Lupus and the Skin

2015 Georgia Lupus Summit

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Lupus and the Skin Outline

- Discuss the importance of skin care in lupus
- Review the different types of cutaneous lupus
- Stress the role of sun protection and avoidance
- Provide an overview of newer therapies for cutaneous lupus

Why is the skin important in lupus?

- Patients with cutaneous lupus have a lower quality of life, particularly from an emotional standpoint
  - No ethnic differences in impact on quality of life
  - The emotional impact is similar to patients diagnosed with diabetes, high blood pressure, and heart attacks
- A flare of cutaneous lupus can lead to a systemic flare of lupus, including nephritis (kidney involvement)

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Forms of cutaneous lupus

- Acute cutaneous lupus erythematosus (malar erythema, photodistributed eruption)→most associated with systemic lupus erythematosus
- Chronic cutaneous LE
  - Discoid lupus (DLE)
  - Tumid lupus
  - Lupus panniculitis
  - Chilblain lupus
- Subacute cutaneous LE (SCLE)

THE AMERICAN COLLEGE OF RHEUMATOLOGY 1982 REVISED CRITERIA FOR CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS*

Criterion	Definition
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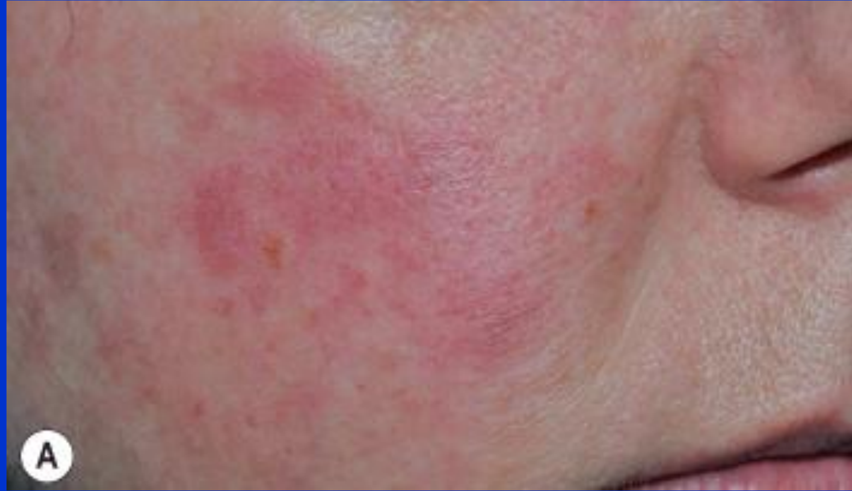
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
5. Arthritis	Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion
6. Serositis	a) **Pleuritis** – convincing history of pleuritic pain, rubbing heard by a physician, or evidence of pleural effusion *OR* b) **Pericarditis** – documented by ECG, rub or evidence of pericardial effusion
7. Renal disorder	a) Persistent **proteinuria** greater than 0.5 g/day or greater than 3+ if quantitation not performed *OR* b) **Cellular casts** – may be red cell, hemoglobin, granular, tubular or mixed
8. Neurologic disorder	a) **Seizures** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance *OR* b) **Psychosis** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance

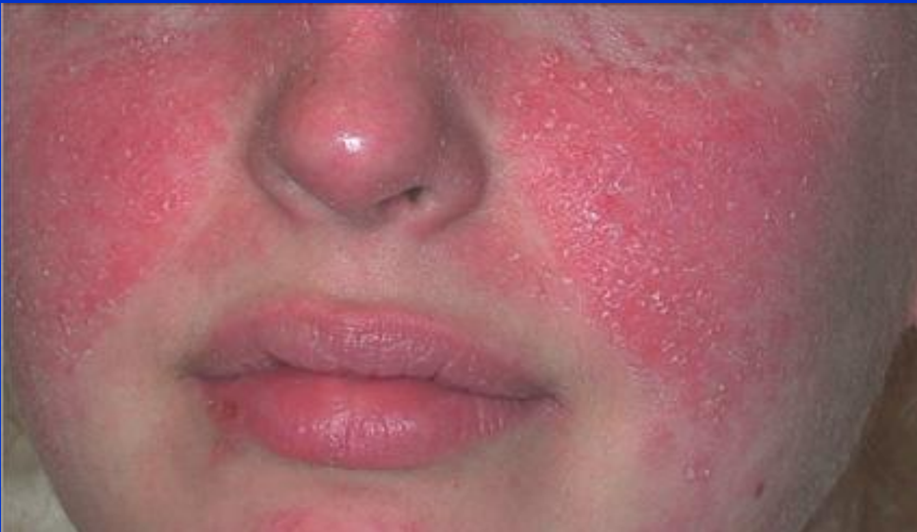
9. Hematologic disorder	a) **Hemolytic anemia** with reticulocytosis *OR* b) **Leukopenia** – less than 4000/mm^3 total WBC on two or more occasions *OR* c) **Lymphopenia** – less than 1500/mm^3 on two or more occasions *OR* d) **Thrombocytopenia** – less than 100 000/mm^3 in the absence of offending drugs
10. Immunologic disorder	a) **Anti-DNA antibody to native DNA** in abnormal titer *OR* b) **Anti-Sm:** presence of antibody to Sm nuclear antigen *OR* c) Positive finding of **antiphospholipid antibodies** based on: (1) an abnormal serum level of IgG or IgM anticardiolipin antibodies; (2) a positive test result for lupus anticoagulant using standard methods; or (3) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test (FTA-ABS)
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome

*The proposed classification is based on 11 criteria. For the purpose of identifying patients in clinical studies, a person shall be said to have systemic lupus erythematosus if any four or more of the 11 criteria are present, serially or simultaneously, during any interval of observation.

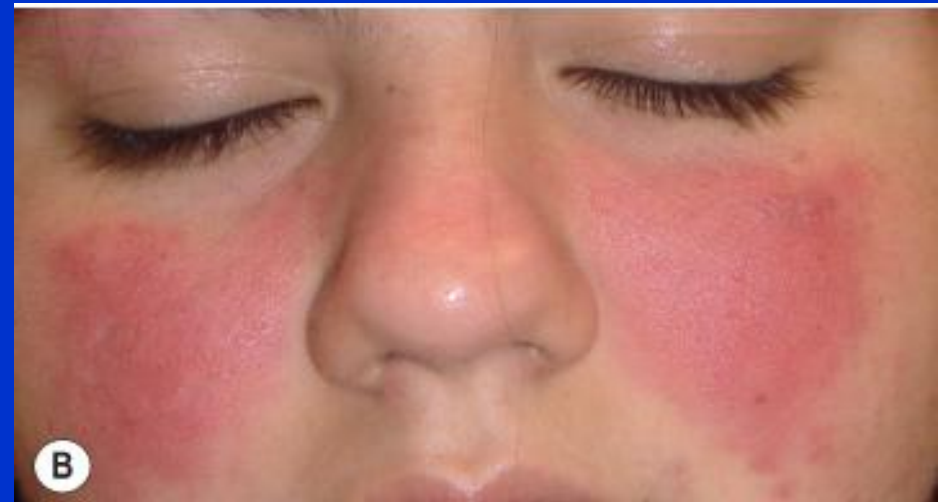
Butterfly rashes of Acute Cutaneous LE



Patchy

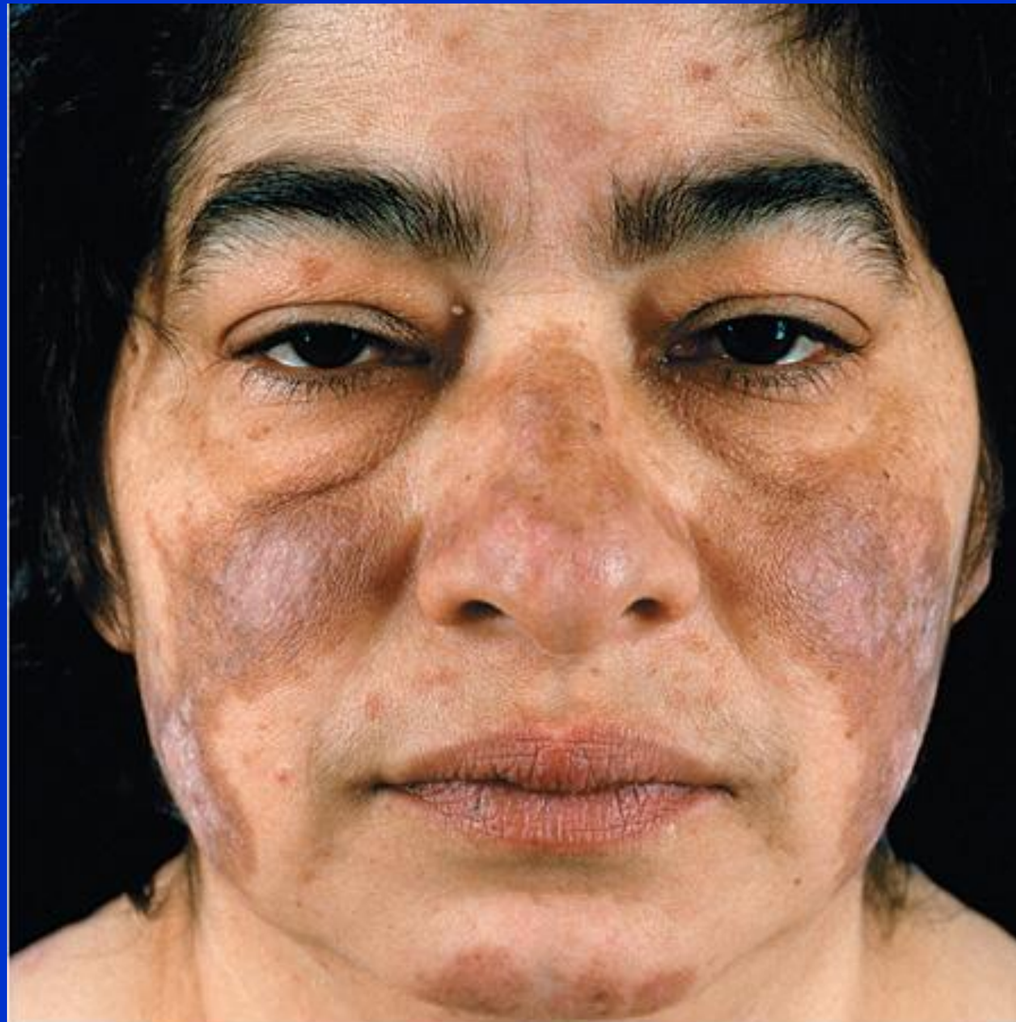


Scaling



Edematous

Post-inflammatory hyperpigmentation from lupus



Source: Wolff K, Johnson RA: *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, 6th Edition*: http://www.accessmedicine.com

