MED437
KING SAUD UNIVERSITY

DERMATOLOGY 437

6-Cutaneous Manifestations of SLE & Other Connective Tissue Diseases

Objectives:

-Differentiate between the various types of Lupus
-Recognize how lupus affect the various systems of the body
-Identify all of the current treatment options available for Lupus
-To learn how to diagnose and investigate dermatomyositis
-To learn the presentation of morphea and systemic sclerosis and ways to manage them.

-This lecture is not meant to be inclusive of all the information about these diseases but to highlight important aspects in their diagnosis and management.

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References: Doctor slides, Team 436

Color Index:

- Important
- Doctor's Notes
- Extra

Editing File

1) LUPUS ERYTHEMATOSUS

It's a designation of a spectrum of diseases that are linked by distinct clinical findings and distinct patterns of polyclonal B cell immunity. (antigen-antibody)

- It ranges from life-threatening manifestations of SLE to the limited and exclusive skin involvement in CCLE. Like discoid lupus erythematosus. It can range from mild nonselective like purpura (differentials of purpura: infection (hep B or C), Drugs, autoimmune (that's why with any purpura we have to check ANA to rule out autoimmune))
- More than 85% of patients with LE have skin lesions, which can be classified into LE-specific & non-specific*.

Revised ACR's Criteria for Classification of SLE

Any 4 of the following criteria are required to make the diagnosis:

Criteria	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	as a result of unusual reaction to sunlight, by patient history or physician observation
Oral ulcer	Oral or nasopharyngeal ulceration, usually **painless**, observed by physician
Arthritis	Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion
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
Renal dis.	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
Neurological dis.	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
Hematological inv.	a) Hemolytic anemia with reticulocytosis OR b) Leukopenia – less than 4000/mm3 total WBC on two or more occasions OR c) Lymphopenia – less than 1500/mm3 on two or more occasions OR d) Thrombocytopenia – less than 100 000/mm3 in the absence of offending drugs
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)
ANA	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.

Lupus Specific eruptions Help a lot to make the diagnosis

1 . Acute cutaneous LE (ACLE) Mallor rash>nonscarring

Localized, generalized (photodistributed)

-involves primarily the epidermis and upper dermis and is usually associated with systemic disease

2. Subacute cutaneous LE (SCLE) usually nonscarring but could be mixed

-involves primarily the epidermis and upper dermis and is associated with anti- Ro/SSA autoantibodies and photosensitivity; the majority of patients do not have significant systemic disease

A. Annular

B. Papulosqamous

C. Syndromes commonly exhibiting similar morphology

1. Neonatal LE (NLE)
2. Complement deficiency syndromes
3. Drug induced (drug induces SCLE is different drug induced lupes)

3. Chronic Cutaneous LE if not treated early patient will have scarring that is permanent (cannot be reversed)

A. Discoid LE (DLE): involve the epidermis, upper and lower dermis, and adnexal structures, and they can scar; the majority of patients do not have significant systemic disease

1. Localized, head and neck.

face and scalp(one of the emergencies hair will never grow again after scarring): Differentials:1. Lichen planus 2.DLE so BIOPSY is important. Also, don't forget to check the ears for brown scaly plaques and follicular

plugging

2. Disseminated (higher chance to have SLE)
3. Verrucous (hypertrophic) DLE

B. Lupus erythematosus tumidus: Involves the dermis but there is no prominent epidermal or adnexal involvement(non scarring no epidermal changes) dermal changes mainly

C. Lupus panniculitis: Involves the subcutaneous tissue and may result in disfiguring depressed scars (it will scar because its an inflammation of subcutaneous fat so requires a DEEP biopsy and aggressive treatment. It's also related to morphea (discussed later))

Erythema nodosum is the commonest type of panniculitis

D. Chilblain LE deep nodules, cold exposure, violaceous & erythematous distal toes

4. Other variance no need to know

-Bullous SLE acute

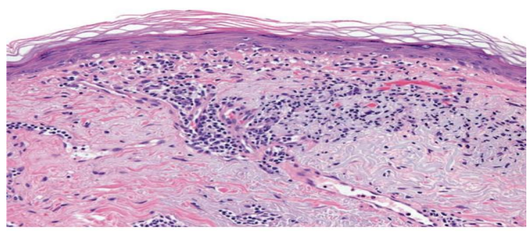
-Rowell's syndrome (SLE clinically looks like erythema multiform) looks like Steven- johnson syndrome. Which involves the SKIN + MUCOS MEMBRANE.

Causes of Steven Johnsen syndrome:

1.mycoplasma pneumonia
2.Drugs
3. SLE (but in lupus it will only affect the skin sparing the lips)

Males slides

PATHOGENESIS



The pathogenesis of cutaneous LE is complex, and it involves an interaction between genetic and environmental factors. The latter include ultraviolet radiation (UVR), medications, and possibly viruses. This interplay triggers a complex inflammatory cascade of cytokine, chemokine and inflammatory cell responses that include cells residing within as well as recruited to the skin. Overall, the lichenoid tissue reaction, defined as epidermal basal cell damage and a band- like lymphocytic infiltrate in the upper dermis, characterizes most subsets of cutaneous LE.

Histopathological feature

- Focal or continuous epidermal atrophy(epidermal thinning)
- Follicular keratin plugs (around hair follicles)
- Vacuolar degeneration along the dermo-epidermal junction zone (we will see a gap)
- Individual necrotic keratinocytes
- Thickening of basement membrane(one of the major criteria)
- Abundant interstitial mucin deposits in the reticular dermis
- Moderate to dense superficial and deep perivascular and periadnexal lymphocytic infiltrate (inflammatory cells)
- Note (melanocyte produce melanin which goes to keratinocytes the question is what will happen if the keratinocytes are destroyed where will the melanin go? It will go to the dermis, It's called melanin incontinence. The dermis will be pigmented

Acute Cutaneous Lupus Erythematosus

- Acute malar " butterfly rash" or more generalized photodistributed eruption.
- Nearly ALL patients presenting with ACLE will have systemic lupus erythematosus (SLE), often in an acute flare
- Patients with ACLE will nearly always have a +ve ANA
- ACLE is transient (hours/days) superficial dermis and may follow sun exposure , improves with improvement of the SLE
- Non scarring
- **Are there any common skin eruptions that may be confused with acute cutaneous lupus erythematosus?** **ACLE > no need biopsy because I know for sure the patient has SLE But for Discoid> I need a biopsy**
- **DO NOT BIOPSY FACE as it will cause scarring.**

- Seborrheic dermatitis erythema and scales (spared nasolabial folds, eyebrows and chest) not difficult to rule out
- Vascular type of rosacea chronic and triggered by sun exposure /No systemic symptoms like arthritis
- Polymorphous light eruption photosensitivity related to sun
- Photo reaction to systemic medications (doxycycline and psoralen) and topical products
- Certain types of porphyria(related to heme synthesis)

- What is the initial workup of ACLE?
  1. History & Physical examination (they usually come due to a photoreaction) ask about arthritis
  2. Skin Biopsy (based on the location, if it was in the face > no biopsy)

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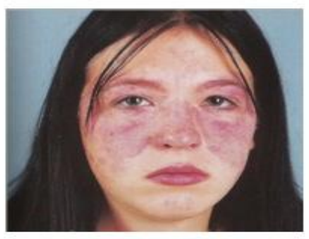
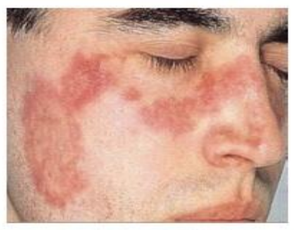
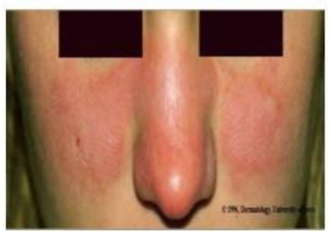
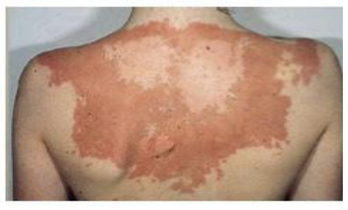
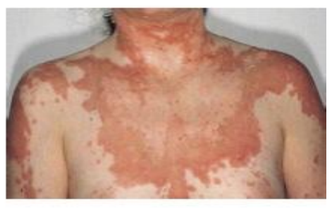




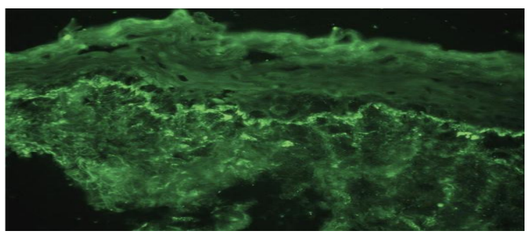






	3. Serology: important A. ANA :+ve in 95% ,VERY SENSITIVE BUT NOT SPECIFIC B. Anti-dsDNA (anti- native DNA): Specific but not very sensitive, indicates high risk for renal disease. (SLE nephritis) C. Anti-smith : most specific +ve in 30% D. Anti-histone Ab (drug induced lupus) E. Rheumatoid factor : +ve in 30% 4. CBC, ESR , CRP (leukopenia and thrombocytopenia in SLE) . 5. Urine analysis (protein and casts because the kidney is silent) 6. C3,C4: : low levels indicate active disease, often with renal involvement. 7. Lupus Band Test : not used routinely • It's preferred to be done on non-lesional non-exposed skin (for SLE) ,but can be performed on lesional skin.(for DLE) • Positive DIF supports the diagnosis of Cutaneous LE, negative DIF does not exclude the diagnosis. • Clinical, histopathology, serology are more important. • Positive antibody of normal appearing skin correlates with SLE. • Granular deposits of immunoglobulins and complement are detected in a band-like pattern at the dermal-epidermal junction.
Acute Cutaneous Lupus Erythematosus	**What I want you to know about ACLE is malar rash and it is usually indicate systemic involvement** **T** •The aim of treatment for cutaneous LE is to alleviate symptoms and to prevent scarring. 1.Sun protective measures why sun is triggering ? Apoptosis, immunological reaction in skin leading to sun burn 2.Potent topical steroids if you dont use it in discoid patient will scar, in acute not that essential 3.Antimalarial drugs. Hydroxycholoroquine to treat skin and joint 4. Oral steroids. Internal organ involvement Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab acute patient rarely scar but if scar go for immunosupressants •The aim of treatment for acute cutaneous LE is to alleviate symptoms and to prevent scarring. 1.Sun protective measures why sun is triggering ? Apoptosis, immunological reaction in skin leading to sun burn 2.Potent topical steroids if you dont use it in discoid patient will scar, in acute not that essential 3.Antimalarial drugs. Hydroxycholoroquine to treat skin and joint 4. Oral steroids. Internal organ involvement Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab acute patient rarely scar but if scar go for immunosupressants

Lupus Band test



Types of Cutaneous Disease in Lupus Erythematosus

There are several variants of cutaneous lupus, defined in part by the location and depth of the inflammatory infiltrate

EVALUATION FOR SYSTEMIC LUPUS ERYTHEMATOSUS

- HISTORY
- PHYSICAL EXAMINATION
- Specific cutaneous lesions
- Nonspecific cutaneous lesions
- Lymphadenopathy, arthritis
- LABORATORY TESTS
- ANA with profile (anti-dsDNA, -Sm)
- Urinalysis
- CBC with differential, platelet count
- Chemistries (BUN, creatinine)
- Erythrocyte sedimentation rate
- Complement levels (C3, C4)

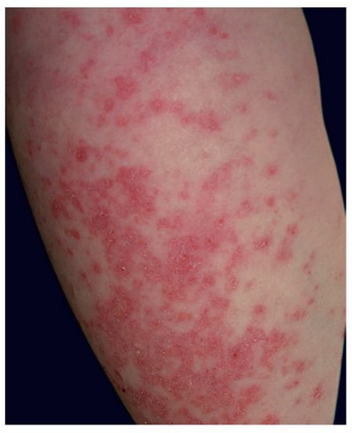
Lupus- nonspecific eruptions

Help support the diagnosis

- **Non-scarring alopecia:**telogen effluvium, Alopecia Areata, lupus hair.
- Scarring alopecia (discoid lupus)
- **Raynaud's syndrome** (mostly in Systemic sclerosis Vasospasm So it turns white then blue due to cyanosis then red due to hyperemia and dilation)
- **Nailfold telangiectasias and erythema**
- **Vasculitis**
  - A)Urticarial vasculitis urticaria : evanescent wheals that disappear within less than 24 hrs, if it persists more than 24 hrs > this is called urticarial vasculitis and we have to look for the cause.
  - B)Small vessel vasculitis (e.g. palpable purpura) pinpoint bleeding most common 3 causes 1. CT DISEASES 2. DRUGS 3.INFECTIONS(strept,hepatitis c)
  - C)Polyarteritis nodosa-like lesions
  - D)Ulcerations
- **Cutaneous signs of antiphospholipid syndrome:**
  - A)Livedo Reticularis comes in the legs like a web (autoimmune)
  - C)Acrocyanosis
  - D)Atrophie blanche-like lesions
- **Periungual erythema** (in dermatomyositis and systemic sclerosis)
- **Papular and nodular mucinosis**
- **Palmar erythema**
- **Oral lesions aphthous ulcers**
- **Bullous lesions (non-specific)**
- **Acanthosis nigricans**
- **Mucinous infiltration**
- **Porphyria cutanea tarda.**
- **Calcinosis Cutis**
- **Photosensitivity**we have to check ANA and anti-ro to rule out AUTOIMMINE

anti-Rho to rule out autoimmune

Subacute Cutaneous Lupus Erythematosus



- More persistent than those of ACLE (weeks- months)
- Scaly, superficial, inflammatory macules, patches, papules and plaques that are photodistributed, particularly on the upper chest & back, lateral neck, and dorsal arms & forearms and The midfacial skin is usually spared(difference between SCLE and ACLE).
- **Morphologic subtypes**: most common cause of annular lesion? Dermatophyte. No need to biopsy start with anti-fungal cream
  - Annular/polycyclic lesions " ring-shaped"
  - Papulosquamous lesions:
    - psoriasiform more likely to progress to systemic
    - pityriasiform
- Lesions often result in dyspigmentation (mainly hypopigmentation) but do not scar.

