
بسم الله الرحمن الرحيم

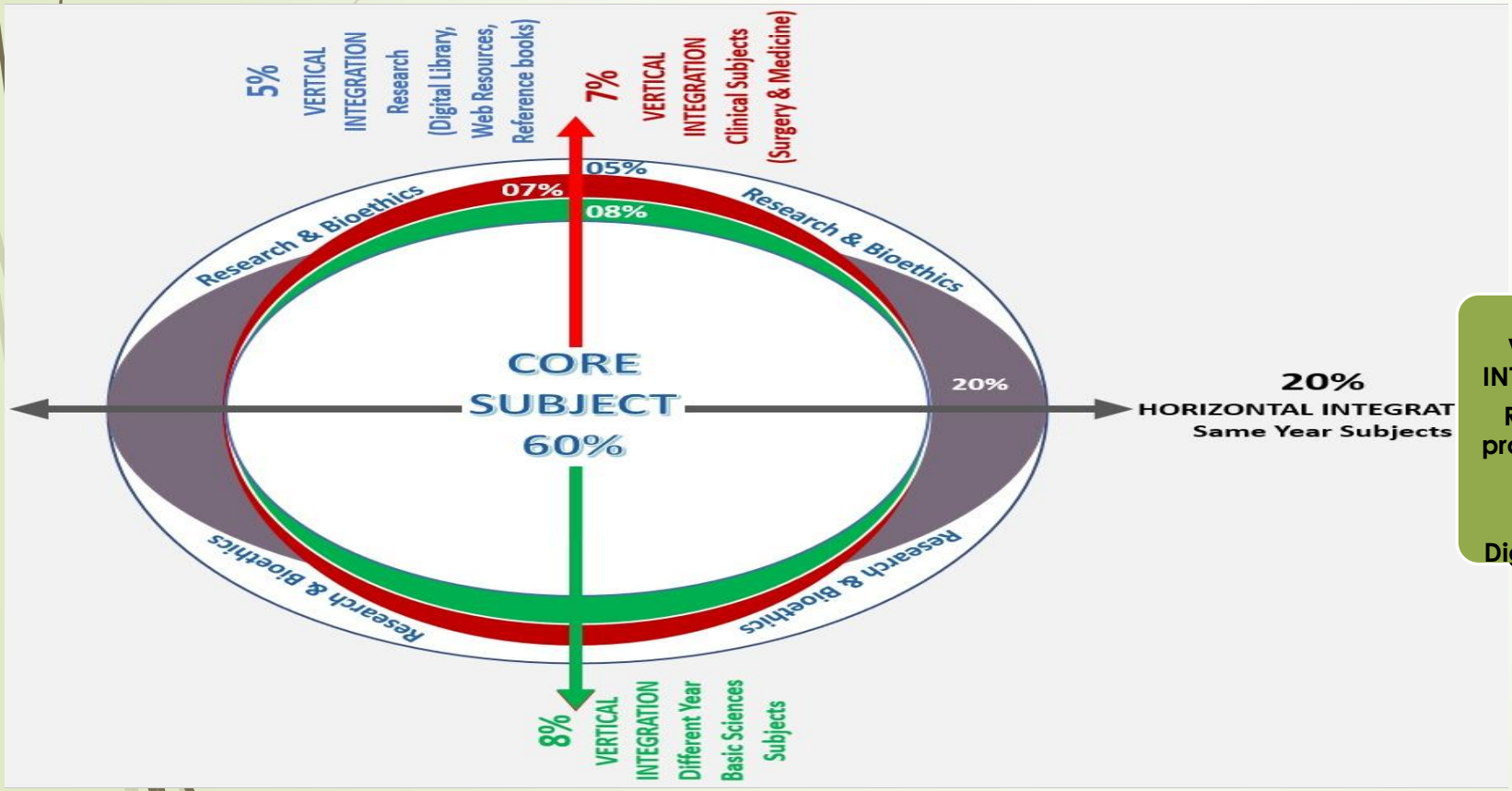

رَبَّنَا لَا تُزِغْ قُلُوبَنَا بَعْدَ إِذْ هَدَيْتَنَا
وَهَبْ لَنَا مِن لَّدُنكَ رَحْمَةً ۚ
إِنَّكَ أَنتَ الْوَهَّابُ ٨
Our Lord! Let not our hearts deviate after You have guided us, and grant us mercy from You. Truly, You are the Bestower.
[Al-Quran 3:8]

Motto

Vision

- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

Professor Umar Model of Integrated Lecture



60% CORE SUBJECT

20% HORIZONTAL INTEGRATION Physiology biochemistry

8% VERTICAL INTEGRATIO N Pathology pharmacolo gy

7% VERTICAL INTEGRATION Clinical integration

5% VERTICAL INTEGRATION Research, professionalis m Ethics Digital library

RHEUMATOLOGY
LECTURE:4

"Systemic Auto-immune Diseases"

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Learning Objectives

At the end of this session students will be able to learn:

- How to diagnose "Lupus and related disorders" on the basis of history and examination
- Relevant Investigations
- Guidelines and recent advances

Rheumatological Diseases

- Joint Diseases (Arthritis)
- Soft tissue Rheumatism
- Systemic Diseases (Auto-immune/Vasculitis)
- Bone Disorders

Core Concept

Case Scenario

25-years old lady presented with complaint of **fatigue**, **arthralgias** (involving small joints of both hands, with EMS lasting for few minutes) and **rash** on her face (cheeks) for 3 months.

