Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Scleroderma Spectrum Disease

Objectives :

- Background
- Scleroderma
- Sjogren's Syndrome
- Inflammatory Myopathies

Done by :

Team leader: Al Hanouf Al Jaloud

Team Members:

Batoul Al Ruhaim
Mansour Al obrah
Wejdan Al Badrani
Gharam Al Julaidan
Rotana Al Khateeb

Revised by: Aseel Badukhon

Resources :

Doctors slide + notes: Mohammed A. omair

Books:

Kumar & Clark's
MKSAP
Step up to medicine
Master of the board

Background

Scleroderma spectrum diseases are a group of heterogeneous diseases that has a predominant feature and share other common features.

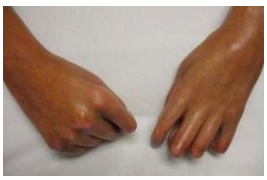
- They are **rare but serious** diseases that are characterized by a specific organ involvement and many other common features.
- Difficult to treat.
- Associated with significant morbidity and mortality due to internal organ damage.
- Therapies used to treat inflammatory manifestations are similar for all conditions.

Scleroderma or systemic sclerosis (SSc)

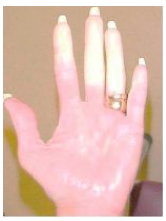
Scleroderma is the **old** name, the **more scientific** name is systemic sclerosis.

SSc is characterized by:

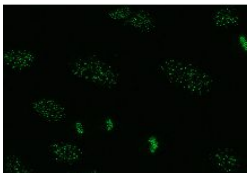
skin thickening



vasculopathy



autoantibody production

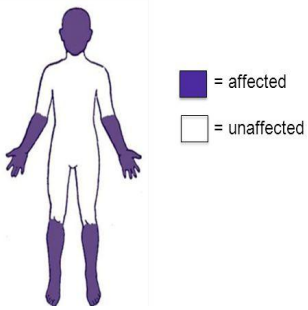
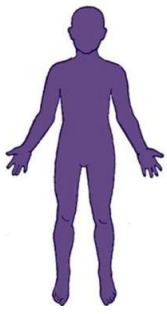


Pathogenic pathways of the disease manifestations:

1. **Fibroblast** activation due to **collagen deposition** which leads to skin thickening and lung fibrosis and myocardial fibrosis.
2. **Vasculopathy** and autonomic neuropathy leading to vascular complications like Raynaud's phenomenon and renal crisis , pulmonary hypertension
3. **Autoimmunity** and inflammation where you will **develop autoantibody** that causes inflammatory manifestations such as arthritis"

Types

Based on **cutaneous involvement**, it is classified into:

Limited 70% of cases Limited Cutaneous Scleroderma (LcSSc)	**Diffuse** 30% of cases Diffuse Cutaneous Scleroderma (DcSSc)
- Often more indolent - Has a **higher risk of pulmonary hypertension** - Associated with Anti-centromere antibodies. - Skin involvement is limited to the hands, Face, feet, forearm - Raynaud's phenomenon starts many years (up to 15) **before** any skin changes. - Has a **Characteristic face features:** • 'beak'-like nose • small mouth (microstomia). - When you have: (**C**alcinosis, **R**aynaud's phenomenon, **E**sophageal involvement, **S**clerodactyly, **T**elangiectasia) it is called **CREST syndrome**	- Associated with more internal organ involvement - Has a worse prognosis - associated with Anti-topoisomerase/RNA polymerase III antibodies. - Edematous in onset, skin sclerosis rapidly follows. - Raynaud's phenomenon starts **just before** or **concomitant** with the edema. - More likely to develop **interstitial lung disease** and **renal crisis**
★ Involves the **hands** up to **the elbow** and **legs** up to **the knees.** ★ Limited subtype is more **indolent**. ★Serious complications such as **pulmonary hypertension** usually occurs after 10 years of the onset.  	★ Involves the **whole body.** ★ The **face** involves in both conditions, so you can't judge a subtype base on the face. ★ Diffuse subtype has more **quicker** course, **worse prognosis**, more internal organ involvement and more **mortality**. 

-**"SSc *sine* scleroderma:** A rare third subtype characterized by visceral disease in the absence of skin involvement. And usually these patients are missed as the predominant feature -which is the skin thickening- is not there.

AutoAntibodies

Scl-70 (topoisomerase)	Associated with **diffuse** subset, ILD, and reduced risk of PAH pulmonary arterial hypertension
Anti-centromere	Associated with **limited** subset, PAH and DU digital ulcers
RNA polymerase III (mainly with DcSSc)	Associated with SRC scleroderma renal crisis, malignancy associated SSc, and mortality.
Scl-PM scleroderma polymyositis	Associated with myositis overlap when you have 2 autoimmune diseases, you call it an overlap.