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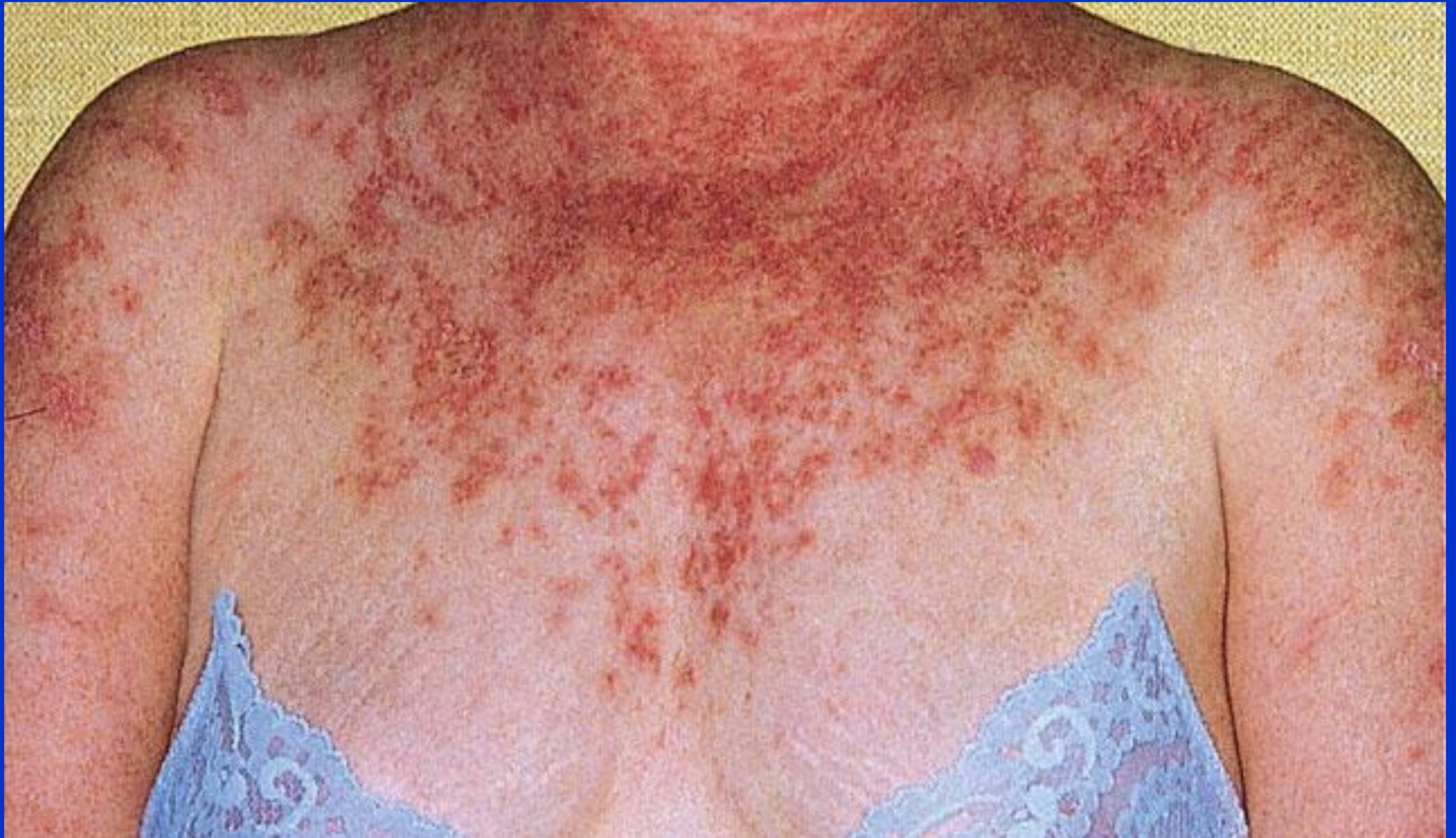
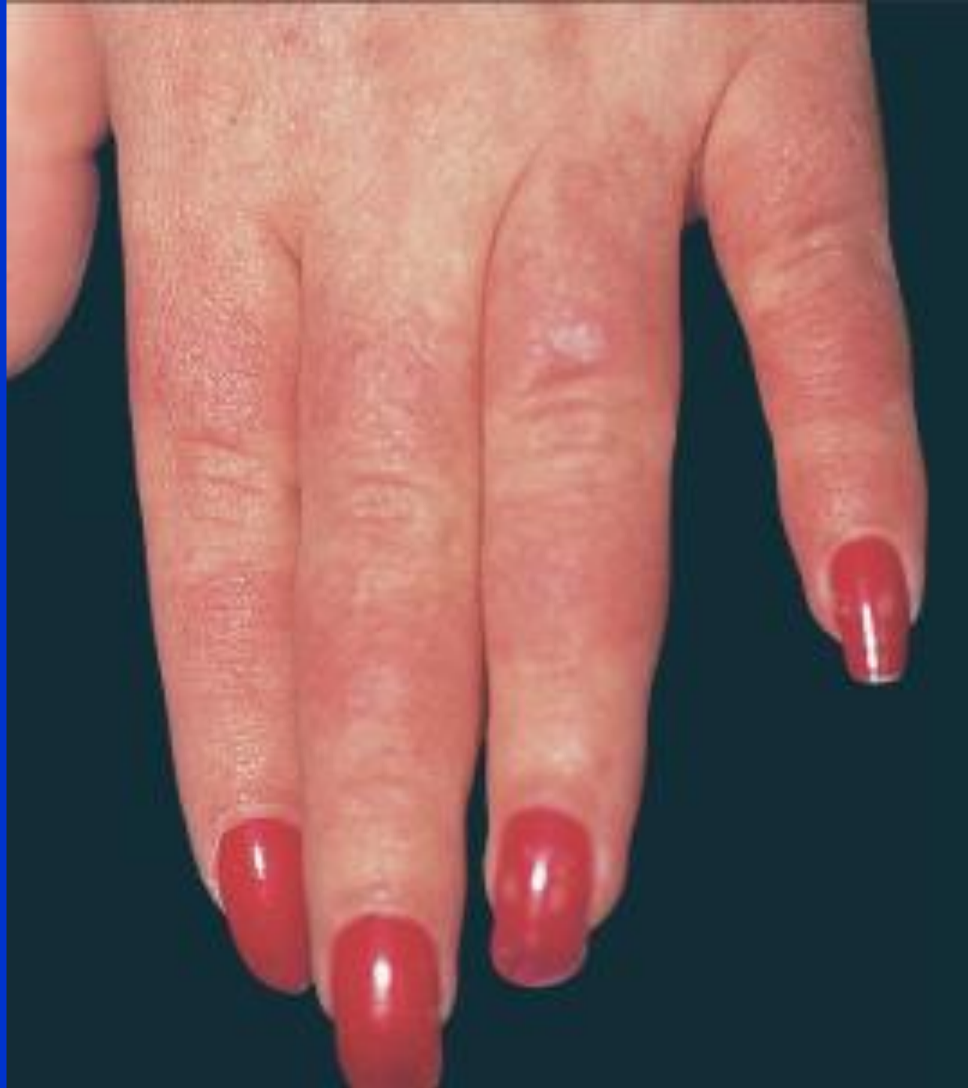
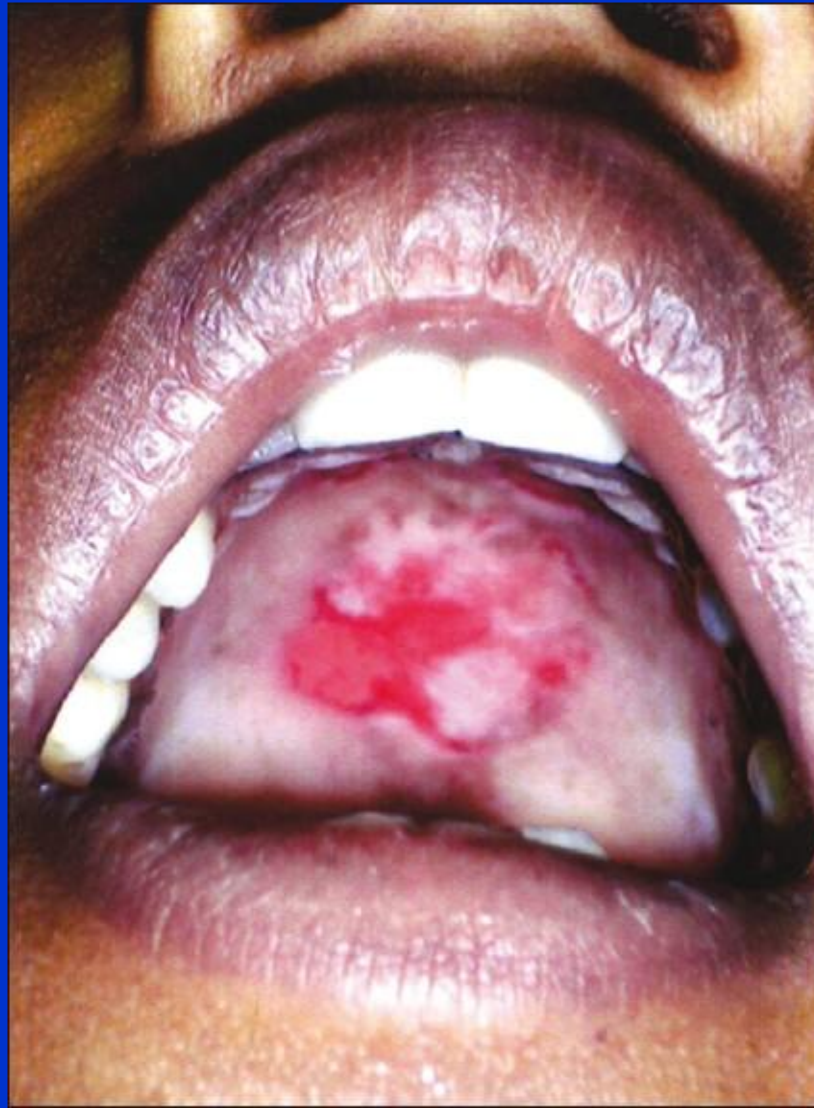
Photodistribution of lupus (in sun-exposed areas)



Hands: Acute cutaneous lupus erythematosus



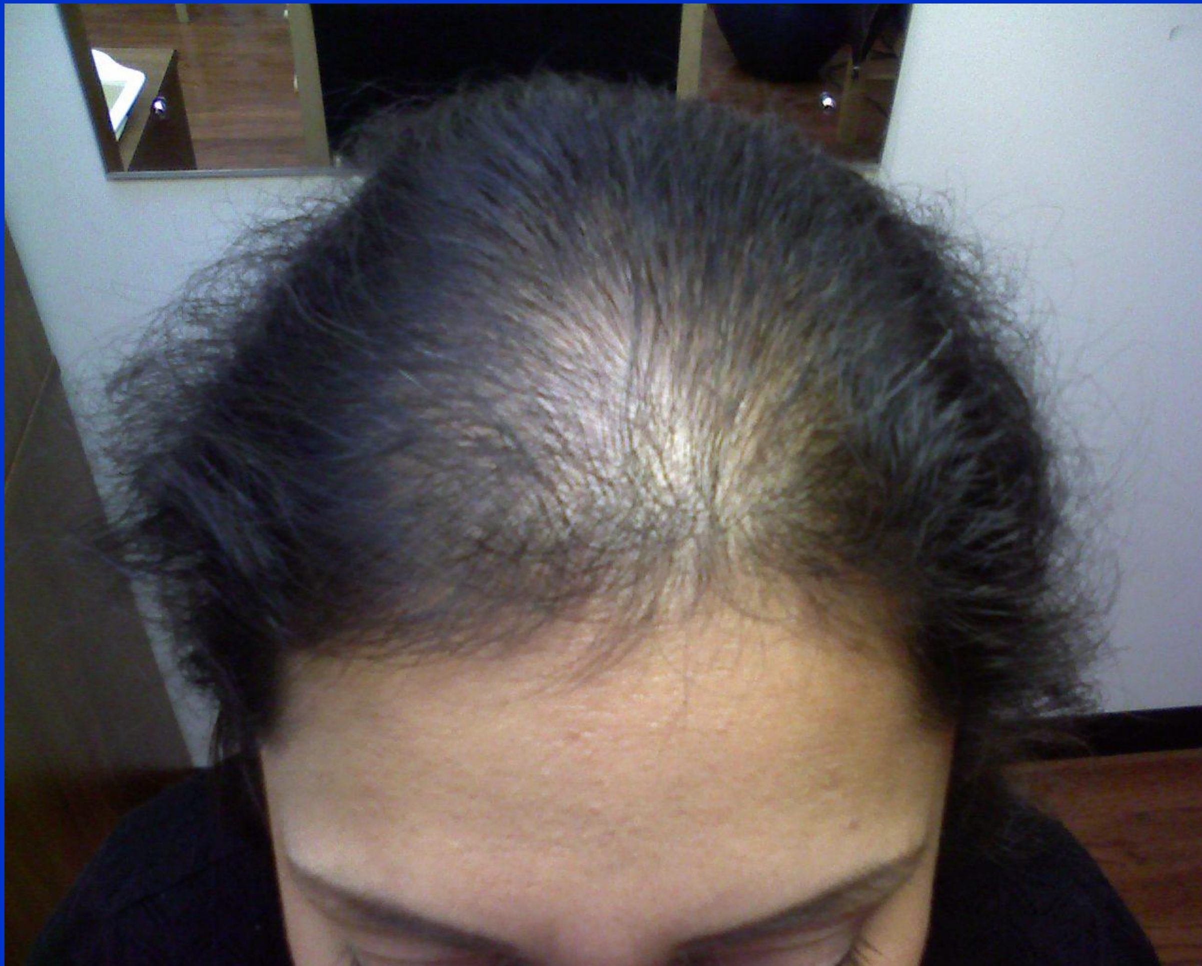
Oral ulcers of LE: both painless or painful



