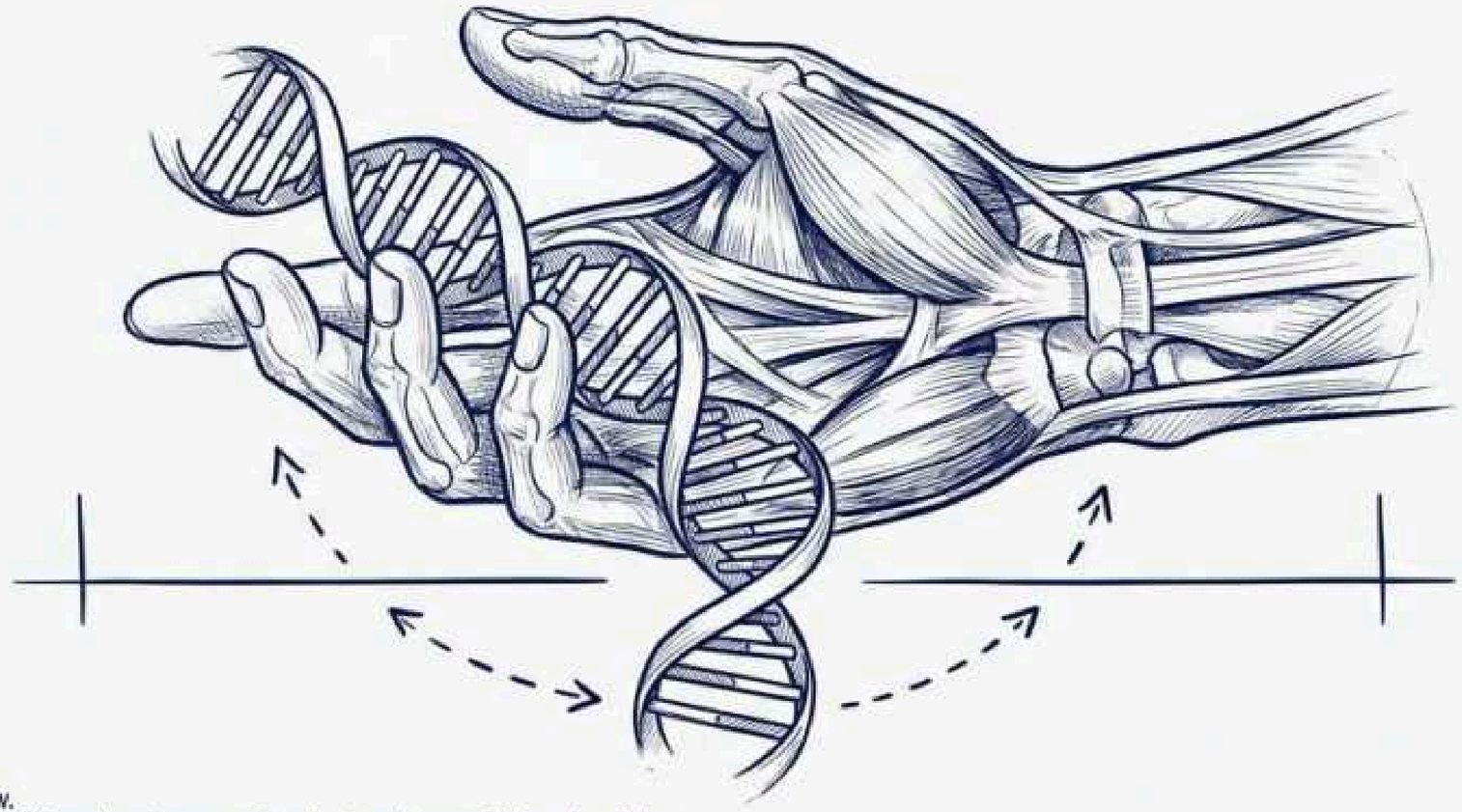
Connective Tissue & Muscle Diseases

Clinical presentations, autoimmune pathology, and inherited myopathies.

