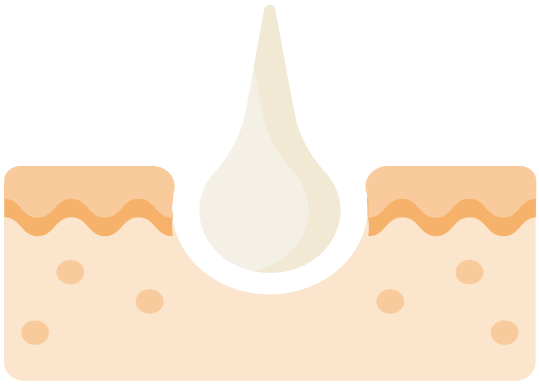

Cutaneous Manifestations Of SLE And Other Connective Tissue Disease

Objectives:

1. Not given
2. The doctor did not give us the slides. So most of the lecture is based on (doctor slide in the previous years) and 437+436 teams.
3. **The slides will be in Black color and anything from the teams will be in Dark gray.**
4. What you need to focus on is the Pictures and the cutaneous manifestations as the difference between doctor's slides this year and the previous years was a lot of pictures about cutaneous manifestations of the connective tissue diseases
5. differentiate between the various types of Lupus
6. recognize how Lupus affects the various systems of the body
7. identify all of the current treatment options available for Lupus
8. recognize the psychosocial effects that Lupus has on the patient and their family.
9. To learn how to diagnose and investigate dermatomyositis.
10. How to manage dermatomyositis.
11. To learn the presentation of morphea and systemic sclerosis and ways to manage them.
12. To recognize other diseases like Rheumatoid nodules and mixed CTD.
13. 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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Lama Alyahya

Done by:
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Lama Alyahya
Taibah Alzaid

Academic leader
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Color index:

- Important
- Doctors Notes
- Female Slides
- Male Slides
- Extra

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Editing file

lupus Erythematosus

Connective tissues diseases: (that will be covered in this lecture)

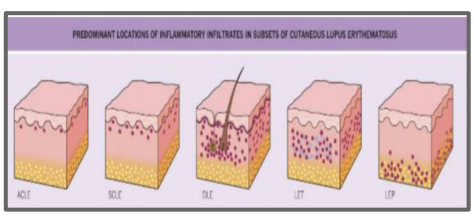
1. Lupus Erythematosus
2. Dermatomyositis
3. Scleroderma (systemic sclerosis)
4. Morphea

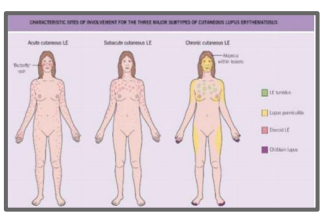
lupus Erythematosus :

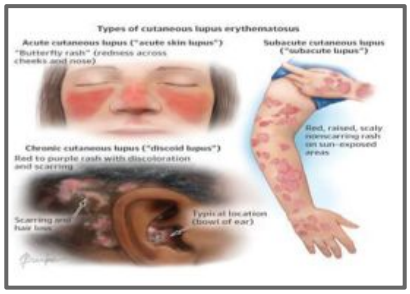
- LE is as an autoimmune diseases associated with antibodies directed against components of cell nuclei.
- A multisystem disorder that predominantly affects the skin.
- Its course and organs involvement are unpredictable (Great mimicker).
- It ranges from life threatening manifestation of SLE to the limited and exclusive skin involvement in chronic cutaneous lupus.
- Our concern here is the systemic involvement that might happen in Cutaneous lupus.
- There are several variants of cutaneous lupus, defined in part by the location and depth of the inflammatory infiltrate
- Lupus may affect any tissue, skin, kidneys, CNS, lungs and others.

Classification:

- **1. Systemic form (SLE):**
  almost always associated with skin manifestations.
- **2. Cutaneous form (CLE)**:
- further divided base on histopathological findings:
- **A. Histopathologically specific CLE:** (the dermo-epidermal junction is the site affected the most).
  - **Acute cutaneous lupus:** (Key Words: Malar rashes, non scarring, photodistributed)
    - → involves primarily the epidermis and upper dermis and is usually associated with systemic disease.
  - **Subacute cutaneous lupus:** (K.W: non scarring, types of lesions: annular, papulosquamous)
    - → 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.
  - **Chronic cutaneous LE (CCLE):** (most common)
  - **i. Discoid lesions of lupus:** (K.W: scarring, follicular bulging, involve face, scalp and ears)
    - → involve the epidermis, upper and lower dermis, and adnexal structures, and they can scar.
    - → the majority of patients do not have significant systemic disease.
  - **ii. Lupus erythematosus tumidus** (rare)**:** (K.W: non scarring (no epidermal changes))
    - → Involves the dermis but there is no prominent epidermal or adnexal involvement.
  - **iii. Lupus panniculitis:**
    - → Involves the subcutaneous tissue and may result in disfiguring depressed scars.
  - **iv. Chilblain LE:**
    - → deep nodules, cold exposure, violaceous & erythematous distal toes.
- **b. Histopathologically nonspecific LE- skin manifestations:**
  - **1- which are not exclusive to LE disease.**
  - **2- Raynaud's, livedo reticularis, palmar erythema, periungual telangiectasia, vasculitis,diffuse non scarring alopecia and ulcers.**
- Note: SLE and CLE can occur simultaneously or separately.







lupus Erythematosus

Cutaneous Findings (Non-specific) Of SLE:

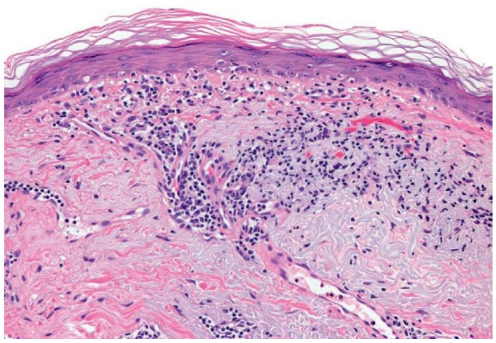
- Diffuse non-scarring alopecia.
- Raynaud's phenomenon.
- Nailfold telangiectasias and erythema.
- Vasculitis (might change the prognosis):
  - Urticarial vasculitis.
  - Small vessel vasculitis (e.g. palpable purpura).
  - Polyarteritis nodosa-like lesions.
  - Ulcerations.
- Cutaneous signs of antiphospholipid syndrome:
  - Livedo reticularis.
  - Ulcerations.
  - Acrocyanosis.
  - Atrophie blanche-like lesions.
- Livedoid vasculopathy.
- Palmar erythema.
- Papular and nodular mucinosis.

Evaluation For Lupus Erythematosus:

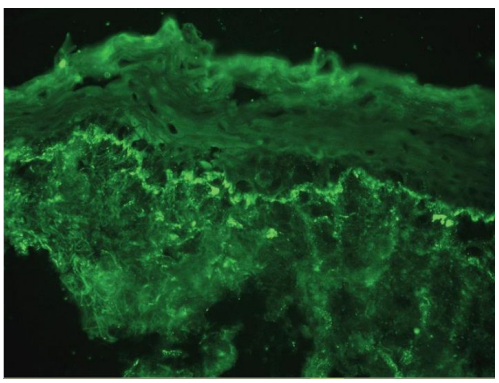
- **HISTORY**
- **PHYSICAL EXAMINATION:**
  - Specific cutaneous lesions.
  - Nonspecific cutaneous lesions.
  - Lymphadenopathy, arthritis.
- LABORATORY TESTS:
  - Skin biopsy (+/- DIF). Almost all cases will need skin biopsy.
  - ANA with profile (anti-dsDNA, -Sm).
  - Urinalysis.
  - CBC with differential, platelet count.
  - Chemistries (BUN, creatinine).
  - Erythrocyte sedimentation rate.
  - Complement levels (C3, C4) The lower the complement level the higher the chance of having nephritis.

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 bandlike lymphocytic infiltrate in the upper dermis, characterizes most subsets of cutaneous LE.



Inflammation in cutaneous lupus mainly in the dermis and dermoepidermal junction (Perivascular).
Perifollicular inflammation more with discoid lupus.