Do patients with SCLE have SLE?

- About 1/2 patients with SCLE will have 4 or more criteria for the classification of SLE
- Skin disease, photosensitivity, musculoskeletal complaints
- 60-100% have anti Ro antibody.
- 10-15% develop significant internal disease including nephritis.
- SCLE could occur in patients with Sjögren syndrome, deficiency of the second component of complement (C2).
- Drug induced SCLE: hydrochlorothiazide, terbinafine, calcium channel blockers, NSAID, TNF-α inhibitors, antiepileptic, minocycline and proton-pump inhibitors. ● The lesions may or may not clear once the medication is discontinued

How do you make the diagnosis of SCLE?

- SCLE is a clinical diagnosis based on presence of:
  - Typical photodistributed eruption
  - Skin biopsy
- Direct Immunofluorescence
- A strong association exists with anti-Ro/SS- A autoantibodies, and a lesser extent will have anti-La/SS-B

What is the initial workup of SCLE?

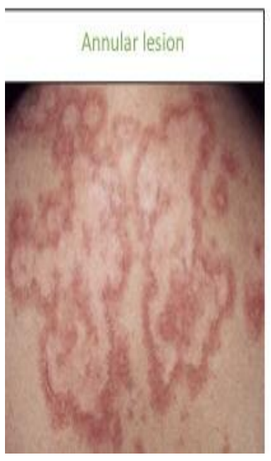
1. History & Physical examination
2. Laboratory testing
3. Medication History

How is SCLE managed ?

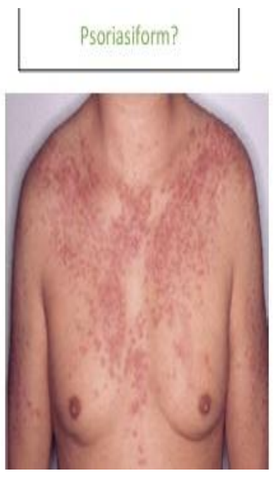
- Broad-spectrum sunscreens
- Sun-protective measures
- Topical steroids
- Antimalarial drugs

Best presentation: annular patch with scaly borders

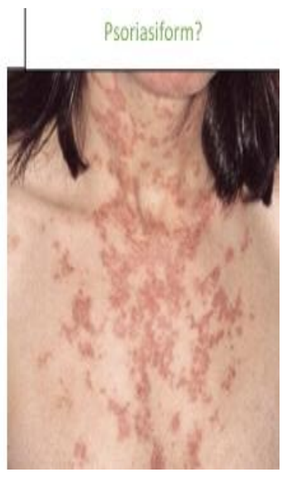
On the neck and back
Papule and plaques
Annular

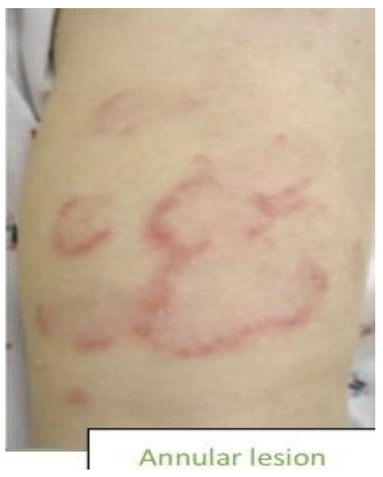


Annular



Christmas tree
Ptyriasiform
papules

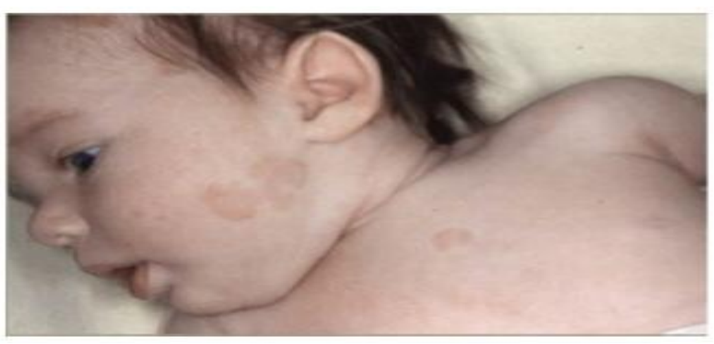


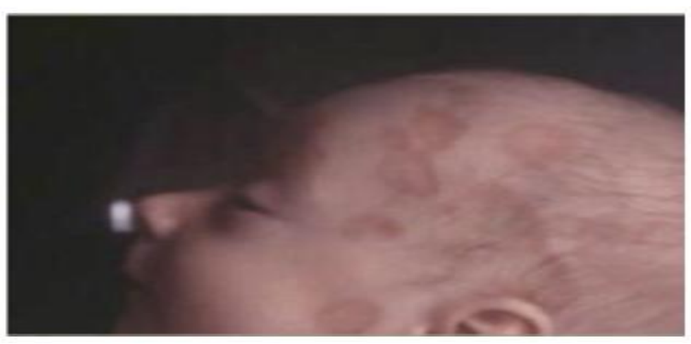


Neonatal Lupus Erythematosus

- The skin lesions occur on the face and head, morphologically resemble SCLE lesions(annular), they are transient, resolving within a few months*.
- In NLE , infants develop skin disease (50%), congenital heart block (50%), or both (10%).
- It's usually permanent and may require a pacemaker.
- 10% of infants with NLE and heart disease die from cardiac complications.
- Thrombocytopenia/ liver disease.
- anti-Ro (100%) and other antibodies as well as the mother.

For mom and baby> we check 1.ANA and anti-rho with anti-la and anti-U1RNP (for CT disease) ,2.ECG, 3. CBC for thrombocytopenia 4. LFT for hepatobiliary disease also 5.biopsy





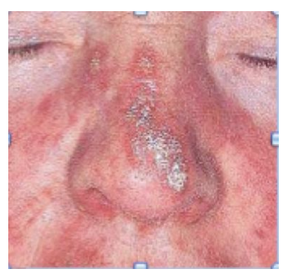
Chronic cutaneous Lupus Erythematosus

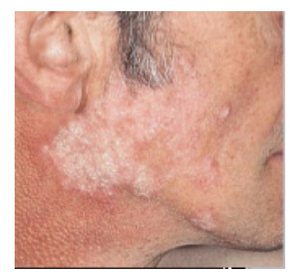
- **What is chronic cutaneous lupus erythematosus?**

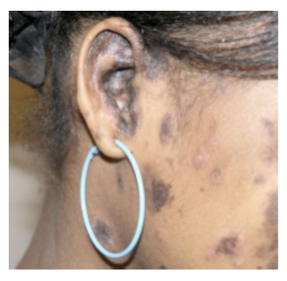
Several types of cutaneous LE that are very persistent are termed chronic cutaneous lupus erythematosus
The most common of these chronic forms is discoid lupus erythematosus 'DLE'
Serologic abnormalities are uncommon only 5% +ve

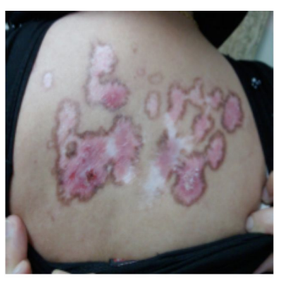
- **Describe the skin changes that occur with <u>discoid lupus erythematosus</u>?**

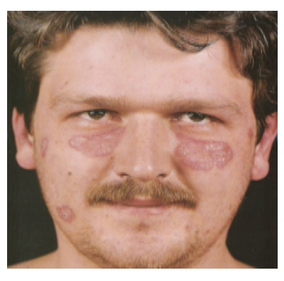
•Localized or generalized
•Chronic, fixed, indurated, erythematous papules and plaques often distributed over the head & neck.
•Scarring indication of potent steroid (requires urgent tx). Unlike the acute is non scarring
•Pigmentary changes (hypo/hyperpigmentation)
•Epidermal changes: scales, keratotic plugging of hair follicles, crusting
•External ears



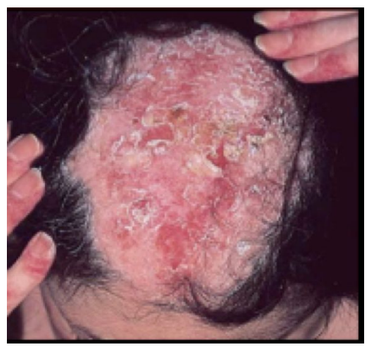




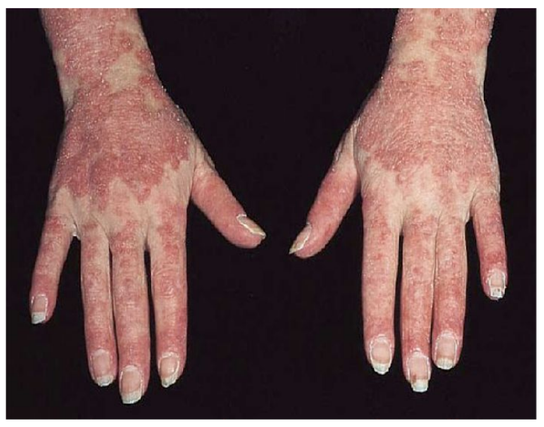


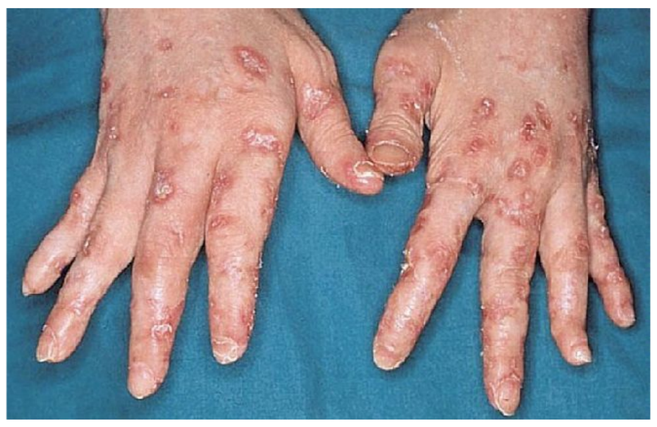


Do patients with DLE develop systemic lupus erythematosus?
•Risk of developing SLE is 5%-15% (slightly higher risk if DLE is generalized).
•25% of SLE patients will develop lesions of DLE at some time during the course of their disease.



How is Discoid Lupus treated?
•Sunscreens
•Sun-protective measures
•Potent topical steroids/ intralesional steroids
•Antimalarial drugs





Mistaken for dermatomyositis.
In DM knuckles are involved unlike here

Drug induced lupus

- **Drug-induced lupus differs from SLE by the following features:**
  - Sex ratios are nearly equal.
  - Arthralgia, myalgia, pleuritis, fever, lacking nephritis, CNS disease.
  - Procainamide, Hydralazine, phenytoin, Penicillamine, Isoniazid, Quinidine, Anti-TNF, IFN…
  - Antihistone antibodies.
  - No antibodies to native DNA or hypocomplementemia are present.
  - When the drug is discontinued, the patient has resolution of clinical manifestations and reverting of abnormal laboratory values to normal.
  - Nephritis and central nervous system features are not commonly present.