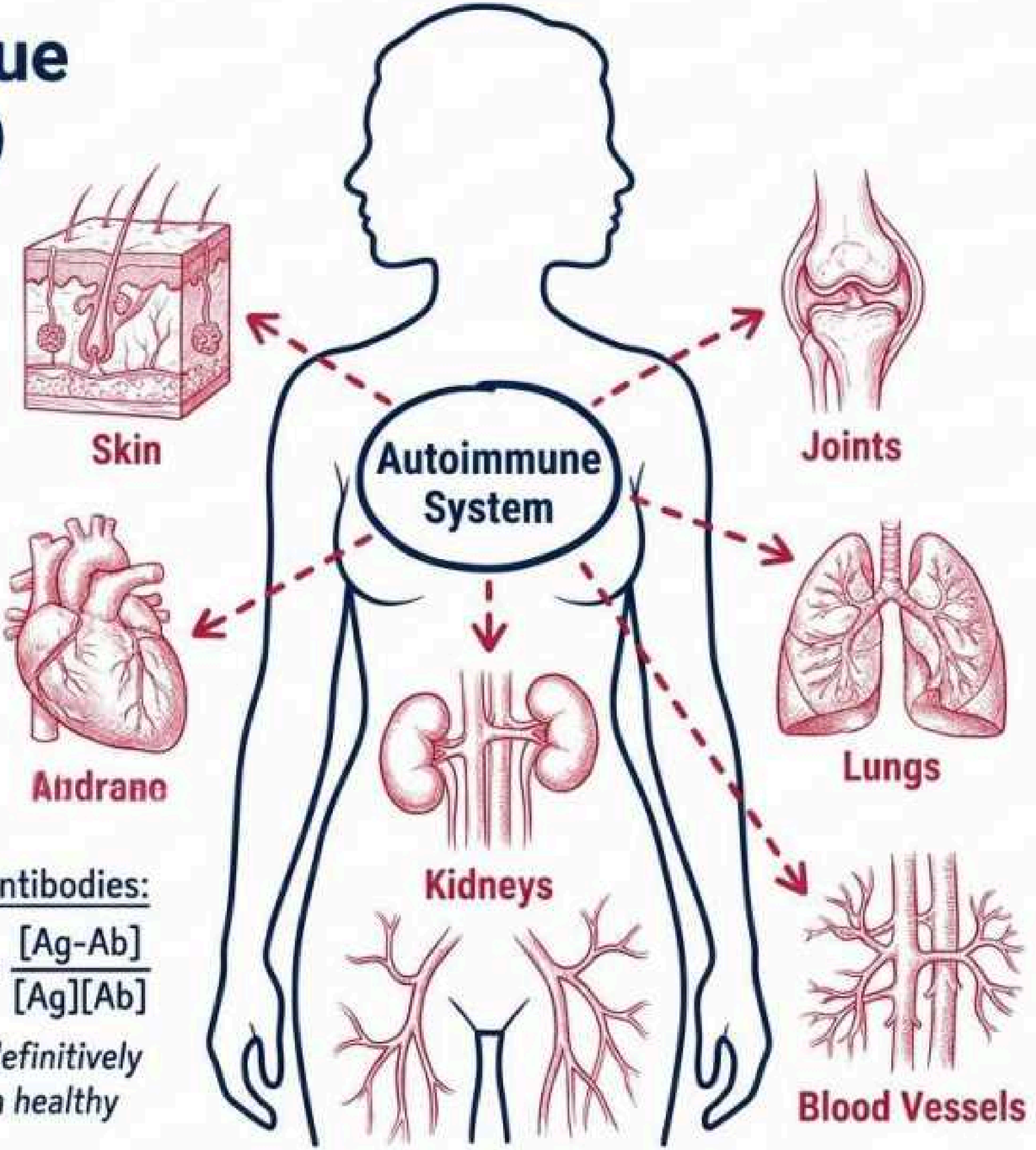


Medical Course 533 B – Lecture 5 Overview.
At a glance: Systemic lupus erythematosus, Sjögren's syndrome, systemic sclerosis, vasculitis, polymyalgia rheumatica, giant cell arteritis, inflammatory myopathies, and inherited muscle diseases.

Connective Tissue Diseases (CTDs)

¶ 5.1

Much commoner in women.



Diagnostic Caveat [ANA Tests]

Blood Tests: Autoantibodies (especially Antinuclear Antibodies / ANA) aid diagnosis.

Warning: A positive test alone is common in healthy people. Positive ≠ Disease.

