thorax and upper extremities, in addition to head and neck
- Less common than localized dle
- All degrees of severity
  - Palms and soles can have painful, erosive lesions
  - Elbow/arm lesions seem to co-occur with acral finger lesions, and more often have active systemic disease
  - Scalp may become bald and have striking areas of hyper and depigmentation
  - Diffuse scarring may involve the face and upper extremities
- Labs – (+) ANA 30-40% of the time, antibodies to ssDNA more common than antibodies to dsDNA (rare) and leukopenia, more common with generalized than localized
Discoid Lupus Erythematosus – Histology

- Patchy perivascular and periadnexal lymphoid inflammatory infiltrate in the superficial and deep dermis
- Characteristically around vessels, follicles and eccrine coil
- MUCH DENSER AND EXTENDING DEEPER THAN SCLE OR ACLE
- Increased mucin (may present as widened collagen bundles)
- Thin epidermis, effacement of rete ridges
- Compact hyperkeratosis (USUALLY NO PARAKERATOSIS compare to SCLE)
- PROMINENT FOLLICULAR PLUGGING
- Hydropic (edematous) degeneration of the basal layer and follicular epithelium -> pigment incontinence.
- Thickening of basement membrane
- Histology varies with stage of lesion
  - 1) acute show patchy lymphoid inflammation and vacuolar interface dermatitis
  - 2) after several months, begin to show hyperkeratosis, basement membrane thickening and dermal mucin
  - 3) chronic, inactive lesions show atrophy with postinflammatory pigmentation and scarring throughout the dermis, but no more signs of inflammation.
- Pilosebaceous units are destroyed, “orphaned” arrector muscles. Dermis appears fibrotic, but elastic tissue stain can distinguish the diffuse dermal scar of lupus from focal wedge-shaped superficial scars of lpp or folliculitis decalvans.
Follicular plug ("carpet tack")
Liquefaction degeneration
Thick basement membrane
Discoid Lupus Erythematosus – Histology - DIF

- DIF testing is (+) >75% of cases,
  - If lesions have been active for several months (early lesions negative or nonspecific immunofluorescent findings).
  - DIF shows granular deposition of Ig and complement at DEJ.
  - Head and neck positive more often (80%) than trunk (20%).
  - Uninvolved skin is negative.
  - Always biopsy well established lesion, older lesions more (+) than younger.
  - If doing dif, transport in ns may give higher yield than freezing or Michel's transport medium, if you can get it there in 24 hrs.
Discoid Lupus Erythematosus – Prognosis and treatment specifics

- **Q** - What is the rate of progression from DLE to SLE?
- **A** - variable, but 95% of cases of DLE confined to skin at outset remain so.
- Progression from cutaneous DLE to SLE is uncommon,
  - Patients with SLE frequently have discoid lesions, but they usually have systemic involvement early, rather than evolution from chronic cutaneous le (DLE lesions seen in ¼ of pts with SLE at some point in their course)
  - If patients have SLE and discoid lesions (common), they often have fever and arthralgia
  - Spontaneous remission occurs occasionally, but rebound after discontinuation of treatment is typical.
  - Death uncommon.
Discoid Lupus Erythematosus – Prognosis and treatment specifics

- **Generalized DLE has a worse prognosis than localized**, with systemic symptoms, check
  - ANA, anti-dsDNA, C1, CBC (leukopenia), UA (hematuria/proteinuria to identify patients with SLE nephritis)
- **Treatment specifics**: slow taper of medications if inactive
- New validated instrument to measure activity of CLE. “Cutaneous Lupus Erythematosus Area and Severity Index”
Summary
Case 5

- A 35 year old woman with a prior diagnosis of DLE presents to clinic complaining of “painful hands.” Her DLE is being controlled with topical Clobetesol, but since it got cold after the holidays, she has been having really painful hands, and a new rash. On physical exam, you notice purple-red patches and plaques that look scarred and atrophic. They do not look like “normal” DLE lesions.
What is your diagnosis?
Lupus specific skin disease – Chilblain Lupus Erythematosus (Hutchinson):