- **What is minocycline-induced lupus?** (minocycline Is used for acne)(you have to follow up)
  - Polyarthralgia, fatigue, fever, elevated liver enzymes, pneumonitis, anemia, lupus specific skin eruption have not been reported
  - All patients have positive ANA

If you have cough, arthritis , or fever > stop the drug
They are bluish patches on the skin and hyperpigmented and discoloration

Chlorpromazine	Isonizide
Hydralazine	procinamide
Methyldopa	Quinidine
Anti- TNF	Minocyclin
Penicillamin	IFN-alpha, IFN-beta

THERAPY OF CUTANEOUS LUPUS

❖ **LOCAL THERAPY**
- Sun protection
- Topical and intralesional corticosteroids
- Topical calcineurin inhibitors
- Topical retinoids

❖ **SYSTEMIC ANTIMALARIAL THERAPY**
- Hydroxychloroquine (200 mg po qd–bid in adults; up to 6.5 mg/kgideal body • weight/day)
- Chloroquine (125–250 po qd in adults; up to 3.5–4 mg/kg ideal body weight/day)
- Quinacrine (100 mg po qd)
- Combination of hydroxychloroquine or chloroquine (Don't give two anti-malarial together, they have adverse effects on the eyes.) and quinacrine but you can add quinacrine to either hydroxychloroquine or chloroquine.

❖ **SYSTEMIC THERAPY FOR ANTIMALARIAL-RESISTANT CUTANEOUS DISEASE**
- Retinoids (e.g. acitretin, isotretinoin)
- Thalidomide (50–100 mg po qd for clearing and, if necessary, 25–50 mg po, qd–twice weekly for maintenance) for vasculities
- Dapsone (primarily for bullous eruption of SLE)
- Immunosuppressive agents (e.g. mycophenolate mofetil, azathioprine)
- Sulfasalazine
- Clofazimine
- Systemic corticosteroids
- Immune response modifiers (e.g., rituximab, abatacept,* belimumab, anti-IL-6 Ab, • anti-IL-10 Ab)

❖ **1st line:** Antimalarials (Hydroxychloroquine,Chloroquine, Quinacrine), Systemic steroids.
  - Antimalarials side effect: xerosis, exanthematous or lichenoid drug eruptions, urticaria, blue-gray skin hyperpigmentation,ocular toxicity, gastrointestinal upset,myopathy, cardiomyopathy, and rare central nervous system side effects (dizziness, headache, insomnia, psychosis).

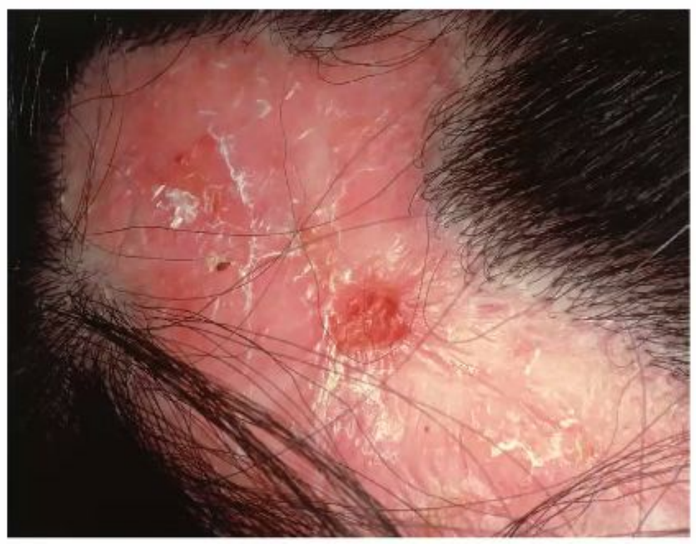
Important pictures for Exam

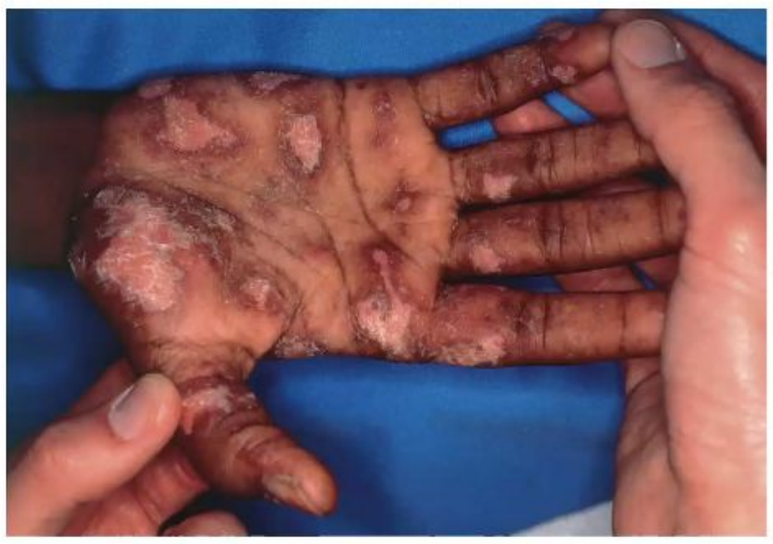
General notes

Primary skin lesion: De novo Secondary: Evolution or due to injury

What the major benefit of differentiating between primary or secondary lesion?

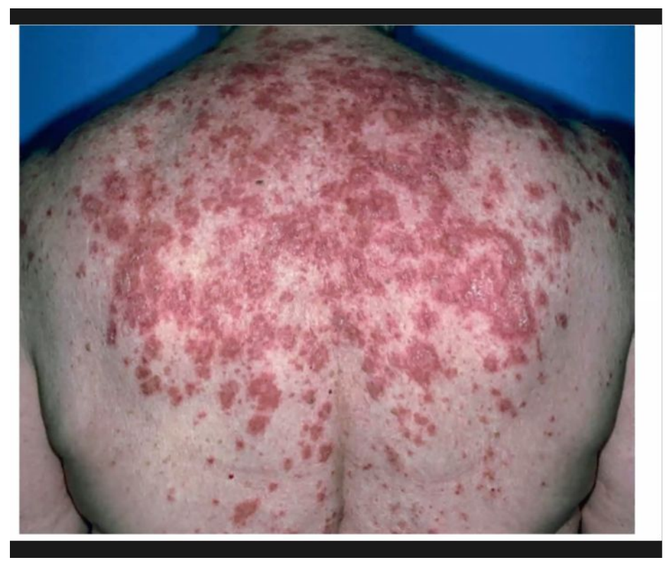
You cannot make a diagnosis with a secondary lesion, you need a primary you to diagnose for example: Herpes (grouping vesicles), *lichoplanus*, psoriasis (*plaques*).





What do you see?

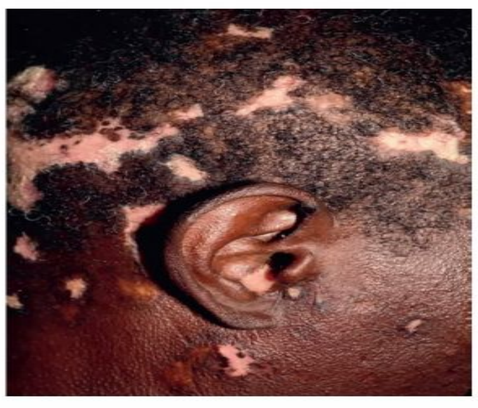
- Area of hair loss with well-defined irregular borders (خط متعرج) 4 by 8 cm with central erosion, area of scarring (opening of hair follicles are lost كانها قطعة وحدة), and there might be some crusts, plus you can see some scales.
- This is typical Discoid (affecting the hairy area and diffuse + causes secondary scarring + Follicular Plugging + Adherent Scales)
- This is not a panniculus because the panniculus affect the deeper tissue plus there will be depression ((انخفاضand no scaling
- 2nd picture: In the palm (atypical location discoid), u must do close up evaluation in the clinic or use microscopy to determine scarring.
- Don’t say Alopecia

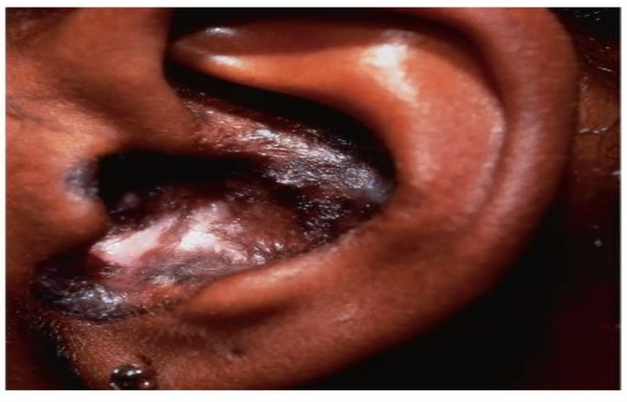


-This is subacute on the upper back Raised,Annular configuration and there are some scales

- Sun exposed
- Subacute cutaneous lupus until proven otherwise

This is not a discoid because there is no follicular plugging and no scarring (it is clear in the center)

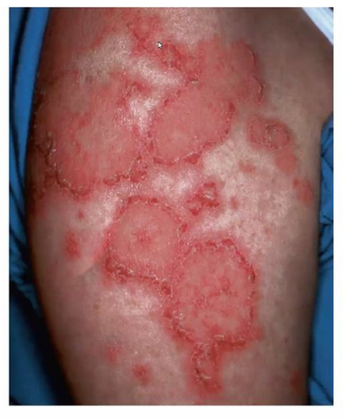


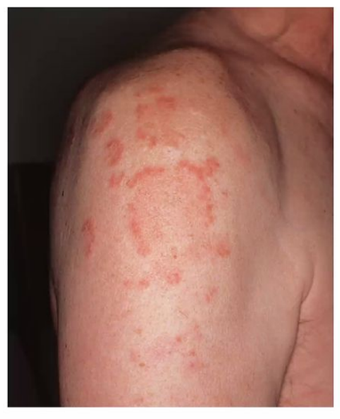


Another Discoid in darkly pigmented skin and It’s all scars
Multiple areas, these two are typical location of discoid

2nd pic: ear and inner penna

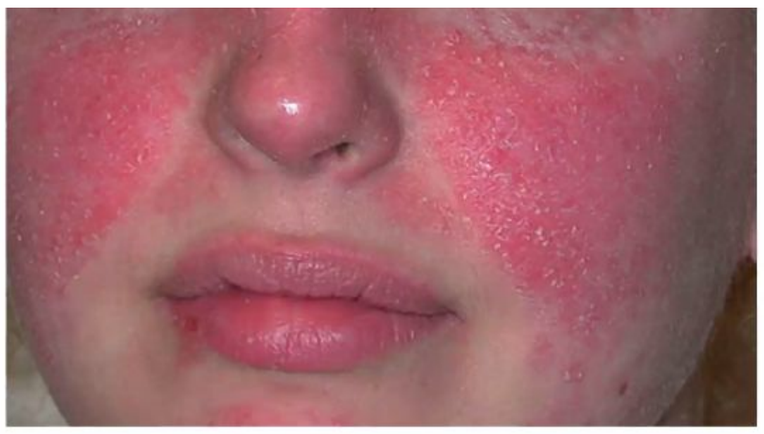
Discoid lupus could be one entity and that’s all or it could be part of Systemic lupus

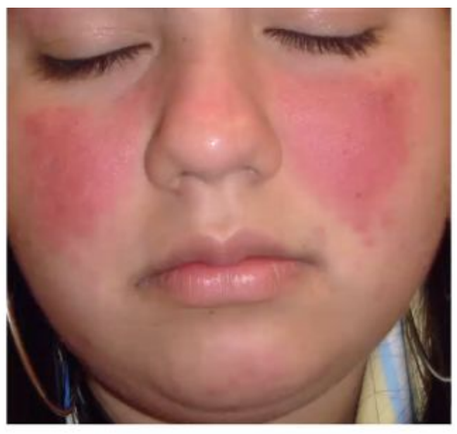




- Multiple more or less ill-defined Erythematous annular plaques with enhanced scales at the border . (you must end ur description with the primary lesion or secondary lesion)
- 2nd : Arcuate:Incomplete

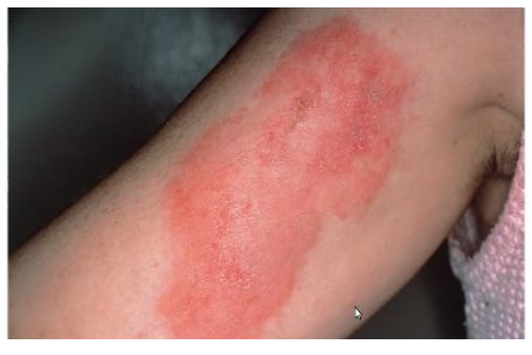
Those are typical subacute cutaneous lupus
Typical of Subacute cutaneous lupus: annular polycyclic and towards having scale and might go piriform.
Important note: annular in the sun exposed areas: upper back chest shoulders وما تكون كثير بالوجه and annular and psoriasiform this is subacute cutaneous lupus (and anti Ro and anti La are positive)