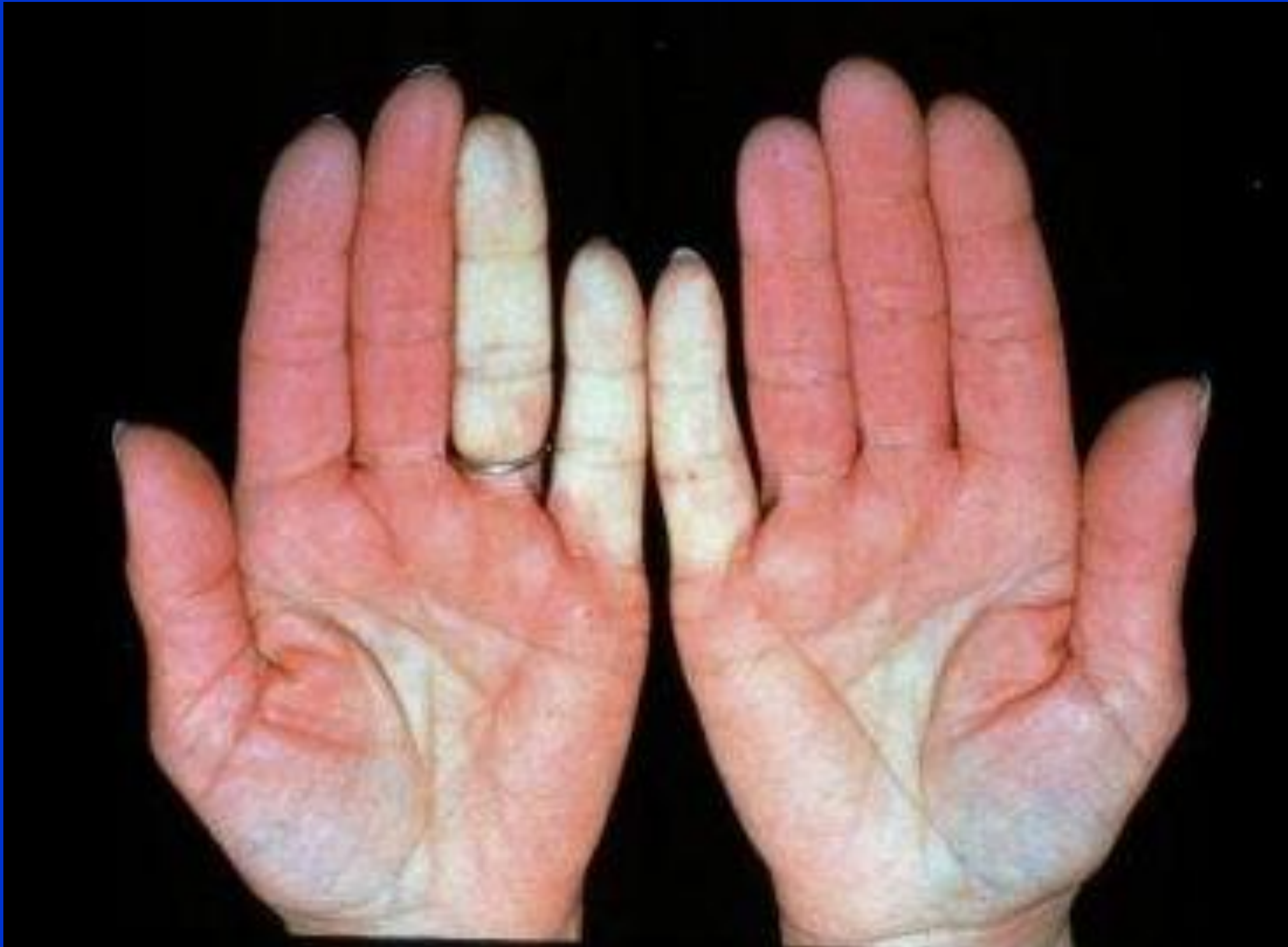
Many skin findings of systemic lupus

CUTANEOUS FINDINGS (NONSPECIFIC) THAT SUGGEST THE DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS
Diffuse non-scarring alopecia
Raynaud's phenomenon
Nailfold telangiectasias and erythema
Vasculitis
• Urticarial vasculitis
• Small vessel vasculitis (e.g. palpable purpura)
• Polyarteritis nodosa-like lesions
• Ulcerations
Cutaneous signs of antiphospholipid syndrome
• Livedo reticularis
• Ulcerations
• Acrocyanosis
• Atrophie blanche-like lesions
• Degos'-like lesions
Livedoid vasculopathy
Palmar erythema
Papular and nodular mucinosis

Flares of lupus cause non-scarring alopecia (hair loss)



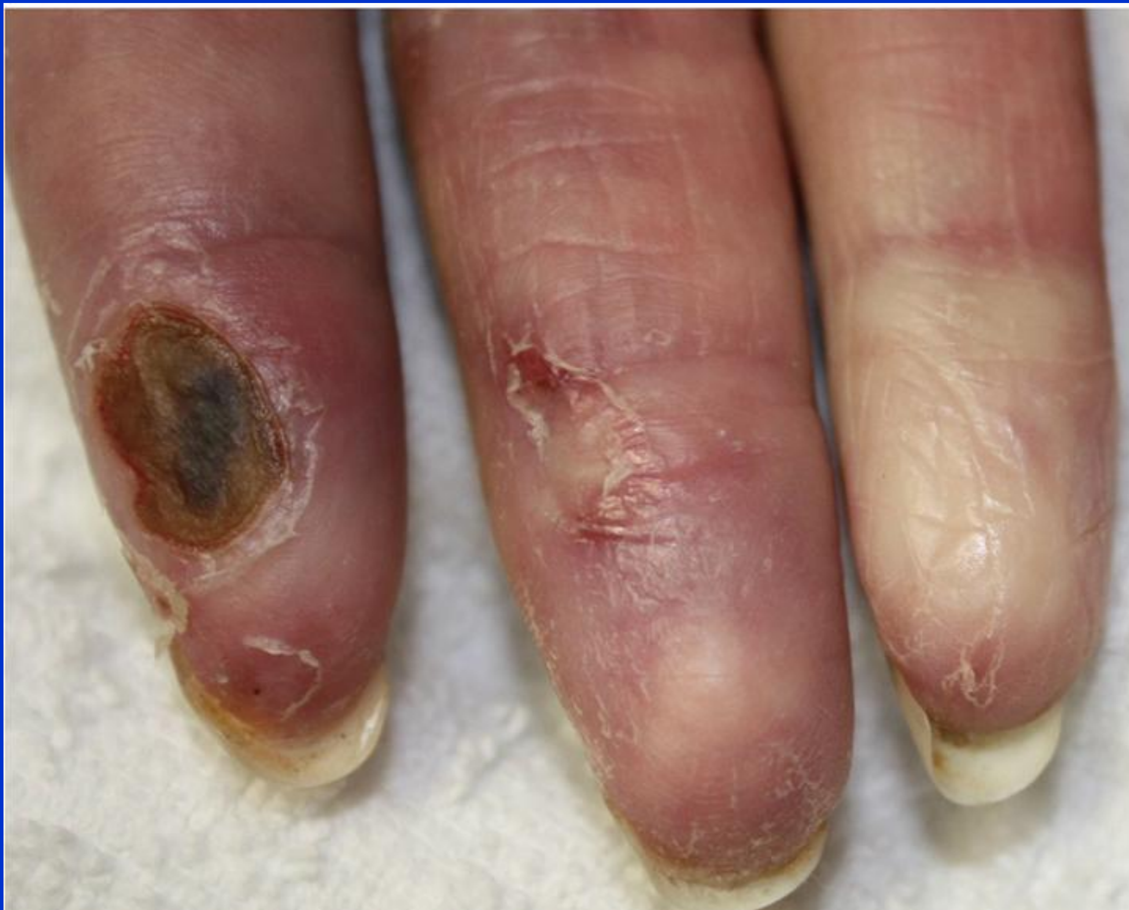
Raynaud’s phenomenon



Raynaud's phenomenon

-3 colors: White, red, blue

-severe cases can ulcerate



Primary (not worrisome) vs. secondary (due to an underlying problem) Raynaud's phenomenon

CLINICAL AND LABORATORY FEATURES OF PRIMARY AND SECONDARY RAYNAUD'S PHENOMENON		
Feature	**Primary Raynaud's**	**Secondary Raynaud's**
Sex	F:M 20:1	F:M 4:1
Age at onset	Puberty	>25 years
Frequency of attacks	Usually <5 per day	5–10+ per day
Precipitants	Cold, emotional stress	Cold
Ischemic injury	Absent	Present
Abnormal capillaroscopy	Absent	>95%
Other vasomotor phenomena	Yes	Yes
Antinuclear antibodies	Absent/low titer	90–95%
Anticentromere antibody	Absent	50–60%
Anti-topoisomerase I (Scl-70) antibody	Absent	20–30%
In vivo platelet activation	Absent	>75%

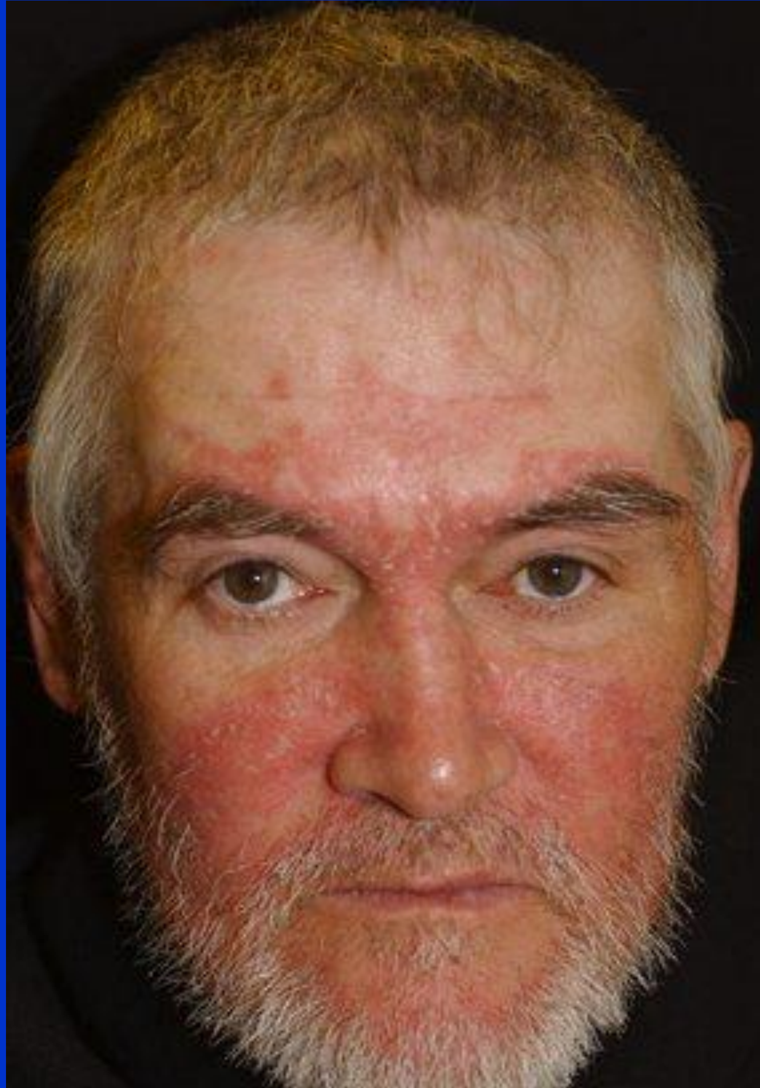
Secondary Raynaud's Phenomenon

- Systemic sclerosis (90 to 95% of patients)
- Mixed connective tissue disease (85%)
- Undifferentiated connective tissue disease

- Systemic lupus erythematosus (10 to 45%)
- Dermatomyositis (20%)
- Primary Sjogren's syndrome (33%)

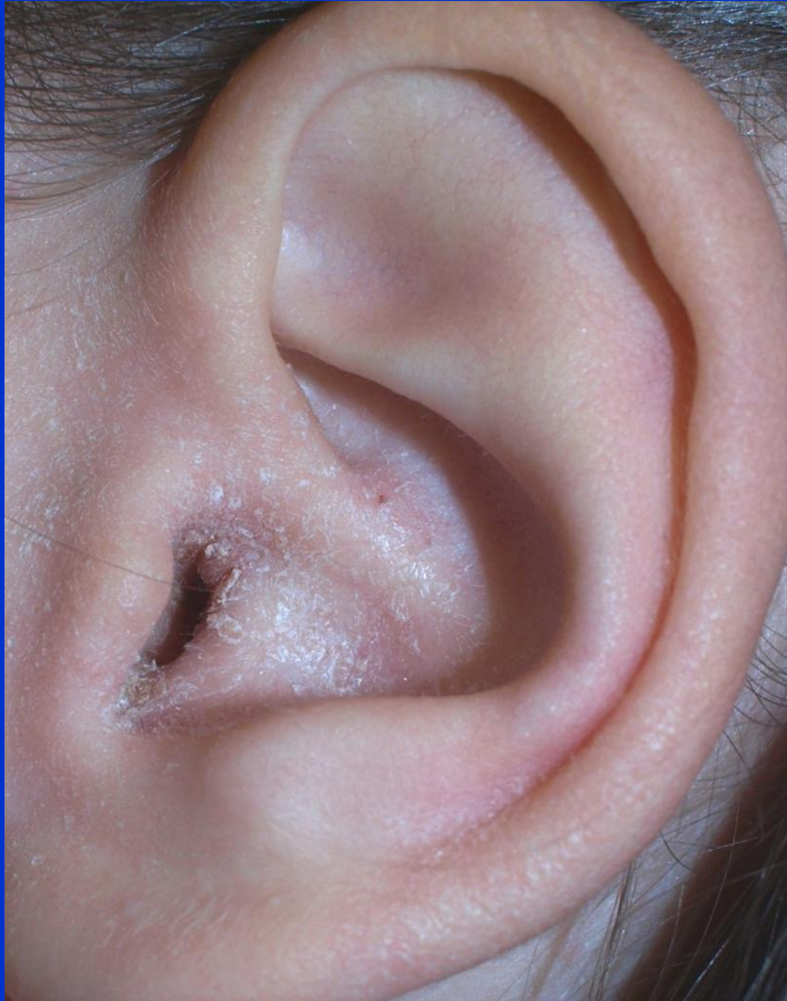
What other conditions can cause a red face?