Case Scenario

Basic labs are notable for a total lymphocyte count of 500, RBC casts and 3+ proteinuria on urinanalysis. Auto-antibody testing is notable for high titers of ANA, anti-dsDNA and anti-smith antibodies.

Case Scenario

- Systemic Lupus Erythematosus

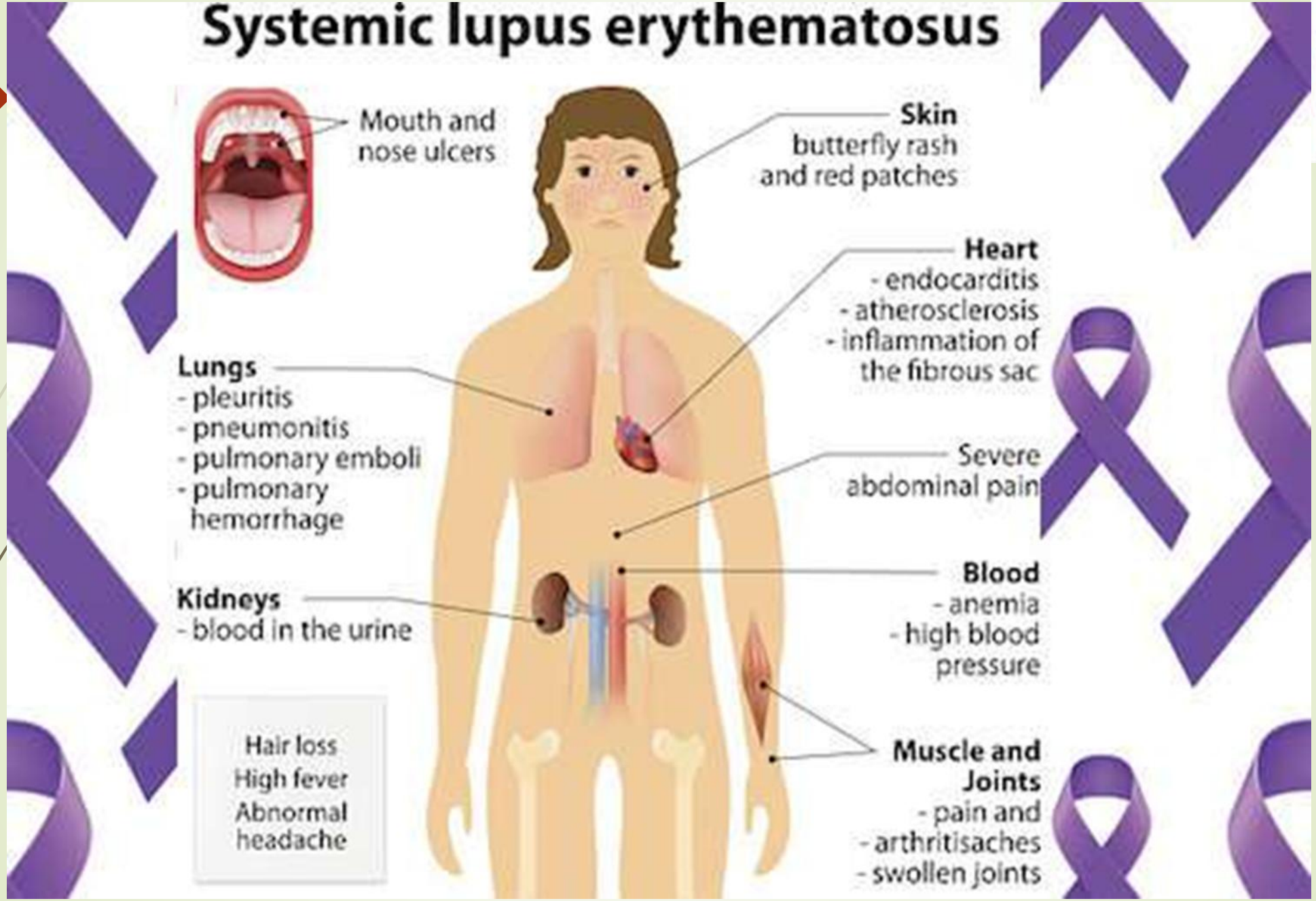
(Prototypic auto-immune disease, mostly involving young females)

Case Scenario

- Every lupus patient is different
  (Organ system /Severity)

- Unique disease course

Systemic lupus erythematosus



Lupus Work-Up

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Initial Test

Anti-nuclear antibodies (ANA)

If positive

SLE-specific Tests

Anti-double-stranded DNA (dsDNA)
Anti-Smith
Anti-ribonucleoprotein (also in Mixed Tissue Connective Disorder)
Anti-LA/SSB (also in Sjögren's syndrome)

Other Labs

CBC
Chem panel
Complement levels
ESR
Urinalysis

Rule out Drug-Induced Lupus

Procainamide, Methyldopa, Quinidine, and Hydralazine
Antihistone antibodies often positive