- **Chronic unremitting form or LE**
- **Clinical**
  - Under recognized entity, but may be one of the most common causes of digital lesions in LE patients
  - Affects fingertips, rims of ears, calves, and heels
  - Usually in women, precipitated by cold, damp climates
  - May be cold induced lesions that then koebnerize DLE lesions
  - Lesions mimic old DLE lesions as they evolve, or may look like lcv
  - Usually preceded by dle on the face, sometimes has systemic involvement
  - Mimicry of sarcoidosis may be striking
- **Workup**
  - Cryoglobulins and antiphospholipid antibody should be sought
  - Seems to be associated with anti-Ro/SSA antibodies
- **Histologically similar to idiopathic chilblains (pernio)**
  - Interface dermatitis superficial and deep perivascular lymphocytic infiltratration, like classic DLE
Case 6

- A 50 year old man with classic DLE lesions on his face and scalp. On his face, palms, extensor surfaces of his arms and soles are massively hyperkeratotic, verrucous-like plaques
What is your diagnosis?
Lupus specific skin disease – Verrucous (hypertrophic) lupus erythematosus

- **Clinical**
  - Non-pruritic papulonodular lesions on extensor arms and hands. Upper back and face.
  - Hyperkeratosis is greatly exaggerated
  - Look like keratoacanthoma or hypertrophic lichen planus

- **Histology**
  - Lichenoid dermatitis, therefore look carefully for other lesions for lichen planus or le as well as DIF (continuous granular in LE).
  - Verrucous LE shares similar histology with DLE (no basement membrane zone thickening, dermal mucin, eccrine coil involvement, subcutaneous nodular lymphoid infiltrates)
  - Think of Hypertrophic LE in cases when only cytoid bodies are present, and are restricted to the dej, rather than deep into follicle or fibrous tract remnants.
  - May simulate SCC histologically
Lupus specific skin disease – Verrucous (hypertrophic) lupus erythematosus

- Differential Diagnosis
  - LP - Lips and scalp - look for lesions that look like either Lupus or Lichen Planus, may need to biopsy
  - LPP (different path - shaggy fibrin in both but deeper in cases of lpp)
- Some have SLE, some only cutaneous, but probably the same risk of SLE as with DLE
- Treat with retinoid (1st line therapy)
Lupus specific skin disease — Lupus-erythematosus-Lichen planus overlap syndrome: (*lupus planus*)

- **Clinically**
  - Looks clinically like verrucous (hypertrophic) lupus, but is a true overlap syndrome.
  - Large, atrophic, hypopigmented red or pink patches and plaques.
  - Pigment abnormalities prominent over time
  - Fine telangectasia and scaling present
  - Extensor aspects of extremities and midline back
  - Prominent palmoplantar involvement - most troublesome part of disease, including nail dystrophy and anonychia
  - Scarring alopecia and oral involvement have been noted in some patients

- **Histology**-feature of both DLE and LP
**Lupus specific skin disease** — Lupus-erythematosus-Lichen planus overlap syndrome: *(lupus planus)*

- DIF-usually suggests LP, but with continuous granular deposition of immunoglobulin (like LE)

**Treatment**

- Response to treatment is poor, but tx includes topical steroids, dapsone, thalidomide, or isotretinoin
- Cellcept or imuran may be needed
- *Antimalarials can occasionally produce a lichenoid drug eruption in patients with LE, which may mimic lupus planus*
Case 7

- A 40 year old woman with SCLE, controlled with Plaquinil, comes in for regular follow-up. In addition to her usual SCLE lesions, the woman also has multiple, annular indurated plaques on her face and chest.