- Acute cutaneous LE will show interface dermatitis and vacuolization of basal keratinocytes (white halo) and sparse superficial lymphoid infiltrates (near the epidermal-dermal junction).
- Chronic discoid LE will show focal dense interface dermatitis with perivascular and periadnexal lymphoid infiltrates throughout the entire dermis (dark areas). A thickened basement membrane is a characteristic finding and can be highlighted by PAS staining.
- Direct immunofluorescence of cutaneous lupus:
  - Will show granular deposits of IgM are present at the dermal–epidermal junction within lesional skin. In Lesional DIF: Granular deposition of IgG/IgM in the DEJ (Dermoepidermal junction) and around hair follicles. However, in Non-lesional DIF (Normal skin) is referred to as ''Lupus band'' test, Positive reaction usually indicates systemic SLE.
  - In Lupus Band Test It's preferred to be done on non lesional non exposed skin.

lupus Erythematosus

CLE Histopathology:

- Focal or continuous epidermal atrophy (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 + Abundant interstitial mucin deposits in the reticular dermis + Moderate to dense superficial and deep perivascular and periadnexal lymphocytic + melanin incontinence (the dermis will be pigmented because the keratinocytes are destroyed).

The American College Of Rheumatology 1982 Revised Criteria For Classification Of Systemic Lupus Erythematosus (not always precise)	
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 Skin rash	• as a result of unusual reaction to sunlight, by patient history or physician observation.
Oral ulcers	• 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 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.
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.
Hematologic disorder	• 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.

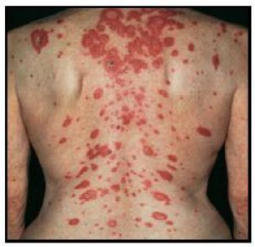
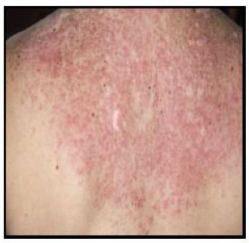
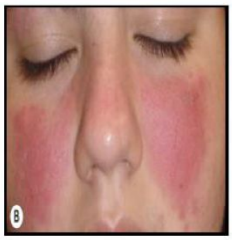
Immunologic disorder	• a) Anti-DNA antibody to native DNA in abnormal titer. **OR**
	• b) Anti-Sm: presence of antibody to Sm nuclear antigen. **OR**
	• c) Positive finding of antiphospholipid antibodies based on:
	  ○ (1) an abnormal serum level of IgG or IgM anticardiolipin antibodies;
	  ○ (2) a positive 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).

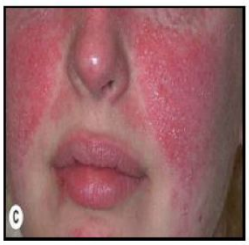
Antinuclear antibody	• An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome.

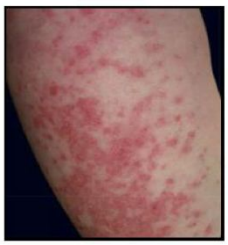
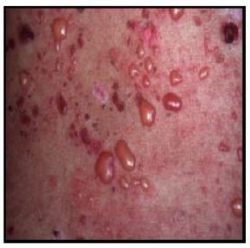
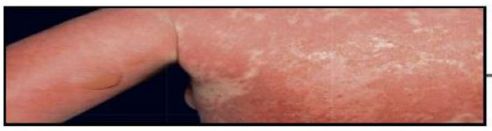
lupus Erythematosus

Acute cutaneous lupus erythematosus (ACLE):

- These patients must be **evaluated carefully for evidence of internal disease.** ACLE usually indicate systemic disease.
- **Bilateral Malar erythema (Butterfly rash). Sparing of the nasolabial folds** helps differentiate lupus from rosacea. (malar is the best presentation for ACLE).
- The lesions tend to be transient, **follow sun exposure** and resolve without scarring.
- The morphology ranges from **mild erythema** (hard to be noticed by the physician) to **intense edema.**
- **Telangiectasias, erosions, dyspigmentation and epidermal atrophy** help distinguish the malar erythema from other facial rashes. Could be **scaly** like **picture c.**
- The duration may range from a few hours to several weeks.
- Sometimes may be more widespread in distribution. Rarely involves areas other than the face.
- **Pic B:** bilateral patch affecting both cheeks with fainting over the nose, with nasolabial fold sparing.
- **Pic next to picture C:** multiple erythematous papules.
- **Pic 6:** clear fluid filled tense bullae, (tense indicates deeper involvement, superficial bullae are more fluctuant and less tense).

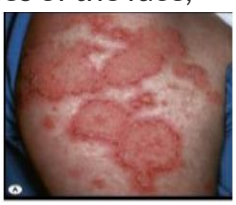


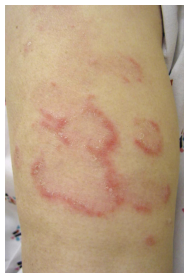
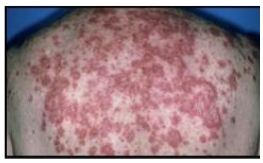
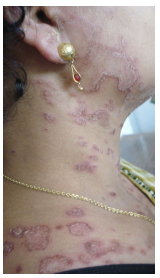
Toxic epidermal necrolysis-like eruption of acute lupus erythematosus.This presentation has also been referred to as a form of acute syndrome of apoptotic pan-epidermolysis (ASAP)

Subacute cutaneous lupus erythematosus (SCLE):

- Non-itchy dry rash appears on the upper back and chest typically **photosensitive**, lesions confined to sun-exposed skin.
- The **midfacial skin is usually spared** (difference between SCLE and ACLE), while the sides of the face, upper trunk and extensor aspects of the upper extremities are commonly involved.
- Subacute LE does not scar does not involve hair follicles.
- Systemic involvement is not usually severe.
- Can be mild, with only a few small scaly patches appearing after sun exposure.
- Lesions may have a:
  - **Annular configuration:** (**first picture:** variably sized multiple annular erythematous patches with enhanced scaly borders (or crust) on sun exposed aspects with coalescence and central clearing).
  - **Papulosquamous**/Psoriasiform type**:** more likely to progress to systemic (**second picture**: Eczematous or psoriasiform appearance on the back (photosensitive area)), best presentation (annular patch with scaly borders).



Scaly and annular (with poly cyclic margin) clear center

- Lesions often result in dyspigmentation (mainly hypopigmentation) but do not scar.
- The long-term prognosis of patients who have SCLE is not completely known.
- 10-15% of SCLE patients will over time develop internal disease, including **nephritis**.
- SCLE is associated with the **anti-Ro (SSA) autoantibody** and anti-la. (Approximately 70%).
- **Drug induced SCLE:**
- SCLE lesions can appear after receiving certain medications including:
  - **Hydrochlorothiazide,terbinafine,** Griseofulvin, Calcium channel blockers, NSAIDs (naproxen), Antihistamines,TNF-α inhibitors, antiepileptic,**Minocycline** and proton-pump inhibitors.
- The lesions may or may not clear once the medication is discontinued

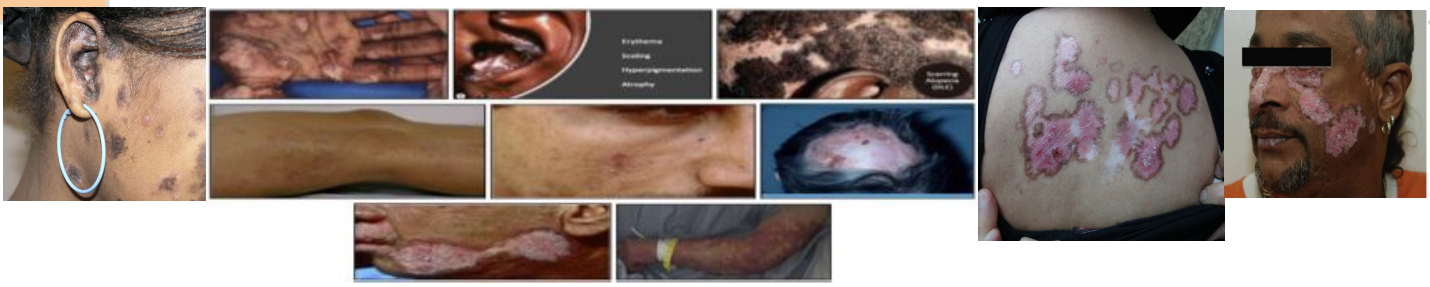
lupus Erythematosus

Chronic CLE:

Discoid lupus erythematosus (DLE)

Annular (coin like lesions)