New EULAR/ACR criteria for the classification of SLE

Clinical domains	Points
Constitutional domain	
Fever	2
Cutaneous domain	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous or discoid lupus	4
Acute cutaneous lupus	6
Arthritis domain	
Synovitis or tenderness in at least 2 joints	6
Neurologic domain	
Delirium	2
Psychosis	3
Seizure	5
Serositis domain	
Pleural or pericardial effusion	5
Acute pericarditis	6
Hematologic domain	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Renal domain	
Proteinuria > 0.5 g/24 hr	4
Class II or V lupus nephritis	8
Class III or IV lupus nephritis	10

Immunologic domains	Points
Antiphospholipid antibody domain	
Anticardiolipin IgG > 40 GPL *or* anti-β2GP1 IgG > 40 units *or* lupus anticoagulant	2
Complement proteins domain	
Low C3 *or* low C4	3
Low C3 *and* low C4	4
Highly specific antibodies domain	
Anti-dsDNA antibody	6
Anti-Sm antibody	6

REFERENCE: Aringer et al. Abstract #2928. 2018 ACR/ARHP Annual Meeting

- ✓ **Classification criteria are not diagnosis criteria**
- ✓ All patients classified as having SLE must have ANA ≥ 1:80 (entry criterion)
- ✓ Patients must have ≥ 10 points to be classified as SLE
- ✓ Items can only be counted for classification if there is no more likely cause
- ✓ Only the highest criterion in a given domain counts
- ✓ SLE classification requires points from at least one clinical domain

@Lupusreference

SLE Treatment

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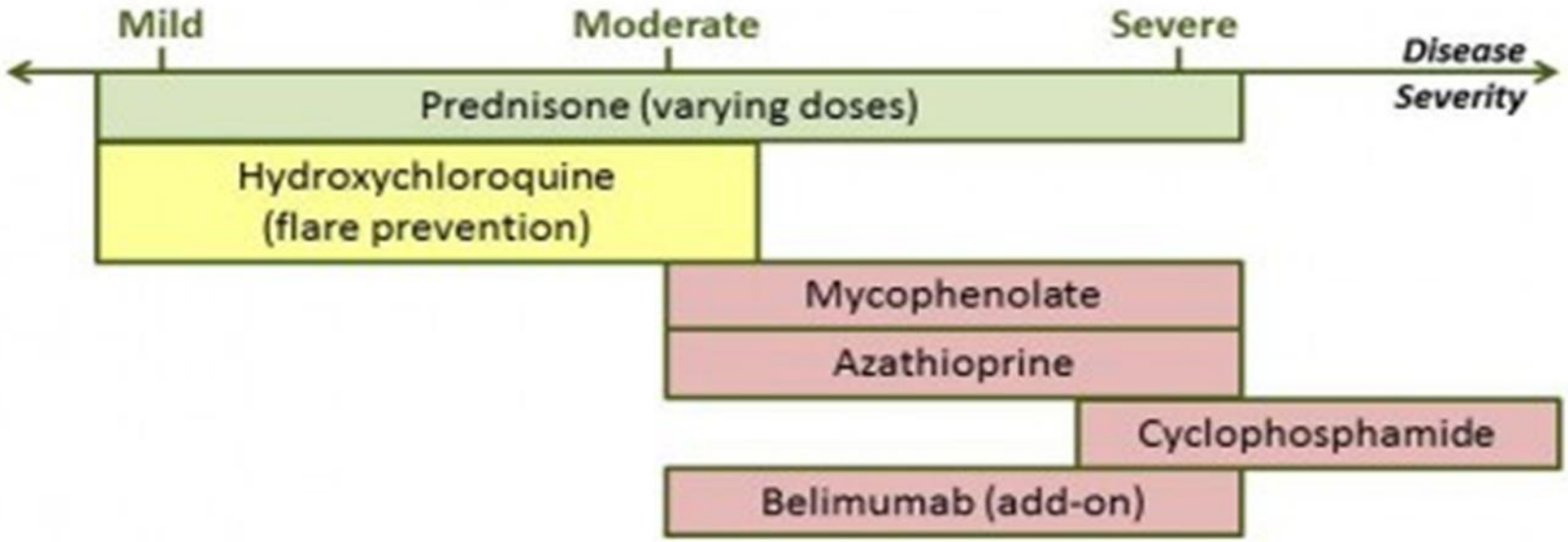


