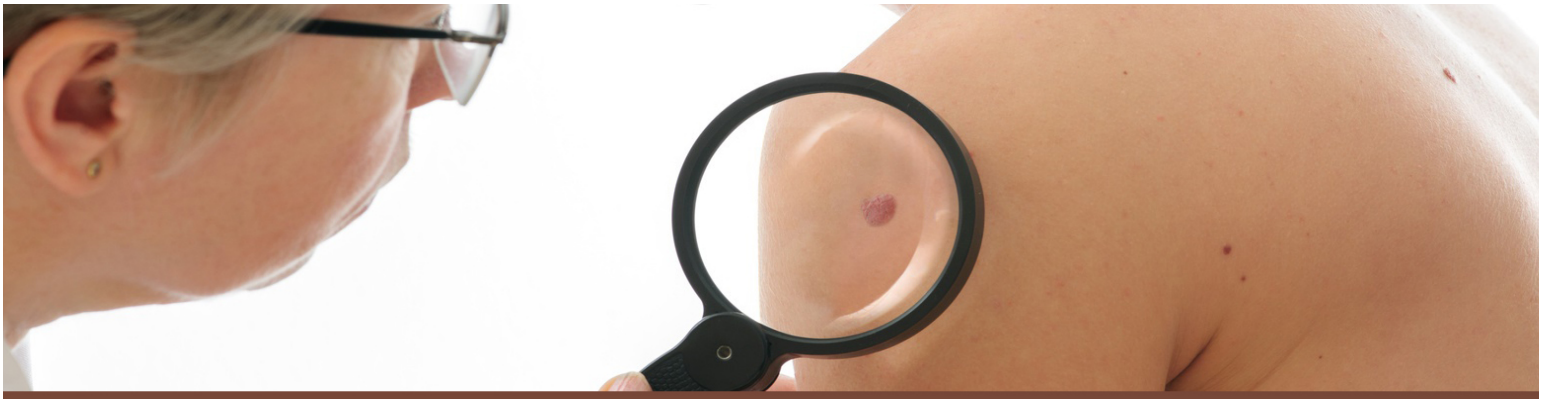

433 Teams

DERMATOLOGY

Lecture (5 & 6)

Cutaneous Manifestations of SLE and Other CTDs (dermatomyositis, scleroderma)

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Objectives:

- ✓ Differentiate between the various types of Lupus.
- ✓ Recognize how Lupus affects the various systems of the body.
- ✓ Identify all of the current treatment options available for Lupus.
- ✓ To learn how to diagnose and investigate dermatomyositis. • How to manage 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.

Kindly note:

- This work is based on Dr. Hadeel Mitwalli's slides + notes during the lecture. (That's why the male's work is deferent)
- Few notes were taken from 432 team.

Color index: slides, important, doctor notes, book Doctor's notes (Group F)

Lupus Erythematosus

- It's a designation of a spectrum of diseases that are linked by distinct clinical findings and distinct patterns of polyclonal (antibodies that are secreted by different B cell lineages) B cell immunity.
- It ranges from life threatening manifestations of SLE to the limited and exclusive skin involvement in CCLE.
- 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 Systemic Lupus Erythematous

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

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulcer
- Arthritis
- Serositis
- Renal disease
- Neurological disease
- Hematological inv.
- Immunological disease
  - ANA

Classification of Cutaneous Disease in Lupus Erythematous

Lupus Specific Eruptions

I. Acute cutaneous LE (ACLE)
- Localized, generalized, bullae

II. Subacute cutaneous LE (SCLE)
- A. Annular
- B. Papulosqamous
- C. Syndromes commonly exhibiting similar morphology
  1. Neonatal LE (NLE)
  2. Complement deficiency syndromes
  3. Drug induced

III. Chronic Cutaneous LE
- A. Discoid LE (DLE)
  1. Localized
  2. Disseminated
- B. Verrucous (hypertrophic) DLE
- C. Lupus erythematosus – lichen planus overlap
- D. Chilblain LE
- E. Tumid Lupus
- F. Lupus panniculitis