- What is your diagnosis?
What is your diagnosis?
Lupus specific skin disease – Tumid Lupus Erythematosus

**Clinical**
- Likely a subset of CCLE
- Rare, but distinctive, may be related to reticular erythematous mucinosis
- Edematous erythematous plaques usually on the trunk
- Little surface change
- Resolve without atrophy or scarring
- Intense photosensitivity, absence of systemic disease, tendency to recur

**Suggested that Jessner lymphocytic infiltrate, REM, and papulonodular mucinosis are all dermal variants of LE-specific skin disease.**
- Lupus has CD4+ lymphocytes, Jessners has mostly CD8+ lymphocytes.

**Histology**
- Not typical of lupus – pronounced dermal lymphoid infiltrate, little to no epidermal change
- striking amounts of mucin

**Treatment** - Respond very well to antimalarials.
Case 8

- A 35 year old woman with DLE presents to your resident clinic. She has noticeable DLE lesions throughout her body, but they are well controlled on her face and scalp.
What is your diagnosis?
Lupus specific skin disease –

Lupus Erythematousus Panniculitis

- **Terminology**
  - Also called *Lupus erythematosus profundus* or *Kaposi-Irgang Disease*
  - Profundus refers to a DLE lesion with underlying panniculitis, panniculitis means only panniculitis

- **Clinical**
  - Chronic, occurs in women 20-45, many have dle at other sites (70%)
  - Overlying skin may be normal, but often has overlying discoid or tumid lesions
  - Sometimes discovered incidentally when unrelated lesion is biopsied
  - Firm, sharply defined, nontender subcutaneous nodules 1-3 cm in diameter
  - Proximal extremities usually involved
  - May heal with deep depressions

- Calcification frequently occurs, and the subsequent pain may be the pt’s main complaint

- In the breast, may produce nodules that mimic cancer (clinically and radiologically)

- 50% of pts have SLE, but less usually not with severe systemic symptoms
Lupus specific skin disease – Lupus

Erythematous Panniculitis - Histology

- **Histology:**
  - Absence of characteristic epidermal and dermal changes of LE.
  - Lobular lymphocytic panniculitis with privascular infiltration
  - Lymphoid nodule in subcutaneous septae, necrosis of fat lobule,
  - Fibrinoid or hyaline degeneration of remaining lipocytes.
  - Overlying epidermis may show basal liquefaction and follicular plugging or may be normal.
  - Not uncommon to see dermal lymphoid nodules or vertical columns of lymphoid cells in fibrous tract remnants
  - Dermal mucin may be prominent and dermal collagen hyalinization (resembling that seen in morphea) may be present

- DIF - Continuous granular deposition of immunoglobulin and C3 seen at dej
Fat necrosis

Lobular panniculitis
Lupus specific skin disease — Lupus

Erythematous Panniculitis - DDX

- Stasis panniculitis (lipodermatosclerosis)
  - which shows “frost on a window pane,”
- SUBCUTANEOUS PANNICULITIS-LIKE LYMPHOMA
  - shows atypical lymphocytes around lipocytes and pt has constitutional symptoms, as well as erythrophagocytosis focally and t-cell clonality
  - CD8 dominant or CD56 (+) (NK cell lymphoma), or
  - CD30 (+) (anaplastic lymphoma)
  - CD5 and CD7 may be reduced (loss of pan t-cell markers).

Difficult to differentiate - CD8 predominance, loss of CD5 or CD7, t-cell clonality, erythrophagocytosis MAY ALSO BE SEEN IN LUPUS PANNICULITIS

Some cases of lymphoma may be indistinguishable from LE panniculitis or some cases of LE panniculitis may represent an abortive lymphiod dyscrasia

Lupus panniculitis responds to antimalarials and does not progress to lymphoma.
Case 9

- The mother is a healthy 24 year old woman who is visiting for a two week post-op for a primary C/S. The pregnancy was otherwise uncomplicated, and she gave birth to a healthy baby girl.