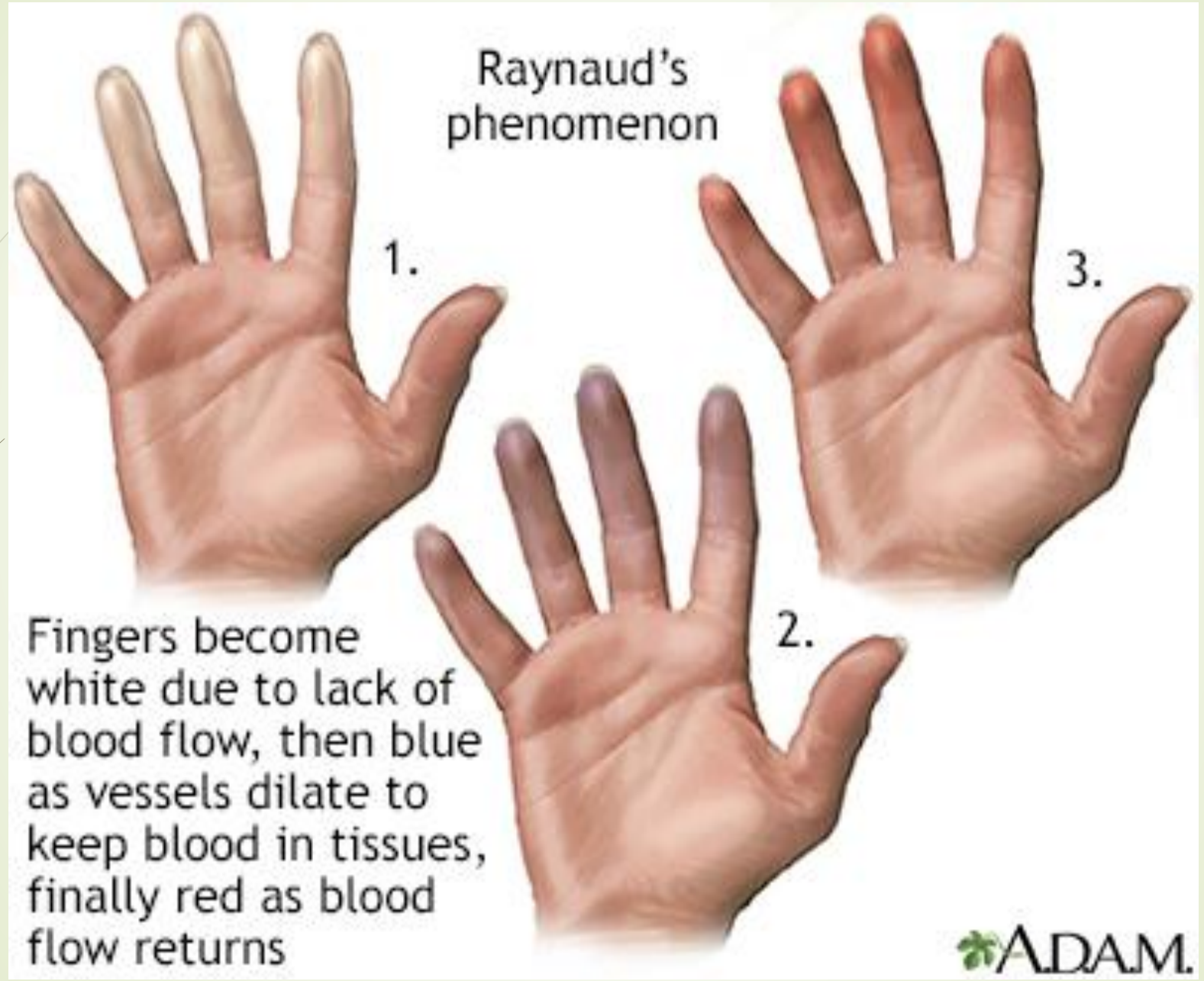
Hydroxychloroquine use requires annual ophthalmology visits due to risk of retinopathy

Case Scenario

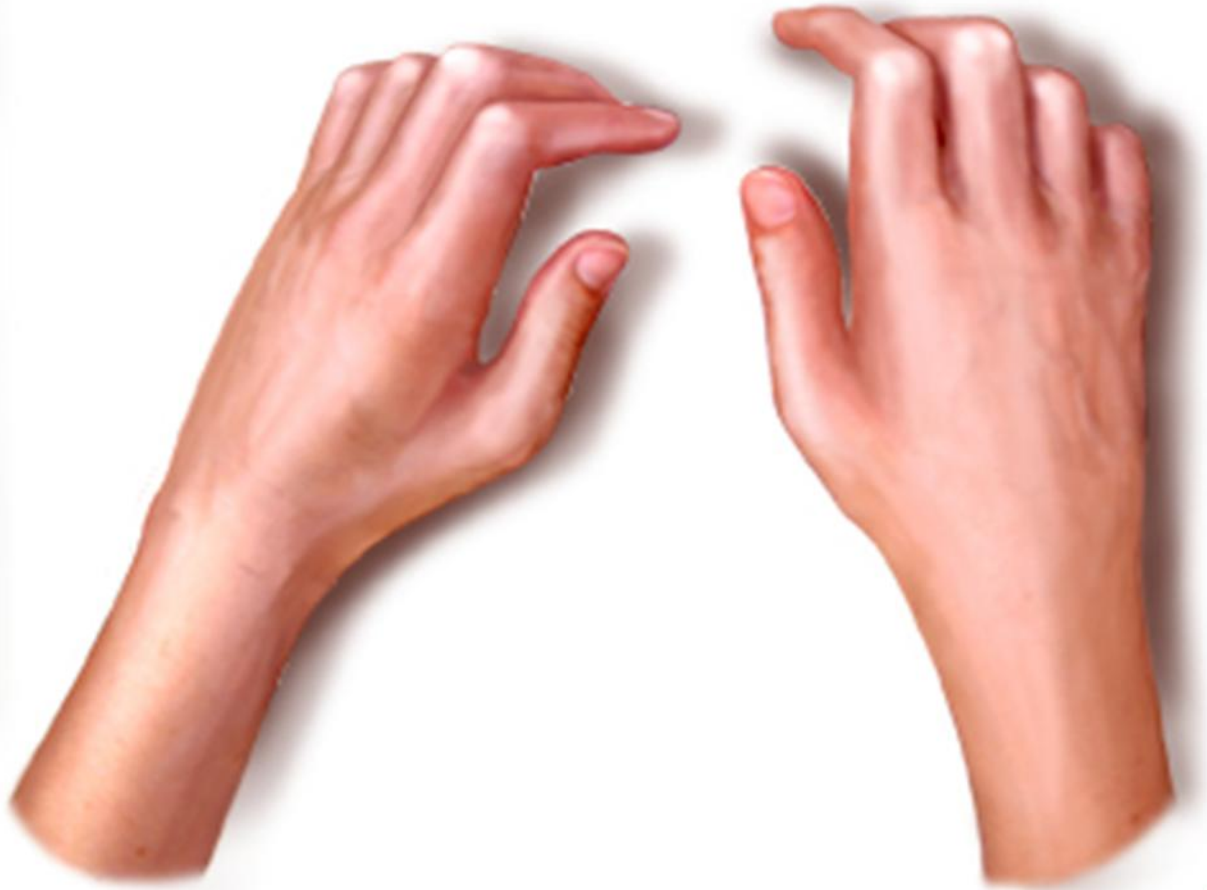
- 35-years old lady presented with complaints of **Raynaud's** phenomenon and **gastroesophageal reflux** for 2 years. Her GPE revealed **sclerodactyly**, **narrow oral aperture** and diffuse **thickening of skin** involving both hands extending upto elbows.