Lupus Nonspecific Eruptions

Nonscarring alopecia
Telangiectasia
Livedo Reticularis
Palpable Purpura
Periungual erythema

Acute Cutaneous Lupus Erythematosus

- **Acute malar "butterfly rash"** or more generalized photo-distributed 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, improves with improvement of the SLE.
- **Non scarring.**

Initial Workup

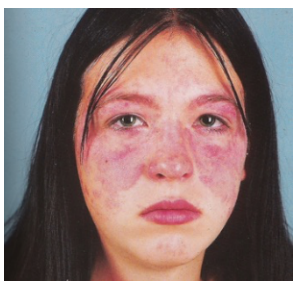
1. History & Physical examination.
2. Skin Biopsy. (Better on non-lesional skin to detect systemic involvement)
3. **Lupus Band Test**
   - It's preferred to be done on non-lesional non-exposed skin, but can be performed on lesional skin.
   - Granular deposits of immunoglobulins and complement are detected in a band-like pattern at the dermal-epidermal junction.
4. **Serology**
   - **ANA**: +ve in 95%, very sensitive but not specific. (screening test)
   - **Anti-dsDNA** (anti- native DNA): Specific but not very sensitive, indicates high risk for renal disease. (432 team: anti-ssDNA in generalize DLE)
   - **Anti-smith**: most specific +ve in 30%.
   - **Anti-histone Ab** (drug induced lupus).
   - **Rheumatoid factor**: +ve in 30%.
5. CBC with deferential, ESR (high)
6. Urine analysis (Proteinuria: > 0.5 g/day)
7. **C3, C4**: low levels indicate active disease, often with renal involvement.

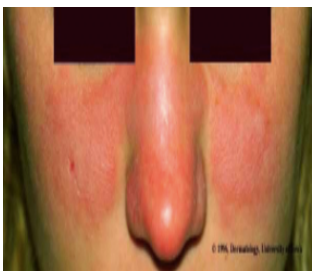
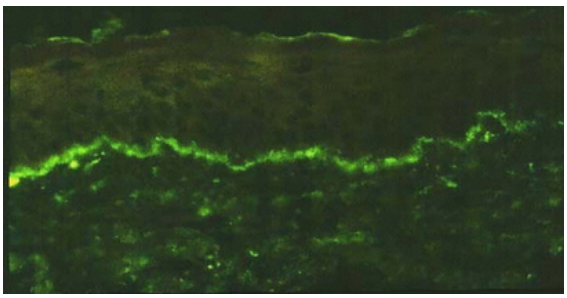
Management

The aim of treatment for cutaneous LE is to alleviate symptoms and to prevent scarring.

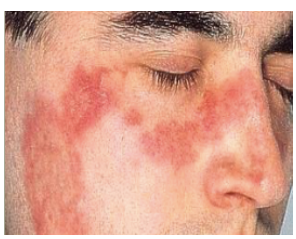
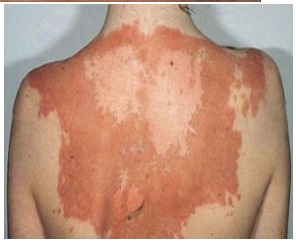
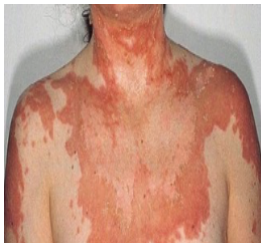
1. **Sun protective measures**
2. **Potent topical steroids**
3. **Antimalarial drugs**
4. Oral steroids
5. Methotrexate, azathioprin, mycophenolate mofetil, cyclosporine, cyclophosphamide, IVIG, and Rituximab. (Steroid-sparing agents; biological treatment)

Examples



Lupus Band Test

Subacute Cutaneous Lupus Erythematosus

- More persistent than those of ACLE (weeks- months).
- Scaly, superficial, inflammatory macules, patches, papules and plaques that are **photo-distributed**, particularly on the upper chest & back, lateral neck, and dorsal arms & forearms.
- Morphologic subtypes:
  - **Annular/polycycliclesions** "ring-shaped"
  - **Papulosquamous lesions**:
    - Psoriasiform
    - Pityriasiform

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**.
- SCLE could occur in patients with Sjögren syndrome, deficiency of the second component of complement (C2d), or it may be drug induced (thiazide diuretics).