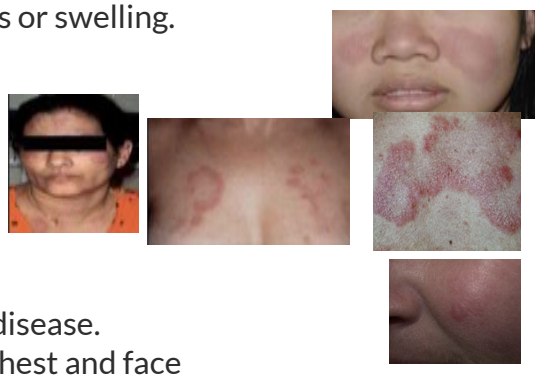
- It is the commonest form of cutaneous lupus usually presents as red scaly patches or plaques that leave dyspigmentation and scarring mostly hypopigmented or depigmented scars.
- It may be localized or widespread.
- Usually affects the cheeks, nose and ears, but sometimes involves the upper back, V of neck, and backs of hands sun exposed areas.
- Unusual to present below the neck without lesions present above the neck.
- Involvement of hair follicles will lead to scarring alopecia
- 10% of DLE patients develop SLE.
- Have a **chronic course**, less chance of remission. More difficult to control
- No clear association between sun exposure and developing DLE lesions..
- Active lesions tend to feel induration on palpation.
- Follicular plugging and scarring alopecia Irreversible hair loss.
- Dyspigmentation (Hypo in the central area and hyper at the periphery).
- Only 5-15% of DLE patients eventually develop clear-cut SLE.
- The risk is higher in patients with widespread discoid lesions.
- Remember: Discoid lesions represent 1 of the 11 ARA criteria for SLE.
- Hypertrophic DLE is an unusual variant (Thick, scaly) mostly on the arms.



DLE Lesions which favor the head and neck region, may show erythema, scaling, atrophy and dyspigmentation in addition to scarring (and alopecia). Less common sites include the palms. 1st pic on the right: Discoid lupus lesions with dyspigmentation and scarring alopecia (well defined multiple coalescent depigmented linear patch). Hypopigmentation often develops centrally with hyperpigmentation at the periphery usually more aggressive in dark skin patients .

Lupus erythematosus tumidus (LET):

- Dermal form of lupus it's deep so it doesn't involve any epidermal changes (scales).
- The rash is characteristically photosensitive, so it affects sun-exposed sites.
- Red, swollen, urticaria-like bumps and patches or swelling.
- Induration and erythema without scaling and follicular plugging.
- Erythematous, edematous, urticarial-like plaques or nodules usually over face
- The epidermis is uninvolved but has intense dermal inflammatory infiltrate.
- Appears on the face and trunk.
- Negative serology, does not lead to systemic disease.
- multiple Annular pink–violet plaques on the chest and face
- forming arcuate configurated plaques with no scaly borders .None of the lesions have epidermal change.

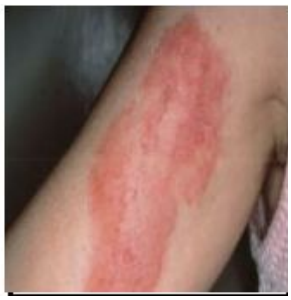


lupus Erythematosus

Chronic CLE (cont'):

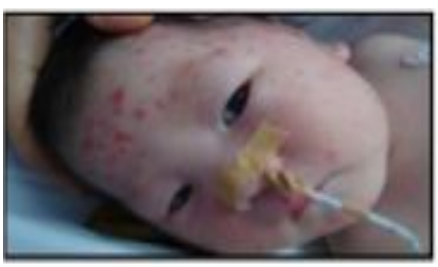
Lupus panniculitis (LEP)

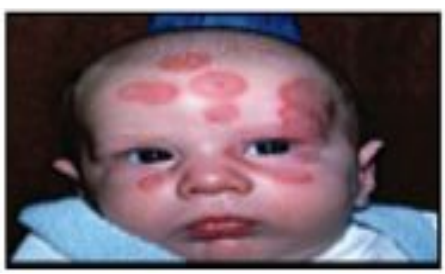
- Involvement of deeper areas of the skin all the way down to the fat (In panniculitis the **subcutaneous tissue** is most affected) hardening of skin in areas with fat tissue (thighs & hips) leading to post inflammation atrophy
- Indurated plaques that can evolve into disfiguring, depressed areas.
- Occur on the face, upper arms, upper trunk, breasts, buttocks and thighs.
- Some patients have discoid lesions overlying the panniculitis (Lupus Profundus).
- Pic : Erythematous plaque on the upper arm. The lesions may resolve with lipoatrophy

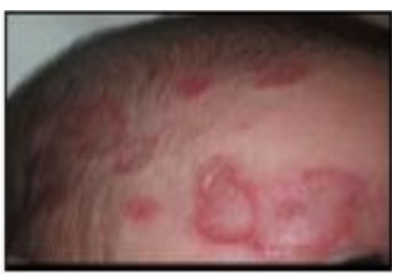


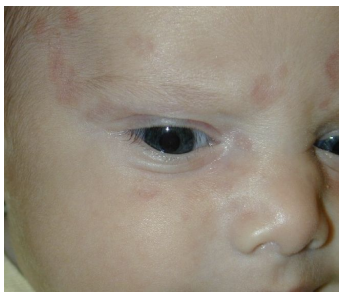
Neonatal lupus:

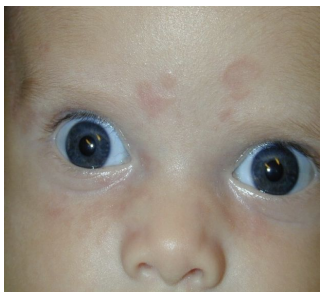
- Newborn babies born to mothers with subacute LE may develop annular rash associated with heart block so need to screen for it, that resolve spontaneously.
- May occur in infants whose mothers have **anti-Ro autoantibodies** anti-La/SSB antibodies and more rarely Ribonucleoprotein (RNP) antibodies.
- **In babies who have NLE, the SCLE-like lesions are histologically identical to those of SCLE in adults.**
- **Almost 100% of babies with NLE have anti-Ro (SSA) antibodies.**
- Unlike SCLE in adults, lesions have a predilection for the face **(Periorbital region) "raccoon or owl eye".**
- Photosensitivity is very common in NLE, but sun exposure is not required for lesions to form. (lesions can be present at birth).
- Lesions typically resolve without scarring, although dyspigmentation and residual telangiectasias may develop.
- The major extracutaneous findings are: **Congenital heart block, hepatobiliary disease and thrombocytopenia.**
- Heart block is almost always present at birth. Cardiomyopathy can occur in a small percentage of patients (neonatal period).
- Cardiac NLE has a mortality of 20% and two-thirds will require pacemakers.
- Hepatobiliary disease and thrombocytopenia, may present at birth or within the first few months of life.
- Hepatobiliary disease ranges from mild elevation of liver enzymes to liver failure.
- All NLE children should be evaluated for internal manifestations with a physical exam in addition to an ECG (cardiac changes), CBC (thrombocytopenia) and LFT (liver involvement).
- Lesions look similar to SCLE (annular). > annular erythematous plaques.
- **Third pic** : multiple annular plaques with enhanced erythematous borders.









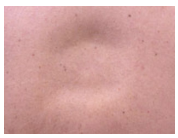


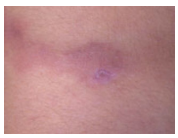
lupus Erythematosus

Chronic CLE (cont'):

Lupus Profundus

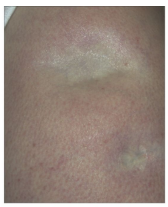
- lupus affecting the fat underlying skin lupus panniculitis.
- it may develop at any age, including children. The face is the most common area to be affected.
- Inflammation of the fat results in firm deep nodules for some months.
- The end result is deep scars on fat layer or lipodystrophy.