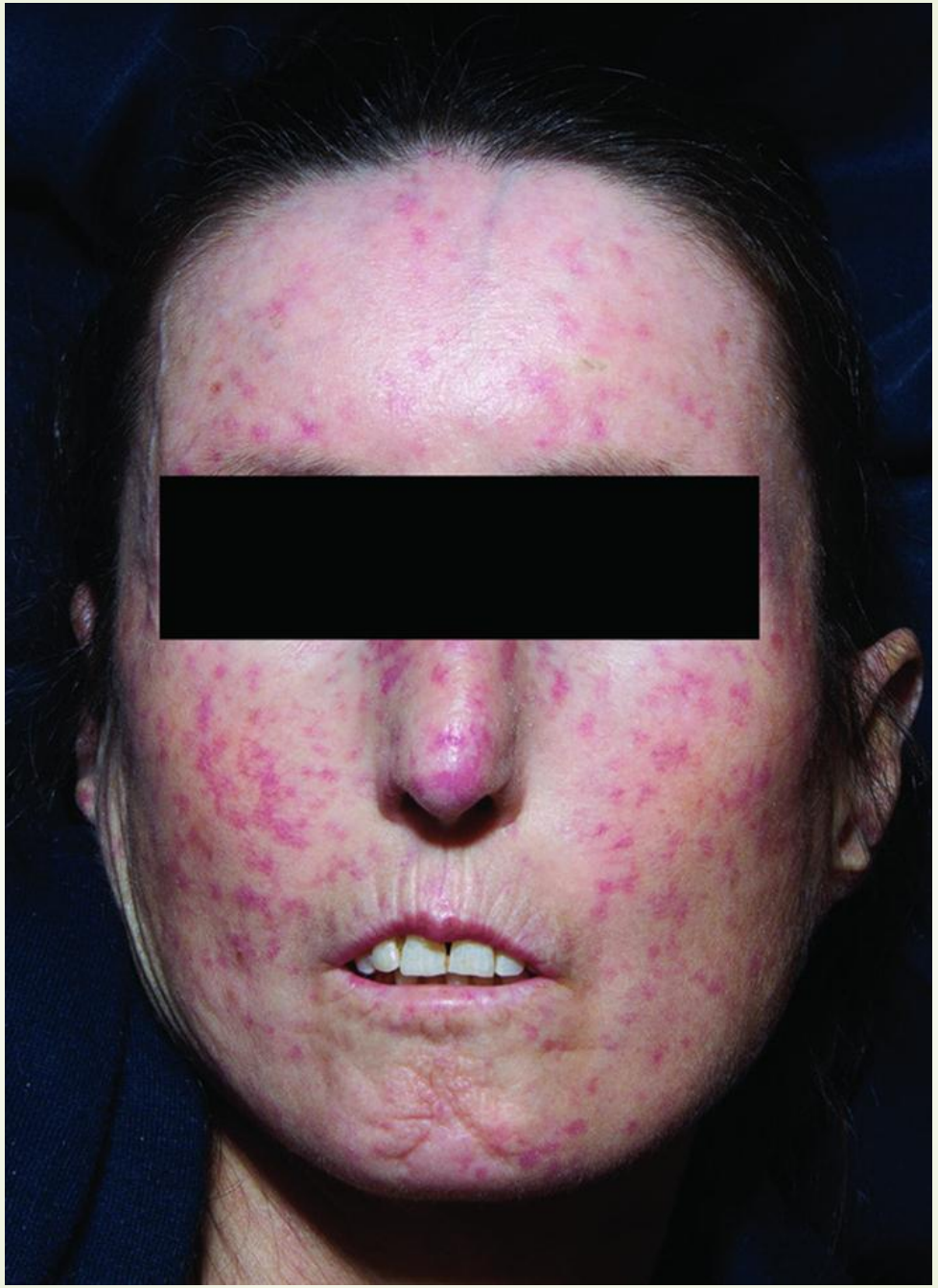
Case Scenario

- Systemic Sclerosis


Raynaud's phenomenon
1.
2.
3.
Fingers become white due to lack of blood flow, then blue as vessels dilate to keep blood in tissues, finally red as blood flow returns
A.D.A.M.