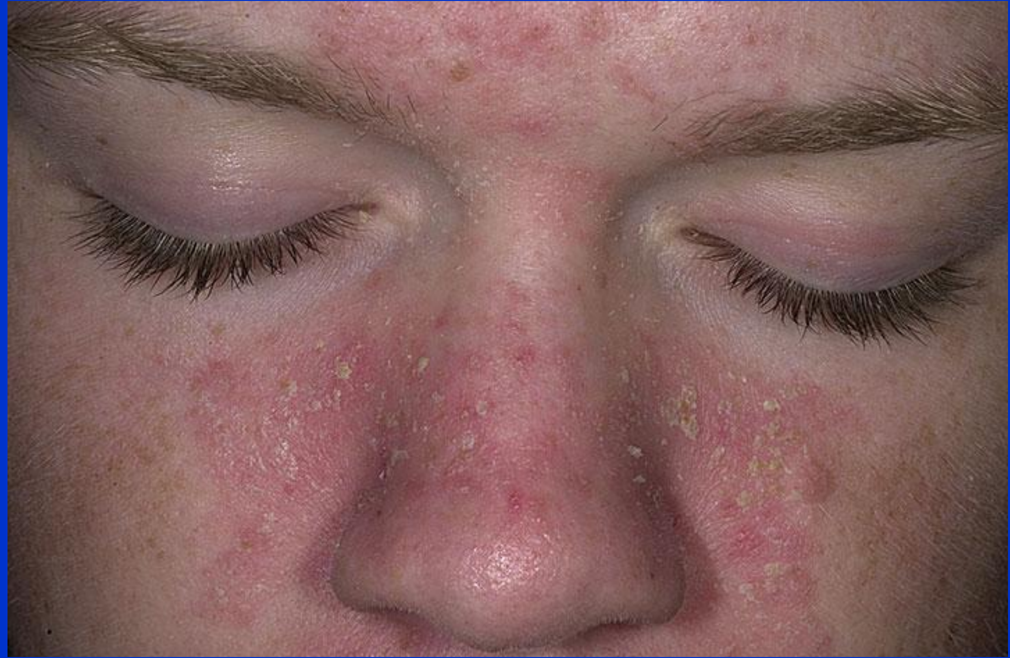
Seborrheic dermatitis can resemble malar erythema



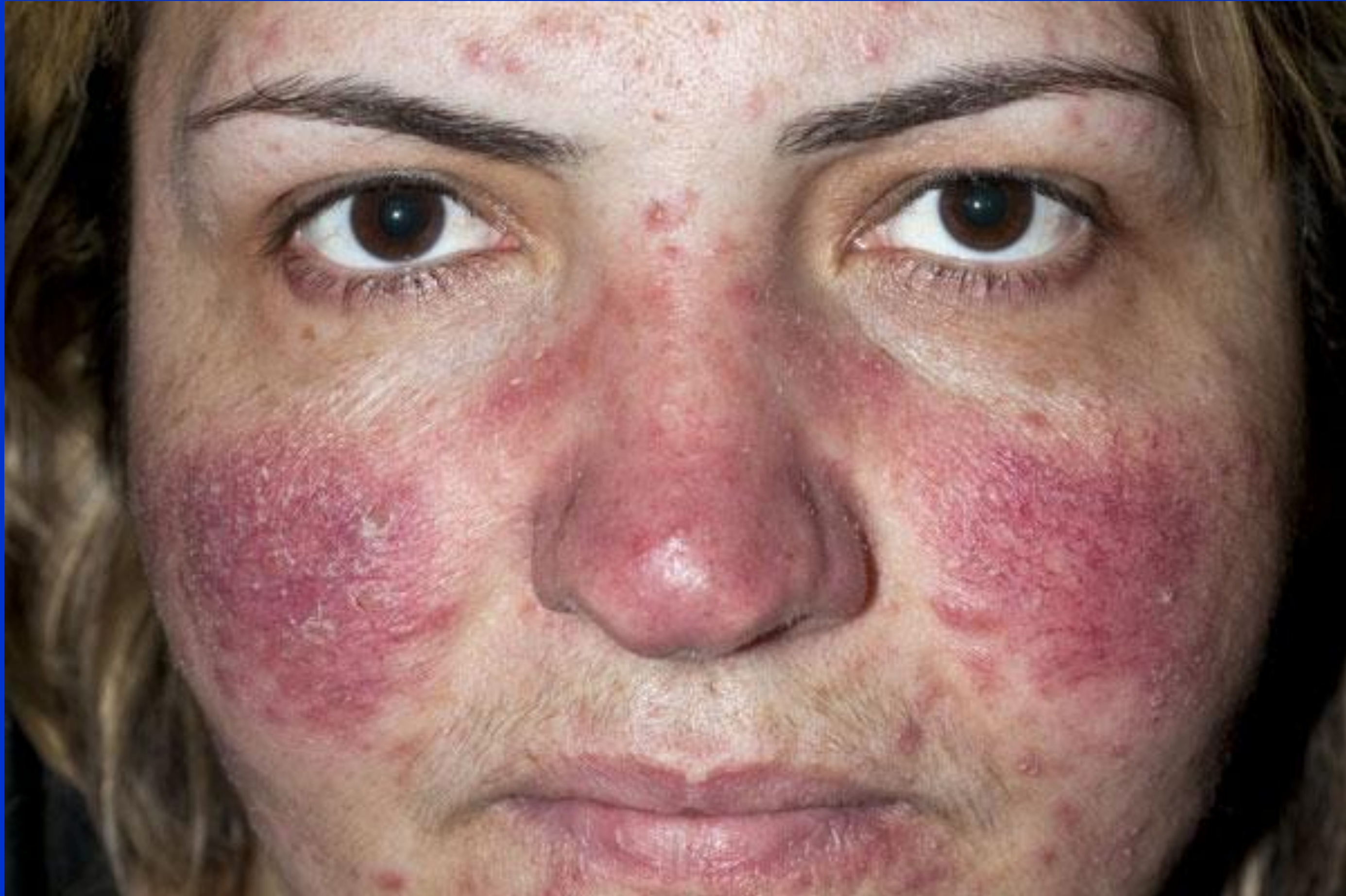
Seborrheic dermatitis can involve the scalp, forehead, eyebrows, ears, beard, chest