Diagnosis

- SCLE is a clinical diagnosis based on presence of:
  - Typical photo-distributed eruption.
  - Skin biopsy.
- Direct Immunofluorescence (Lupus band test).
- A strong association exists with **anti-Ro/SS-A** autoantibodies and a lesser extent will have anti-La/SS-B.

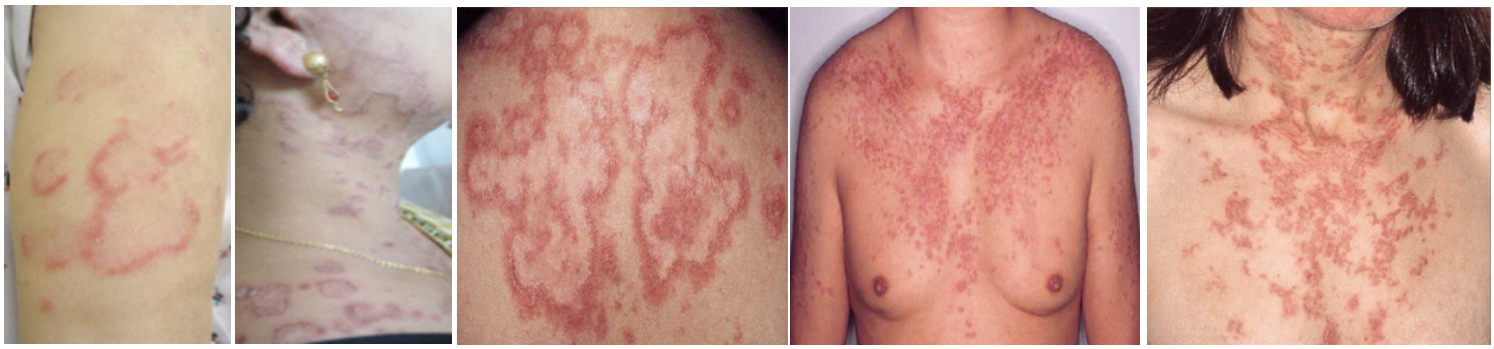
Initial Workup

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

Management

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

Examples



Chronic Cutaneous Lupus Erythematous

- 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.

Describe the skin changes that occur with discoid lupus erythematosus?

- Localized or generalized.
- Chronic, fixed, indurated, **erythematous papules and plaques** often distributed over the head & neck.
- **Scarring**.
- Pigmentary changes (**hypo**/hyperpigmentation).
- Epidermal changes: scales, keratotic plugging of hair follicles (scarring alopecia), crusting.
- **External ears**.

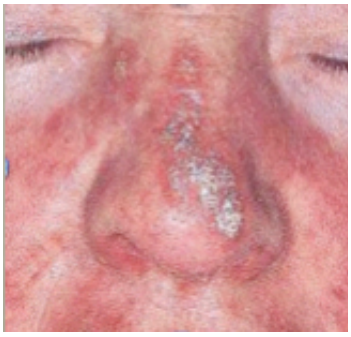
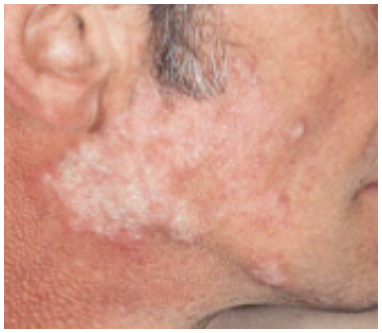
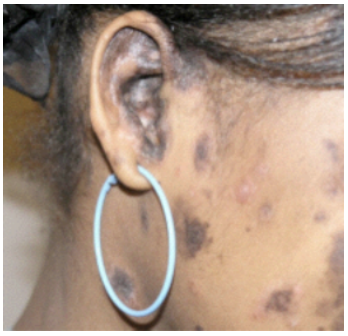
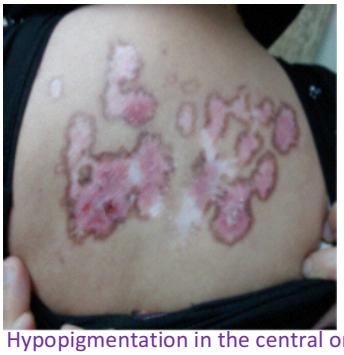
Do patients with DLE develop systemic lupus erythematosus?