-ANA positive in 95%. -RF positive in 30%

2013 Criteria for the Classification of Systemic Sclerosis

Table 1
The ACR/EULAR criteria for the classification of SSc

Category		Subitems	Weight
Skin[a]	Enough to make a diagnosis if no other explanation is there **Sufficient Criterion**	Skin thickening of the fingers of both hands extending proximal to the MCPs[b] metacarpophalangeal	9
		Puffy fingers	2
		Whole finger, distal to MCP	4
Fingertip lesions[a]		Digital tip ulcers	2
		Pitting scars	3
Telangiectasia		—	2
Abnormal nail fold capillaries		—	2
PAH and/or interstitial lung disease		—	2
Raynaud's Phenomenon (RP)		—	3
Scleroderma-related antibodies (any of anticentromere, anti–topoisomerase-I [anti–Scl-70], anti–RNA polymerase-3)		—	3
—		Total score:	

★ If you have a patient who has **skin thickening involving the tip of the fingers extending proximal to the MCP** and there is *no other clear reason*, this is systemic sclerosis. You have to have a score of **nine**, so just having this manifestation is enough to diagnose systemic sclerosis and this is what we call a **sufficient criteria**.

Organ Involvement in SSc

- SSc is a disease that is **difficult** to evaluate, treat, and monitor.
- It is very **heterogeneous** and usually diagnosed late.
- Pathogenesis in each organ involved is not the same it could be (Neurovascular/fibroproliferative/inflammatory).
- There is no single drug that treats everything.
- A strategy should be adopted to evaluate each manifestation and organ involved on a regular basis.
- **Skin is the Largest and Most Important Organ in SSc (and all women).**

★ In systemic sclerosis because there are **3 different pathogenic pathways**, each manifestation should be assessed **individually** and managed in a different way. This is a CHALLENGE.

Skin Involvement

★ Initially the patients have the **inflammation** of their skin, the inflammation will activate the **fibroblast** and will add to more **collagen deposition** and **skin thickening+fibrosis**.

- Skin involvement has been considered a **reflection** of internal organ involvement.
- The **level of skin involvement predicts severe disease and mortality.** (More skin involvement = worse prognosis)
- Skin loosening occurs 5 years after the onset of the disease. The skin is not very responsive. The response takes 1-2 years to be seen.
- Treatment is usually initiated when active skin inflammation is apparent or progressive skin thickening. Once they have the **inflammation** you have to treat with Immunosuppressants
- SKIN INVOLVEMENT ALWAYS STARTS IN THE FINGERS AND TOES (distally) AND EXTENDS PROXIMALLY. And when the disease gets better it's always from proximal to distal
- Contractures of the fingers and disability are preventable with **stretching exercise.** patients who keep on exercising even if they have an aggressive disease this reduce the disability by **70-80%**).
- Patients should be advised to use **emollients** and creams at all time.

Treatment of skin involvement

- Methotrexate (if no ILD or renal failure use other drugs in this case) because this drug can cause pneumonitis and it will accumulate in the body with renal impairment increasing its toxicity
- Mycophenolate mofetil
- Cyclophosphamide
- Rituximab
- With some steroids (steroids is a significant risk factor for **SRC** Scleroderma renal crisis and is best to be avoided in patients with DcSSc.

Raynaud's Phenomenon and Digital Ulcers (Pain at the tip of your fingers)

- Spasm of the digital arteries, usually precipitated by cold and relieved by heat. If there is no underlying cause, it is known as Raynaud's disease.
- Affects 5% of the population, mostly women.
- Usually bilateral and fingers are affected more commonly than toes.
- Vasoconstriction causes skin pallor followed by cyanosis due to sluggish blood flow, then redness secondary to hyperaemia.
- In chronic severe disease tissue, infarction and digital loss can occur.

★ It's an **exaggerated** response of trigger (cold – stress - medications such as: **Beta blockers**).

➢ RP and DU are 2 faces of the same coin.
➢ There is some difference between the underlying pathogenesis of both conditions.
➢ 95% and 50% of SSc have RP and DU respectively, but RP tends to occur years before the diagnosis of SSc unlike DU that usually occur in the first 5 years after the development of the non-RP manifestation.

★ During the **exam** or **cold** weather what happened to your body physiologically?
Peripheral blood vessels **constrict** to maintain the heat, but once your stress is gone blood vessels dilate. But patients with RP & UD have exaggerated and prolonged vasoconstriction.

★ **Secondary RP** could be due to **systemic sclerosis**. The most important complication is **digital ischemia**, they could develop an ulcer or gangrene (becomes black).

★ What are the **colors** of RP? 1) White due to **vasoconstriction**. 2) Blue-purple due to **cyanosis**. 3) Red due to **vasodilatation**.

Treatment modalities in secondary **Raynaud's Phenomenon (RP)**

➢ Never underestimate **non-pharmacological** treatment. Patients should avoid cold by wearing gloves and warm clothes, and stop smoking. & to cope with stress.

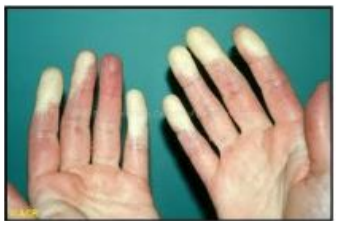
➢ **Treat pain adequately.** Pain will cause more spasm > ↑ vasoconstriction > ↑ ischemia > ↑ pain "viscous cycle"

➢ **Calcium channel blockers** are effective in treating RP with the cost of side effects and intolerance.