Seborrheic dermatitis can resemble malar erythema



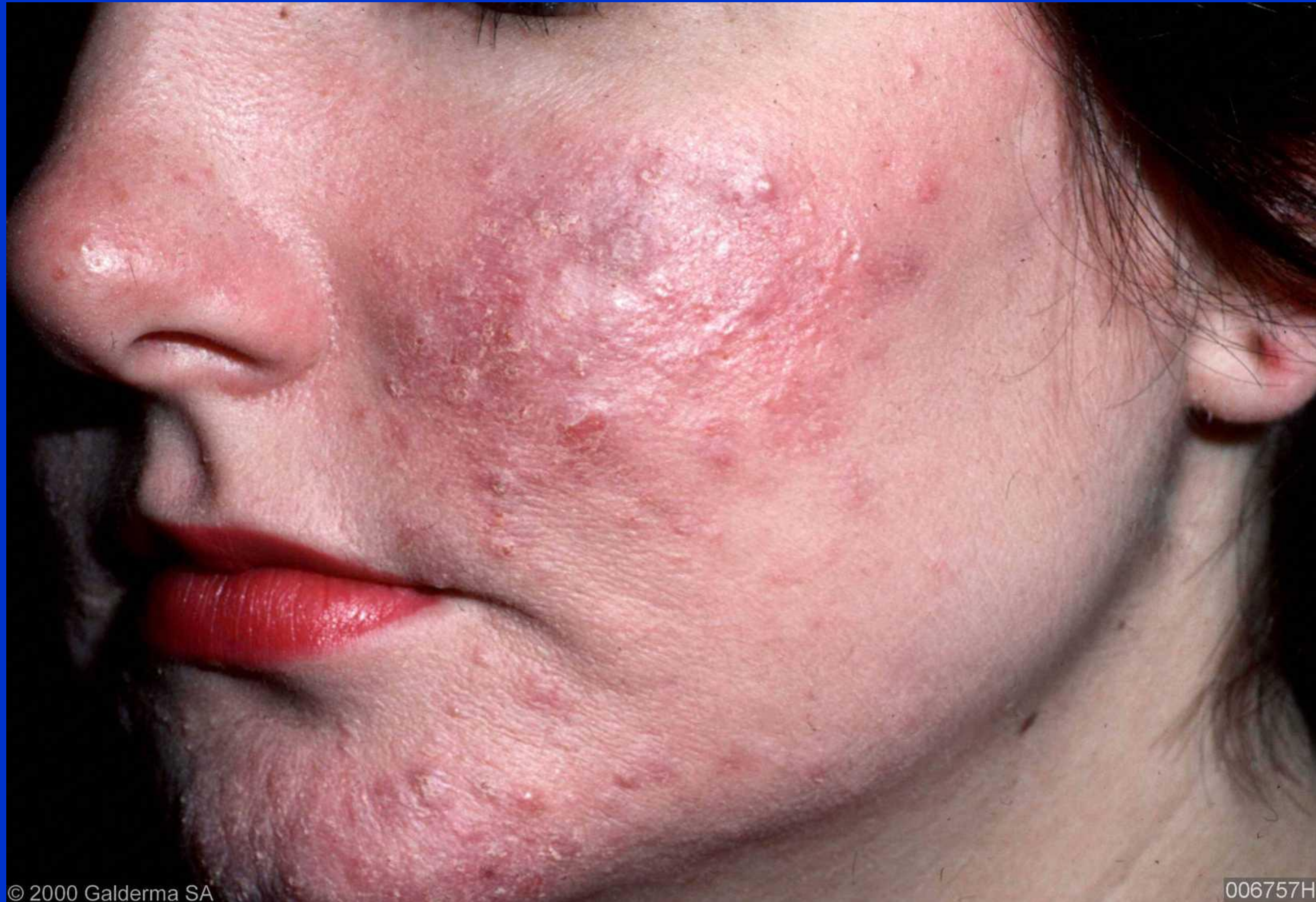


Rosacea can resemble malar erythema

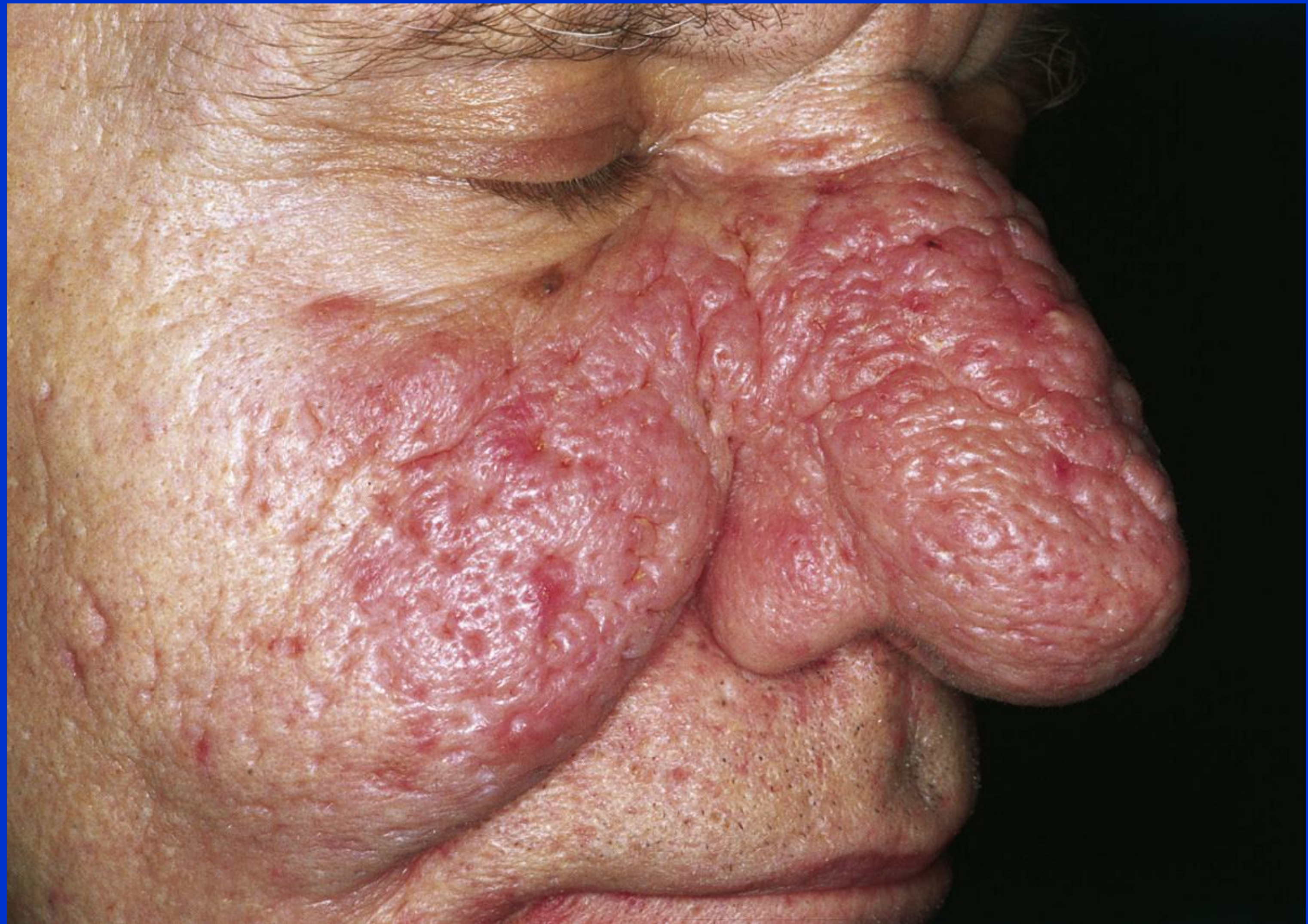


Examination more likely rosacea if:
-Presence of red bumps and pus
-Redness crosses nasolabial folds

Another example of rosacea

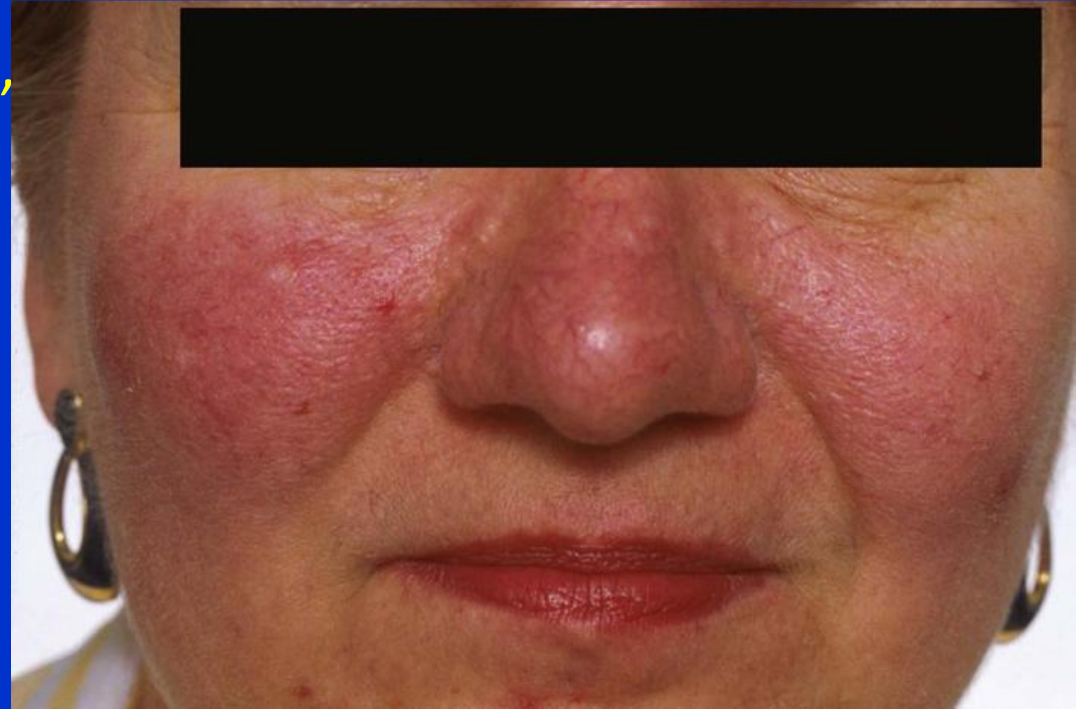


Rhinophymatous rosacea



Sometimes rosacea vs. malar erythema is very difficult to differentiate

- Timing: Acute or chronic?
- Triggers: Stress, heat, alcohol, spicy foods?
- Any pimples ever?
- Other rashes?
- Photosensitivity (can be both)
- Associated symptoms: joint aches, fatigue more than usual, eye symptoms
- Labs: Role of ANA?



Forms of cutaneous lupus

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Discoid lupus is in the criteria for systemic lupus, however, a patient can have discoid lesions commonly without systemic lupus

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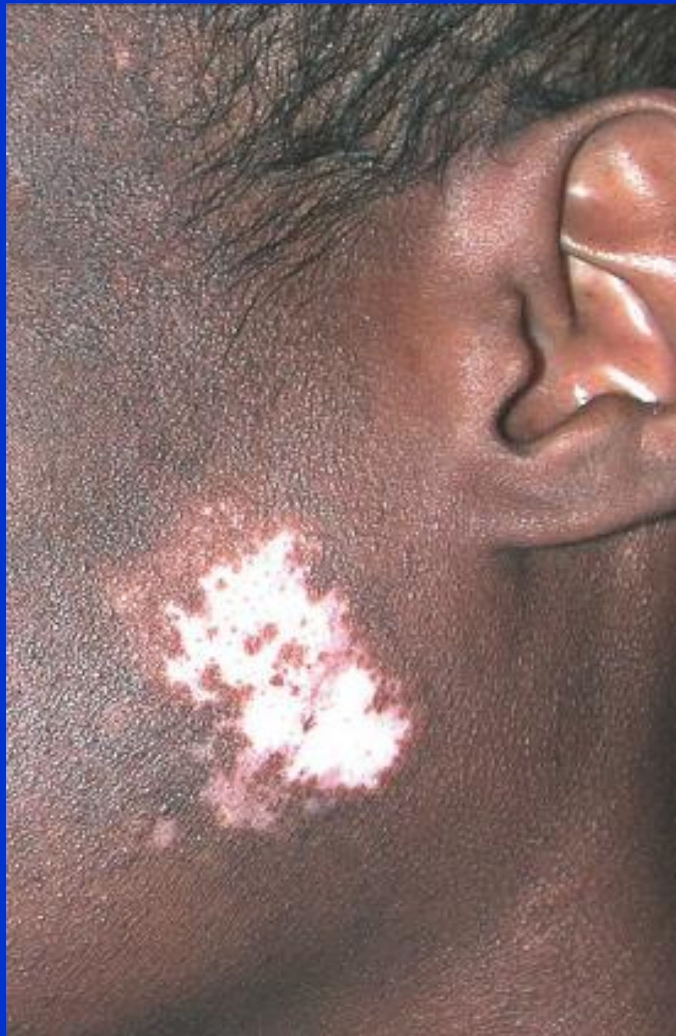
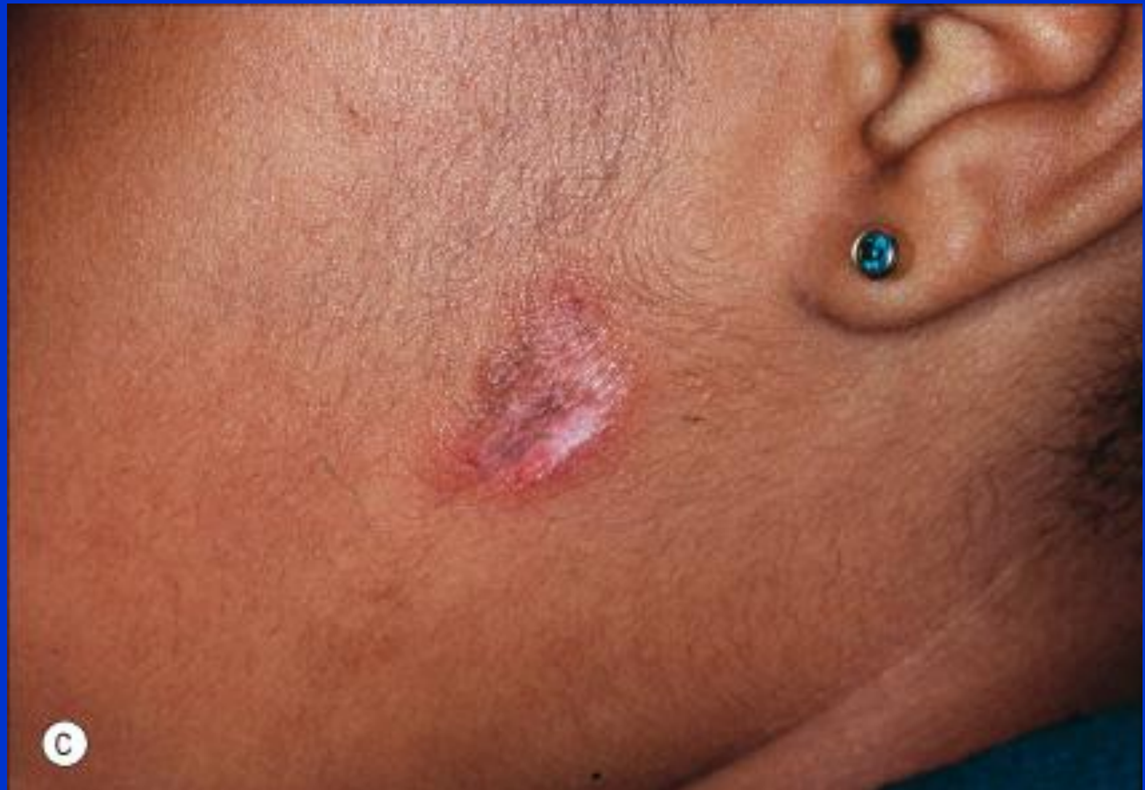
Various clinical presentations of discoid lupus erythematosus (DLE)