In scleroderma, the abnormal build-up of fibrous tissue in the skin can cause the skin to tighten so severely that the fingers curl and lose their mobility





Box 1 - American college of rheumatology diagnostic criteria for systemic sclerosis.*

Major criterion

- Proximal sclerodermatous skin changes (proximal to the metacarpophalangeal joints)

Minor criteria

- Sclerodactyly
- Digital pitting scars of fingertips or loss of substance of the distal finger pads
- Bibasilar pulmonary fibrosis

* The patient should fulfill the major criterion or two of the three minor criteria.

Management

- Raynaud's
- Skin tightness
- Lung fibrosis
- Scleroderma renal crisis

Case Scenario

- 55-years old lady with no co-morbids, has noted difficulty in getting up from chair and reaching for items above her head.

- On proximal muscle testing, she can raise her thighs and arms against gravity but cant hold them there even against slight resistance.Distal muscle strength, reflexes and sensations are intact

Case Scenario

- The laboratory tests are remarkable for an elevated creatinine kinase of 3000U/L.

- Further work up revealed evidence of inflammation in bilateral thigh muscles on STIR MRI and EMG consistent with inflammatory myopathy and normal NCS.

Case Scenario

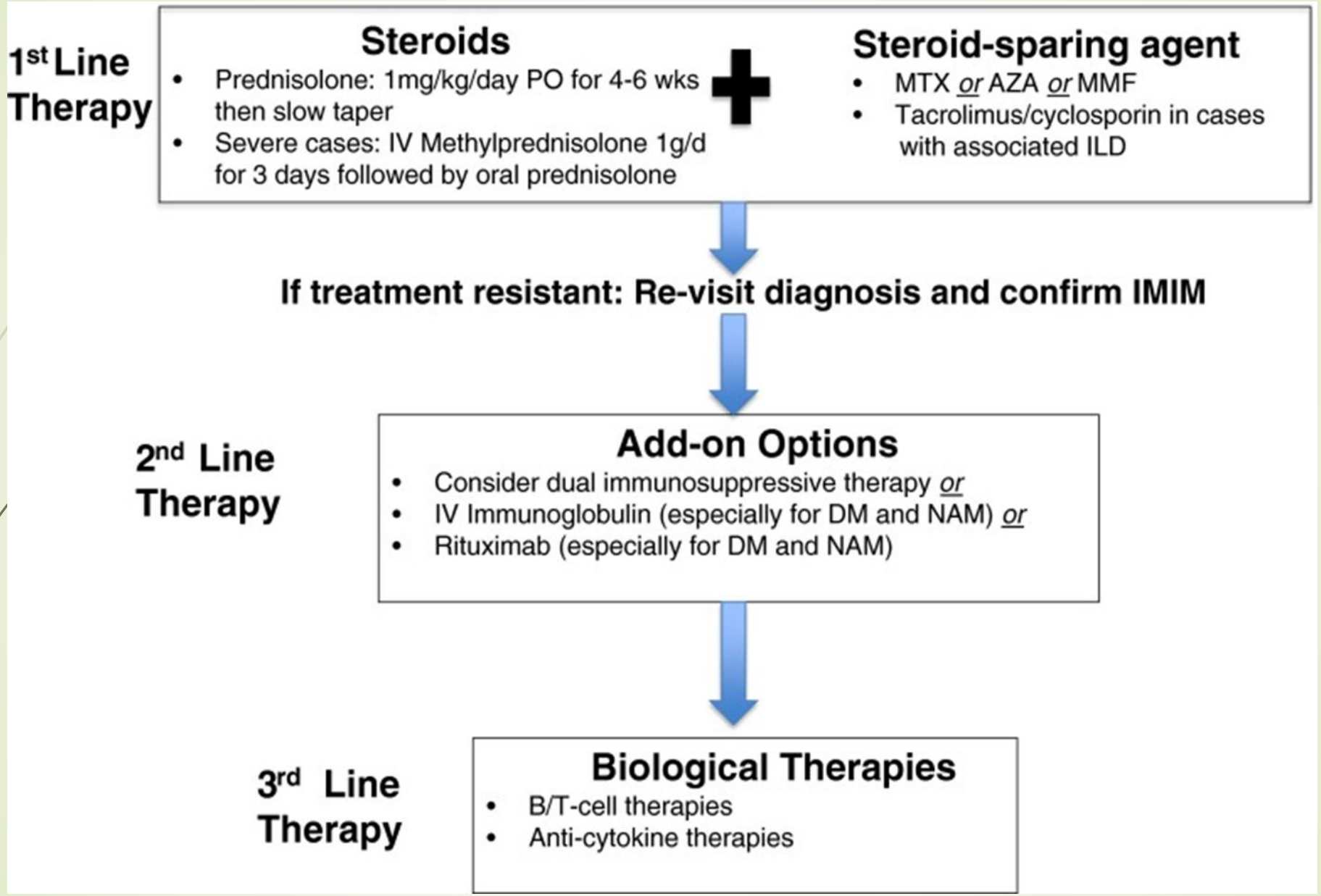
Inflammatory myopathy

(Polymyositis & Dermatomyositis)