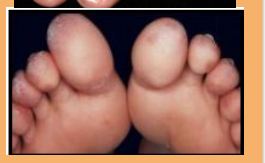


Dimpling post inflammation

Cryotherapy is the same mechanism

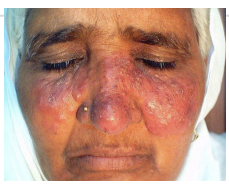


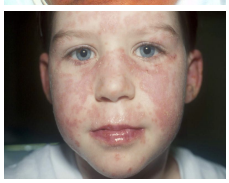
Chilblain lupus



- Itchy and/or tender red or purple bumps that usually come on from cold exposure but can sometimes be precipitated by sun exposure or smoking.
- Redor dusky purple papules and plaques on the toes,fingers, and sometimes the nose, elbows, knees and lower legs
- .They are considered to be a form of skin vasculitis (blood vessel inflammation).
- Usually they have no circulating antibodies.
- The lesions are brought on or exacerbated by cold.
- Appears after exposure to cold weather.
- The lesions may represent the concurrence of ordinary chilblains
- with LE,although, with time, the lesions may develop a discoid lesion.
- Pic : Violaceous plaques, some with scale, on toes. If there is a family history of this disorder, the possibility of mutations in TREX1, which encodes a DNA exonuclease, can be considered.
- The main treatment is to avoid precipitating factors
- Purplish discoloration of acral areas (toes & fingers) worsen by cold but is there all the time, While a frost bite remits after cold is removed, Raynaud's is the range of colors (hypoxia then hypermedia) and pain.
- Now we have COVID chilblain (leads to same manifestations)
- MCQ: mention aggravating factors for this condition? Smoking, sun exposure.

Systemic Lupus Erythematosus:





- Only a few patients with cutaneous LE also have SLE.
- The most common presentation is with a malar eruption or butterfly.
- Other skin changes in SLE are photosensitivity, mouth ulcers, and diffuse hair loss.
- SLE may also affect joints, kidneys, lungs, heart, liver, brain, blood vessels and blood cells

Investigations

- SLE is always with positive ANA.
- antiRo/La antibodies, is nearly always present in patients with subacute LE.
- Leucopenia tends to be more pronounced in patients with systemic LE

Malar rash is the first and most common cutaneous signs

Table 2. Clinical Features of SLE

System	Presentation
Constitutional	Fatigue, fever (in absence of infection), weight loss
Musculoskeletal	Arthritis, arthralgia, myositis
Skin	Butterfly rash, photosensitivity, mucous membrane lesion, alopecia, purpura, urticaria, vasculitis
Vascular	Raynaud's disease
Renal	Hematuria, proteinuria, renal casts, nephrotic syndrome
Gastrointestinal	Nausea, vomiting, abdominal pain
Pulmonary	Pleurisy, pulmonary hypertension
Cardiac	Pericarditis, endocarditis, myocarditis
Reticuloendothelial	Lymphadenopathy, splenomegaly, hepatomegaly
Hematologic	Anemia, thrombocytopenia, leukopenia
Neuropsychiatric	Psychosis, seizures, organic brain syndrome, transverse myelitis, cranial neuropathies, peripheral neuropathies

SLE: systemic lupus erythematosus.
Source: Reference 13.

Lupus:

- Skin biopsy may be diagnostic especially in discoid lupus erythematosus.
- Direct immunofluorescence tests may show positive antibody deposition along the basement membrane (lupus band test).

lupus Erythematosus

Drug induced lupus:

- Sex ratios are nearly equal.
- Nephritis and central nervous system features are not commonly present.
- Anti-DsDNA –ve, Anti-Histone AB +ve.
- When the drug is discontinued, the patient has resolution of clinical & laboratory abnormalities.
- Procainamide, Hydralazine, phenytoin, Carbamazepine , Lithium , Sulphonamides , Minocycline, Penicillamine, Isoniazid, Quinidine, Anti-TNF, IFN, etc.

Autoantibodies:

- Specific but not Sensitive:
  - Anti-dsDNA (lupus nephritis).
  - Anti-Sm,
- Sensitive but not specific:
  - ANA (>95%),
  - ssDNA (70%).
- Drug-induced lupus:
  - Anti-Histone Ab.

CLE Management:

- The aim of treatment for cutaneous LE is to alleviate symptoms and to prevent scarring.
- Smoking cessation will help Raynaud's phenomena and chilblain lupus . Smoking aggravates the symptoms and decreases response to treatment.
- Sun protection: Education against sun exposure + the use of sunscreen .very important!
- Topical therapy:
  - Topical steroids.
  - Topical Calcineurin inhibitors e.g. Tacrolimus.
  - Topical Retinoids.
- Oral steroids.
- Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab.
- Intralesional steroids AKA (ILK injections) more aggressive.
- **Systemic Antimalarials Therapy** (Can effect the disease course (weak disease modifying agents)):
  - Hydroxychloroquine (200 mg po qd–bid in adults; up to 6.5 mg/kg ideal 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 and quinacrine (increase the efficacy of Tx).
  - Don't give Hydroxychloroquine and Chloroquine together as it leads to ocular toxicity.
  - 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).
- Systemic Therapy For Antimalarial-Resistant Cutaneous Disease:
  - Retinoids (e.g. acitretin, isotretinoin).
  - **Thalidomide (teratogenic)** (50–100 mg po qd for clearing and, if necessary, 25–50 mg po qd–twice weekly for maintenance).
  - **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).

Dermatomyositis

Introduction:

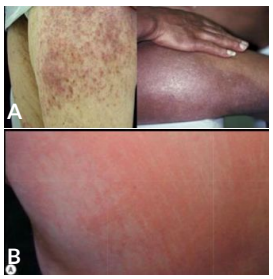
- Dermatomyositis is classified as one of the idiopathic inflammatory myopathies
- . An uncommon inflammatory disease affects adults between 40-60 (females mainly) and children 5-15.
- Skin changes. A violet-colored or dusky red rash on face and eyelids and on areas around nails, knuckles, elbows, knees, chest and back. The rash, which can be patchy with bluish-purple discolorations, is often the first sign of dermatomyositis.
- Is a disease of presumed autoimmune pathogenesis (relatively rare) that presents with a symmetric, proximal extensor inflammatory myopathy and a characteristic cutaneous eruption.
- Malignancy in DM is about 10% to over 50% in adults (Most common are: Ovarian, and colon cancer but can include: breast, lung, gastric, pancreatic, lymphomas , and ¼ of adults with DM have an associated occult malignancy (unknown origin).
- The risk of malignancy may return to normal after 2-**5 years.** So, **Our concern here In DM is malignancy.**
- Skin manifestations often precede the onset of symptoms related to malignancy.
- Some pts doesn't have evidence of muscle inflammation **(Amyopathic dermatomyositis)** and Some doesn't have muscle symptoms but if you test them there is inflammation **(Hypomyopathic dermatomyositis)**.

Classification System For Dermatomyositis:

- Adult-onset:
  - Classic DM
  - Classic DM with malignancy.
  - Classic DM as part of an overlapping connective tissue disorder.
  - Clinically amyopathic DM.
  - Amyopathic DM.
  - Hypomyopathic DM
- Juvenile-onset:
  - Classic DM.
  - Clinically amyopathic DM.
  - Amyopathic DM.
  - Hypomyopathic DM.

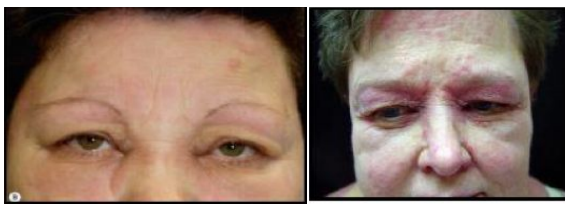
Cutaneous Manifestations Of Dermatomyositis (Uncommon)

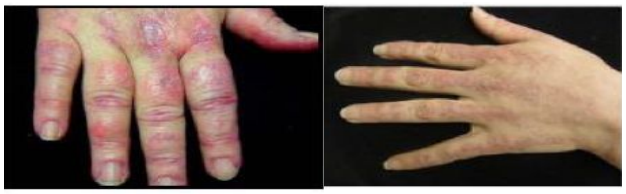
- Cutaneous erosions or ulcerations.
- Holster sign (poikiloderma of the lateral thighs) **(A)**.
- Flagellate erythema **(B)**.
- Vesiculobullous lesions.
- Exfoliative erythroderma.
- Panniculitis.
- Gingival telangiectasias.
- Pustular eruption of the elbows and knees.
- Lipoatrophy (especially in juvenile dermatomyositis).
- Small vessel vasculitis (especially in juvenile dermatomyositis).