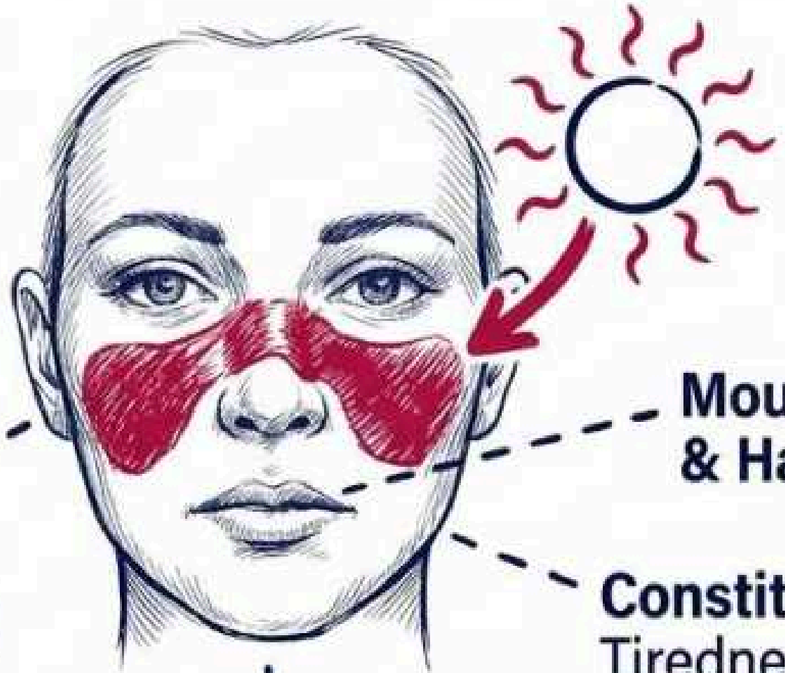
Receptor-Binding Kinetics of Autoantibodies:

$$[Ag] + [Ab] \rightleftharpoons [Ag\text{-}Ab] \Rightarrow K_a = \frac{[Ag\text{-}Ab]}{[Ag][Ab]}$$

(Presence of autoantibodies does not definitively equal pathogenic complex formation in healthy individuals).

Systemic Lupus Erythematosus (SLE)

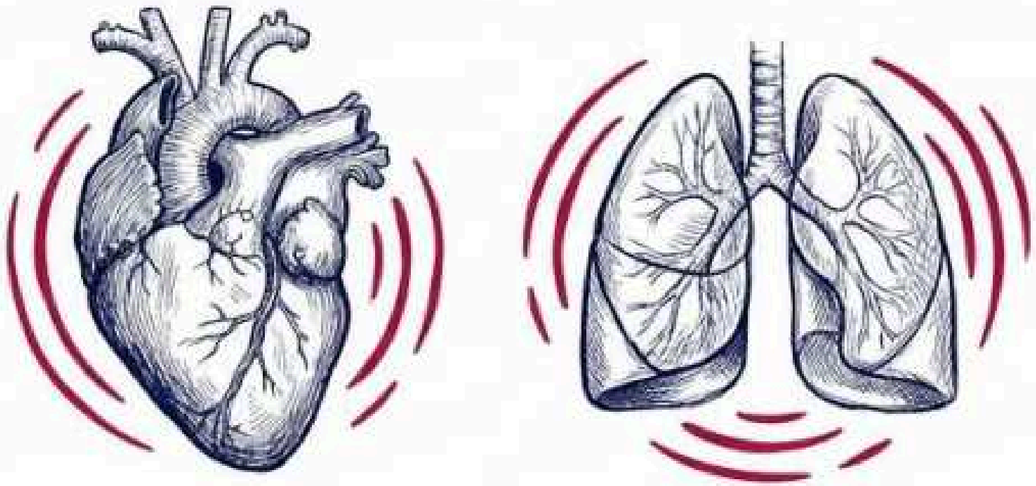
Usually called lupus; can affect almost any organ.



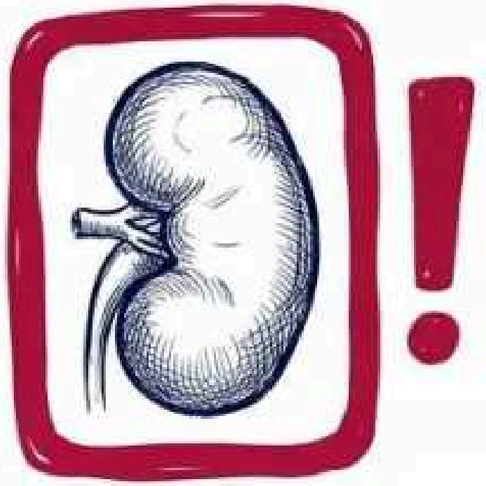
Rash across cheeks/nose (worsens in sunlight)