- Risk of developing SLE is 5% (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.

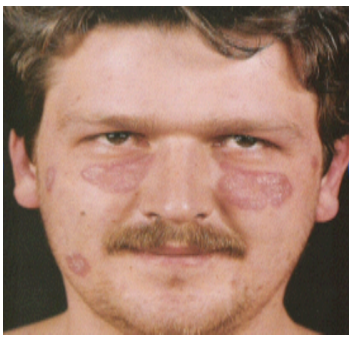
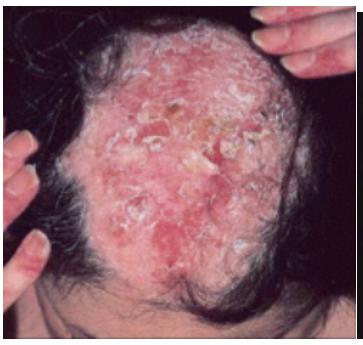
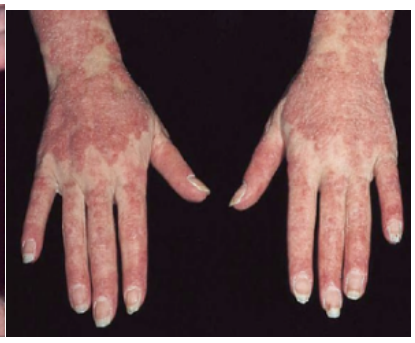
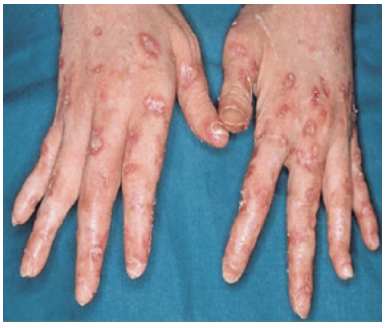
How is Discoid Lupus treated?

- Sunscreens
- Sun-protective measures
- Potent topical steroids / **intralesional steroids**
- Antimalarial drugs

Examples

Hypopigmentation in the central or inactive area and hyperpigmentation at the active border with Scaring and telangiectasia.

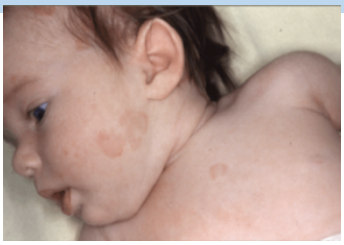
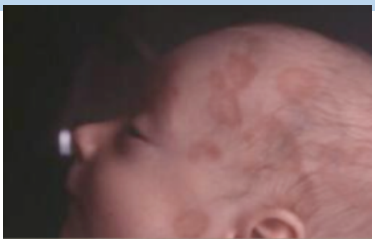





Scarring alopecia

Neonatal Lupus Erythematosus

- The skin lesions occur on the face and head, morphologically resemble SCLE lesions, they are transient, resolving within a few months.
- In NLE, infants develop skin disease (50%), heart disease (50%), or both (10%).
- The heart disease usually manifests as **isolated complete heart block**.
- It's usually permanent and may require a **pacemaker**.
- 10% of infants with NLE and heart disease die from cardiac complications.
- **Thrombocytopenia** / **liver disease**.
- Nearly all have anti-Ro/SS-A and sometimes anti-La/SS-B antibodies, **as well as their mothers**.