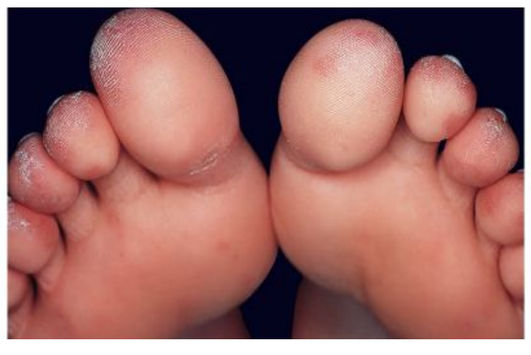




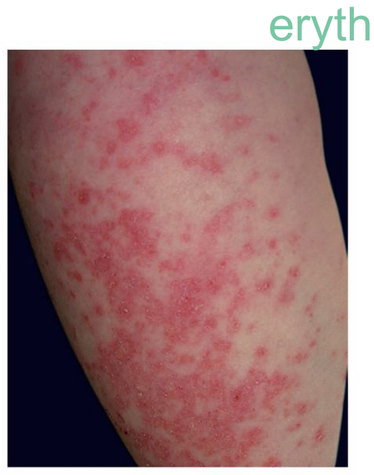
- Well defined erythematous patch affecting the cheeks sparing the nasolabial fold *(~and sometime crossing the bridge of the nose*) = Malar rash
- The left pictures have scaling secondary to cream usage (malar rash usually there isn’t but present in conditions like sebhoric dermatitis)
- **Acute cutaneous lupus**

Important pictures for Exam

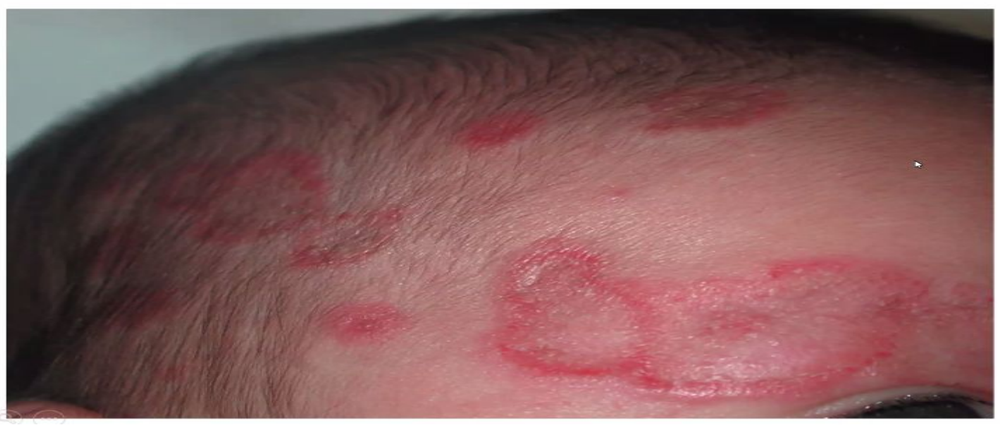




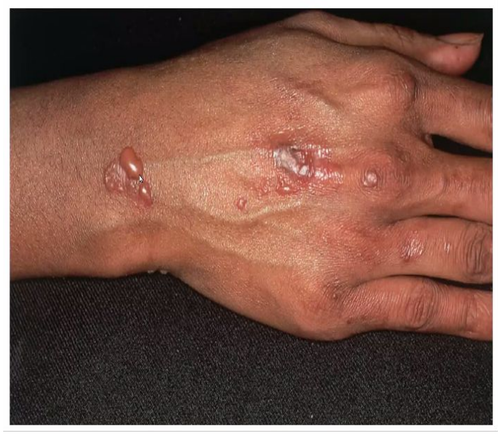
- "Well Defined light to brown erythematous area/patch with central clearing with brown firm to hard consistency atrophy"
- Area of erythematous irregular patch with some scaling as a secondary change and *lightning/clearing center and some brownish discoloration with little bit of scale* (Secondary change of lupus panniculitis= Dermal atrophy)
- Scarred atrophy and depression and inflammation
- On the right pic you could see "*chill prains???* On the tip of the toe which could be seen as mild erythematous areas + usually painful" nonspecific feature of lupus



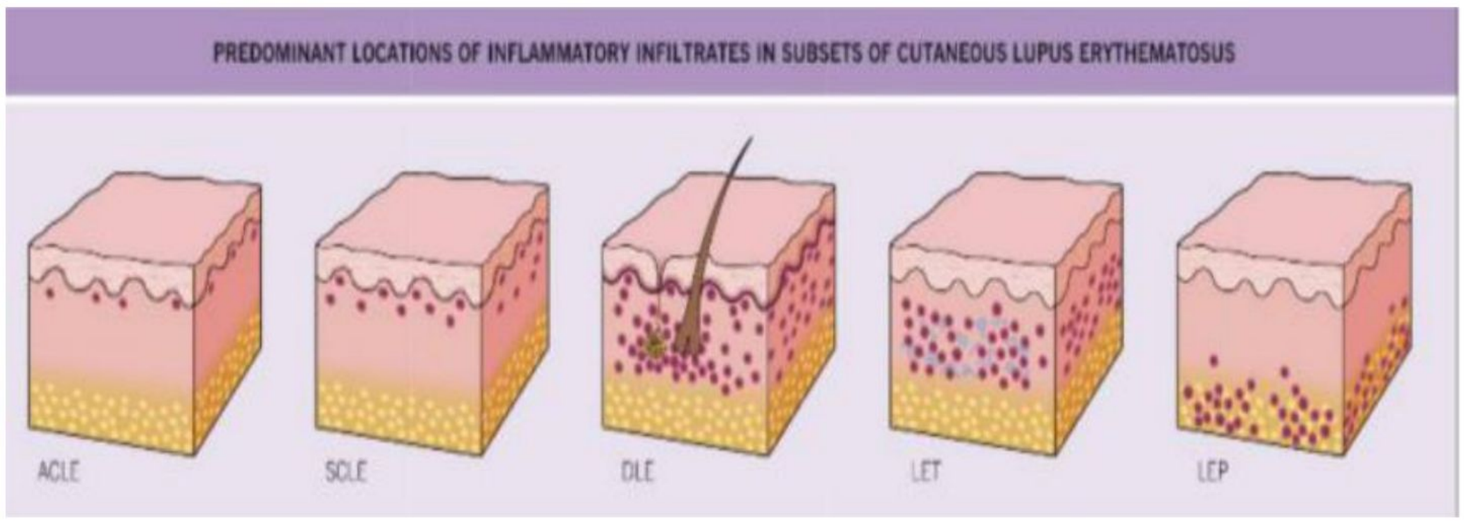
Subacute CLE, psoriasiform

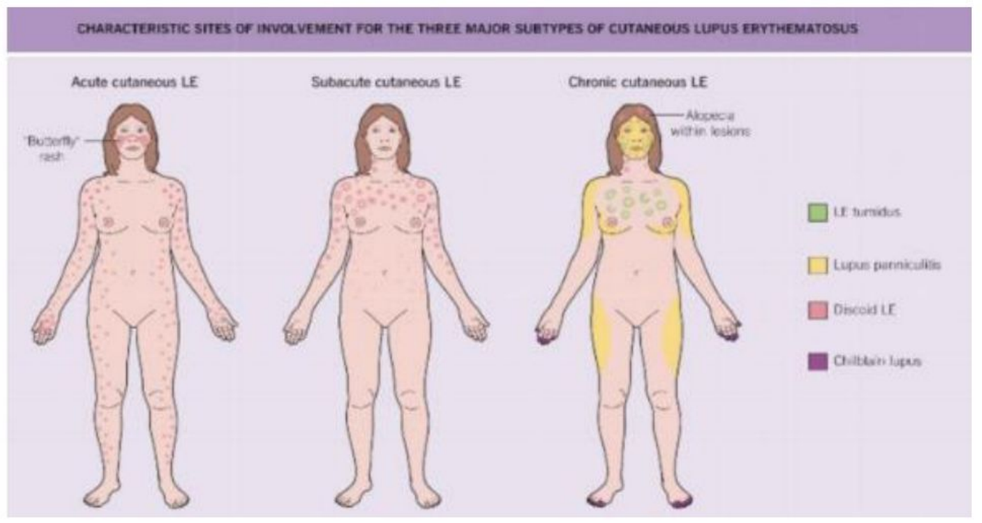


- Annular configuration is clear in this picture
- **Neonate with affection of the head with multiple erythematous annular plaques = Neonatal lupus**
- **The cutaneous manifestation resolves on its own later after few months but the cardiac doesn't.**

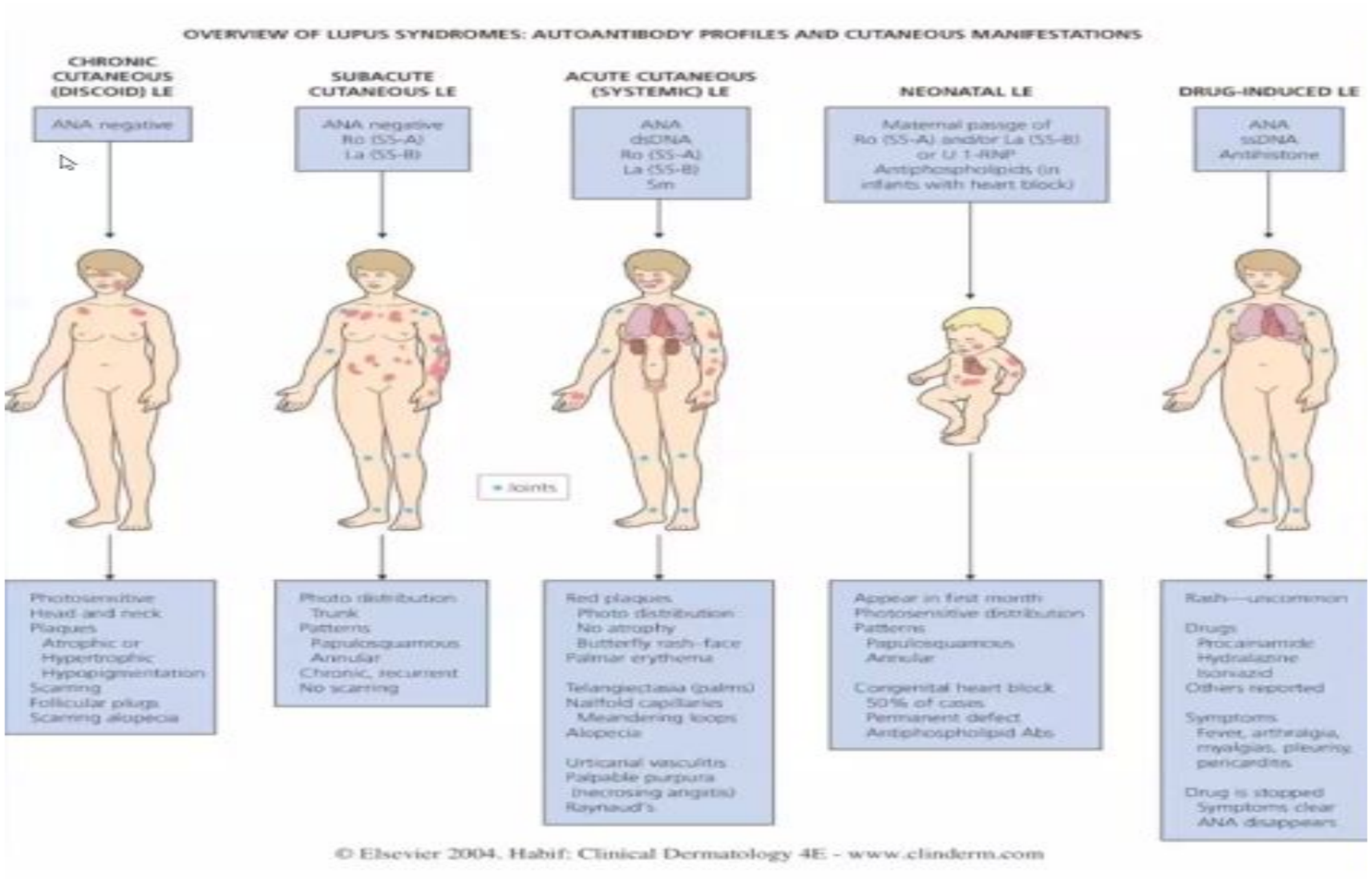


- Blisters (Tense blister ثابتة = meaning its deeper {DEJ or even subepidermal}) with tiny vesicles (discoid lupus)





Predominant locations of inflammatory infiltrates in subsets of cutaneous lupus erythematosus. The types of cutaneous lupus erythematosus are: (ACLE),(SCLE), (DLE),(LET) and (LEP); the latter three are forms of chronic cutaneous lupus erythematosus. The primary locations of the infiltrates are as follows: superficial dermis, ACLE and SCLE; superficial plus deep dermis and periadnexal, DLE; superficial and deep dermis, LET; and subcutaneous fat, LEP. The final diagnosis requires clinicopathologic correlation



Dermatomyositis

•Autoimmune disease of uncertain etiology.