➢ Prazosin not working well. can cause severe postural hypotension that's why it is better to avoid it

➢ Efficacy of oral and IV prostaglandins.

➢ IV iloprost better than nifedipine.



Treatment modalities in **Digital Ulcer**

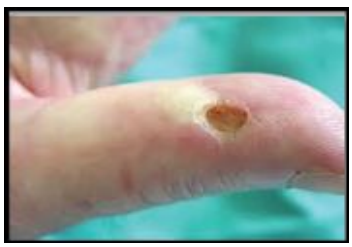
➢ Aim of treatment includes: healing and prevention of new ulcers at the end of the study.

➢ CCB are commonly used but no evidence in healing DU

➢ Endothelin receptor antagonist (bosentan) has been shown to prevent new ulcers and is believed to be a disease modifying agent for SSc

➢ Phosphodiesterase-5 inhibitors has a positive effect on healing and preventing ulcers.

➢ Prostacyclin has been shown to heal DU and prevent new ulcers.



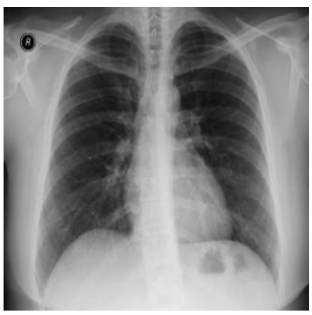
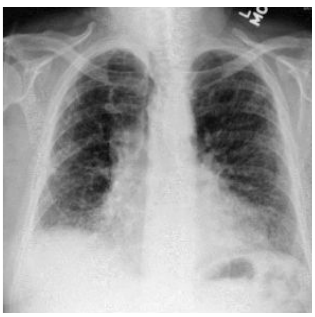
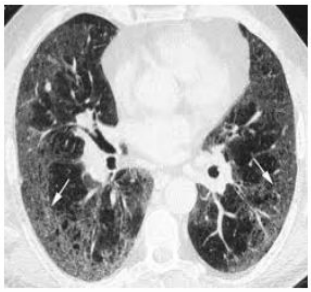
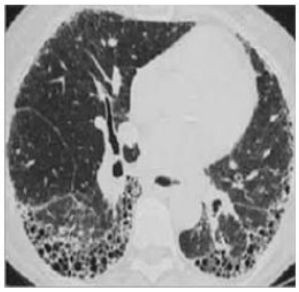
Interstitial Lung Disease

Mostly with DcSSc

★ ILD is a **very common**, about **70%** of systemic sclerosis patients have ILD. It could be very mild or diffuse.

- ILD: is defined as a specific form of chronic, progressive **fibrosing** interstitial pneumonia leading to progressive loss of pulmonary function, and **respiratory failure.**
- Who should be screened for ILD: EVERYBODY how? By doing high-resolution CT scan (HRCT) it will show ground glass appearance + bibasal fibrosis.
- It affects usually the **bases** of the lungs.
- Diagnosis is made by a combination of imaging and pulmonary function test (PFT).

Clinical findings in ILD:	**PFT** in ILD shows:
• Tachypnea • Tachycardia • Cyanosis • Clubbing • Reduced chest expansion • Fine early inspiratory crackles	• Low forced vital capacity (FVC) • Low forced expiratory volume in one second (FEV1) • Normal or high FVC/FEV1 ratio • Low diffusion capacity of carbon monoxide (DLCO) because the gas exchange is abnormal due to fibrosis of lung • ILD is a restrictive lung disease • Both FVC & FEV1 will be decreased with more decrease in FVC • **FEV1/FVC ratio will be normal or elevated!**

You do chest x-ray but **you don't relay on it**, because even if the patient has significant disease the chest x-ray can be **normal**.

Treatment Options

- **Cyclophosphamide** is up to today the standard of care used as treatment induction in ILD.
- Alternative could be: MMF (Mycophenolate mofetil) or rituximab.
- Maintenance includes: MMF, AZA (Azathioprine) and RTX (Rituximab).
- Steroids are a part of induction and maintenance.

DO NOT USE METHOTREXATE HERE!!

Pulmonary Arterial Hypertension

Mostly with LcSSc

★ Exactly what happens to the fingers with RP and DU happens here, you have **abnormality in the blood vessels** and **significant vasoconstriction** and then **PAH** and its symptoms (**dyspnea - palpitation - syncope**).

- PAH is defined as **PAP ≥ 25 mmHg** at rest or 30 mmHg after exercise
- Pulmonary **wedge pressure ≤ 15 mmHg.**
- PAH has become a very important cause of mortality along with ILD they are the cause of 33% of death.
- Affects 8-13% of SSc (RHC criteria)

Solutions to **Reduce PAH-related Mortality and Morbidity:**

Early detection

Aggressive treatment

Early referral for lung transplant

Primary causes of death in 234 patients with SSc

	N	%
All death cases	234	100
SSc-related death cases	128	55
Pulmonary	78	33
Pulmonary fibrosis	45	19
Isolated PAH	33	14
Myocardial	33	14
Arrhythmia	14	6
Left heart failure	8	3
Right heart failure	5	2
Biventricular heart failure	4	2
Pericarditis (constriction and/or tamponade)	2	1
Renal	10	4
Renal crisis	10	4
Gastrointestinal	7	3

How to diagnose PAH in SSc

- Clinical findings include:
  - Desaturation
  - Tachycardia
  - Palpable P2 and parasternal heave
  - Loud 2nd heart sound
  - Signs of right sided heart failure because of the back flow.
  - PFT may show isolated low DLCO All other PFTs would be normal because the problem is in the vessels not the lungs (the lungs are normal).
- The **first** investigation to order is **echocardiography**. Echo + Low DLCo are used for screening for PAH
- The **gold** diagnostic tool is right sided heart catheterization.