Polymyositis / Dermatomyositis

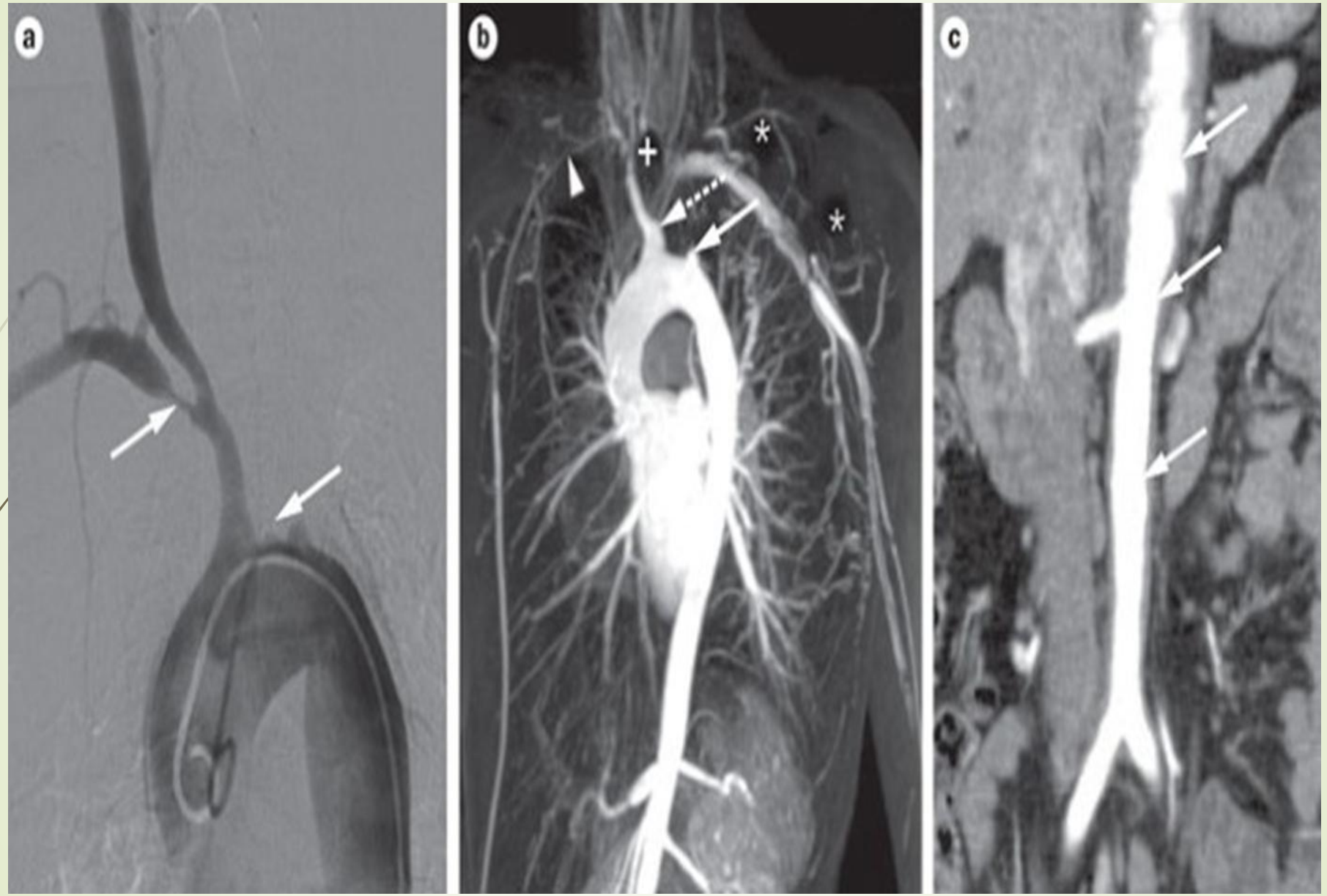
- **Diagnostic criteria**
  1. Proximal muscle weakness
  2. Elevated serum CK
  3. Myopathic changes on EMG
  4. Muscle biopsy demonstrating lymphocytic inflammation
  5. Dermatomyositis: Skin rash as well as criteria above
     - Definitive diagnosis with four criteria having been met
     - Probable with three
     - Possible with two

Bohan & Peter (1975). *NEJM.*


1st Line Therapy
Steroids
Prednisolone: 1mg/kg/day PO for 4-6 wks then slow taper
Severe cases: IV Methylprednisolone 1g/d for 3 days followed by oral prednisolone
Steroid-sparing agent
MTX or AZA or MMF
Tacrolimus/cyclosporin in cases with associated ILD
If treatment resistant: Re-visit diagnosis and confirm IMIM
2nd Line Therapy
Add-on Options
Consider dual immunosuppressive therapy or
IV Immunoglobulin (especially for DM and NAM) or
Rituximab (especially for DM and NAM)
3rd Line Therapy
Biological Therapies
B/T-cell therapies
Anti-cytokine therapies