•Involving skin and proximal muscle weakness. Shoulder and pelvis

•Juvenile, adult onset.

•Amyopathic dermatomyositis- in some instances, muscle involvement may not be detectable.

•Making early diagnosis is important because it is a serious but treatable multi system disease

Criteria for diagnosing dermatomyositis:

➢Progressive proximal symmetrical weakness difficulty combing hair, sitting up from ground or chair, dysphagia

➢ Elevated muscle enzyme levels
➢ Abnormal findings on electromyograms
➢ Abnormal findings from muscle biopsy.
➢ Compatible cutaneous disease.

Diagnosis:

Proximal muscle weakness with two of the three laboratory criteria

Are there skin changes that are diagnostic of dermatomyositis?

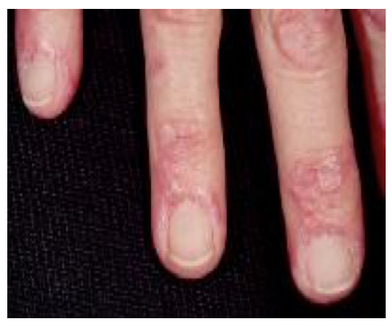
Two cutaneous findings have been describes as "pathognomonic" of dermatomyositis:

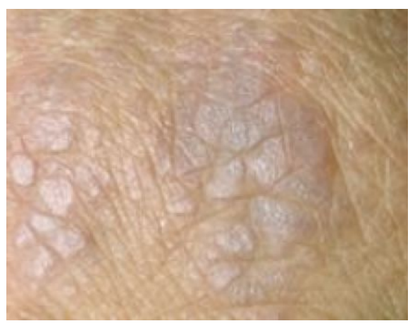
1.Gottron's papules

2.Gottron's sign

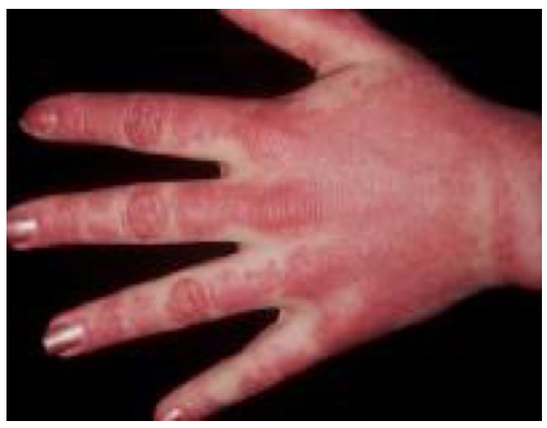
What is the difference between Gottron's papules and Gottron's sign?

•Gottron's papules- are erythematous to purplish flat papules on the extensor surfaces of the interphalangeal joints



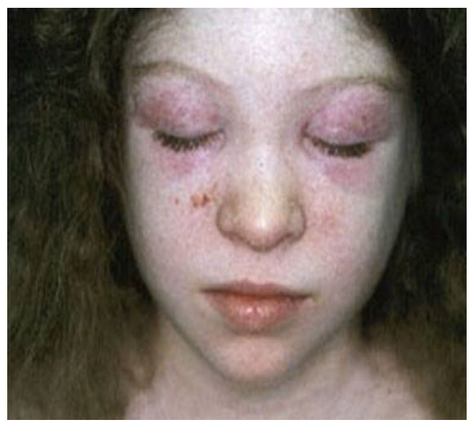


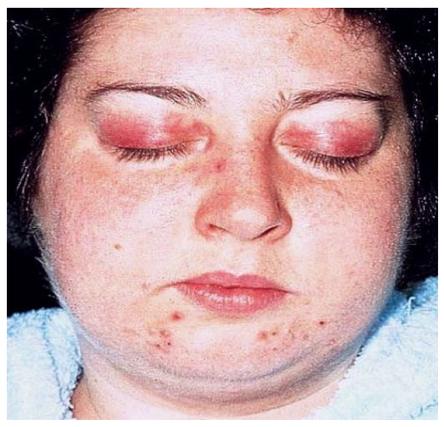
•Gottron's sign- consist of symmetric violaceous erythema, sometimes with edema, over the dorsal knuckles of the hands, elbows, knees, and medial ankles.



- **Are there other skin findings that are characteristic of dermatomyositis?**

•**Heliotrope rash**- symmetrical periorbital edema with a violaceous (lilac) dusky erythema

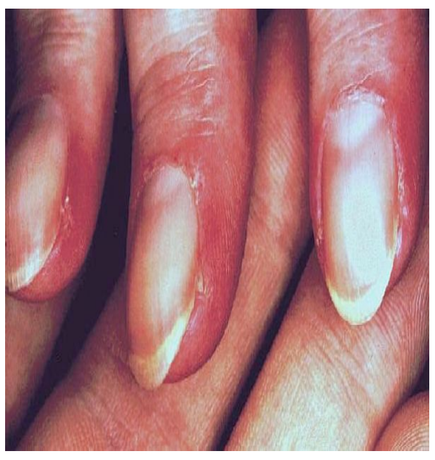




Dermatomyositis

•Periungual telangiectasia with cuticle atrophy

Mechanic hands



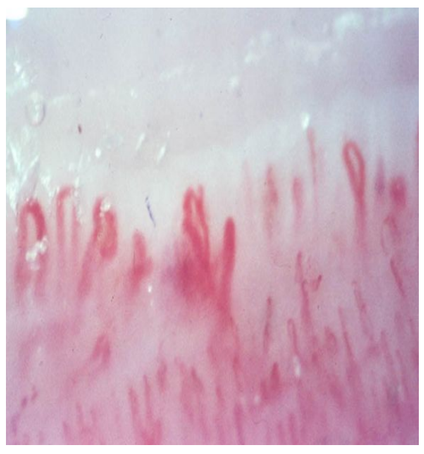
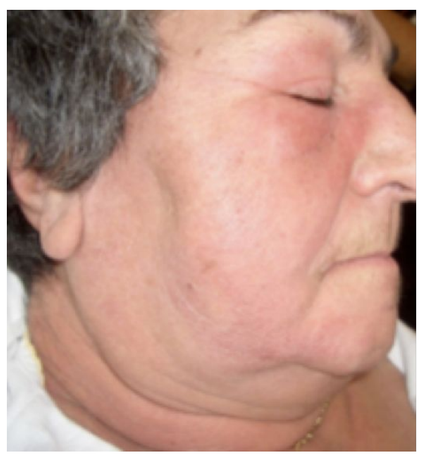
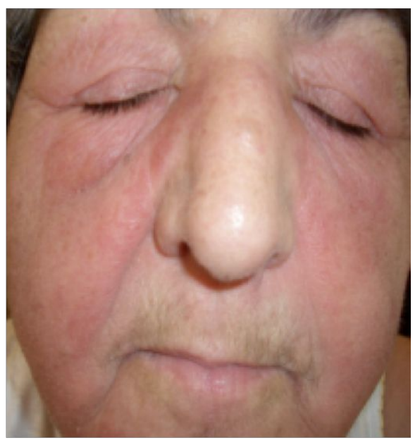
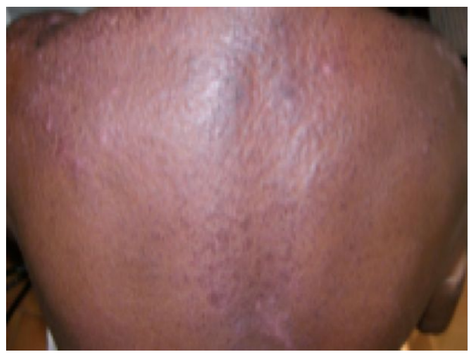


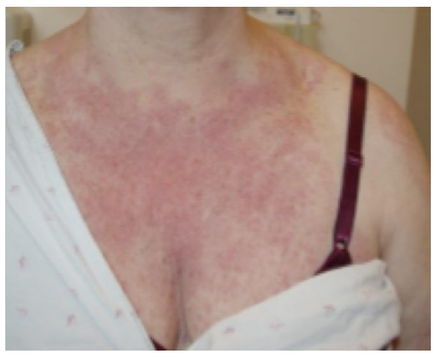
Photo distributed violaceous erythema of the face, sun-exposed areas of the neck, upper chest, shoulders, dorsal arms, forearms, and hands blotches of erythema





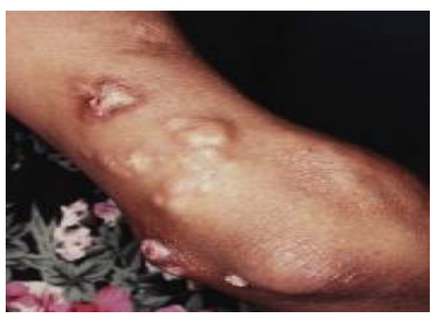
Shawl sign- highly associated with interstitial lung disease





Calcinosis- of the skin or the muscle.

•manifests as firm, yellow or flesh-colored nodules, often over bony prominences. (juvenile DM) in 25%-70% of patients



Are there any diseases associated with dermatomyositis?

•It can be associated with other connective tissue diseases such as lupus, rheumatoid arthritis, scleroderma and Sjogren's syndrome.

•25% of adults with DM have associated malignancy.

•Female patients should be carefully screened for ovarian cancer.

•Juvenile type associated with calcinosis cutis.

•Fulminant lung disease is reported in amyopathic DM and underlying malignancy, therefore both malignancy screening and systemic involvement are recommended irrespective of muscle involvement.

•Oropharyngeal and upper esophageal muscle involvement may lead to dysphagia, nasal regurgitation or aspiration.

•Respiratory failure due to weakness of the diaphragm and chest wall muscles.

•What is a serious complication in DM?

•ILD in 10% of cases

•often occurs with antisynthetase antibodies (t-RNA) antibodies to aminoacyl-transfer ribonucleic acid synthetase enzymes

•30% of DM have antisynthetase syndrome (ILD raynaud’sphenomenon, arthritis, mechanics hands)

Dermatomyositis

How do you diagnose dermatomyositis?

- History & Physical examination
- Serum levels of muscle enzymes
  - Creatine phosphokinase (CPK) level is most reliable indicator of disease activity. Other muscle enzymes: aldolase, AST, ALT, LDH.
- Serology-
  - ANA in < 60%
  - Anti-Jo-1 (anti-histidyl-t-RNA synthase) in 30%
  - Anti-Mi-2 (**highly specific**), but it lacks sensitivity because its present in only 25% of patients, indicates good prognosis.
- Magnetic resonance imaging (MRI), sensitive, not specific.
- U/S of muscle.
- Electromyogram, sensitive. Not specific. Normal in 10% of patients
- Muscle biopsy- **Inflammatory cell infiltrations & necrosis of muscle cells.** Best to choose biopsy side based on MRI findings.
- Skin biopsy- **suggestive but not diagnostic**(unlike DLE), shows interface dermatitis.
- PFTs, Co diffusion
- CXR, high resolution chest CT
- ECG
- **GIT symptoms:** barium swallow
- CMP, CBC, diff, ESR
- Malignancy screen for adults

What are the indicators of poor prognosis?

- Malignancy
- Cardiac involvement
- Older age
- Progressive disease
- Initiation of therapy after 24 months of muscle weakness
- Longer duration of symptoms before diagnosis
- Pulmonary disease
- Dysphagia
- Extensive cutaneous involvement of the trunk

How is dermatomyositis treated?

- Oral steroids are the mainstay treatment.
- Steroid sparing agents- Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab.
- **Topical** steroids and antimalarial medications are used to **improve the cutaneous rashes.**
- Physiotherapy to improve strength and flexibility of the muscles.
- For Calcinosis cutis: diltiazem and or surgical excision, low dose warfarin

3) Scleroderma

• An autoimmune connective tissue disease of unknown etiology
• Chronic disease that involves the microvasculature and connective tissue and results in fibrosis.
• There is an increase in dermal collagen & decrease in the elastic tissues which leads to typical thickening & immobility (absent creases)
•It may be localized, as in morphea, or more generalized and involving visceral organs, as in progressive systemic sclerosis.
•Onset typically between 30 -50 years old.
•Significant mortality rate, overall 10 yr survival of less than 70%. This is why It's very important to diagnose and treat early.