Remember you can have pulmonary hypertension secondary to ILD which makes diagnosis and management **more complex.** PAH can be primary or secondary to HF, lung disease.

★ On physical exam (**hypoxia - low BP**, due to decreased preload, pulmonary pressure is high & systemic pressure is low)

Treatment of PAH

- **Endothelin Receptor Antagonists:**
  - **Bosentan**
  - Ambrisentan
- Macitentan
- **Phosphodiesterase-5 Inhibitors**
- **Prostacyclins** (I.V)

Gastrointestinal System Involvement

★ Crohn's disease involves GI tract from mouth to the anus, same thing happens to systemic sclerosis EVERYTHING IS INVOLVED.

- GIT is the most **common** internal organ to be involved (95-99%) which includes:
  - Esophagus "the most common visceral involvement": dysmotility and **reflux** leading to strictures
  - Stomach: gastroparesis, **watermelon appearance** with telangiectasia it is called (GAVE) gastric antral vascular ectasia. Which can lead to upper GI bleed -> anemia.
  - Small bowel: blind loop syndrome complicated by **bacterial overgrowth** manifesting as chronic diarrhea and **malabsorption**.
    - Primary treatment is sequential antibiotics but stomas and TPN can be offered in advanced cases
  - Large bowel: chronic **constipation**, fish mouth diverticula.
    - Treatment includes laxatives
  - Anorectal: fecal **incontinence** is a devastating complication and difficult to manage but one option could be to clear bowel frequently before going out.

*know how each part of the GI manifest.

diverticula.

Kidney Involvement

Scleroderma Renal Crisis

Mostly with DcSSc

- Patients with SSc usually have low BP, once you see **high BP suspect SRC.**
- The primary histopathologic changes in the kidney are localized in the small arcuate and interlobular arteries and the glomeruli.
- The **characteristic** finding is intimal proliferation and thickening that leads to narrowing and obliteration of the vascular lumen, with concentric "**onion-skin**" hypertrophy.
- This will lead to activation of the **aldosterone-renin-angiotensin pathway.** So they have **severe malignant hypertension** and they develop vasoconstriction of the afferent blood vessel in the kidneys.
- Precipitating factors include: high dose **steroids**, cyclosporin, **pregnancy**.
- Anemia in SSc is usually iron deficiency, once you see **microangiopathic hemolytic anemia suspect SRC.** It means the RBCs are destroyed because of the abnormal blood vessels, it's not a hemolysis due to autoantibodies. So Coombs' test is negative **MCQ!!**

★ SRC was the leading cause of death of systemic sclerosis patients till patients took **ACE inhibitors.**

Clinical Lab Findings

- Any new onset HTN with a BP of >150/85 or 20 mmHg increase from baseline is critical to recognize.
- Normotensive renal crisis can occur
- Urinalysis might show proteinuria and hematuria but **no RBC cast.** Because there is no GN!
- High creatinine is almost universal
- Anemia with positive hemolytic workup points to **microangiopathic hemolytic anemia**

Treatment

- Treatment is **control of BP** by reducing it 10 mmHg every 24 hours
- **Best** (and only) drug **Angiotensin Converting Enzyme Inhibitors** if there's allergy, use ARBs.
- Even if progress to ESKD 40% might recover and get back to near normal function.

Other Manifestation

Cardiac: Myocardial fibrosis leading to conduction abnormalities and arrhythmias, cardiomyopathy, and accelerated coronary artery disease.

Arthritis: similar to RA with erosions and joint destruction.

Myositis: manifested by weakness with no pain and high muscle enzymes.

Extra from books

Management in a nutshell:

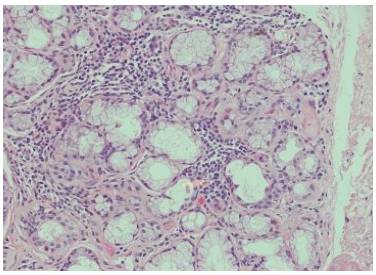
All patients should:
1)be educated 2) do stretching exercise regularly 3) use skin lubricants.

for:
Raynaud's: CCB
Interstitial lung disease: Cyclophosphamide
Pulmonary HTN: Endothelin receptor antagonist (bosentan) / Prostacyclin
Renal involvement: 1st drug ACEIs (Controls HTN and prevent SRC)
Esophageal symptoms: PPI / antacid
Malabsorption: Nutritional supplement + rotational ABx

Sjogren's Syndrome (SS)

-20% of patients with SSc have Sjögren Syndrome.