Mouth ulcers & Hair loss

Constitutional: Tiredness & Joint pain



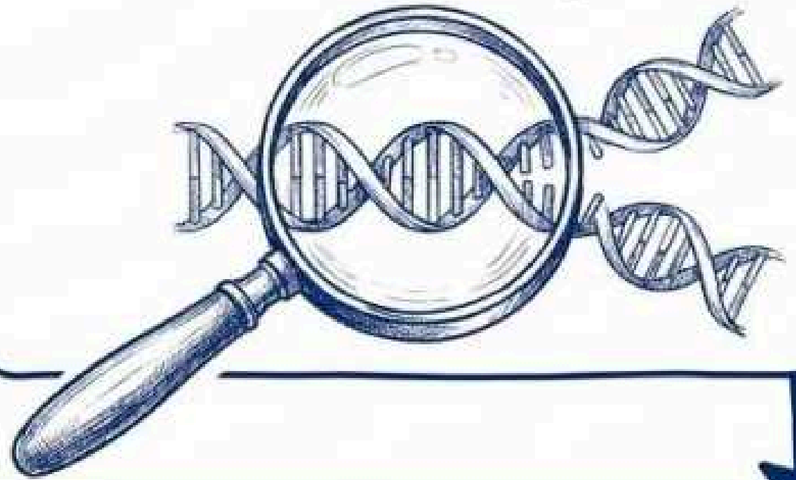
Cardiopulmonary: Inflammation of organ linings (pleurisy/pericarditis).



Renal Threat: Lupus nephritis (one of its most serious forms, as described in Medicine 523 B).

Diagnosing & Treating Lupus

Diagnosis: Clinical + Serological



Confirmed by combining clinical physical features with blood markers.

Key Biomarkers: Antibodies to double-stranded DNA (anti-dsDNA) & complement levels.

Stepped Treatment Protocol:

Step 1: Baseline

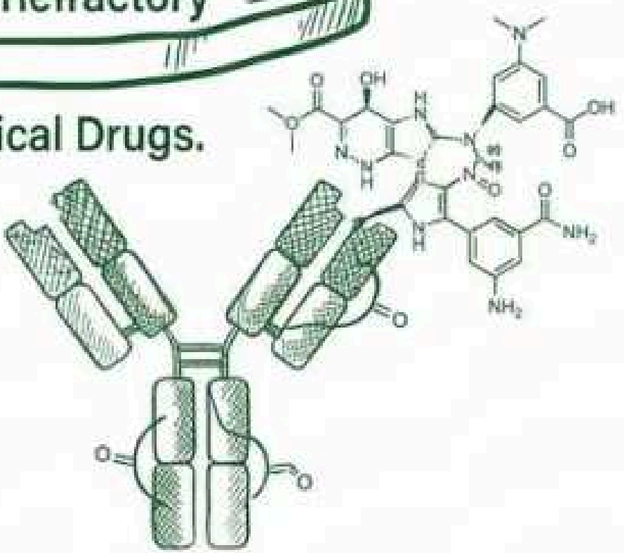
Hydroxychloroquine.
Originally an antimalarial drug.
Recommended for almost everyone (reduces flares, improves survival).

Step 2: Organ Involvement

Steroids & Immune-Suppressing Drugs.

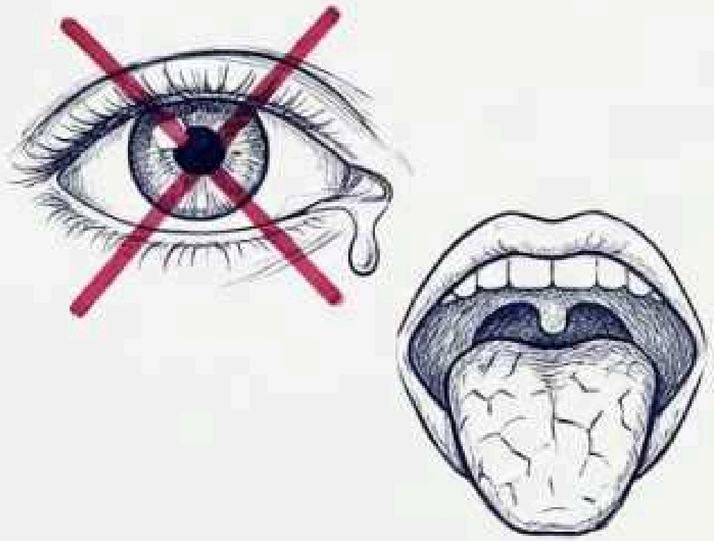
Step 3: Advanced/Refractory

Biological Drugs.