- In the past 3 days, the girl has developed a strange rash. Her face is edematous, and is covered with annular erythematous macules and papules with slight scale. In her diaper area, she also has telangiectatic macules.
What is your diagnosis?
Lupus specific skin disease – Neonatal Lupus Erythematosus

- Most girls born to Ro/SSA (+) mothers
  - strong association with Ro/SSA, some La/SSB (+) as well
  - In unselected women with anti-Ro antibodies, only 1-2% will have an affected child

- Clinically
  - Lesions not present at birth, but develop during the first few weeks of life
  - Annular erythematosus macules and plaques on head and extremities (otherwise SCLE like)
  - Raccoon eyes (periocular involvement)
  - Telangiectatic macules or angiomatous papules may be found in sun-protected sites (diaper area) independent of active lupus skin lesions
  - Lesions fade with time and become atrophic
Lupus specific skin disease – Neonatal Lupus Erythematosus

- **Prognosis for child**
  - Resolve spontaneously by 6 months, usually heal without scarring
  - Dyspigmentation and telangiectasias may be present for months to years
  - 50% of neonates have an associated congenital heart block (usually 3rd degree) which is permanent (not if pt is only U1RNP(+)). Sometimes this is the only manifestation of the disease (no female predominance).
  - If there is cutaneous disease, thrombocytopenia and hepatic disease are as common as cardiac involvement
  - Japanese infants different-they express anti-dsDNA antibodies and 8% progress to SLE

- **Prognosis for mother**
  - 50% of mothers are asymptomatic at time of delivery, but will often develop arthralgia, sjogrens syndrome, or other mild systemic findings
  - Risk of second child having neonatal LE is about 25%
As previously stated: Cutaneous manifestations were traditionally divided into lesions
  1. showing characteristic histological changes of LE (LE-Specific Skin disease), or
  2. those not distinct, histopathologically, for LE (may be seen as a feature of another disease)

History of exposure to excessive sunlight before onset of disease or before an exacerbation is common (especially facial eruption)
  - Photosensitivity (abnormal response to UVR) in 50-93% of pts with SLE

Systemic Lupus Erythematosus: ACR’s 11 criteria (need 4+ for diagnosis)
  - 3 rashes – Malar, Discoid, Photosensitivity
  - 5 “itis”- oral ulcers (stomatitis), arthritis, nephritis (proteinuria >0.5g/d or casts), neurologic disorders (meningitis), Pleuritis/pericarditis
  - 3 lab abnormalities – blood abnormalities (hemolytic anemia, leukopenia, thrombocytopenia), ANA, Immunologic disorders (anti dsDNA antibodies, anti smith antibodies, antiphospholipid syndrome
Findings occur in >50% of cases of lupus
- Fingertips or toes show edema, erythema, or telangiectasia
  - Seen in lupus, but much more exaggerated and common with DM
  - If (+), good indicator of SLE: 76% of pt’s with DLE and this finding had SLE, in patients with DLE and not SLE, none had it
- Telangiectasia in Nailfold capillary loops in
  - LE: wandering glomeruloid loops
  - Dermatomyositis and scleroderma loops show symmetric dilation and dropout of vessels
  - Osler-Weber-Rendu syndrome show ectasia of half of the capillary loop
- Red or spotted lunulae may be present in patients with SLE
- Diffuse nonscarring hair loss is common.
  - Short hairs in the frontal region “lupus hairs” due to chronic telogen effluvium and increased hair fragility,
  - Occurs when ACLE is flaring
Systemic Lupus Erythematosus - LE non specific skin disease – Vascular Lesions

- Raynaud phenomenon
  - Most common vascular reaction in lupus patients (in ~15% of patients)
  - Seems to herald a worse prognosis, but less renal disease
  - May correlate with DLE lesions of the hands
  - May lead to focal ulcerations and subsequent disease
- Leg ulcers-deep punched out with very little inflammation, on pretibial or malleolar areas
Q – What is Sneddon Syndrome?
A – Sneddon syndrome - livedo reticularis and strokes related to hyalinizing vasculopathy
Livedo is a separate LE-non specific cutaneous vascular reaction, but has clear overlap with vasculopathy
Livedoid pattern is associated with antiphospholipid antibodies
Systemic Lupus Erythematosus - LE non specific skin disease – Vascular Lesions