- It is a systemic chronic inflammatory disorder characterized by **lymphocytic infiltrates** in **exocrine organs.** Especially the **lacrimal** and **salivary** glands



- Most individuals with Sjögren's syndrome present with sicca (**dryness**) symptoms, such as:
  - Xerophthalmia (dry eyes) Keratoconjunctivitis Sicca
  - Xerostomia (dry mouth)
  - Vaginal dryness
  - Parotid gland enlargement because of severe **lymphocytic infiltration** leading to obstruction.
  - **GI problems**, because they might have reduced fluid secretion in the gut. Having **constipation**.

★ It's an **Underdiagnosed** disease
When it comes along with a connective tissue disease such as RA, SSc, SLE.. etc its called secondary SS

Criteria of SS

Diagnosis of primary SS:
at least 4 of the criteria listed below (you must have number 5 or number 6)

1. Ocular dryness
2. Oral dryness
3. Ocular signs (Schirmer test) A standard strip of filter paper is placed on the inside of the lower eyelid; wetting Of <10 mm in 5 min indicates defective tear production.-Kumar.
4. Oral signs (sialogram, scintigraphy or sialometry findings)
5. Positive minor salivary gland biopsy findings showing lymphocytic infiltration.
6. Positive anti–SSA anti-sjogren syndrome A or anti–SSB anti-sjogren syndrome B antibody results

-The best initial test is Schirmer test, while the most accurate is a lip or parotid gland biopsy. -Master.

Treatment of Glandular Manifestation

- Oral hygiene bc saliva inhibits bacteria
- Avoid sugars
- Florid products
- Parasympathomimetics (pilocarpine) will increase the secretion of saliva and tears.
- Artificial eye and mouth moisturizers
- Creams and lotions
- Vaginal lubricants

Extraglandular manifestations of SS

- Arthritis
- Myositis
- Pancytopenia
- Palpable purpura
- ILD
- Demyelinating disease like multiple sclerosis.
- Renal tubular acidosis **type 1**(Distal) Remember rheumatology is always type 1 ;p
- Interstitial nephritis
- Severe unexplained Fatigue

Treatment Extraglandular manifestations of SS

- Treatment of all include **immunosuppressive agents:**
  - Steroids
  - MTX **(except for ILD)**
  - Azathioprine
  - Cyclophosphamide
  - Rituximab
- For RTA (renal tubular acidosis) you just need to give NaHCO3 you don't give immunosuppressant because the damage has already happened.

Complications

- SS patients are at risk of developing Non-hodgkin's B cell **lymphoma** 20 times more than the general population
- Look for persistent LAP leukocyte alkaline phosphatase or disappearance of RF (usually it is positive)

★ Patient with SS coming with **fever**, **night sweat** and **lymphadenopathy** you have to suspect lymphoma

Most common cause of death in SS is malignancy. -Step up.

Idiopathic inflammatory Myopathies (IIM)

- Are a group of autoimmune myopathies that are characterized by symmetrical muscle **weakness mainly in the proximal muscles.** Mainly **striated (skeletal)** but can also involve the smooth muscles.
  Almost always the involvement is in the **proximal** muscle, only have distal muscle involvement in severe cases and if not treat it for long period
- It is **insidious** (never acute) and progressive.
- Pharyngeal muscle involvement can present as **dysphagia** and can lead to **aspiration pneumonia.**
- Chest wall weakness can present as **dyspnea** and lead to **type II respiratory failure.**
  1. Type I = only hypoxemia
  2. Type II = hypoxemia + hypercapnia
  - Myositis may lead to ILD causing type I respiratory failure so **ABG** is important to differentiate and know the site of pathology -either lung (type I) or muscles (type II)
- Can affect the heart and lead to **cardiomyopathy** very rare

Types of IIM

1. **Primary idiopathic polymyositis (PM)** inflammation and necrosis of skeletal muscle fibers only.
2. **Primary idiopathic dermatomyositis (DM)** when you have polymyositis with skin involvement "Rashes"
3. Polymyositis or dermatomyositis associated with malignancy
4. Childhood polymyositis or dermatomyositis
5. Polymyositis or dermatomyositis associated with another connective-tissue disease
6. Inclusion body myositis. very rare.
7. Miscellaneous (eg, eosinophilic myositis, myositis ossificans, focal myositis, giant cell myositis)

★ to make things easier:
When you only have proximal skeletal muscle weakness its **Polymyositis** when you have proximal skeletal muscle weakness+the characteristic skin rashes its **Dermatomyositis**!