◆ Pathogenesis:

- Individual genetic background
- Exposure to environmental triggers(virus, drugs, vinyl chloride, silica and nanoparticles from traffic-derived pollution).
- Inducing vascular damage and fibroblast
- Activate cells that have ability to give origin to endothelial cells, or collagen producing cells
- These cells will migrate into injured tissues to differentiate into both endothelial cells and fibroblasts, to cause defective vasculogenesis or fibrosis or both, and to have immunomodulatory effects.
- The B cells in SScare activated and produced anti-topoisomerase I and anti-centromere antibodies

Scleroderma

Localized scleroderma

Systemic scleroderma

Morphoea

Linear scleroderma
or panniculitis (agressive treatmentc cz it goes down to the bone) or guttate

Limited systemic sclerosis
Crest

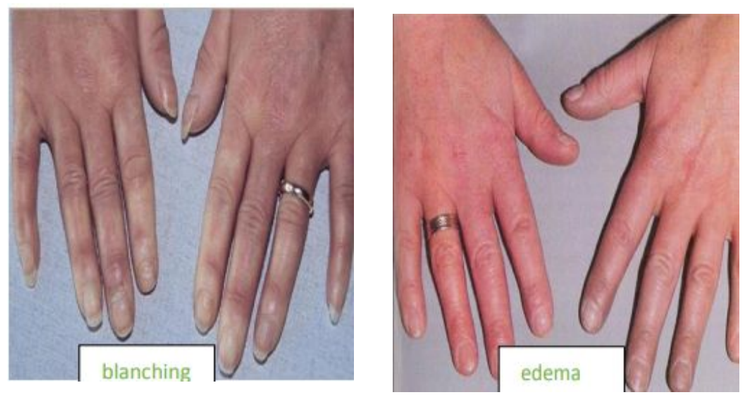
Diffuse systemic sclerosis
peaked nose, limited mouth opening, no crrases

Systemic sclerosis sine scleroderma
no skin involvement but could have dysphagie

limited systemic scleroderma CREST Syndrome	**Progressive Systemic Sclerosis** **What are the cutaneous findings inprogressive/diffuse systemic sclerosis?**
• Induration is limited to the distal extremities and face. • Tend to develop internal involvement late in the course of disease (decades) • It's considered a type of limited systemic scleroderma – C = Calcinosis cutis – R = Raynaud's phenomenon – E = Esophageal dysfunction – S = Sclerodactyly (tightening of fingers) – T = Talangiectasia • Pulmonary hypertension • Most patients with CREST syndrome have circulating antibodies To centromeres called "anti-centromere antibodies"	1.Swelling of the hands and feet and/or Raynaud's phenomenon 2.Telangiectasia 3.Proximal nail fold changes (avascular areas) 4.Thickening and sclerotic changes involving the face& extrimities- progressive ● Sclerodactyly- tapering of fingers, with waxy , shiny hardened skin,which is tightly bound down & doesn't permit folding or wrinkling ● Loss of normal facial lines (mask like) patient looks younger than they are ● Thinning of lips, microstomia, radial perioral furrowing , small sharp nose 5.Digital ulcers +/- loss of digits

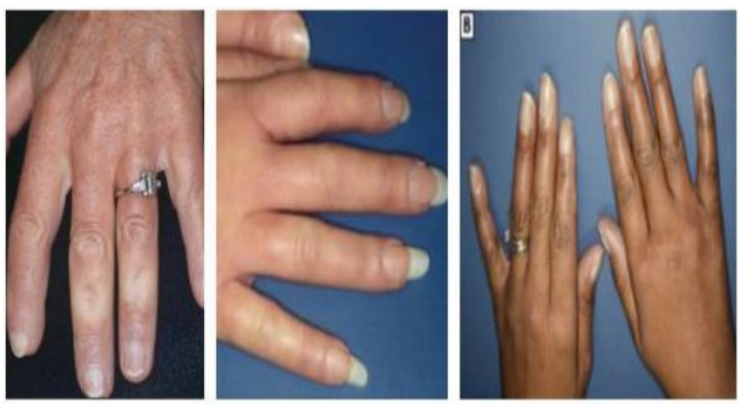
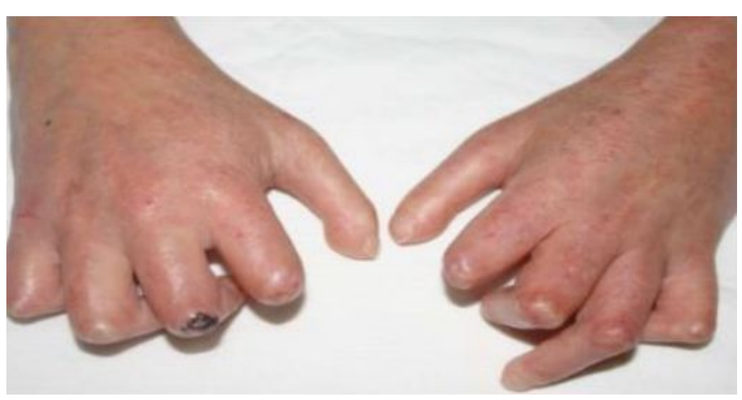
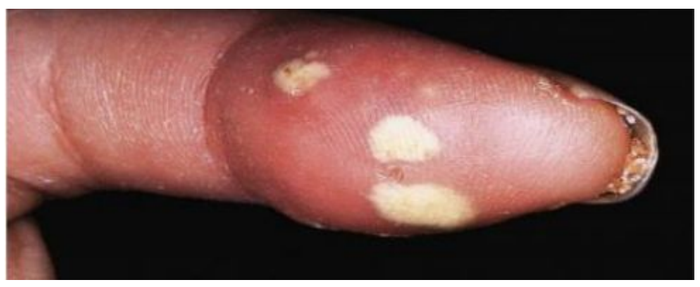
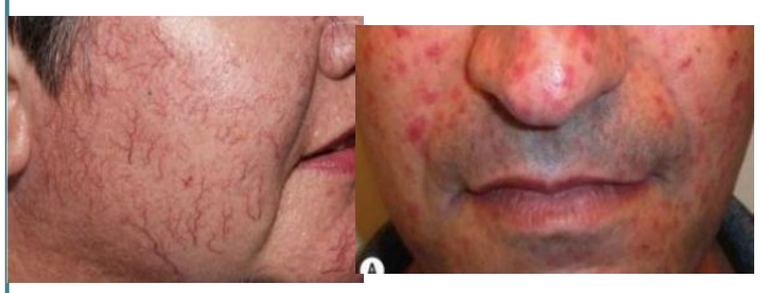
CREST syndrome

Progressive Systemic Sclerosis



◆ Cutaneous features of systemic disease:

- Digits:Early pitting edema (early on),• Sclerodactyly- tapering of fingers, with waxy , shiny hardened skin,which is tightly bound down & doesn't permit folding or wrinkling (later on).
- Face:Beaked nose, microstomia (small mouth) and a youthful appearance.
- Thinning of lips, microstomia, radial perioral furrowing , small sharp nose (can't open mouth by 3 fingers)
- Dyspigmentation:Salt & pepper.
- Telangiectasias:Matted(squared off) on the Face, lips and palms.
- Nailfold capillary abnormalities: in 90% (Capillary drop out alternating with dilated loops).
- Dystrophic Calcinosis Cutis.
- Raynaud's phenomenon.
- Cutaneous ulcer

 Early phase of SSc ●Early, edematous phase of V systemic sclerosis. ●: Note the demonstration of pitting edema on two of the digits. ●Edematous and shiny fingers ● Swelling and sclerosis reduce hand movements, so patients may be unable to make a fist, or to place thepalmar surfaces together - the 'prayer sign'. ●Fingertips may have pitting, ulcers or loss of bulk from finger pads	 Late phase - Contractures, thick skin, ulceration and scars - Late stage of systemic sclerosis with diffuse cutaneous scleroderma. - Note the fixed flexion contractures, sclerodactyly, and the digital ulceration overlying the third proximal interphalangeal joint	 Calcinosis cutis white spots or ulcerations and may bequite painful.
 Pitted scars scars of the digital pulp that form in distal areas	 Salt and pepper pigmentation Areas of hyper and hypopigmentation The "salt and pepper" sign. Leukoderma with retention of perifollicular pigmentation in a patient with systemic sclerosis.	 1st picture: regular telangiectasia (long and tortuous) seen in rosacea 2nd picture: matted telangiectasia seen in scleroderma (flat and rounded)

Raynaud's Phenomenon can be primary or secondary

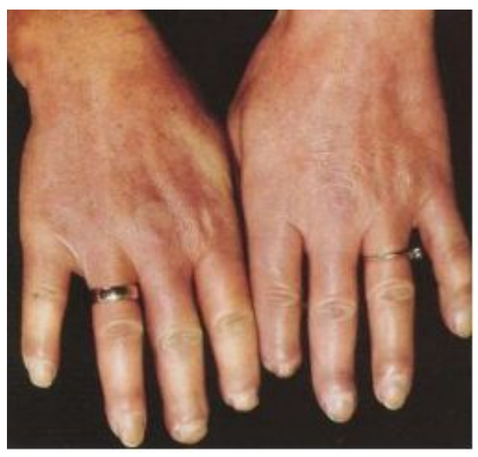
• It is digital ischemia that occurs on exposure to cold and/ or as a result of emotional stress.

Causes: 1- Rheumatic disorders(SS 85%,SLE 35%, DM 30%, RA, PAN)

2- Diseases with abnormal blood proteins (cryoprotein, macroglobulins)

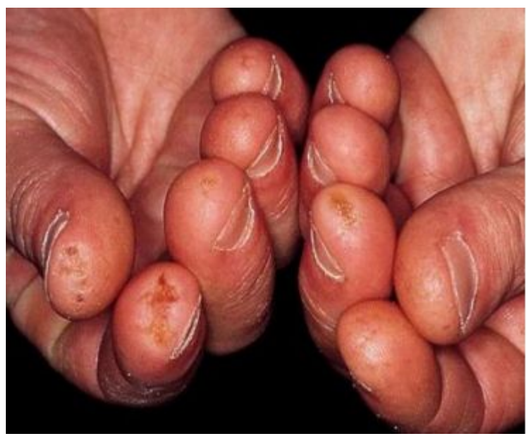
3- Drugs (b-adrenergic blockers, nicotine,cyclosporine)

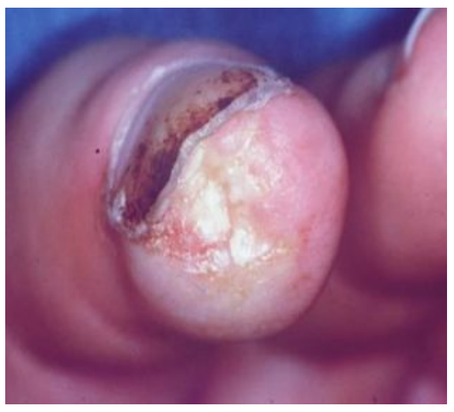
4- Arterial disease (atheriosclerosis obliterans)

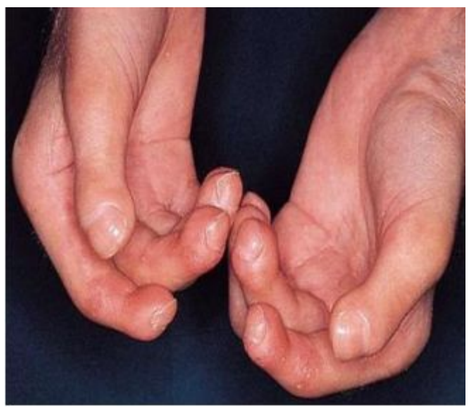


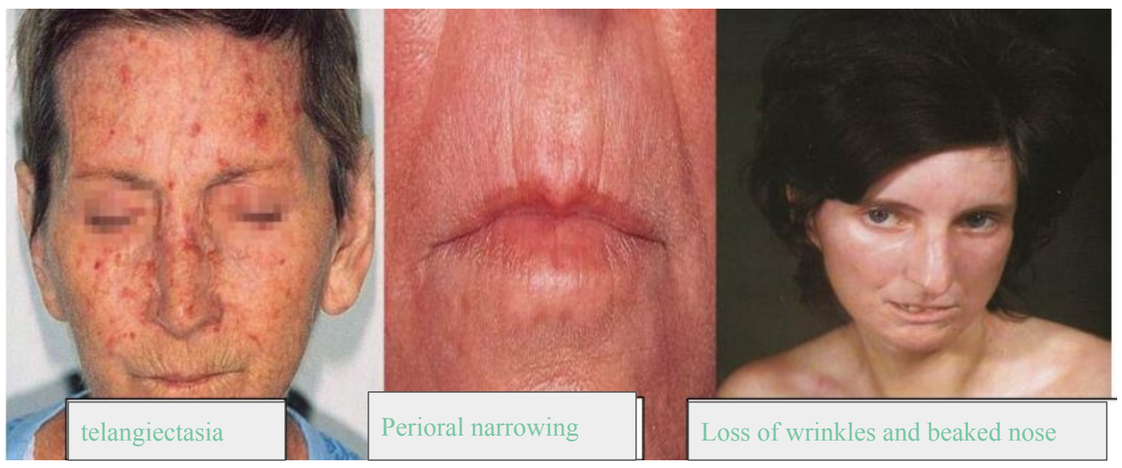
Nonpitting edema of the hands & feet.