Case Scenario

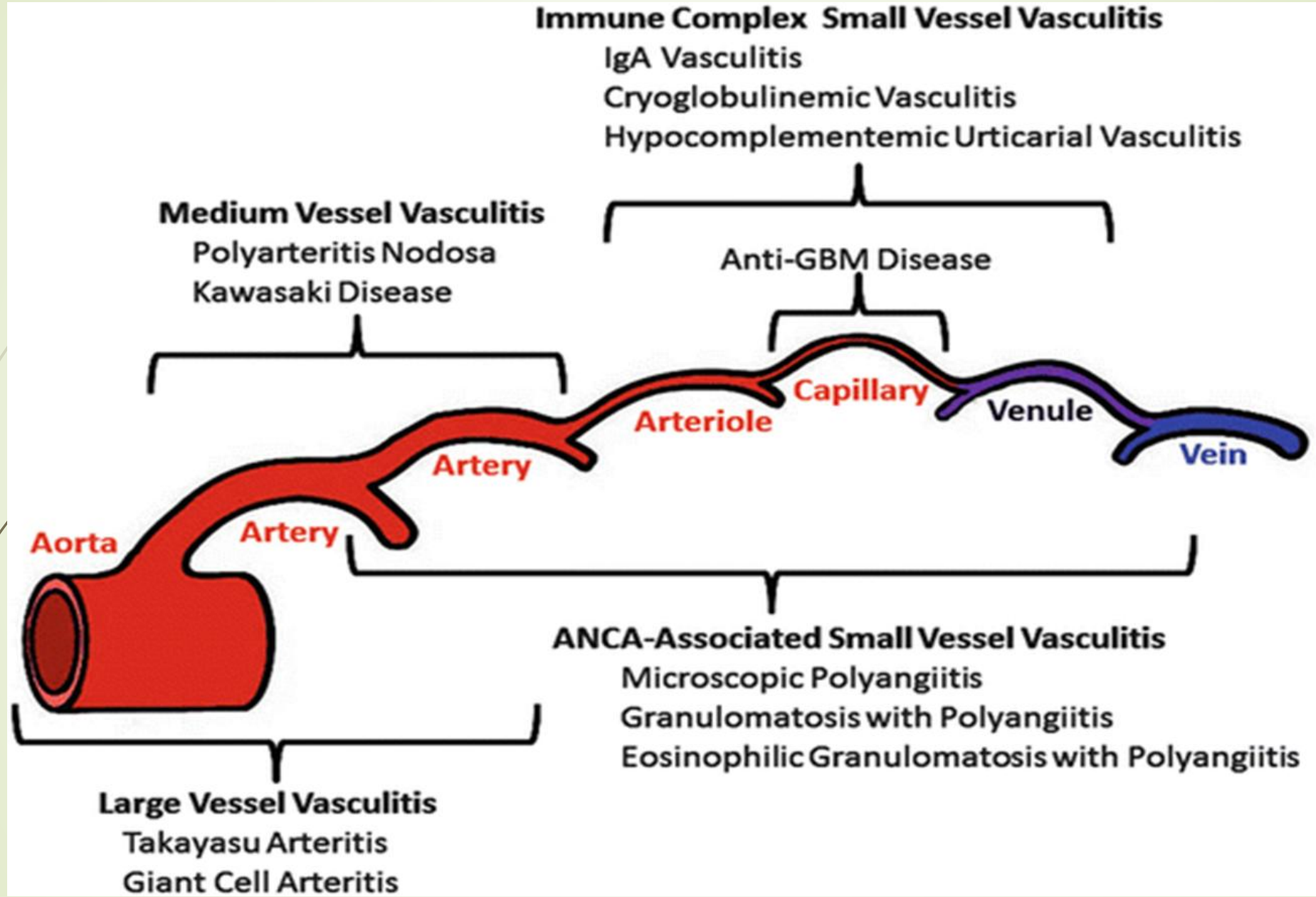
24-years old lady presented with complaints of feverish feeling and fatigue for last 1 year. On GPE, her **right radial and brachial pulses were not palpable**. She had audible **bruits** over bilateral sub-clavian and renal arteries.


a
b
c

Case Scenario

Takayasu's Arteritis

(Large vessel Vasculitis)


Immune Complex Small Vessel Vasculitis
IgA Vasculitis
Cryoglobulinemic Vasculitis
Hypocomplementemic Urticarial Vasculitis
Medium Vessel Vasculitis
Polyarteritis Nodosa
Kawasaki Disease
Anti-GBM Disease
Capillary
Arteriole
Venule
Vein
Artery
Artery
Aorta
ANCA-Associated Small Vessel Vasculitis
Microscopic Polyangiitis
Granulomatosis with Polyangiitis
Eosinophilic Granulomatosis with Polyangiitis
Large Vessel Vasculitis
Takayasu Arteritis
Giant Cell Arteritis

Take home message

- Systemic Lupus Erythematosus is a prototypic auto-immune disease with multi-system involvement.

- Every lupus patient is different in terms of organ system involvement and severity and needs multi-disciplinary care (rheumatologist, dermatologist, neurologist and nephrologist as indicated).

Recent Advances

- Belimumab is novel biologic which was initially approved for management of non-renal, non-neurological lupus has now been approved for management of 'Lupus Nephritis'

References

- Davidson's textbook of Internal Medicine
- American College of Rheumatology guidelines for management of Systemic Lupus Erythematosus

جَزَاكَ ٱللَّهُ خَيْرًا