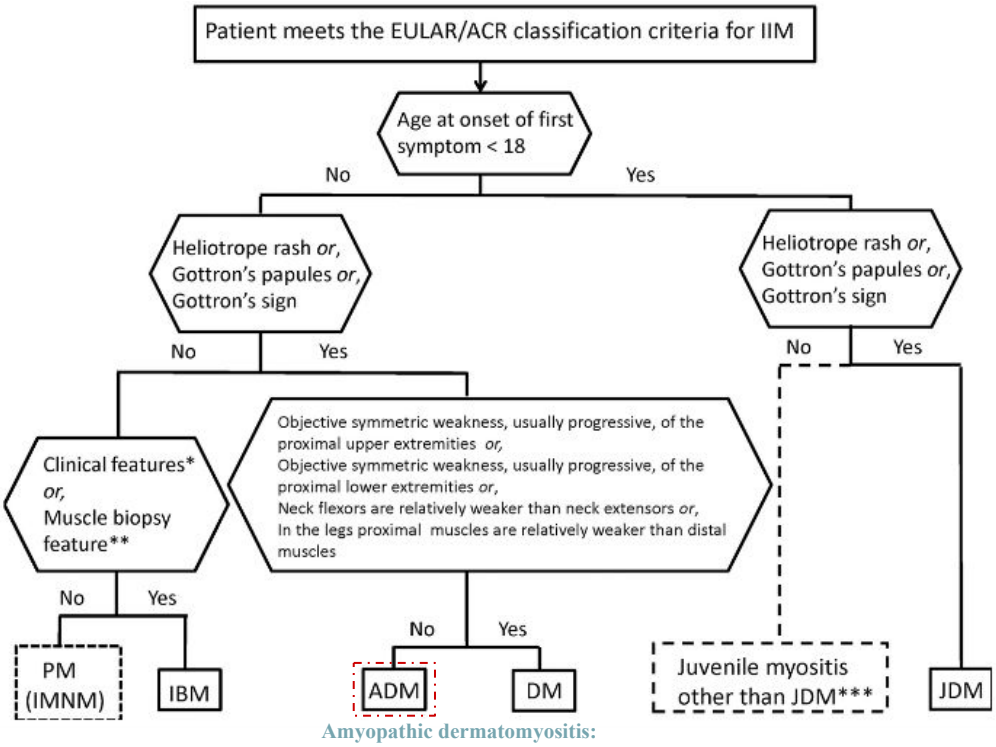
Don't memorize the criteria

Variable	muscle biopsy	muscle biopsy	Definition
Age of onset			
Age of onset of first symptom assumed to be related to the disease ≥18 years and <40 years	1.3	1.5	18 ≤ age (years) at onset of first symptom assumed to be related to the disease <40
Age of onset of first symptom assumed to be related to the disease ≥40 years	2.1	2.2	Age (years) at onset of first symptom assumed to be related to the disease ≥40
Muscle weakness			
Objective symmetric weakness, usually progressive, of the proximal upper extremities	0.7	0.7	Weakness of proximal upper extremities as defined by manual muscle testing or other objective strength testing, which is present on both sides and is usually progressive over time
Objective symmetric weakness, usually progressive, of the proximal lower extremities	0.8	0.5	Weakness of proximal lower extremities as defined by manual muscle testing or other objective strength testing, which is present on both sides and is usually progressive over time
Neck flexors are relatively weaker than neck extensors	1.9	1.6	Muscle grades for neck flexors are relatively lower than neck extensors as defined by manual muscle testing or other objective strength testing
In the legs, proximal muscles are relatively weaker than distal muscles	0.9	1.2	Muscle grades for proximal muscles in the legs are relatively lower than distal muscles in the legs as defined by manual muscle testing or other objective strength testing
Skin manifestations			
Heliotrope rash	3.1	3.2	Purple, lilac-colored, or erythematous patches over the eyelids or in a periorbital distribution, often associated with periorbital edema
Gottron's papules	2.1	2.7	Erythematous to violaceous papules over the extensor surfaces of joints, which are sometimes scaly. May occur over the finger joints, elbows, knees, malleoli, and toes
Gottron's sign	3.3	3.7	Erythematous to violaceous macules over the extensor surfaces of joints, which are not palpable
Other clinical m…			
Dysphagia or …	0.7	0.6	Difficulty in swallowing or objective evidence of abnormal motility of the esophagus
Laboratory mea…			
Anti–Jo-1 (an… autoantibod…	3.9	3.8	Autoantibody testing in serum performed with standardized and validated test, showing positive result
Elevated serum … lactate dehy… aminotransf… aminotransf…	1.3	1.4	The most abnormal test values during the disease course (highest absolute level of enzyme) above the relevant upper limit of normal
Muscle biopsy fe…			
Endomysial in… surrounding, but not invading, myofibers		1.7	Muscle biopsy reveals endomysial mononuclear cells abutting the sarcolemma of otherwise healthy, non-necrotic muscle fibers, but there is no clear invasion of the muscle fibers
Perimysial and/or perivascular infiltration of mononuclear cells		1.2	Mononuclear cells are located in the perimysium and/or located around blood vessels (in either perimysial or endomysial vessels)
Perifascicular atrophy		1.9	Muscle biopsy reveals several rows of muscle fibers, which are smaller in the perifascicular region than fibers more centrally located
Rimmed vacuoles		3.1	Rimmed vacuoles are bluish by hematoxylin and eosin staining and reddish by modified Gomori trichrome stain