- Degos like lesions
Systemic Lupus Erythematosus - LE non specific skin disease – Mucous membrane lesions

- **Seen in 20%-45% of SLE patients**
  - can be either LE non-specific or LE specific on histology (if they are DLE lesions)
- **Conjunctivitis, episcleritis, nasal and vaginal ulcerations may occur**
- **Oral mucosal hemorrhages, erosions, shallow angular ulceration with surrounding erythema and gingivitis common**
- **Erythema, petechiae, and ulceration on hard palate**
Systemic Lupus Erythematous - LE non specific skin disease -- Other cutaneous findings

- Rarely, TEN may be associated with lupus (ACLE, SCLE > DLE)
- Multiple eruptive dermatofibromas have been described with SLE
- Calcinosis cutis is uncommon, but may be dramatic
- Palisaded neutrophilic and granulomatous dermatitis –
  - Symmetric popular eruption of the extremities
  - Skin colored to erythematous lesions with a smooth, ulcerated or umbilicated surface
  - Histology: vasculitis or palisaded granulomatous inflammation
- Infrequently may see plaque-like or papulonodular depositions of mucin (reddish purple or skin colored lesions on trunk and arms or head and neck)
Systemic Lupus Erythematosus - LE non specific skin disease — Other cutaneous findings

- Urticarial Vasculitis (tender urticarial plaques and papules over bony prominences lasting >24 hrs) common
- Urticaria-chronic urticaria found in 44-73% of pts with SLE
- Arthalgia, earliest, deforming arthropathy and acute migratory arthritis resembling rheumatoid arthritis as well as avascular necrosis of fem head.
- Can have erythromelalgia, (differs from raynaud in that it flares with heat as opposed to cold)
A patient with Systemic Lupus Erythematosus presents for a flare of ACLE. She has the typical malar rash, her arthritis is causing her terrible pain, and she has an appointment with her rheumatologist after clinic to check her kidney function. She is noticeably concerned. She says she has recently developed blisters all over her skin. On physical exam, on her extensor arms, chest and face, including her tongue, you notice widespread grouped vescicles and bullae. She says they do not hurt or itch.
What is your diagnosis?
Systemic Lupus Erythematosus - LE non specific skin disease – Bullous Lesions of LE

- Very confusing subject, may be LE specific or LE nonspecific
- **LE Specific**
  - As previously stated, bullous lesions may be exaggerated liquefactive degeneration of basal cell layer in ACLE and SCLE, resembling TEN
  - Occasionally, but rarely, develop in DLE
- **LE non-specific**
  - The entity normally described as bullous le, is a le non-specific on biopsy
  - Also called *DH-like vesiculobullous LE* or *epidermolysis bullosa acquisita-like vesiculobullous LE*
  - Seen typically in patients who have or develop active SLE including nephritis
  - **Clinically**
    - Single or grouped vescicles or bullae often widespread, in sun exposed areas
    - Rarely they itch
Systemic Lupus Erythematosus - LE non specific skin disease – Bullous Lesions of LE

- Histology – NEUTRAPHILS at dej and within papillae. Subepidermal bulla containing neutrophils (similar to DH) and inflammatory variant of EBA
  - fluorescence with IgG, IgM, IgA of C3 present in a granular or linear pattern at the basement membrane zone on DIF (similar to LE). Found in or below lamina densa on immunoelectron microscopy. Most HLA-DR2 (+).
Systemic Lupus Erythematosus - LE non specific skin disease – Bullous Lesions of LE