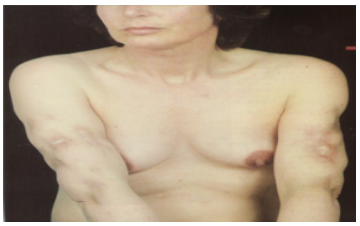
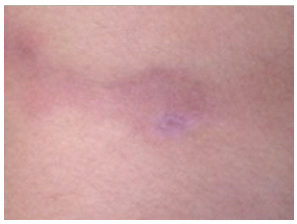
Examples

Lupus Panniculitis

- Inflammation involving the **subcutaneous tissue**, resulting in **inflamed nodules** that often resolve with **depressed scars**.
- They could have overlying DLE lesions "**Lupus Profundus**"
- About 1/2 of patients will have four or more criteria for urge classification of SLE.
- Diagnosis confirmed by **excisional biopsy**.
- Treatment of choice: **Antimalarial drugs**.

Examples

Drug-Induced Lupus Erythematous

Drug-induced lupus differs from SLE by the following features:

- Sex ratios are nearly equal.
- Nephritis and central nervous system features are not commonly present.
- 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.

Drugs associated with lupus erythematosus: (Important)

- **Chlorpromazine**
- **Hydralazine**
- **Methyldopa**
- **Anti-TNF**
- **Penicillamin**
- **Isonizide**
- **Procinamide**
- **Quinidine**
- **Minocyclin**
- **IFN-alpha**
- **IFN-beta**

Dermatomyositis

- An idiopathic chronic inflammatory disease involving the skin and skeletal muscles.
- Muscle involvement usually presents with **proximal muscle weakness**.
- **Amyopathic dermatomyositis**- in some instances, muscle involvement may not be detectable.

Criteria for diagnosing dermatomyositis:

- Progressive **proximal symmetrical weakness**.
- Elevated **muscle enzyme** levels.
- Abnormal findings on **electromyograms**. (Short duration, polyphasic)
- Abnormal findings from **muscle biopsy**. (Best location is triceps)
- **Compatible cutaneous disease.**

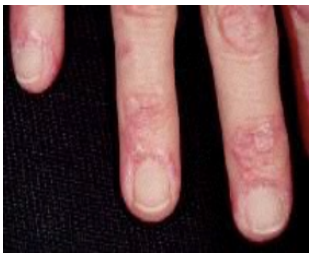
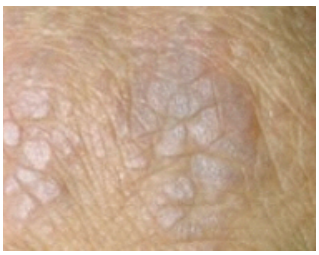
Diagnosis: Proximal muscle weakness with two of the three laboratory criteria.

Are there skin changes that are diagnostic of dermatomyositis?

Two cutaneous findings have been describing as "**pathognomonic**" of dermatomyositis:

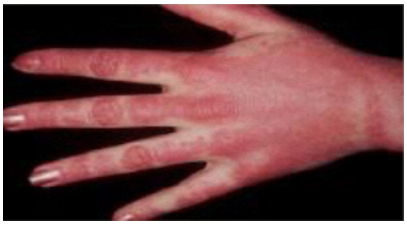
1. **Gottron's papules**

Erythematous to **purplish flat papules** on the extensor surfaces of the interphalangeal joints.

2. **Gottron's sign**

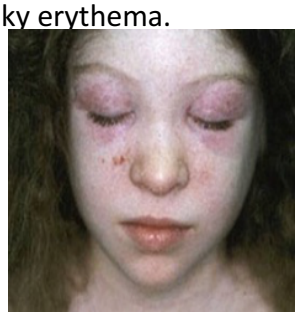
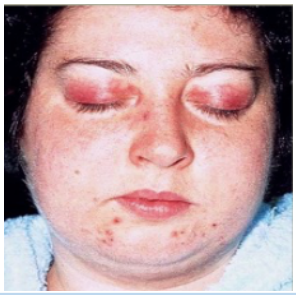
Consist of symmetric violaceous erythema, sometimes with edema, over the dorsal knuckles of the hands, elbows, knees, and medial ankles.



Are there other skin findings that are characteristic of dermatomyositis?

Heliotrope rash

Symmetrical periorbital edema with a violaceous (lilac) dusky erythema.