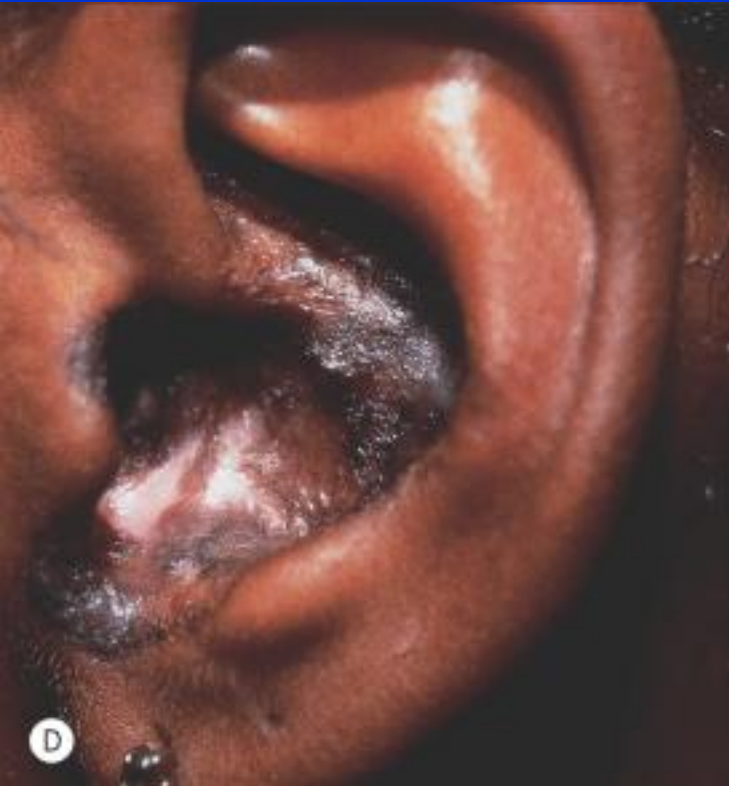


Vitiligo-like lesions



Active purple border with hypopigmentation and scar

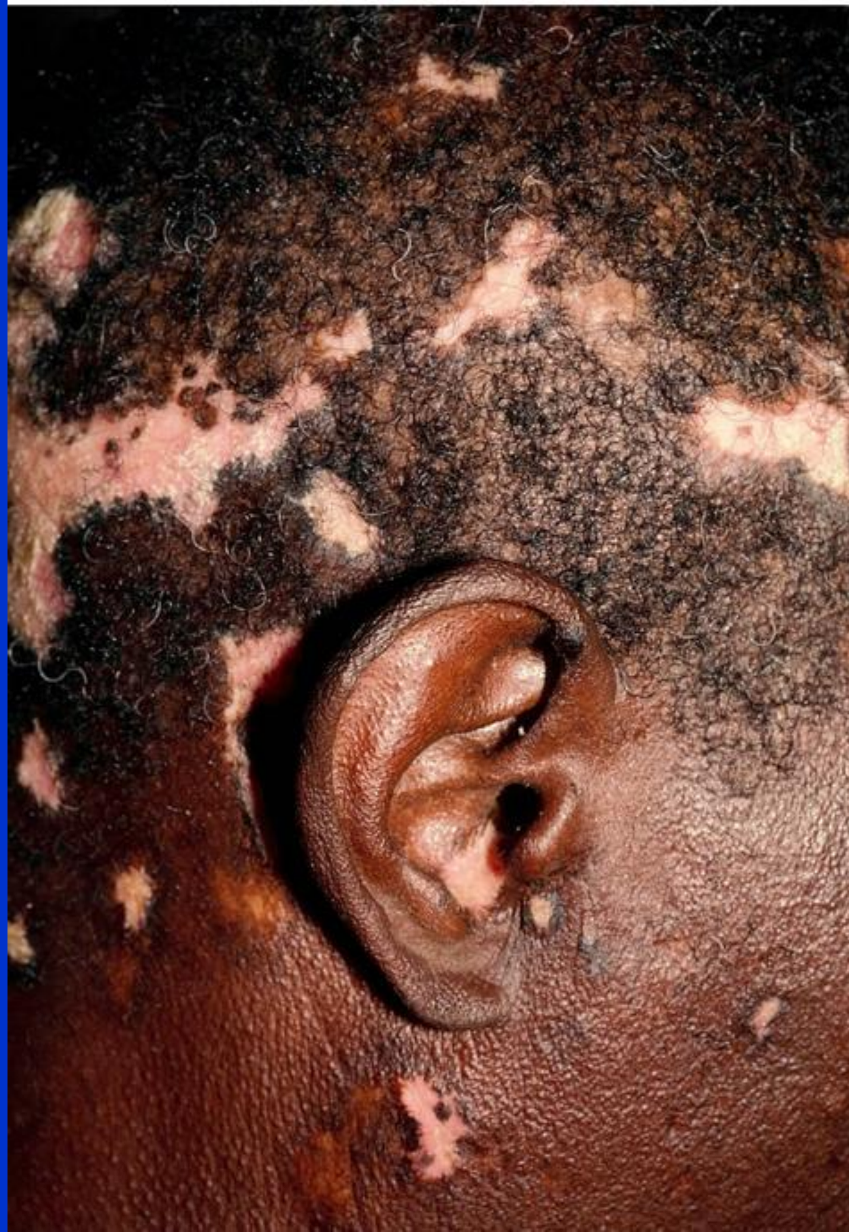
DLE can be destructive



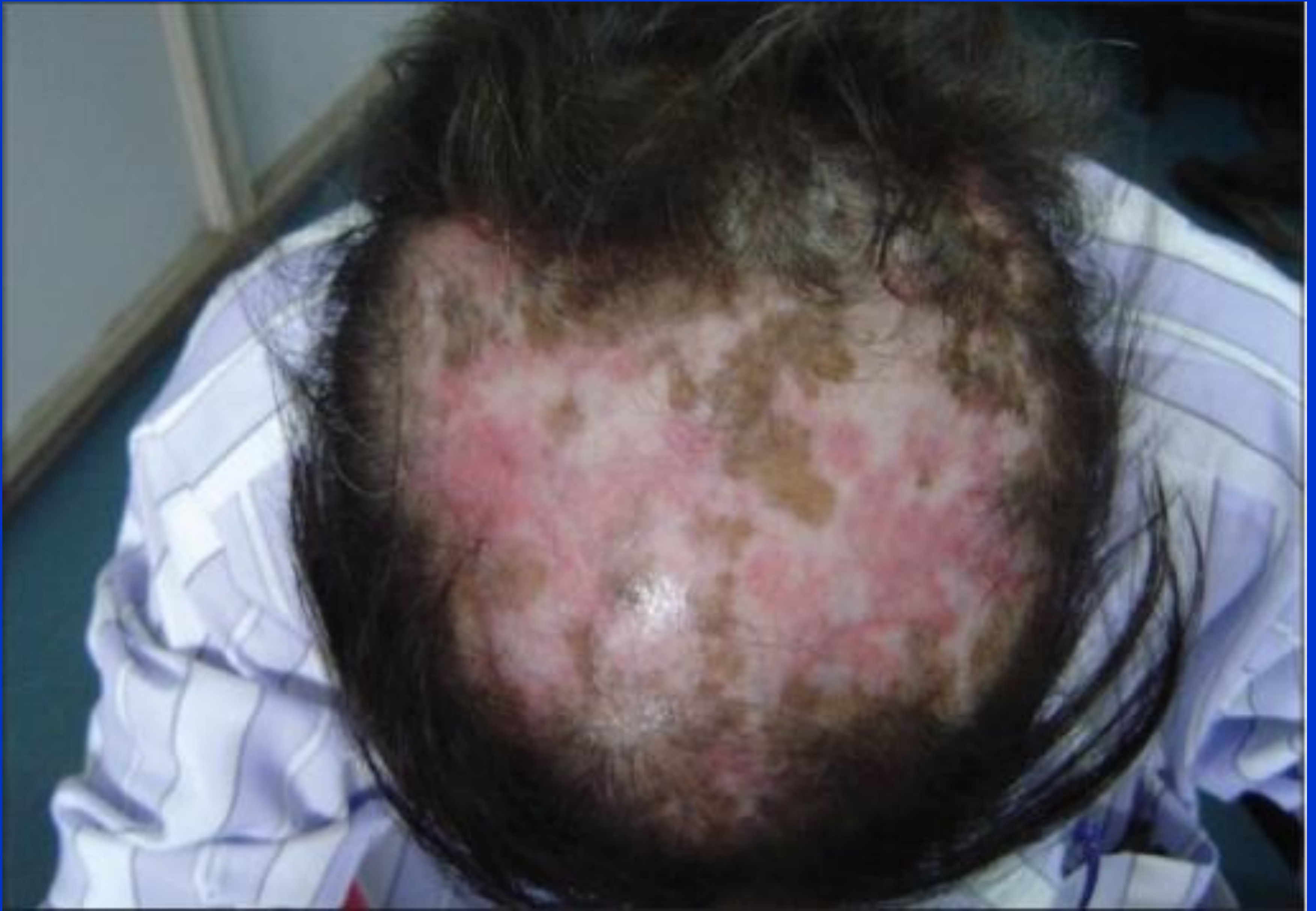
Conchal bowls in the ear
are a common site for DLE

E

Scarring alopecia due to DLE



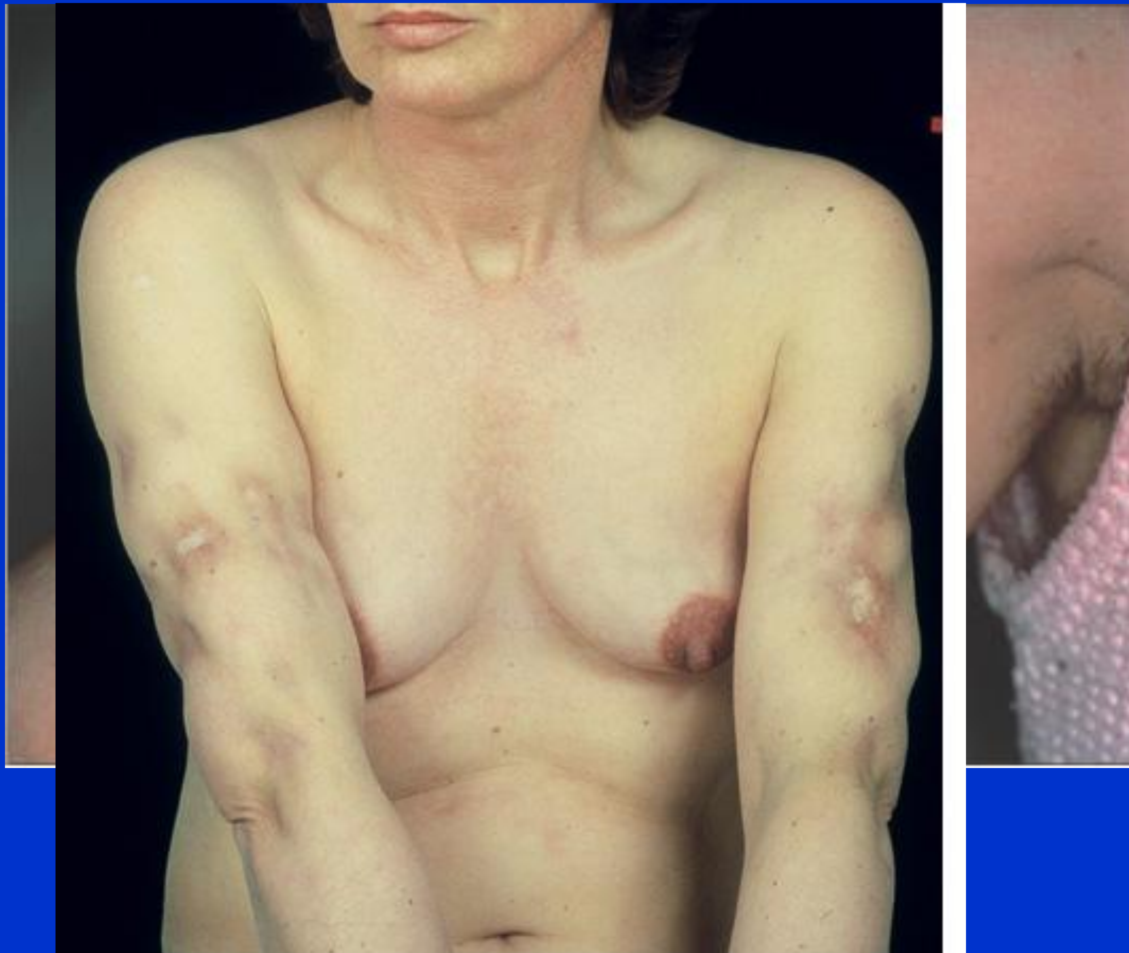
Discoid lupus erythematosus (DLE)



Clinical tips about DLE

- Rarely progresses to systemic lupus erythematosus (SLE) --only 5-15%
  - Though patients with SLE can have DLE lesions
  - More likely to progress to SLE if widespread
- Patients can have arthralgias (joint aches)
- 24% can have lesions in the mouth
- Can develop squamous cell carcinomas (cancers) in chronic lesions