For your interest

Diagnosis is made if the score is
Without biopsy ≥ 7.5
With biopsy ≥ 8.7

Algorithm for IIM

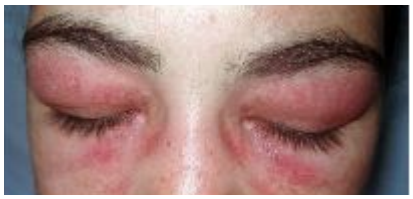


Amyopathic dermatomyositis:
Only skin manifestation with no muscle weakness

Rashes of DM

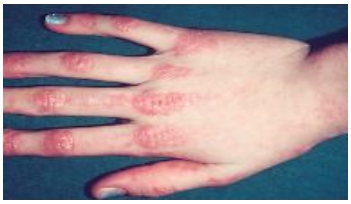
Most characteristic skin changes in DM

Heliotrope rash



purple discoloration is accompanied by periorbital edema

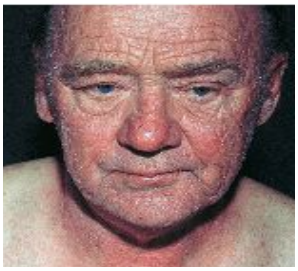
Gottron's papules/sign



purple-red, raised patches over the knuckles

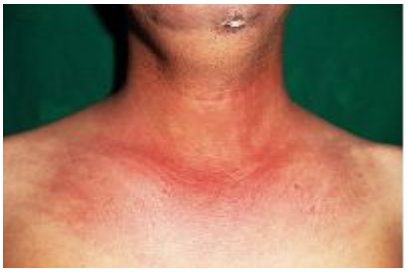
Photosensitivity

exaggerated reaction to light exposure.



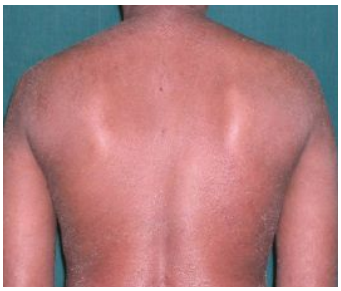
Shawl rash

لان شكله زي الشال



Erythroderma

Everything is red



Investigation

- Muscle enzymes are elevated:
  -CK -LD -AST -ALT -Aldolase
- Autoantibodies: **Anti Jo-1**
- MRI muscle: showing muscle edema **not specific**, any inflammation of the muscle will show edema.
- Muscle biopsy: lymphocytic infiltration
- EMG: myopathic changes we don't do it anymore.
- MOST IMPORTANT: **RULE OUT OTHER CAUSES OF MYOPATHIES.** Only diagnosed after FULL WORKUP!
- **Muscle biopsy** is the definitive test! Establishing diagnosis and excluding other causes of myopathies.

The challenge in the **scleroderma** is the treatment (management), in **Sjogren** the challenge is to bring the patient, in **Myositis** it's always a challenge to diagnose these patients.

Extramuscular manifestations

- Arthritis
- RP
- ILD (antisynthetase syndrome)

Treatment of all manifestations

- **Steroids** انغرقهم فيه!
  Oral prednisolone is the treatment of choice
- Methotrexate
- Mycophenolate mofetil
- Azathioprine
- Rituximab
- Intravenous immunoglobulins (with pharyngeal involvement, muscle chest wall involvement, rapidly progressive disease and refractory to other medications).

Summary

Scleroderma or systemic sclerosis (SSc)

SSc is characterized by **skin thickening, vasculopathy and autoantibody production.**

Based on cutaneous involvement, it is classified to:

Diffuse disease	Limited form
• more internal organ involvement • Anti-topoisomerase/RNA polymerase III antibodies • worse prognosis.	• has a higher risk of PAH • anti-centromere antibodies • more indolent

Autoantibodies

- **Scl-70 (topoisomerase):** is associated with diffuse subset,ILD, and reduced risk of PAH.
- **Anti-centromere:** limited subset, PAH and DU.
- **RNA polymerase III:** associated with SRC, malignancy
- associated SSc, and mortality.
- **Scl-PM:** associated with myositis overlap.

Skin the Largest and Most Important Organ in SSc

Treatment

Skin involvement	Raynaud's phenomenon	Digital Ulcer
• Methotrexate • Mycophenolate mofetil • Cyclophosphamide • Rituximab • With some steroids	• Treat pain adequately. • Calcium channel blockers • oral and IV prostaglandins. • IV iloprost better than nifedipine.	•Calcium channel blockers • Endothelin receptor antagonist (bosentan) • Phosphodiesterase inhibitors • Prostacyclin

Other manifestation

ILD

is a specific form of chronic, progressive fibrosing interstitial pneumonia leading to Progressive loss of pulmonary function, and respiratory failure.

• Diagnosis: imaging and (PFT).

• Treatment:

• Cyclophosphamide (standard for induction)

• Alternative could be: MMF or rituximab.

•Maintenance includes: MMF, AZA and RTX.

• Steroids are a part of induction and maintenance.

PAH

defined as PAP ≥ 25mmHg with a pulmonary wedge pressure ≤ 15 mmHg.

• Diagnosis:

• The first investigation to order is echo.

• PFT may show isolated low DLCO

• The gold diagnostic tool is right sided heart catheterization.