Periungual talangiectasia with cuticle atrophy

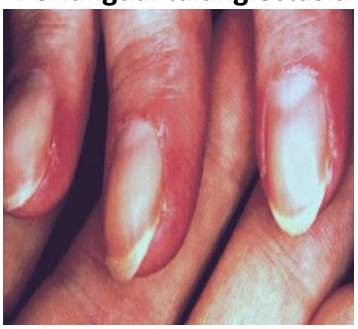
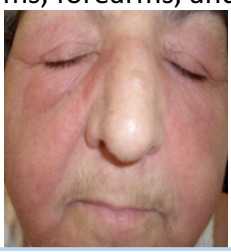
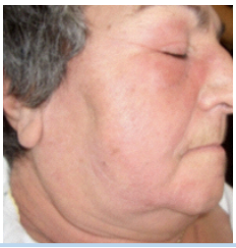
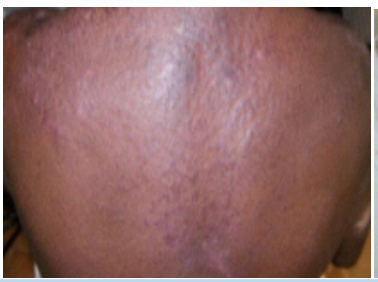
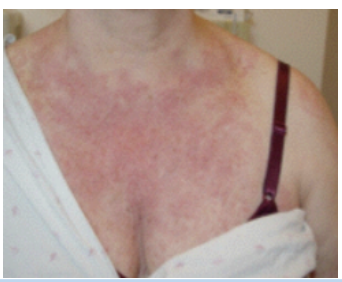
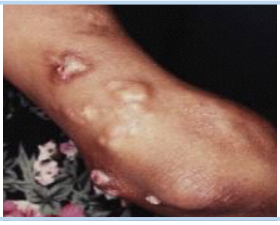



Photo-distributed violaceous erythema of the face, sun-exposed areas of the neck, upper chest, shoulders, dorsal arms, forearms, and hands.

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.

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.
- Adults with dermatomyositis have been reported to have a variety of **malignancies** (cervix, lungs, pancreas, breasts, ovaries and gastrointestinal tract) that sometimes follow a clinical course of exacerbation and remission in concert with the dermatomyositis.
- Female patients should be carefully screened for **ovarian cancer**.

How do you diagnose dermatomyositis?

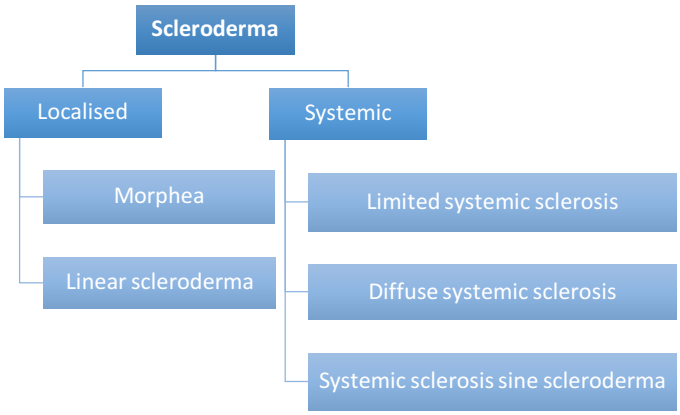
1. History & Physical examination.
2. Serum levels of muscle enzymes- **creatine phosphokinase (CPK)** level is most reliable indicator of disease activity.
3. Serology
   - ANA in < 60%
   - **Anti-Jo-1** (anti-histidyl-t-RNA synthase) in 30%. (lung disease & mechanical hands)
   - **Anti-Mi-2** (highly specific), but it lacks sensitivity because its present in only 25% of patients, indicates good prognosis.
4. Magnetic resonance imaging (MRI).
5. Electromyogram.
6. Muscle biopsy- Inflammatory cell infiltrations & necrosis of muscle cells.
7. Skin biopsy- suggestive but not diagnostic, shows interface dermatitis.

Treatment

- **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.
- Surgical excision or Co2 laser could be utilized to remove tender calcium deposits.