Progressive Systemic Sclerosis









telangiectasia

Perioral narrowing

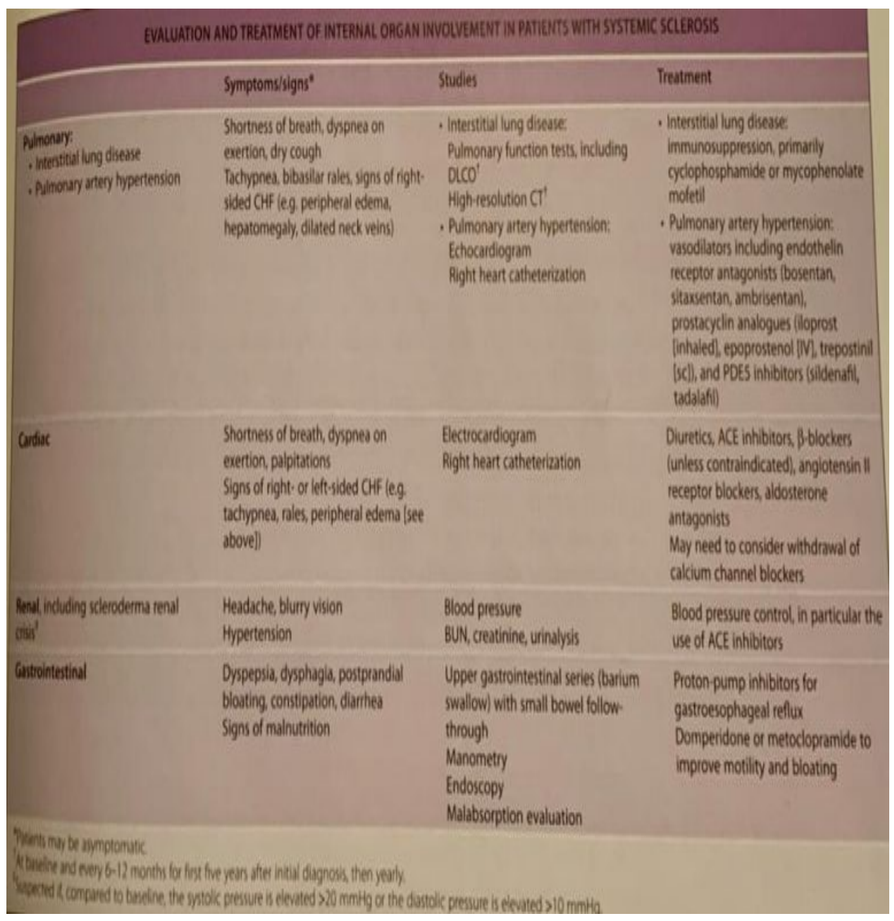
Loss of wrinkles and beaked nose

Digital ischemia and loss of digits

How do you diagnose scleroderma?

1. History & physical examination- characteristic skin changes
   - Either one Major criterion
     - Symmetric cutaneous sclerosis proximal to the MCP or MTP joints.
   - Or Two or more Minor criterion:
     - Sclerodactyly (localized
     - thickening and tightness of the skin of the fingers or toes).
     - Digital pitted scars.
     - Loss of substance from finger pads.
2. Serology
   - ANA (often +ve)
   - Anti-centromere antibodies
     - 71% LSSc "CREST"
     - 21% of DSSc "progressive"
   - Anti-Scl-70 "anti-topoisomerase I"
     - 33% of dSSc
     - 18% of CREST
3. Skin biopsy- skin atrophy with preservation of skin appendages.

This table is not important



EVALUATION AND TREATMENT OF INTERNAL ORGAN INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

	Symptoms/signs*	Studies	Treatment
Pulmonary: • Interstitial lung disease • Pulmonary artery hypertension	Shortness of breath, dyspnea on exertion, dry cough Tachypnea, bibasilar rales, signs of right-sided CHF (e.g. peripheral edema, hepatomegaly, dilated neck veins)	• Interstitial lung disease: Pulmonary function tests, including DLCO† High-resolution CT† • Pulmonary artery hypertension: Echocardiogram Right heart catheterization	• Interstitial lung disease: immunosuppression, primarily cyclophosphamide or mycophenolate mofetil • Pulmonary artery hypertension: vasodilators including endothelin receptor antagonists (bosentan, sitaxsentan, ambrisentan), prostacyclin analogues (iloprost [inhaled], epoprostenol [IV], trepostinil [sc]), and PDE5 inhibitors (sildenafil, tadalafil)
Cardiac	Shortness of breath, dyspnea on exertion, palpitations Signs of right- or left-sided CHF (e.g. tachypnea, rales, peripheral edema [see above])	Electrocardiogram Right heart catheterization	Diuretics, ACE inhibitors, β-blockers (unless contraindicated), angiotensin II receptor blockers, aldosterone antagonists May need to consider withdrawal of calcium channel blockers
Renal, including scleroderma renal crisis‡	Headache, blurry vision Hypertension	Blood pressure BUN, creatinine, urinalysis	Blood pressure control, in particular the use of ACE inhibitors
Gastrointestinal	Dyspepsia, dysphagia, postprandial bloating, constipation, diarrhea Signs of malnutrition	Upper gastrointestinal series (barium swallow) with small bowel follow-through Manometry Endoscopy Malabsorption evaluation	Proton-pump inhibitors for gastroesophageal reflux Domperidone or metoclopramide to improve motility and bloating

*Patients may be asymptomatic.
†At baseline and every 6–12 months for first five years after initial diagnosis, then yearly.
‡Suspected if, compared to baseline, the systolic pressure is elevated >20 mmHg or the diastolic pressure is elevated >10 mmHg.

How do you manage a patient with scleroderma?

- Treatment is symptomatic.
- Raynaud's phenomena:
  - Stop smoking
  - keep hands warm and decrease trauma
  - calcium channel blockers* (nifedipine)
  - aspirin
  - vasodilating drugs (iloprost)
- Calcinosis cutis: nifedipine, surgical or laser excision.
- Skin sclerosis: physiotherapy, phototherapy.
- GI: proton pump inhibitor, surgery for strictures.
- Kidney: ACE inhibitors. IMP
- In severe cases: immunosuppressant , D-Penicillamine might be used (blocks aldehyde groups involved in intermolecular cross-links in collagen)

***An important thing to remember in SLE is antiphospholipid syndrome in which there will be recurrent abortions and tendency for thrombosis(CVA or stroke) , they will also have elevated PTT

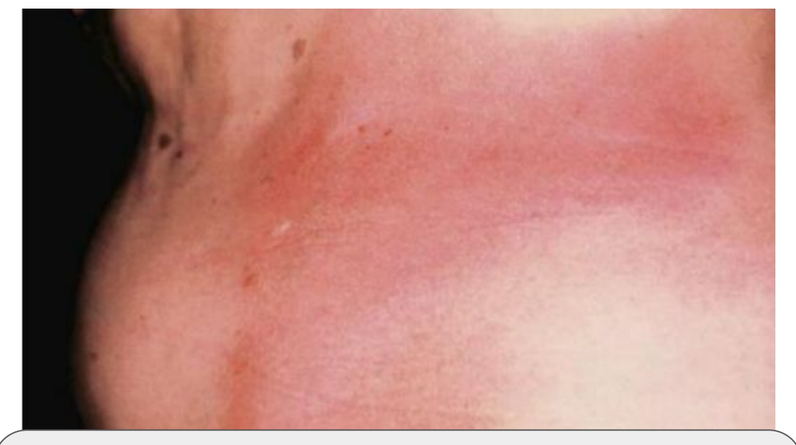
Males slides

4) Morphea

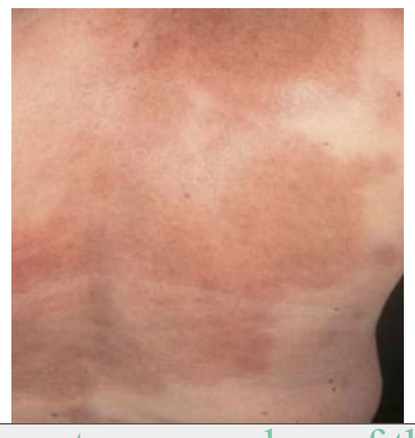
- An inflammatory skin disease that primarily affects the dermis and may extend to subcutaneous structures and lead to scar-like sclerosis.
- Does not lead to involvement of internal organs.
- Some people consider morphea as a subtype of scleroderma (localized scleroderma) and some people consider it as a different entity. The doctor likes to consider it as a different disease.
- Clinicaltypes:
  - plaque type (56%).
  - Linear (20%).
  - Generalized (13%).
  - Deep morphea (11%).

◆ Plaque Morphea:

- Most common type of morphea
- Insidious onset of a slightly elevated, erythematous or violaceous, somewhat edematous plaque that undergoes centrifugal expansion.
- Asymptomatic, can go unnoticed by the patient.
- The central part of the progressing lesion starts to transform into sclerotic, scar-like tissue and the skin becomes more indurated.
- Centrally, it can acquire a shiny white color, and peripherally, a violaceous or ‘’Lilac’’ Ring.
- As the lesion matures, post-inflammatory hyperpigmentation dominates the center over the white sclerosis.
- Most commonly affects the trunk,usually multiple and asymmetric.
- In most patients, morphea progresses over 3-5 years, then arrest and eventually resolves spontaneously. (residual atrophy/pigmentation are commonly observed)



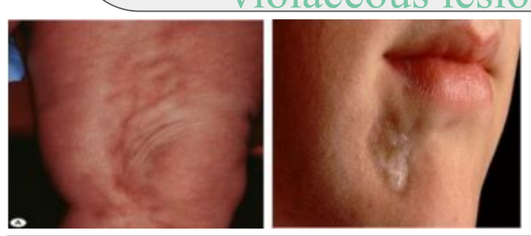
Early-stage lesion presenting as an erythematous edematous plaque not very specific



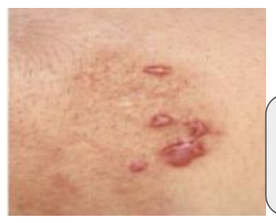
Plaque-type morphea of the back.Multiple, large hyperpigmented plaques, several of which have an inflammatory border. Advanced lesion Red and violaceous lesions

◆ Other variants of morphea: Not important

- Guttate Morphea: multiple, nummular, small plaques.
- Atrophoderma of Pasini and Pierini: hyperpigmented patches on the posterior trunk.
- Deep Morphea: Deep dermis and fat (or deeper). May impair motility of the skin and calcify (osteoma cutis).
- Nodular/Keloid Morphea: keloid-like nodules.
- Bullous Morphea: Very rare



Deep morphea
severe atrophy up to the subcutaneous tissue



Keloidal morphea

4)Morphea

Describe the skin changes that occur with morphea?

Sclerotic, indurated plaques that may be solitary, multiple, linear, or generalized.

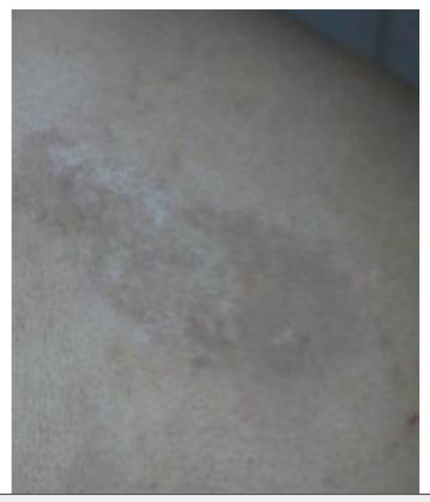
The surface is usually smooth, with the center of the lesion a whitish or ivory color, whereas the border of active lesions is usually violaceous.

It usually involves the skin and subcutaneous tissues but involve deeper structures, even bone.

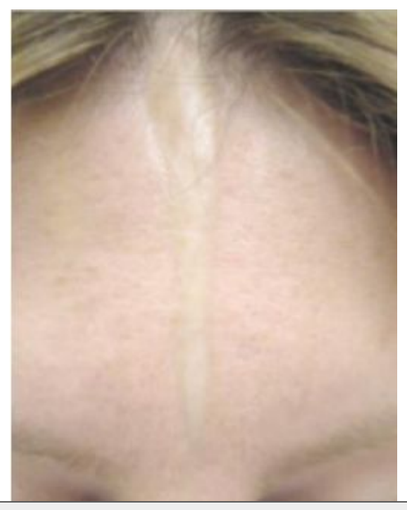
Do patients with morphea develop systemic sclerosis?