• Treatment:

• Endothelin Receptor Antagonists

• Phosphodiesterase Inhibitors

• Prostacyclins

Summary

GI involvement

• is the most common internal organ to be involved
which includes:
- Esophagus: dysmotility and reflux leading to strictures
- Stomach: gastroparesis, watermelon appearance with telangiectasia.
- Small bowel: blind loop syndrome, chronic diarrhea and malabsorption.
- Large bowel: chronic constipation, fish mouth diverticula.
- Anorectal incontinence

Scleroderma Renal Crisis

• Patients with SSc usually have low BP, **once you see high BP suspect SRC.**

• Diagnosis:
• Any new onset HTN with a BP of >150/85 or 20 mmHg increase from baseline is critical to recognize.
• Proteinuria and hematuria but no RBC cast.
• High creatinine is almost universal.
• Microangiopathic hemolytic anemia.
• Treatment:
• ACE inhibitors (best and only)

Sjogren's Syndrome (SS)

• *is a systemic chronic inflammatory disorder characterized by lymphocytic infiltrates in exocrine organs.*

Symptoms
- Xerophthalmia (dry eyes)
- Xerostomia (dry mouth)
- Vaginal dryness
- Parotid gland enlargement

Extraglandular manifestations of SS
• Arthritis
• Myositis
• Pancytopenia
• Palpable purpura
• ILD
• Demyelinating disease
• Renal tubular acidosis type 1
• Interstitial nephritis
• Fatigue

Treatment
• Steroids • MTX (except for ILD)
• Azathioprine • Cyclophosphamide • Rituxmiab

Idiopathic inflammatory Myopathies (IIM)

• *Are a group of autoimmune myopathies that are characterized by muscle weakness mainly in the proximal muscles.*
• Pharyngeal muscle involvement can present as dysphagia and can lead to aspiration pneumonia.
• Chest wall weakness can present as dyspnea and lead to type II respiratory failure.
• Can affect the heart and lead to cardiomyopathy

Investigation • MOST IMPORTANT: RULE OUT OTHER CAUSES OF MYOPATHIES.

Treatment
• Steroids
• Methotrexate
• Mycophenolate mofetil
• Azathioprine
• Rituximab
• Intravenous immunoglobulins

Questions

1-A 45-year-old woman has pain in her fingers on exposure to cold, arthralgias, and difficulty swallowing solid food. She has a few telangiectasias over the chest but no erythema of the face or extensor surfaces. There is slight thickening of the skin over the hands, arms, and torso. What is the best diagnostic test?

a. Rheumatoid factor
b. Antinuclear, anti-topoisomerase I, and anticentromere antibodies
c. ECG
d. BUN and creatinine

2-A 60-year-old woman complains of dry mouth and a gritty sensation in her eyes. She states it is sometimes difficult to speak for more than a few minutes. There is no history of diabetes mellitus or neurologic disease. The patient is on no medications. On examination, the buccal mucosa appears dry and the salivary glands are enlarged bilaterally. Which of the following is the best next step in evaluation?

a. Lip biopsy
b. Schirmer test and measurement of autoantibodies
c. IgG antibody to mumps virus
d. A therapeutic trial of prednisone for 1 month

3-A 45-year-old woman presents to the rheumatology clinic with a three-month history of itchy, dry eyes and a persistently dry mouth. She also mentions that her fingers have been extremely cold, occasionally turning blue after going outside in the morning. Shirmer's test is positive. What is the most likely diagnosis?

a. Systemic sclerosis
b. Raynaud's disease
c. SLE
d. Primary Sjögren's syndrome

4-A 24-year-old woman presents to her GP complaining of cold hands and feet. This has been ongoing for the past three months and is especially bad when she goes out in the mornings and may last for hours. On further questioning, she mentions that her hands sometimes turn blue or red and that gloves are unhelpful. She has otherwise been feeling well and has no past medical history. What is the most appropriate treatment?

a. Propranolol
b. Aspirin
c. Nifedipine
d.Prednisolone

Answers: 1:B, 2:B, 3:D, 4:C

Questions

5- A 45-year-old woman presents to her physician with an 8-month history of gradually increasing limb weakness. She first noticed difficulty climbing stairs, then problems rising from a chair, and, finally, lifting her arms above shoulder level. Aside from some difficulty swallowing, she has no ocular, bulbar, or sphincter problems and no sensory complaints. Family history is negative for neurological disease. Examination reveals significant proximal limb and neck muscle weakness with minimal atrophy, normal sensory findings, and normal deep tendon reflexes. Which of the following is the most likely diagnosis in this patient?

a. Polymyositis
b. Cervical myelopathy
c. Myasthenia gravis
d. Mononeuritis multiplex

6- Over the last 6 weeks a 35-year-old nurse has developed progressive difficulty getting out of chairs and climbing stairs. She can no longer get in and out of the bathtub. She has no muscle pain and takes no regular medications. She does not use alcohol and does not smoke cigarettes. On examination she has a purplish rash that involves both eyelids. There is weakness of the proximal leg muscles. What is the best next diagnostic test?

a. Vitamin B 12
b. Chest x-ray
c. HLA B27 level
d. Creatine kinase (CK)

Answers: 5:A, 6:D