Scleroderma

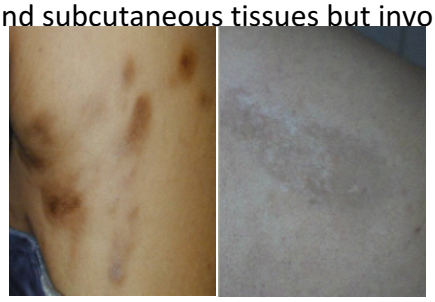
- It's a chronic disease that involves the microvasculature and connective tissue and results in fibrosis.
- There is an increase in dermal collagen & decrease in the elastic tissues which leads to typical **thickening & immobility.**
- It may be localized, as in **morphea**, or more generalized and involving visceral organs, as in **progressive systemic sclerosis.**

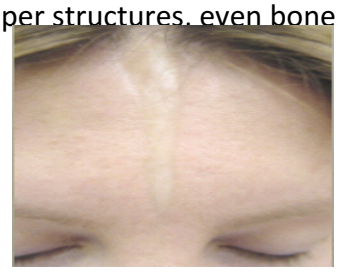


A. Morphea

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 <u>whitish or ivory color</u>, whereas the border of active lesions is usually <u>violaceous</u>. (1st manifestation is erythematous spot)
- It usually involves the skin and subcutaneous tissues but involve deeper structures, even bone.





en coup de sabre (Linear morphea)

Do patients with morphea develop systemic sclerosis?

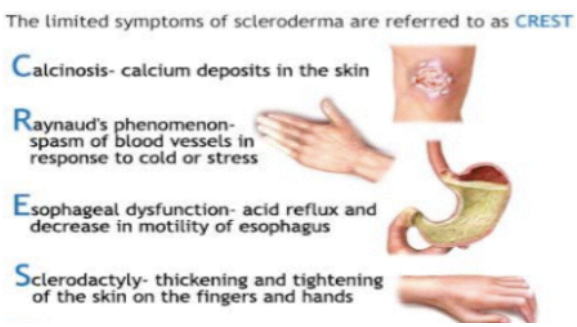
They don't develop SLE.

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.

B. CREST Syndrome

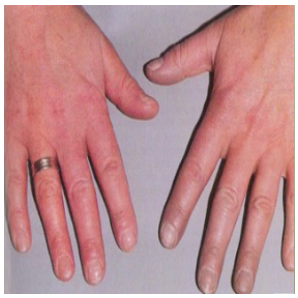
- It's considered a type of <u>limited</u> systemic scleroderma.
  - C = Calcinosis cutis
  - R = Raynaud's phenomenon
  - E = Esophageal dysfunction
    (Lower 2/3 with SS, upper 1/3 with Dermatomyositis)
  - S = Sclerodactyly
  - T = Talangiectasia
- Most patients with CREST syndrome have circulating antibodies to centromeres, called "anti-centromere antibodies".

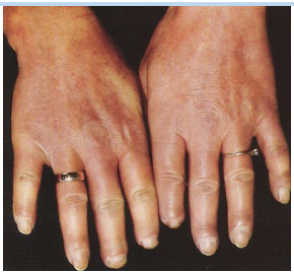


C. Progressive Systemic Sclerosis

What are the cutaneous findings in progressive/ diffuse systemic sclerosis?

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 & extremities- progressive.
   - Sclerodactyly- tapering of fingers "madonna 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.



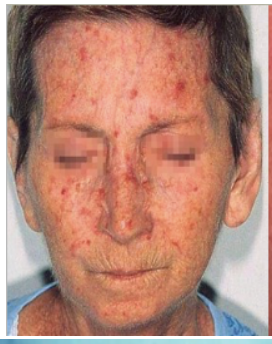


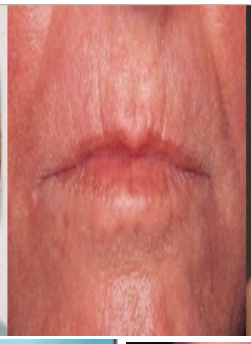
Nonpitting edema of the hands & feet

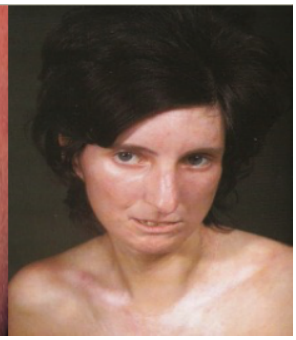
Raynaud's Phenomenon (start as white pallor ischemia then blue stenosis then red active hyperemia)