Sjögren's Syndrome & Systemic Sclerosis

Sjögren's Syndrome

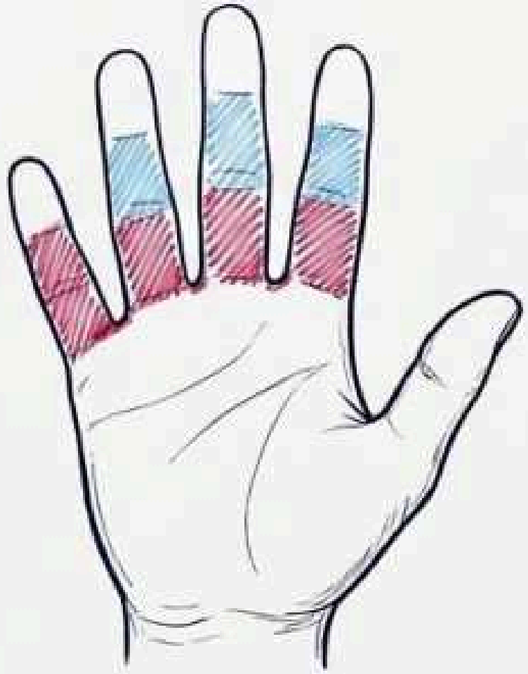


Mechanism: Immune attack on exocrine (tear/saliva) glands.

Symptoms: Dry eyes, dry mouth, tiredness, joint pain.

Risk: Small increased risk of lymphoma.

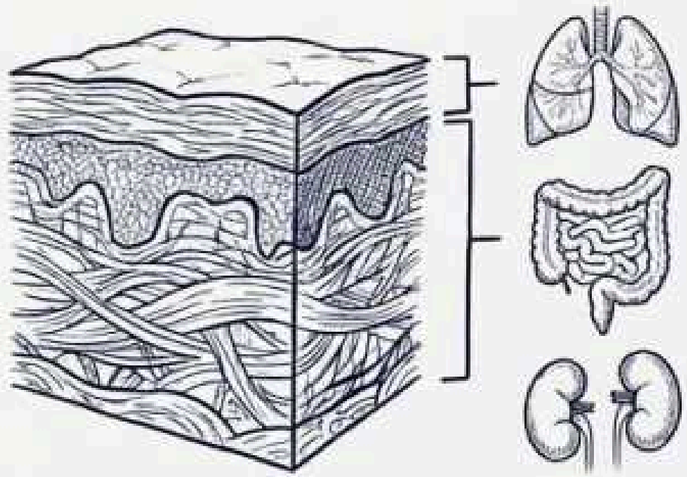
Shared Early Feature: Raynaud's Phenomenon



Fingers transition in the cold: White ➡ Blue ➡ Red.

Caveat: Most isolated Raynaud's has no underlying disease.

Systemic Sclerosis (Scleroderma)

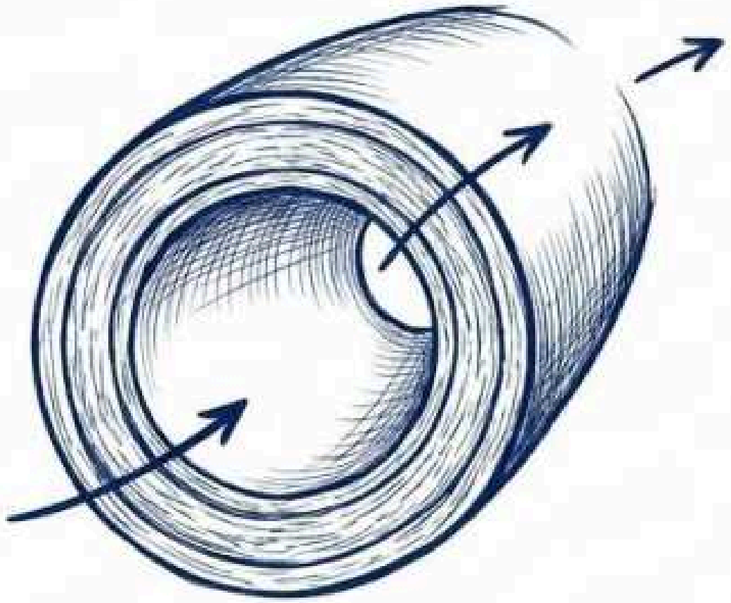


Mechanism: Pathological thickening and hardening of the skin.