Lupus panniculitis—a form of cutaneous lupus in the fat



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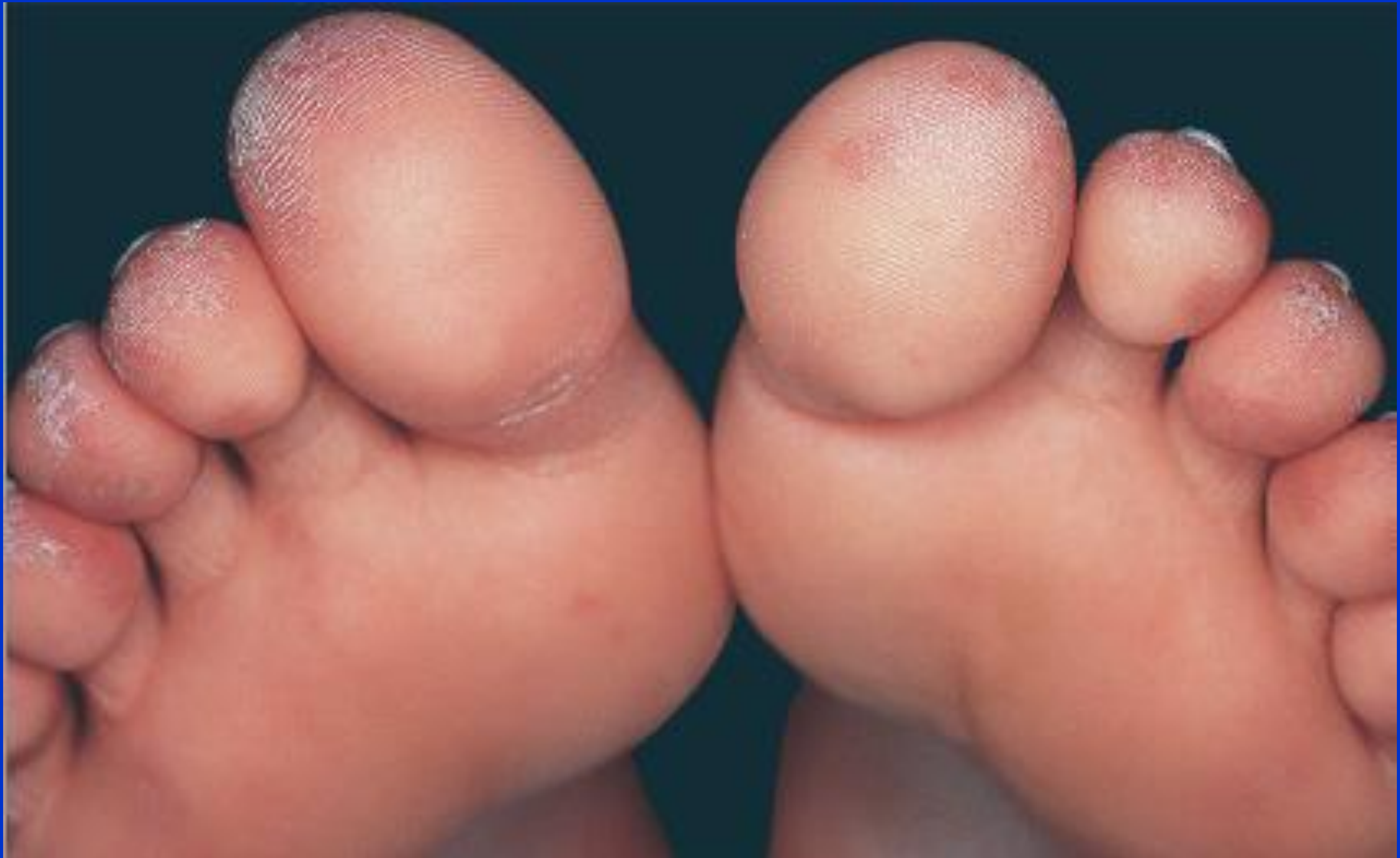
Chilblain lupus—a form of lupus that can appear on the toes, ears, nose



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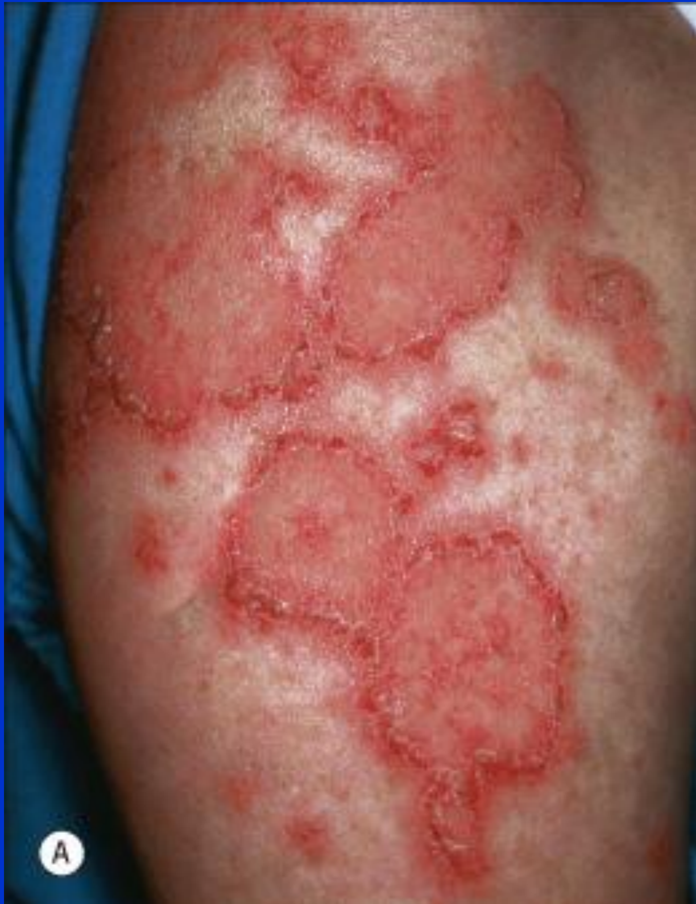
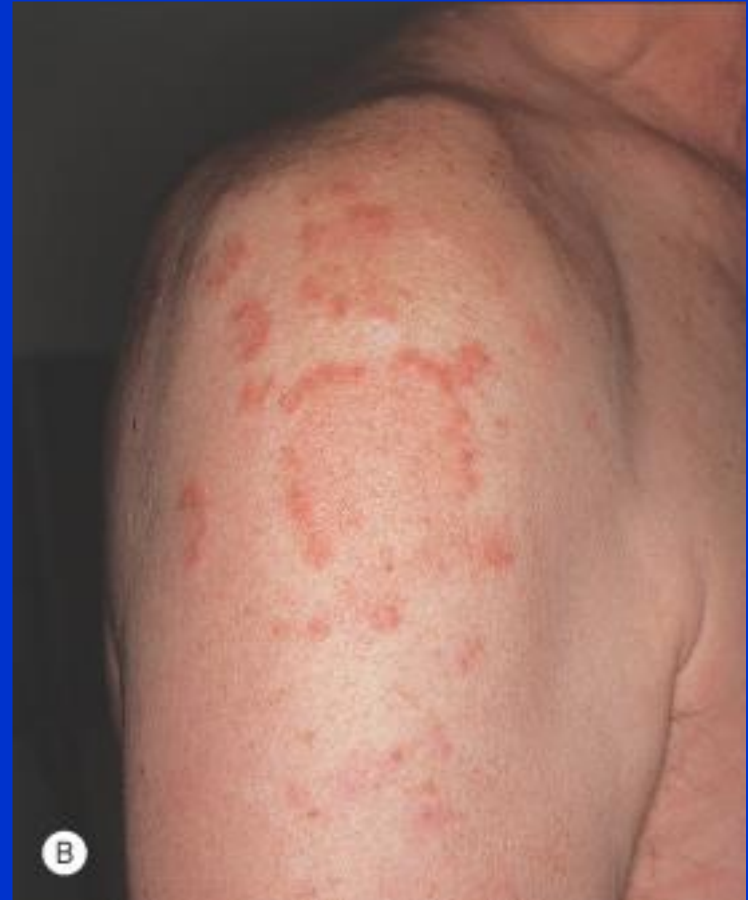
SCLE (Subacute cutaneous lupus erythematosus)

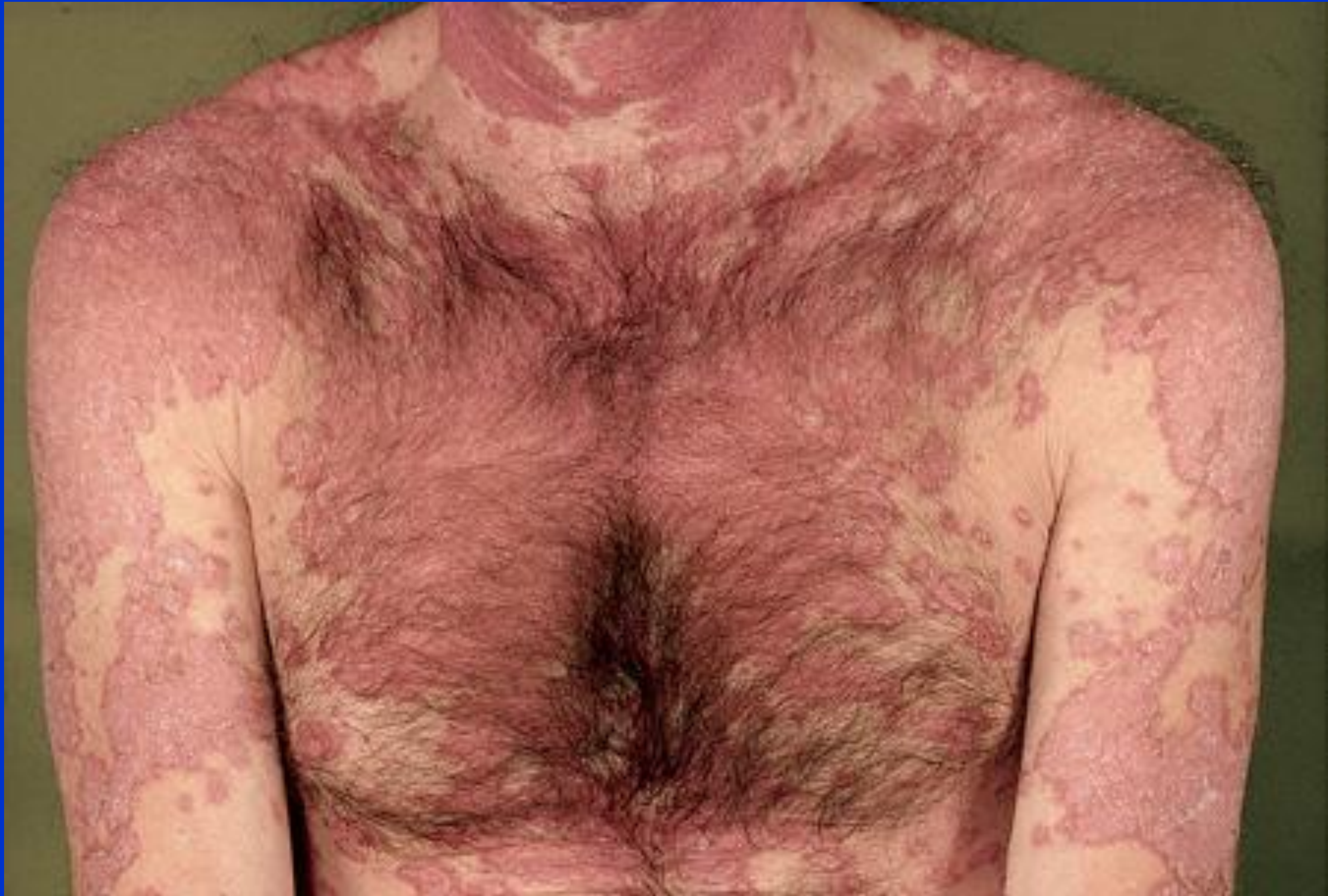
- Two variants
  - Annular (round)
  - Psoriasiform (looks like psoriasis)
- Photodistributed, nonscarring
- Photosensitivity: 50%
- Labs: Often ANA + (80%), SSA +
- Some patients will meet SLE criteria
  - 75% with arthritis or arthralgias
  - 20% with leukopenia
- Recently, many of these patients have an associated medication causing their disease