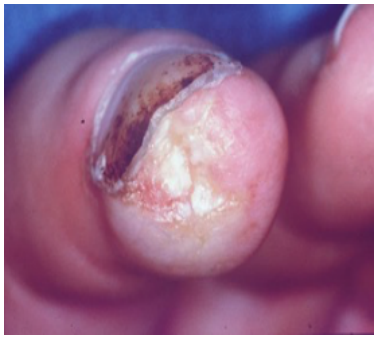
- It is digital ischemia that occurs on exposure to cold and/ or as a result of emotional stress.
- Causes
  1. Rheumatic disorders (SS 85%, SLE 35%, DM 30%, RA, PAN)
  2. Diseases with abnormal blood proteins (cryoprotein, macroglobulins)
  3. Drugs (b-adrenergic blockers, nicotine, cyclosporine)
  4. Arterial disease (atheriosclerosis obliterans)

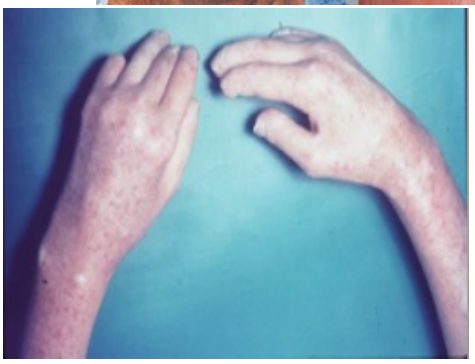
Examples of Progressive Systemic Sclerosis

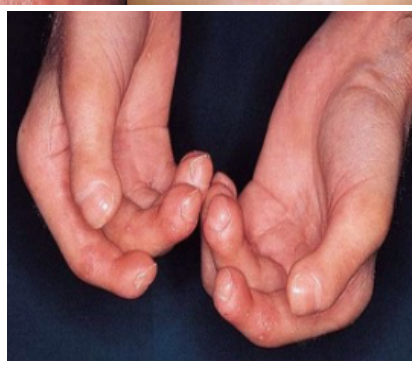


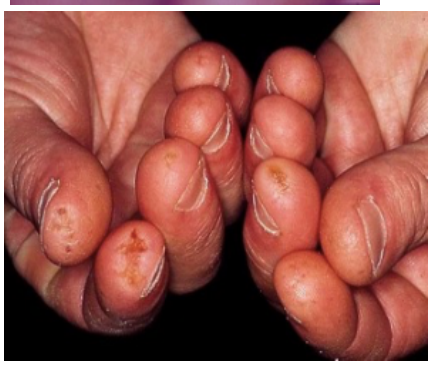












Scleroderma

Diagnosis

1. History & physical examination- characteristic skin changes.
2. Serology:
   - **ANA** (often +ve)
   - Anti-centromere antibodies
     - 71% limited systemic sclerosis “CREST”
     - 21% of diffuse systemic sclerosis “progressive”
   - **Anti-Scl-70** “anti-topoisomerase I”
     - 33% of diffuse systemic sclerosis
     - 18% of CREST
3. **Skin biopsy**- skin atrophy with preservation of skin appendages.

Management

- Treatment is **symptomatic**.
- **Raynaud's phenomena**:
  - Stop smoking
  - Keep hands warm and decrease trauma
  - Calcium channel blockers (dihydropyridines: **nifedipine**)
  - Aspirin and
  - Vasodilating drugs (iloprost)
- **Calcinosis cutis**: nifedipine, surgical or laser excision.
- **Skin sclerosis**: physiotherapy, phototherapy.
- **GI**: proton pump inhibitor, surgery for strictures.
- **Kidney**: **ACE inhibitors**. (It’s important to know about it)
- **In severe cases**: immunosuppressant, D-Penicillamine might be used (blocks aldehyde groups involved in intermolecular cross-links in collagen).

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