- DRAMATIC RESPONSE TO DAPSONE
- EBA is histopathologically and immunopathologically identical since both diseases are medicated by circulating antibodies against type VII collagen (in some patients), but EBA does not respond to dapsone
- May occasionally arise as a result of liquifactive degeneration of the basal cell layer or full thickness epidermal necrosis resembling TEN
- Anecdotally linked to LE-BP, PE (Senear-Usher), DH, PCT, but no clear association
Systemic Lupus Erythematosus - Systemic Findings

- Systemic Manifestations:
  - Most due to immune complex disease, especially vasculitis
  - Thrombosis of various sized vessels-  
    - Lupus anticoagulants are most common cause  
    - These plus increased homocysteine may each increase thrombosis risk. Assoc with early onset organ damage.  
    - Most common form of death from SLE after 5 years (before is infections)
- Renal  
  - Either nephritic or nephritic  
  - Can cause chronic renal insufficiency with proteinuria and azotemia.  
  - Anti-dsDNA and anti-C1q antibodies high specificity for active nephritis.  
  - Active nephritis unlikely if anti-dsDNA (-)  
  - Immunoglobulin and complement components found localized to basement membrane of glomeruli – wire-loop vasculitis lesion
Systemic Lupus Erythematosus – Systemic Findings

- Myocarditis –
  - cardiomegaly and gallop rhythm.
  - Nonspecific EKG changes.
  - Pericarditis and endocarditis also occur.
- CNS –
  - vasculitis, hemiparesis, convulsions, epilepsy, diplopia, retinitis, choroiditis, psychosis, personality disorders.
  - livedo is a marker for CNS disease
- ITP- occasionally forerunner of SLE.
- GI – n/v/d (vasculitis)
- Pulmonary – effusions, interstitial lung disease, acute lupus pneumonitis
- Overlap with Sjogren syndrome (keratoconjunctivitis sicca) and hashimoto thyroiditis, as well as any connective tissue diseases
- Hypercholesterolemia and hypoalbuminemia may occur.
- Coombs (+) hemolytic anemia, neuropenia, lymphopenia
Systemic Lupus Erythematosus – Drug induced

- Hydralazine, Procainamide, Sulfonamides, Penicillin, Anticonvulsants, Minocycline, Isoniazid
- Penicillamine induces or unmasks true lupus
- Most are ANA (+), antihistone antibodies (+)
- L-Canavanine (amino acid in alfalfa sprouts and tablets) can worsen SLE
- Some reports of SLE being aggravated by excess calories, excess protein, high fat (saturated and omega-6 polyunsaturated fatty acids), excess zinc, and excess iron, but no good studies done.
Systemic Lupus Erythematosus - Laboratory findings

- ESR is greatly elevated during active disease
- Coombs test may be (+)
- Many have false (+) RPR.
- RF may (+)
- Levels of IgG may be high, albumin to globulin ratio is reversed.
- Serum globulin increased, especially gamma globulin or $\alpha_2$ fraction
Childhood Systemic Lupus Erythematosus

- Different than neonatal LE, which is a version of SCLE
  - Between 3 and 15 years old
  - Girls:boys - 4:1

- Skin manifestation
  - Typical butterfly eruption on the face with photosensitivity
  - Morbilliform, bullous, purpuric, ulcerating, nodose lesions
  - Oral mucosa is frequently involved

- Associated with systemic complications
Pregnancy and Systemic Lupus Erythematosus

- May have difficulty conceiving, increased number of miscarriages
- SLE may get better or worse during pregnancy
- Risk of fetal death increased if anticardiolipin or Ro (+) therefore will give low dose ASA
Immunohistochemistry general - Systemic Lupus Erythematosus

- Helpful in confirming the diagnosis of LE specific, but not uncommon to see negative IF in pt’s with known disease, and false (+) studies in normal controls.
- IgG, IgA, IgM and complement in continuous granular pattern at the dej in lesional and nonlesional skin
- Q-Medicine just paged me asking for us to biopsy for a Lupus Band Test on one of their patients. What is the Lupus Band Test?
  - A- It is a confusing term.
    - Nonlesional lupus band test – When sun-protected non lesional skin is sampled, specificity is very high if 3+ immunoreactants present at DEJ.
    - (+) test correlates with risk for developing nephritis, but not more than dsDNA serology.
sle ana indirect if ana (+)
Cutaneous LE treatment – General preventative measures/local therapy