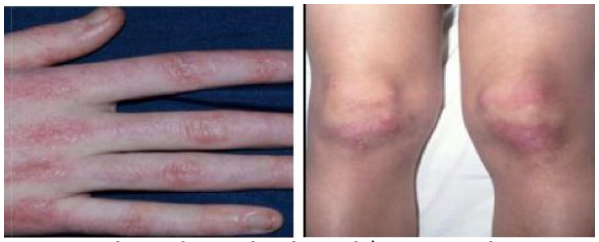


Cutaneous Manifestations Of Dermatomyositis (common) "the first 3 signs are **pathognomonic**"

Heliotrope rash	• Violaceous to dusky erythematous rash with or without edema in a symmetrical distribution involving upper palpebra skin. • Classical picture of the characteristic dermatomyositis rash.
Gottron's papules	• Slightly elevated, erythematous to violaceous papules and plaques that occur symmetrically over the extensor (dorsal) aspects of finger joints (the metacarpophalangeal (MCP) and interphalangeal (IP) joints) sometimes they are shiny.
Gottron's sign	• Symmetric, non-scaling, violaceous to erythematous macules or patches, often atrophic, in the same distribution as Gottron's papules. • Some people define them as gottron's papules, but patches not bump, and some define them as gottron's papules in areas other than the hand (no papules are present in gottron's sign).





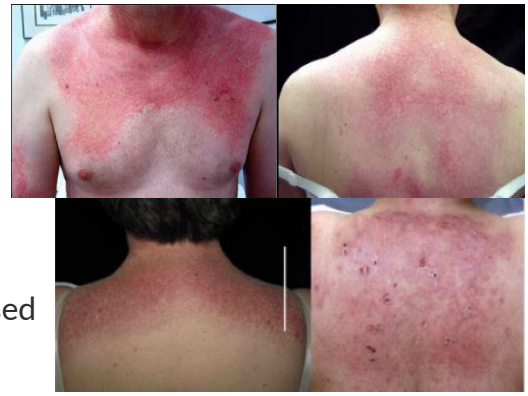


Dermatomyositis

Cutaneous Manifestations Of Dermatomyositis (common) (cont')

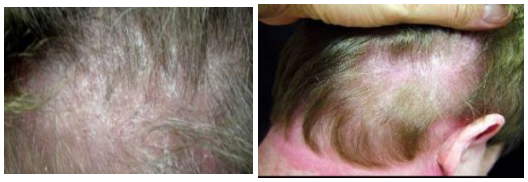
Photodistributed poikiloderma (includes facial erythema)

- V-sign Poikiloderma a rash that has: hyperpigmentation, hypopigmentation, atrophy, and telangiectasia
- Poikiloderma over the upper back (shawl sign) Poikiloderma refers to skin that demonstrates both hyperpigmentation and hypopigmentation, as well as telangiectasias and epidermal atrophy. In DM, patients may demonstrate poikiloderma in any photo-exposed site; however, classic areas of involvement are the upper back (shawl sign).



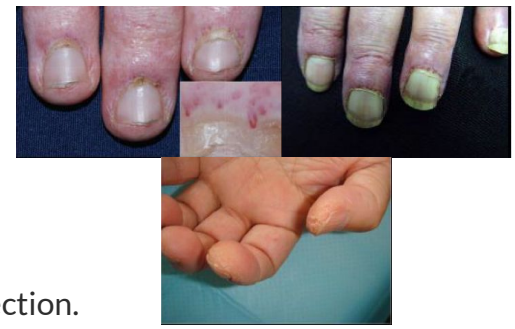
Scalp poikiloderma

- Erythematous to violaceous, psoriasiform dermatitis.



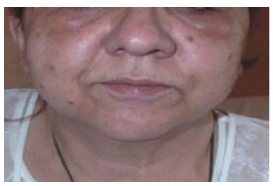
Nail fold changes

- Includes ragged cuticles (Pathognomonic), nailfold telangiectasias.
- Periungual and cuticular changes: Dilation of capillary loops at the proximal nailfold Ragged and thickened cuticles, cuticular overgrowth, and periungual erythema.
- Fragmentation over the cuticle area breach which make pt. prone to bacteria entry and infection.
- Mechanic's hand :Cracking and fissuring of the skin of dermatitis the fingertips.



Others

- **Eyelid edema**
- **Non-scarring alopecia.**
- **Calcinosis cutis** (especially in juvenile dermatomyositis).



Systemic DM manifestations:

- Myopathy: affects proximal muscle groups, mainly the extensor groups (Triceps and quadriceps) in a symmetric fashion. Progressive proximal muscle weakness involves the hips, thighs, shoulders, upper arms and neck.
- Calcinosis: More common in Juvenile DM, favors sites of trauma and can be painful (Calcinosis :stony hard papules with cheesy material , do x-ray , it might be excised)can also be found in scleroderma.
- Pulmonary disease: 15-30%, generally presents as diffuse interstitial fibrosis.
- Patients may also develop ARDS.
- Cardiac disease: Usually asymptomatic (Arrhythmias, conduction defects).
- Gastrointestinal: Symptoms such as dysphagia should prompt investigation for overlap with scleroderma.
- Photosensitivity
- Raynaud's phenomenon
- Dysphagia, gastrointestinal ulcers
- Muscle pain or tenderness
- Fatigue, fever and weight loss
- Calcinosis cutis especially in children
- Interstitial lung disease.

It can be associated with:

- Other connective tissue diseases such as lupus, rheumatoid arthritis, scleroderma and Sjogren's syndrome.
- Cancer, Especially in older patients, particularly of the cervix, lungs, pancreas, breasts, ovaries and gastrointestinal tract.
- Cancer could precede, coincide or follow the diagnosis of DM.

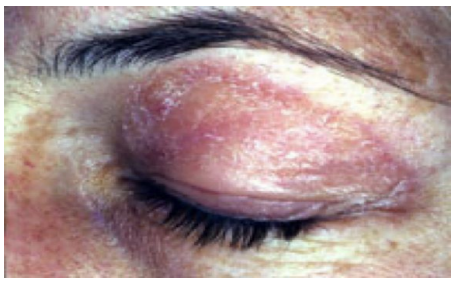
Dermatomyositis

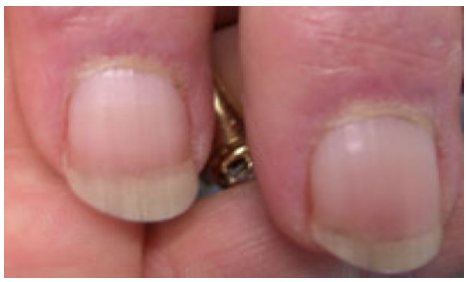
Investigations

- Magnetic resonance imaging (MRI).
- Electromyography.
- Muscle biopsy.
- Blood tests: creatine kinase (CK) and aldolase. Increased CK and aldolase levels can indicate muscle damage and CK is useful to monitor the treatment of DM.
- autoantibodies
- Skin biopsy is suggestive but not diagnostic that shows interface dermatitis.

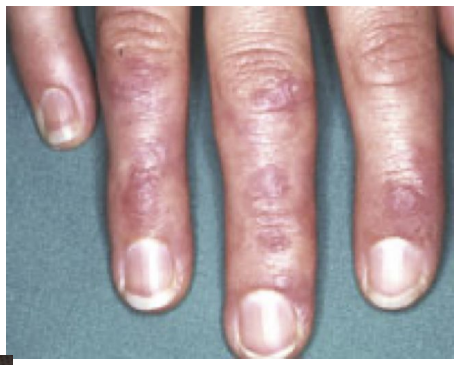
Treatment

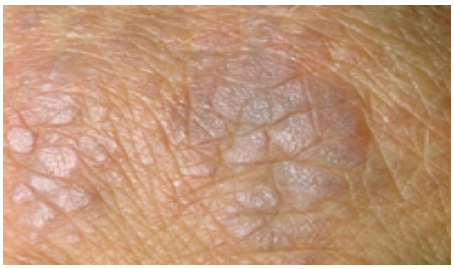
- Oral steroids are the mainstay treatment.
- Steroid sparing agents are:
- Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab.
- Topical steroids and antimalarial medications are used to improve the cutaneous rashes.
- Physiotherapy to improve strength and flexibility of the muscles.
- Surgical excision or Co2 laser could be utilized to remove tender calcium deposits .