How is morphea treated ? depends on type

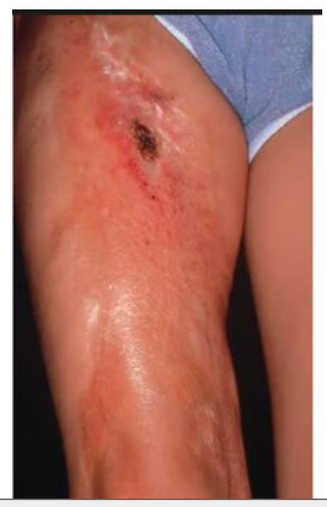
- Morphea has no known cure.
- Treatment of morphea focuses on **controlling signs and symptoms** and slowing spread.
- **Topical and intralesional steroids** , phototherapy, systemic steroids, azathioprine, methotrexate, and cyclosporine might be used in severe cases.
- Physical therapy could be of help if the involvement is close to joints and cause contracture and difficulty in movement.



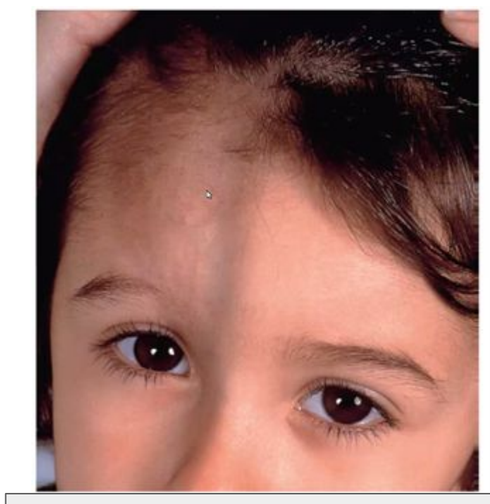
Pigmentation and ivory white When touch skin, we cant pinch it



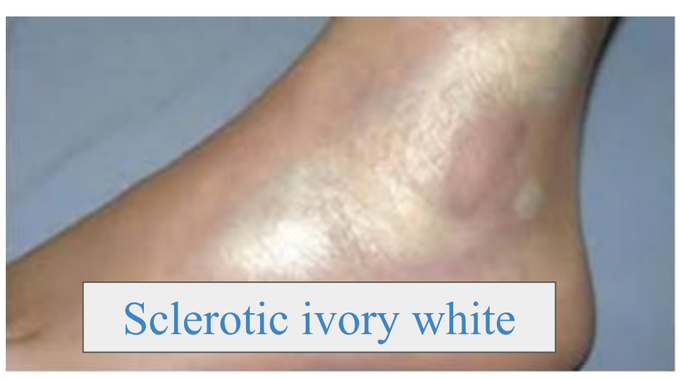
Inco desabri
ضربة السيف
Up to bone and muscle



Localized linear scleroderma
Causes disfigurement
But not systemic
(localized: Linear and morphea)

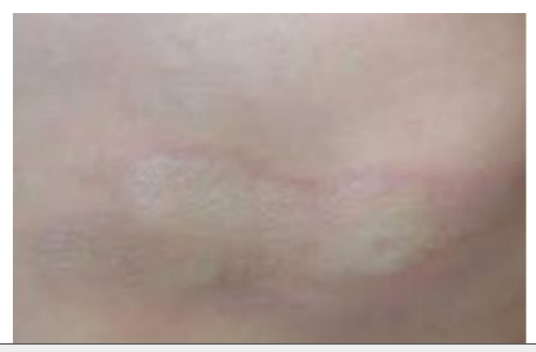


Morphea
sclerosis (localized)

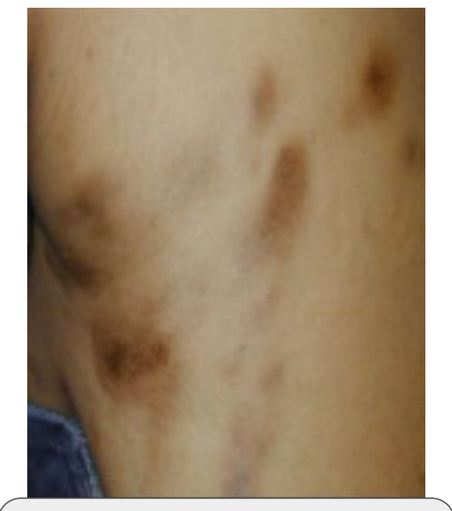


Sclerotic ivory white

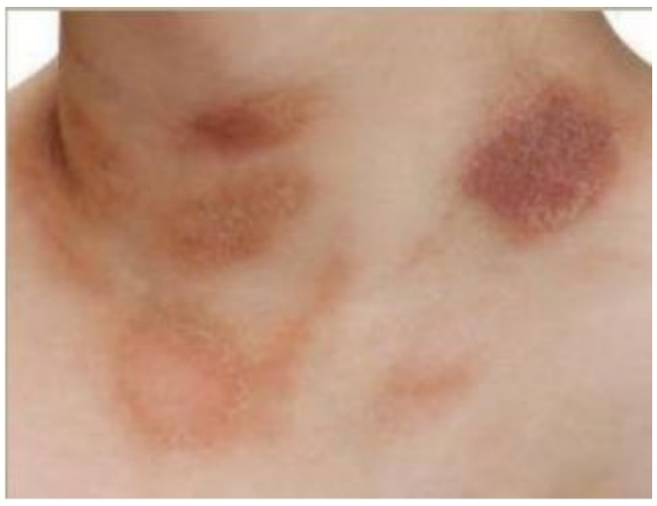
More deep, depressed

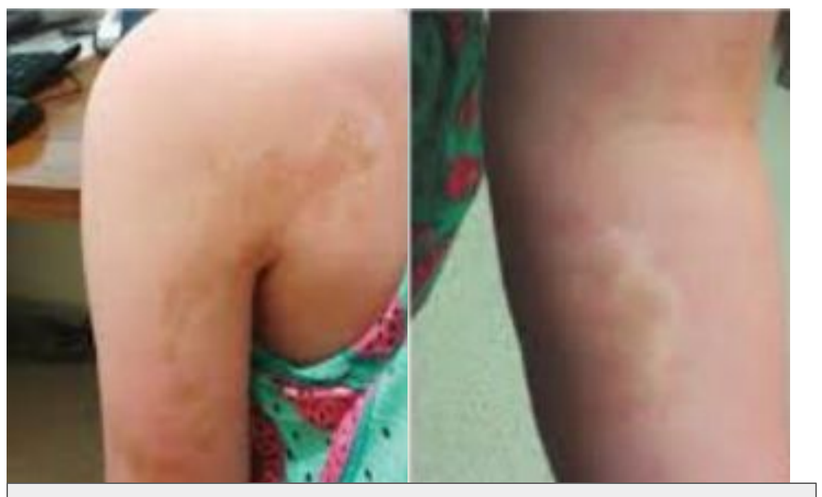


Typical early lesion: violaceous erythema in border and ivory white in center with hardening sclerotic skin



Burned out morphea , pigmentation





Linear morphea

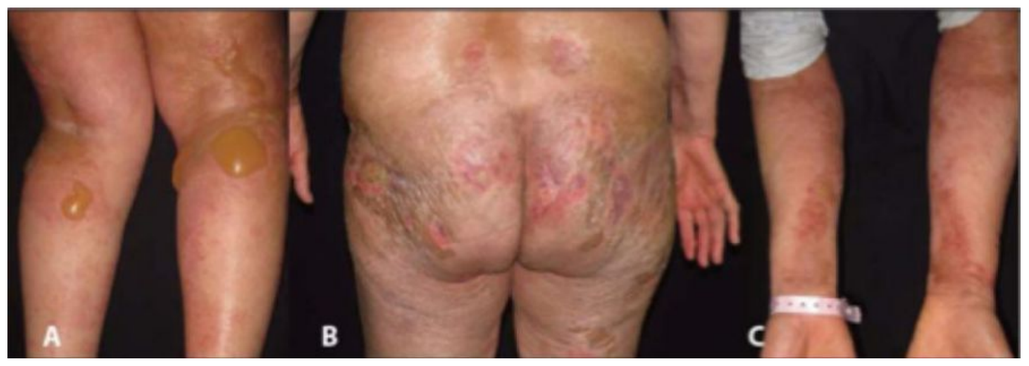
Males slides

◆ Childhood morphea:

- 20% of Morphea patients are children and teenagers.
- 2:1 female to male ratio, mean age of disease onset is 7 years.
- ⅔ of of linear morphea patients are under the age of 18.
- Linear morphea in children can affect the growth of a limb and lead to limb asymmetry as well as decrease range of motion of joints.

◆ Bullous morphea:

- is characterized by tense sub-epidermal bullae in the presence of typical morphea or deep morphea. sometimes comes with severe inflammation causing bullae



Investigations:

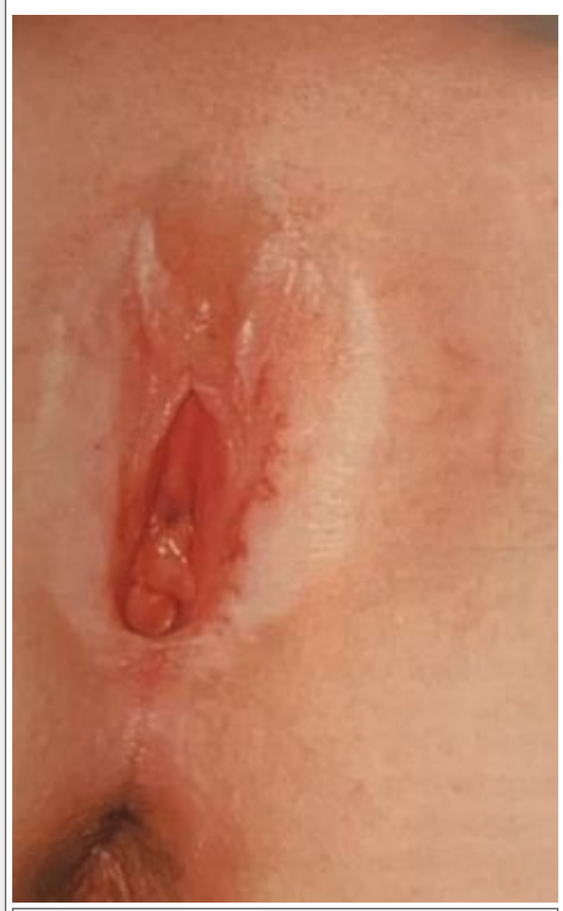
- Lab -work is usually negative in Morphea except generalized & Linear Morphea (ANA +ve in 40-80%)
- Pathology: Helpful (similar to systemic sclerosis). Must be deepsample.

5) Lichen Sclerosus Atrophicus (LSA)

• Sclerotic, ivory white, flat papule and plaques with epidermal atrophy and in extra mucosal sites, follicular plugging . if LSA involves the skin> rule out mucosa

• Most commonly affects female or male genitalia (prepubertal children) , less often extra genital skin may cause scarring of the vaginal introitus or phimosis if not diagnosed and treated early
• Vulval pruritus that's not due to candida or warts
• No systemic manifestations
• Diagnosed by skin biopsy!
• Treatment of choice potent topical steroids (clobetasone dipropionate for longer period to prevent scarring) is not given PRN . If you give 7 year steroids > you will prevent strictures but don't give PRN (intermittent).

Its an autoimmune condition
Could be a subset of morphea (a lot of similarities between them)
Excoriations > take biopsy
If treated early > you will prevent strictures



Sclerosis around (whitish)
Purpuric lesion
Excoriation

Questions

1) You see a patient with chronic scarring alopecia. On examination, you notice fixed, indurated, erythematous papules and plaques on the face and ears. There are also areas of scarring, hyperpigmentation and hypopigmentation. On the scalp, there is scale and keratotic plugging of the hair follicles. What is the most likely diagnosis?
A- Tinea capitis
B- Discoid Lupus Erythematosus.
C- Lichen planus
D- Psoriasis

2) Patient complaining of Raynaud's phenomenon, what is the drug that can cause it?
A- Doxycycline.
B- Beta blockers.
C- Clindamycin.
D- Calcium Channel blockers.

3) Patient came to the ER complaining of SLE like manifestation taking minocycline. What is the first step to manage him?
A- Discontinue the minocycline.
B- Systemic Steroids.

4) Which of the following is a Clinical pathognomic feature of dermatomyositis :
A-Gottron papules
B-vasculitis
C- poikiloderma
D- calcinosis

5) Which one of the following is a very characteristic histopathological feature of scleroderma:
A-increased collagen
B-decreased blood vessel
C-normal eccrine gland size and number
D-normal hair follicle number

6) 19 years old girl presented with arthritis and photosensitive rash on her face, what is the diagnosis:
A- Scleroderma
B- SLE
C- Dermatomyositis
D- Vitiligo

7) Which one of the following is not included in the criteria for diagnosing SLE?
A- Pericarditis
B- Muscle pain
C- Seizure
D- Oral lesion

8) Which one of the following is not considered as part of the diagnostic approach of Dermatomyositis?
A- Magnetic resonance imaging (MRI)
B- Electromyography (EMG)
C- Muscle biopsy
D- Skin biopsy

1	2	3	4	5	6	7	8
B	B	A	A	A	B	B	D