Annular variant of SCLE





Psoriasiform SCLE



Lupus and the Skin Outline

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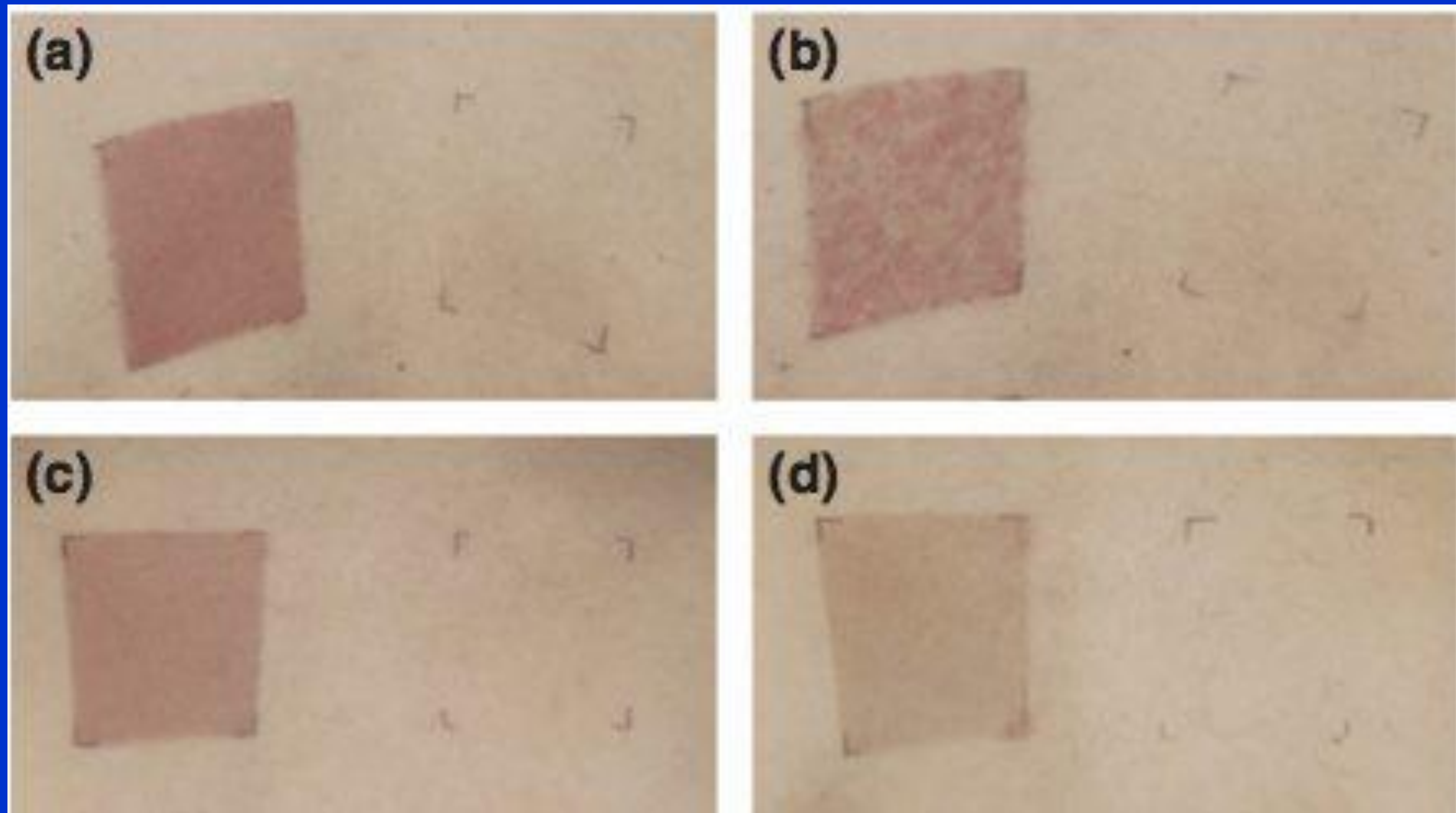
Sunscreens

- Suggest broad-spectrum UVA and UVB SPF 50 and above sunscreen.
  - Apply every 2 hours while outside and more often if still symptoms
  - Apply 15 minutes prior to sun exposure
  - One ounce of sunscreen to exposed areas
  - Best ingredients (physical sunblocks): titanium dioxide, zinc oxide
    - Tend to not absorb that well, but better

There is proof that broad spectrum sunscreen works in lupus



In A-D: The skin was irradiated with UVA and UVB.
Left box (no sunscreen) and right box (with sunscreen)

Kuhn Experimental Derm 2012

Sun avoidance

- It’s important to also avoid the sun
  - Prefer to stay in the shade
  - Avoid sun at peak hours between 11am-3pm

Polypodium leucotomos (Heliocare) might make lupus patients less photosensitive

- Polypodium leucotomos: fern plant extract marketed as an "oral sunscreen"
- Polypodium leucotomos dose
  - Mechanism: Scavenges free radicals, less production of TNF-alpha
  - 480 mg per day (2 pills)
  - $25-$60 for 60 pills

Sun protective clothing

- Regular clothing does not protect well against UV light

- Increasingly there is sun-protective clothing (available online) that can block 98% of UV radiation

- Additive into the laundry: Can use a powder (can search for “Sung Guard) in the laundry to protect against UV light

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Smoking cessation

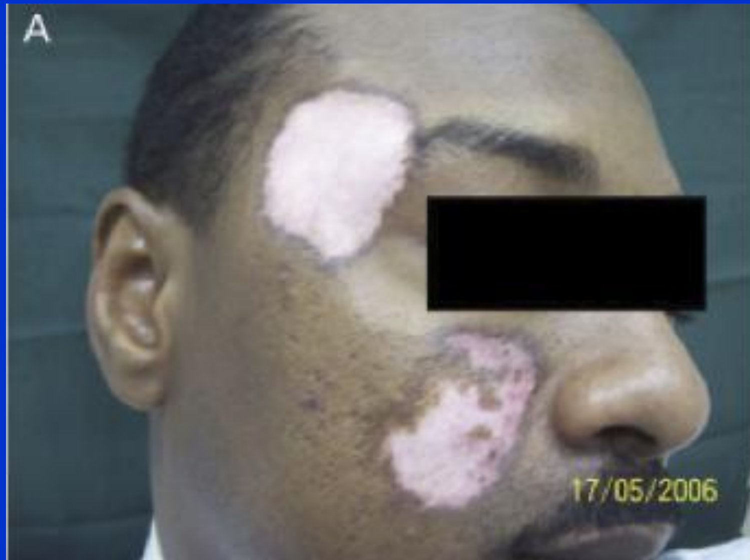
- There is a link between smoking cigarettes and worse skin in lupus
  - Patients also tend to be less responsive to antimalarial treatments when they smoke cigarettes

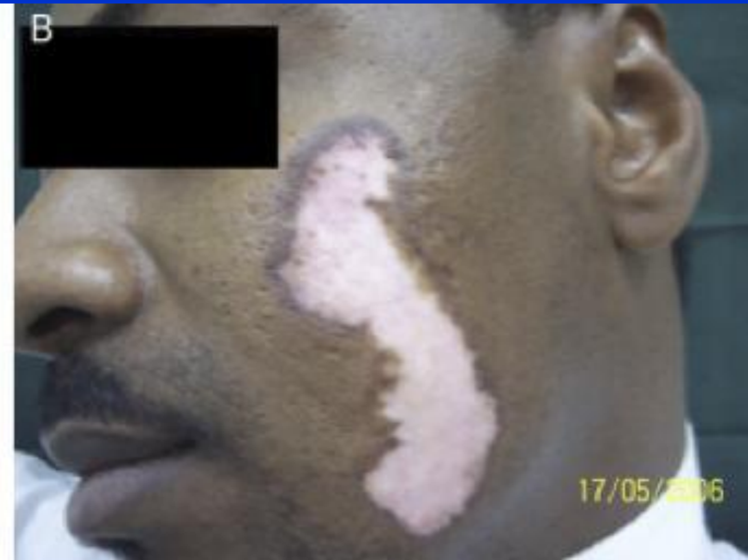
- Need to make attempts to quit smoking

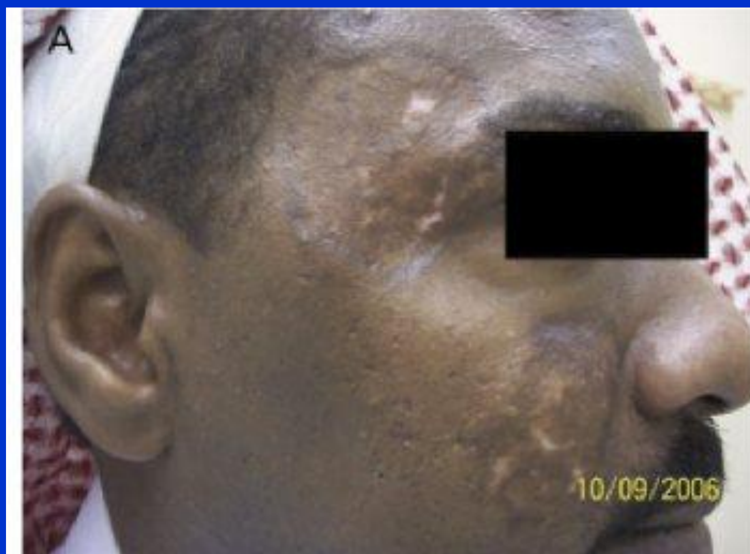
Traditional therapies for cutaneous lupus

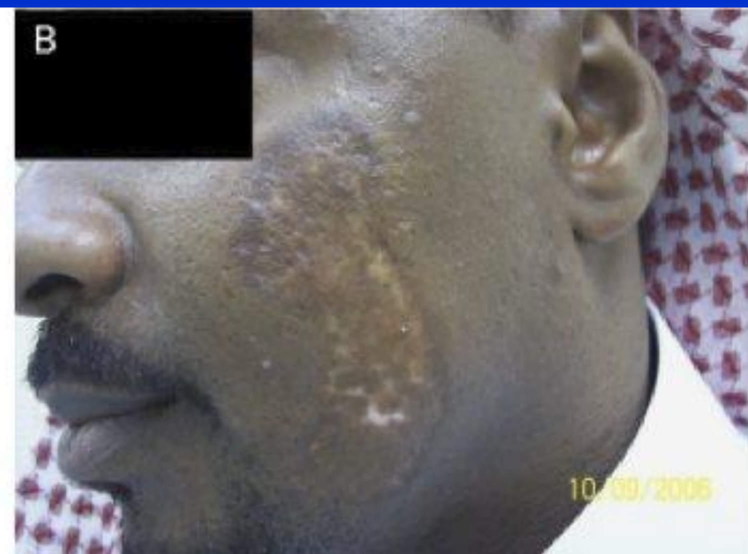
- Topical
  - Corticosteroids
  - Calcineurin inhibitors: tacrolimus (protopic), pimecrolimus (Elidel)
- Systemic
  - Anti-malarials
    - Hydroxychloroquine (Plaquenil)
    - Chloroquine
    - Quinacrine
  - Corticosteroids
  - Methotrexate
  - Dapsone
  - Azathioprine
  - Mycophenolate

Melanocyte-keratinocyte transplantation to improve DLE hypopigmentation

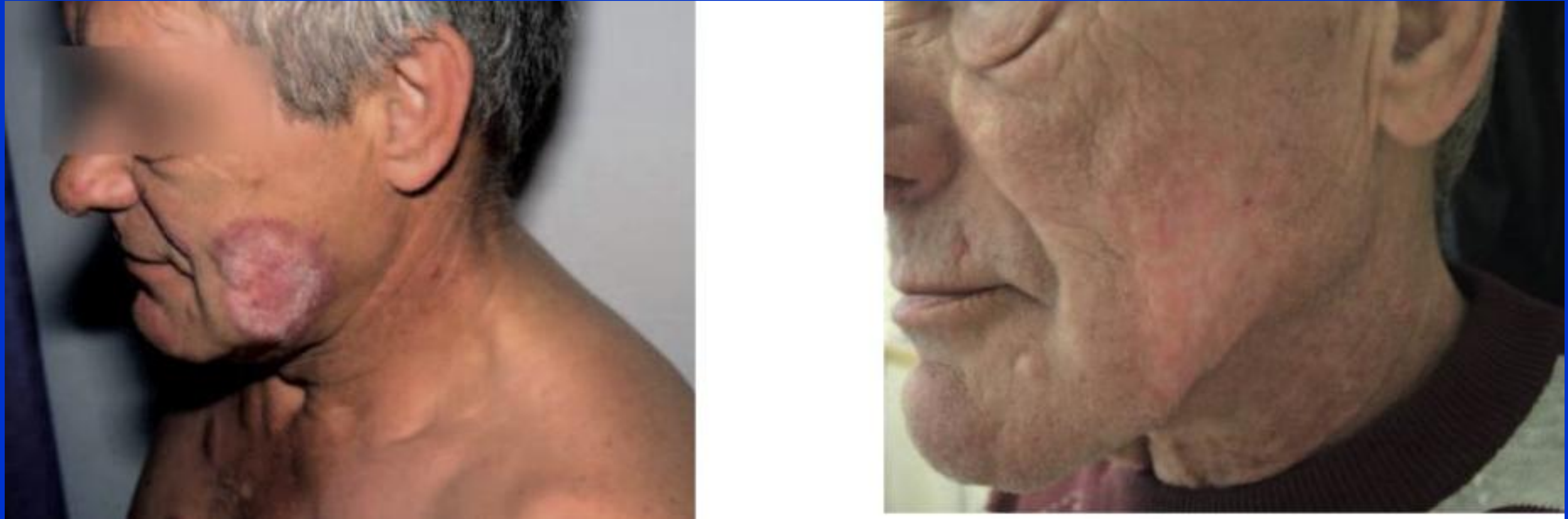








Pulsed dye laser to treat active DLE lesions



6 years later

Belimumab (Benlysta) is a new treatment for SLE

- Mechanism
  - Antibody to B lymphocyte stimulator (BLyS) involved in B cell activation. Depletes activated and naïve B cells and plasma cells.
  - IV infusion: 0, 14, 28 and every 28 days
- Indications: For patients with active, autoantibody positive SLE without renal or CNS disease who have failed conventional therapy or have contraindications
- Some benefit in controlling disease. Skin disease responds slowly
- Unknown answers:
  - What is the role of combination therapy?
  - Does it have any effect as a first-line treatment?
  - Will it help renal or CNS disease?

Still unanswered questions

- What's the extent of the impact of the following on cutaneous lupus?
  - Hormones/Gender?
  - Genetics?
  - Environmental exposures?
  - Viruses/infections?

QUESTIONS?