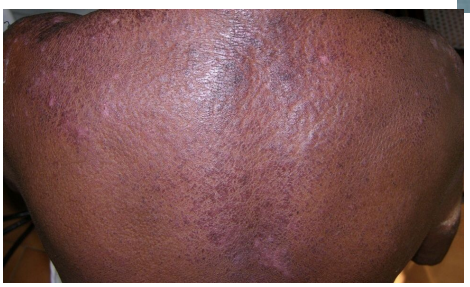




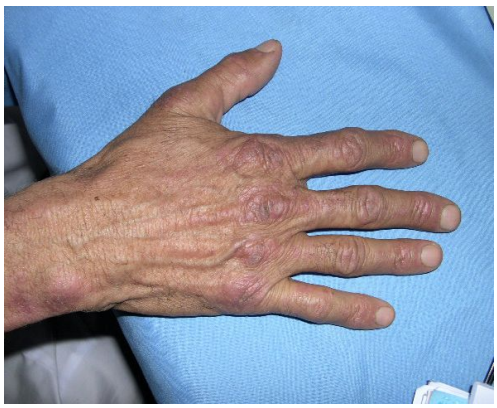
Mechanical hand (dilated capillaries In nails bed)

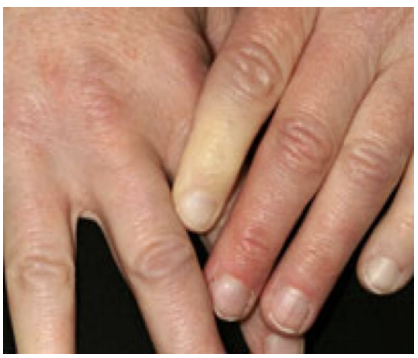


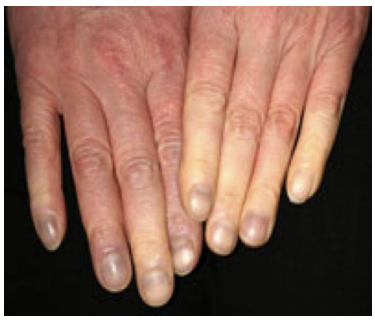


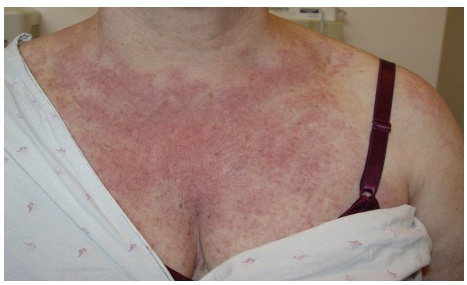


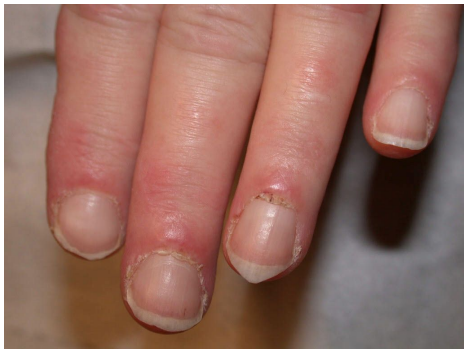
Gottron sign or papule

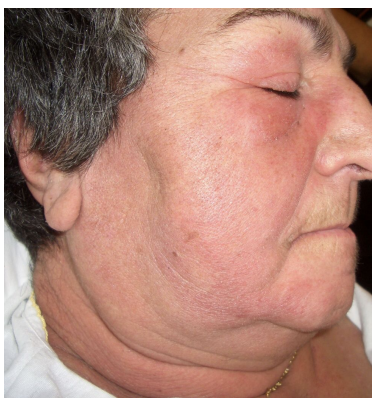












Helitrope sign

Shawls sign (Erythema and edema over photosensitive areas)
40+ female getting dermatomyositis for the first time screen for breast, ovaries and GI tract

Dermatomyositis

Evaluation Of The Patient With Dermatomyositis:

- **HISTORY:**
  Including potential triggers and previous malignancies, and a review of systems.
- **PHYSICAL EXAMINATION:**
  Skin, muscle and complete general examination (including, in adults, breast and pelvic [women], testicular and prostate [men] and rectal [both sexes]).
- **LABORATORY EVALUATION:**

- **Pulmonary:**
  - Pulmonary function tests (PFTs) with CO diffusion.
  - Chest X-ray and/or high-resolution chest CT.
- **Cardiac:**
  - Electrocardiogram (EKG)
  - If symptomatic. echocardiogram and/or Holter monitor.
- **Esophageal:**
  - If symptoms, barium swallow.
- **General :**
  - Complete blood count.
  - Comprehensive metabolic panel.
  - Fasting levels of glucose and lipids.
  - Autoantibody panel.

- **SPECIFIC LABORATORY EVALUATION:**
  - Cutaneous: Skin biopsy (not diagnostic).
  - Muscle: Serum creatine kinase, serum aldolase, occasionally urine creatine, Electromyography (EMG), Muscle biopsy (very conclusive).
  - Serum enzymes are important for diagnosis and even for management.
  - MRI or U/S (if EMG or muscle biopsy are negative)
  - SEROLOGY (ANTIBODIES) : **High specificity: P155** (increased risk of malignancy), **Mi-2** (good prognosis), **Jo-1** (Antisynthetase syndrome), **SRP** (Fulminant DM, cardiac involvement). **Low Specificity: ANA**.
- **MALIGNANCY SCREEN (ADULTS):**
  - Urinalysis, stool occult blood testing.
  - Serum prostate-specific antigen (PSA) [men], Serum CA125 [women].
  - Mammogram and transvaginal pelvic U/S [women].
  - CT of chest, abdomen and pelvis.
  - Colonoscopy, if age-appropriate, iron deficiency anemia, occult blood in stool, or symptoms.
  - Upper endoscopy – if colonoscopy negative in the setting of iron deficiency anemia, occult blood in stool, or symptoms.
  - If planning chronic systemic Corticosteroids DEXA bone density scan.

TREATMENT (CUTANEOUS)

- **Sunscreens (high sun protection factor including protection against UVA).**
- **Topical corticosteroids.**
- **Topical tacrolimus.**
- **Hydroxychloroquine (200 mg twice daily; increased frequency of drug eruptions in patients with dermatomyositis).**
- Hydroxychloroquine (200 mg twice daily) plus quinacrine (100 mg/day).
- Low-dose weekly methotrexate (5–15 mg weekly).
- Mycophenolate mofetil • High-dose IVIg (2 g/kg/month).
- Retinoids, Dapsone, Thalidomide.
- Leflunomide.
- Antiestrogens (e.g. tamoxifen, anastrozole).
- TNF-α inhibitors (e.g. infliximab, etanercept).
- Rituximab.

IF there a big list of treatment it means no effective treatment :)

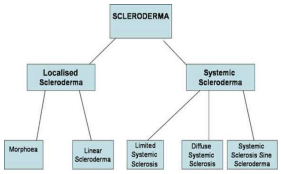
Scleroderma

Scleroderma:

- **SCLERODERMA.**
- **SYSTEMIC SCLEROSIS.**
- **PROGRESSIVE SYSTEMIC SCLEROSIS.**
- **ACROSCLEROSIS.**
- **CREST SYNDROME.**
- **LOCALIZED SCLERODERMA.**
- **LINEAR MORPHEA.**
- **MORPHEA.**

SYSTEMIC SCLEROSIS:

- Systemic sclerosis (SSc, scleroderma) is an autoimmune connective tissue disease of unknown etiology that affects the skin, blood vessels and internal organs.
- The hallmark of the disease is thickening and tightness of the skin.
- characterized by fibrosis of the skin as well as internal organs, e.g. lung, heart, gastrointestinal tract (most common), and kidneys.
- The name systemic sclerosis is meant to convey the systemic nature of the disease, which has two major clinical subtypes: limited and diffuse.
- More common in females.
- 30-50 years.
- Not hereditary (but could be familial).
- Not invariably progressive and fatal (Our concern here is the patient Quality of life).



Classification	
Limited	**Diffuse**

• Limited SSc is characterized by fibrotic skin changes that are limited to the fingers, hands and face and includes the CREST syndrome.
• Tend to develop internal involvement late in the course of disease (decades)
• **CREST Syndrome:** describes the clinical features in a subset of patients with limited SSc.
  ○ **C**alcinosis
  ○ **R**aynaud's phenomenon
  ○ **E**sophageal involvement
  ○ **S**clerodactyly
  ○ **T**elangiectasia
	• In diffuse SSc, generalized fibrotic skin changes are seen and they usually start in the fingers and hands but spread to involve the forearms, arms, trunk, face and lower extremities.
	• Typically associated with early internal organ involvement (within 5 yrs of onset) and a worse prognosis.
	• Positive anti topoisomerase antibodies (**anti scl-70**).

Diagnostic criteria:

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.