- Most important - Exposure to sunlight and all UVR (including artificial sources), must be avoided (high spf) even if pt denies photosensitivity
  - Blocking films applied to home and car windows
  - Acrylic diffusion shields should be placed over fluorescent lights
  - Education about photosensitizing drugs such as HCTZ, Tetracycline, Griseo, Piroxicam
- Cigarette smoking is associated with increased disease activity in SLE and can interfere with effects of antimalarial drugs
- Avoid Keobnerization!
  - Avoid exposure to excessive cold, to heat, and to localized trauma
  - Biopsies an scar revision will often provoke a flare of disease
  - Avoid collagen/filler for atrophic lesions
- Pulsed dye laser effective for some erythematous lesions, but may cause flares.
- UVA-1 useful adjuvant treatment in some patients, proceed with caution, as many lesion keobnerize
- Treat discoid lesions aggressively to avoid scarring
Cutaneous LE treatment – Topical/Local Therapy

- Potent or superpotent topical corticosteroids is beneficial, with occlusion (special made for oral lesions)
  - Clobetesol bid x 2 wks to active lesions then 2 wks of rest
  - Rarely does topical corticosteroids alone adequately treat scle or ccle
- Individual lesions
  - Single most effective treatment is injection of steroids into active border of lesion
  - Kenalog 2.5-10 mg/ml q 4-6 wks, do not use more that 40 mg total at one time).
  - More useful for treating dle.
  - Risk of steroid atrophy must be balanced with atrophy and scarring due to the disease.
  - Better to err on the aggressive side.
- Topical calcineurin inhibitors as a second line therapy
- Nonimmunosuppressive treatment preferred for SCLE and CCLE.
- Maximize local measures, use systemic agents if local activity persists
Cutaneous LE treatment - Systemic Therapy
- Antimalarials

- Antimalarials are the safest.
- Plaquenil 6.5 mg/kg/day.
  - Load with 400mg/d for first 6-8 wks, then decrease to 200mg/d for at least 1 year before tapering.
  - Treat for 3 moths before switching or adding Quinacrine 100 mg/d (does not increase risk of retinal toxicity, but has higher risk of disfiguring pigmentation).
- Chloroquine
  - Effective at 250 mg/d (esp. for CCLE) but difficult to procure.
  - Do not use with plaquenil.
- Can stop during winter months sometimes
- Ocular toxicity is rare with plaquenil doses equal or less than 6.5 mg/kg/d, but get ophthalmology consult before and q6 months.
- Constriction of visual fields to a red object and parentral scotomas are rare, if they occur, stop treatment.
Cutaneous LE treatment - Systemic Therapy

- Retinoids second line, except with hypertrophic le.
  - Isotretinoin 1mg/kg/d, but may have rapid release when drug discontinued.
- Dapsone for bullous systemic le
- Systemic immunsuppressents third line (Cellcept, Imuran, Methotrexate, Leflunomide)
- **Thalidomide works well for CLE refractive to other medications, with response rates between 85-100%**
- PO steroids - save for flares!
  - Usually get rebound flare upon cessation of steroid.
  - If nec, use for 3 wks or less, or possibly only during the loading phase for plaquenil.
  - If giving prednisone, divide the doses, it has a greater le suppressing activity than the same dose given once a day, and much less adrenal-supressing activity
  - Women with SLE have an increased risk of osteoporosis, even without steroid therapy
  - If using, begin bisphosphonate treatment early!
SLE – Future treatment?

- Administration of 200 mg DHEA for 7-12 mo reduced corticosteroid requirements and frequency of disease flares