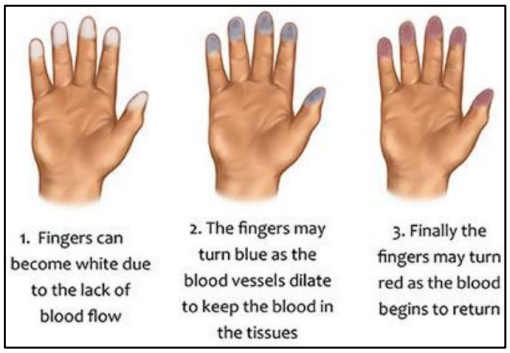
Pathogenesis:

- Individual genetic background and 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

Cutaneous features of systemic disease:

- Digits: Early pitting edema ,hardening, taut and shiny appearance (later on).
- Face: Beaked nose, microstomia (small mouth) and a youthful appearance.
- 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.

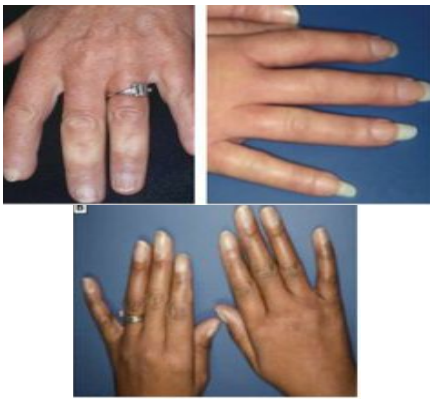


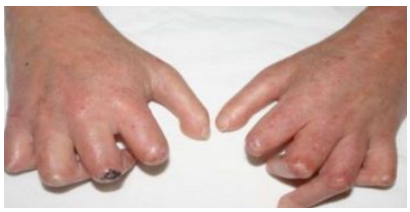
Cutaneous features of systemic disease:

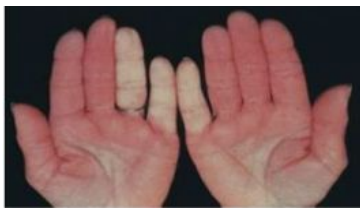
Early phase of SSc	• Early, edematous phase of systemic sclerosis • Note the demonstration of pitting edema on two of the digits. • Edematous and shiny fingers • Swelling and sclerosis reduce hand movements, so patients may be unable to make a fist, or to place the palmar surfaces together the 'prayer sign'. • Fingertips may have pitting, ulcers or loss of bulk from finger pads
Late phase	• Contractures, thick skin, ulceration and scars • Late phase of systemic sclerosis with diffuse cutaneous scleroderma. • Note the fixed flexion contractures, sclerodactyly, and the digital ulceration overlying the third proximal interphalangeal joint.

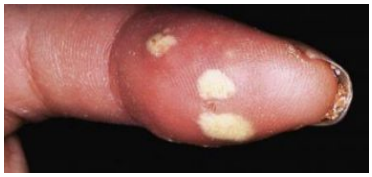
Raynaud's phenomenon	• Vasospasm of the digital microvasculature resulting in:
	  ○ Digital ischemia (pallor)
	  ○ Digital hypoxia (cyanosis)
	  ○ Digital reactive hypermedi (erythema)
	• pale then blue then red, indicates more progressive illness.

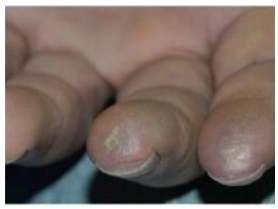
Calcinosis cutis	• white spots or ulcerations and may be quite painful.
Pitted scars	• Pitted scars of the digital pulp That form in distal areas.



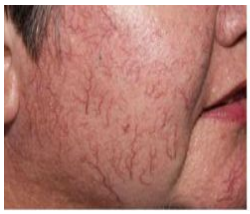
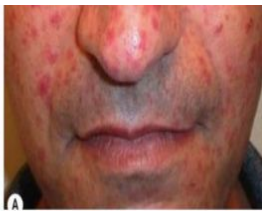








Scleroderma

Cutaneous features of systemic disease:		
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.	
Telangiectasia	• 1st picture: regular telangiectasia (long and tortuous) seen in rosacea and other skin conditions. • 2nd picture: matted telangiectasia seen in scleroderma (flat and rounded)	 

WORK UP:

- Skin biopsy (histopathology): (One of the criteria to diagnose Scleroderma)
  - Compact collagen (Thick areas of collagen in the dermis), loss of subQ fat, deep lymphocytic infiltrate and trapped adnexal structures.
- **Serology (autoantibodies):** (First 3 autoantibodies are of the criteria to diagnose Scleroderma)
  - **ANA.**
  - **Anti-Scl-70 (Anti-Topoisomerase):** AKA **RNA polymerase T (Scl 70)** → diffuse disease, ILD.
  - **Anti Centromeres (ACA):** → Limited disease (CREST syndrome).
  - **Anti-RNP.**
  - **Anti-RNA Polymerase I:** → Diffuse disease.

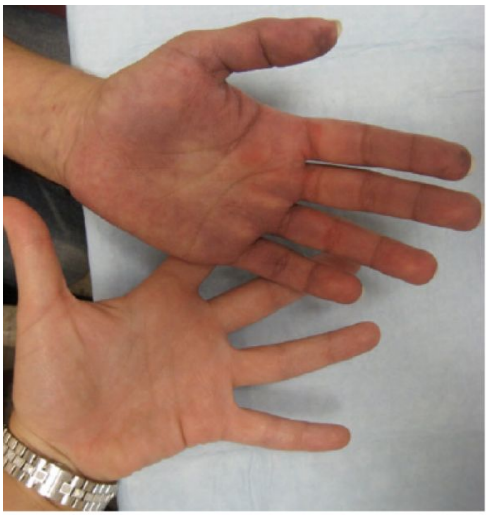
TREATMENT:

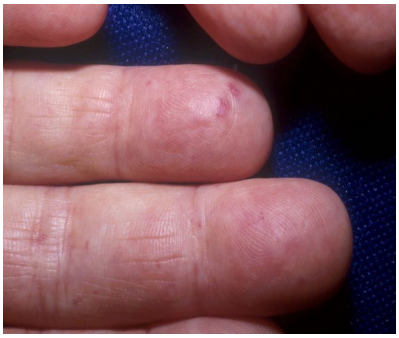
- **"SYMPTOMATIC"**
- Most interventions focus on internal organs and unfortunately, have no significant impact on cutaneous manifestations.
- Raynaud's Phenomenon → Keep warm, CCB (Nifedipine), Angiotensin II receptor blockers (Losartan), Phosphodiesterase type inhibitors (Sildenafil). Stop smoking, decrease trauma. calcium channel blockers, aspirin and vasodilating drugs including nifedipine and iloprost infusions
- Calcinosis cutis: nifedipine, surgical or laser excision.
- Skin sclerosis: physiotherapy, phototherapy.
- GI: proton pump inhibitor, surgery for strictures.
- Kidney: ACE inhibitors.
- In severe cases: immunosuppressant , D-Penicillamine might be used.
- Cutaneous ulcers → Bosentan.
- Fibrosis.
- Morphea.
- Other skin issues: Matted Telangiectasias → Pulse dye laser, Calcinosis cutis → nifedipine, surgical or laser excision.
- Internal organs: ACE inhibitors is used to treat scleroderma renal crisis, GI → PPI or surgery for strictures, Cyclophosphamide → interstitial lung disease, Oral immunosuppressants.

Systemic Scleroderma

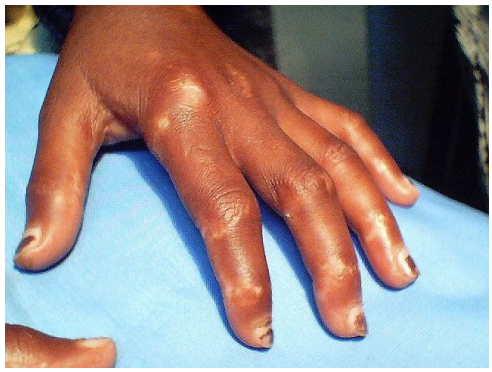
Systemic Sclerosis:

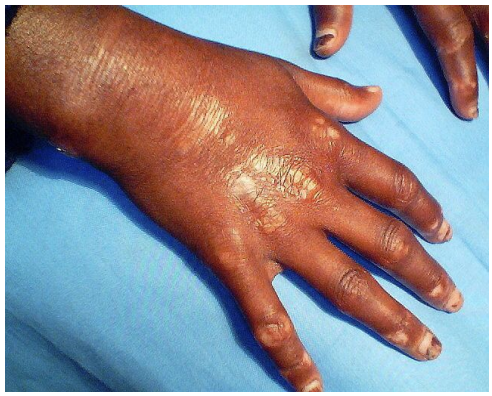
- An autoimmune multisystem disease that results in fibrosis and vascular abnormalities in association with autoimmune changes.
- usually starts between 30-40 years in women who are more affected and later in men.
- Pathophysiology :may involve some injury to the endothelial cells and this results in excessive activation of the dermal connective tissue cells, the fibroblasts
- Usually presents with Raynaud's phenomenon,
- Thickening of the skin of the fingers, then atrophy and sclerosis.
- The fingers become spindle-shaped (sclerodactyly) from resorption of the fingertips.
- Fragile nails become smaller with ragged cuticles
- The tight shiny skin may affect most parts of the body, including the face, resulting in loss of expression and difficulty opening the mouth properly.
- telangiectasia appear on the fingers, palms, face, lips, and chest.
- Ulcers may follow minor injuries over the joints, or on the tips of fingers and toes. Ulceration can lead to dry gangrene and eventual loss of the tips of the fingers
- Joint contractures. Patients will be bed ridden with time.
- Esophageal reflux and dysphagia.
- Lung and heart involvement may manifest as shortness of breath, high blood pressure, chest pain, pleurisy, pneumothorax, pericarditis arrhythmias, general heart enlargement and heart failure.
- Progressive kidney disease resulting in proteinuria, high blood pressure and eventually renal failure.
- Diagnosis is made based on clinical features and presentation.
- Skin biopsy will show skin atrophy with preservation of skin appendages.
- ANA is usually positive.
- Anti topoisomerase I (Scl 70) is characteristic for it especially in severe cases.



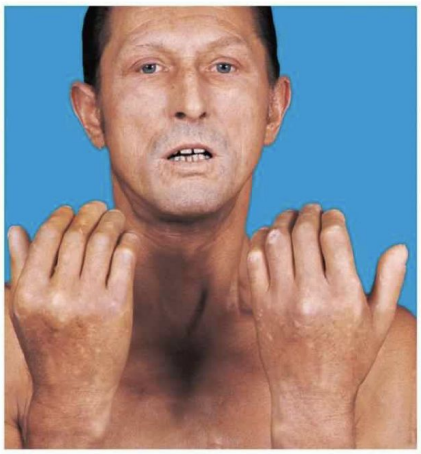


Presence of telangiectasia





Starting to lose distal phalanx
Earliest sign is the inability to pinch skin



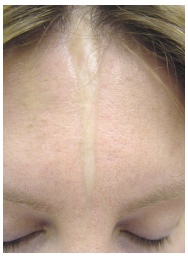
Prayer sign

some is already written but because it's too crowded too add we decided to write everything written in the female slides in one page

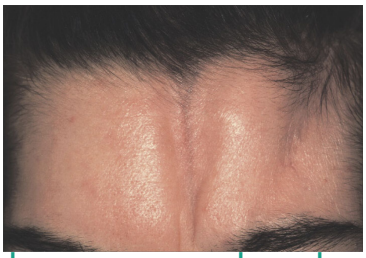
Scleroderma

Linear Scleroderma:

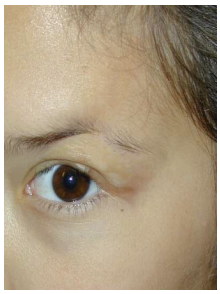
Disease of children



- Linear lesions extend to length of arms or leg
- Begin first decade of life
- May also occur parasagitally down the forehead, known as en coup de sabre

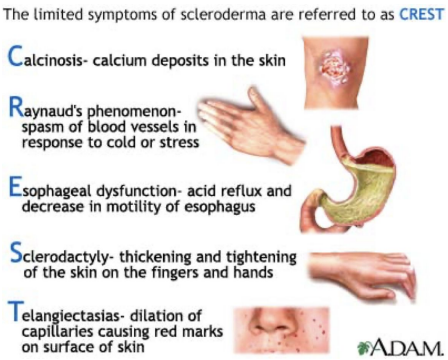


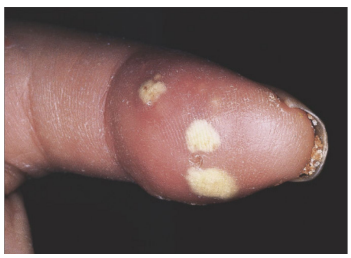
Morphea en coup de sabre



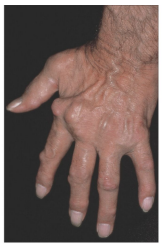
CREST Syndrome:

- Is a limited form of systemic sclerosis in which there is Calcinosis, Raynaud's phenomenon, Esophageal involvement, Sclerodactyly and Telangiectases.
- Anticentromere antibodies are characteristic for this syndrome.





Calcinosis cutis of the thumb in a patient with scleroderma
Very painful when ulcerated



Rheumatoid Nodules:

Differential: gout

- 20-30% of RA patients
- Subcutaneous nodules
- Found anywhere on the body
- Histologically shows dense foci of fibrinoid necrosis surrounded by histiocytes in palisaded arrangement

Mixed Connective Tissue Disease:

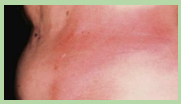
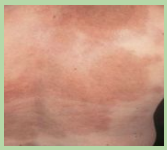
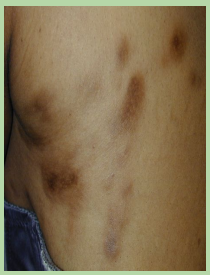
- Mixed features of scleroderma, SLE, and dermatomyositis
- Raynaud phenomenon, sausage-shaped fingers, and swelling of the dorsa of the hands that never becomes sclerodactyly are the most typical features
- Alopecia, facial erythema, periungual telangiectasia, and pigmentary disturbances.
- Painful dermal nodules may appear on the hands or elbows.
- Cutaneous ulceration due to subcutaneous dystrophic calcification

Anti-Rhe antibody is associated with mixed type

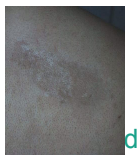
Morphea

Morphea

INFO

- An inflammatory skin disease that primarily affects the dermis and may extend to subcutaneous structures and lead to scar-like sclerosis
- A rare skin condition that causes oval reddish or purplish patches and plaques on the skin.
- Sometimes in linear distribution on face and extremities.
- It subsides on its own over time leaving dyspigmentation and scars. Lillie ring surround morphea (erythematous ring around)—presence is bad because it means it will .

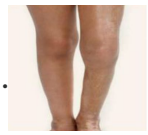
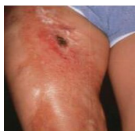


- Does not lead to involvement of internal organs.
- Some people consider morphea as a subtype of scleroderma (localized scleroderma) and some people consider it as a different entity.
- Sclerotic, indurated plaques that may be solitary, multiple, linear, or generalized.
- The surface is usually smooth, 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.
- Confirmed by skin biopsy which usually shows thickening of collagen bundles and loss of skin appendages like sweat glands and hair follicles.Either with scalpel or with punch bx via size 5 then size 3 to go deeper

Clinical types:

- Plaque type , Linear, Deep morphea , Generalized.

Plaque Morphea

- Most common type of morphea with Insidious onset of Asymptomatic slightly elevated, erythematous or violaceous, somewhat edematous plaque that undergoes centrifugal expansion.
- 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)

Linear Morphea

En coup de sabre:

- A term used for linear morphea of the forehead and scalp. Basically, morphea of the forehead and scalp
- Normally unilateral and extends from the forehead into the frontal scalp and leads to hair loss.
- Paramedian location is more common than a median location.

Hemifacial atrophy (Parry-Romberg syndrome):

- A very severe variant of linear morphea. Some people consider it as a different entity
- Progressive loss of subcutaneous fat, but little or no sclerosis.
- Linear morphea tends to involve the underlying fascia, muscle and tendon.

Treatment

- 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.

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- Which of the following is a Clinical pathognomic feature of dermatomyositis?

A) Gottron papules
B) Vasculitis
C) Poikiloderma
D) Calcinosis

3- 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

4- 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

Answers:
1 : B, 2 : A, 3 : A, 4 : B