Internal organ involvement: Lungs, gut, kidneys.

Vasculitis

Inflammation of blood vessels. It can affect vessels of any size, damaging the organs they supply.

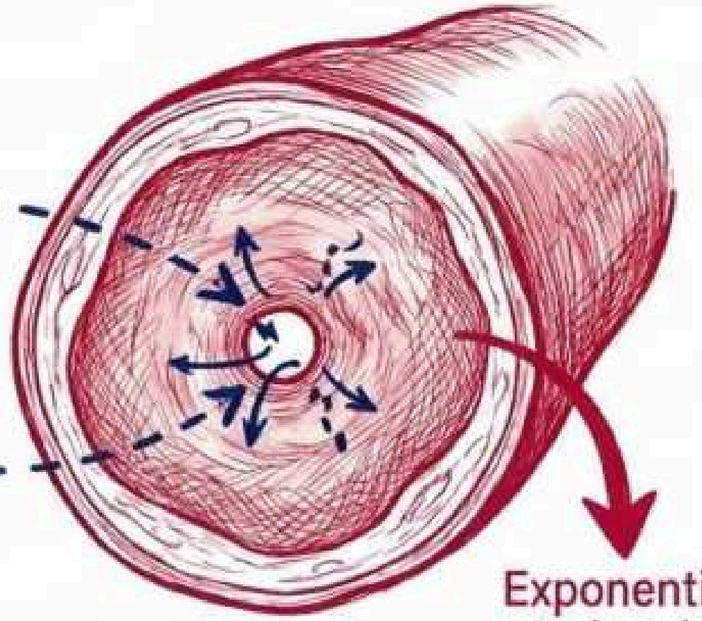


Healthy Vessel

Poiseuille's Equation for Fluid Flow:

$$Q = \frac{\pi \Delta P r^4}{8 \eta L}$$

Because flow (Q) is proportional to the radius to the 4th power (r^4), inflammatory thickening of the vessel wall causes exponential tissue ischemia.



Inflamed Vessel

Exponential Ischemia

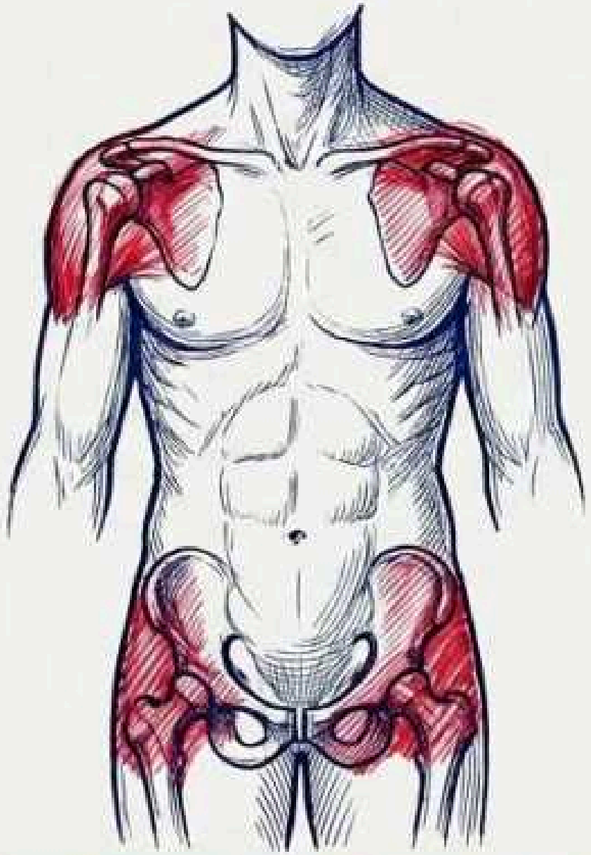
- Disease Spectrum:
  - Large-vessel: e.g., Giant Cell Arteritis.
  - Small-vessel: Often affects critical filtration organs like kidneys and lungs.

Prognosis Shift: Treatment with steroids and immune-suppressing drugs has transformed what were once frequently fatal diseases into manageable ones.

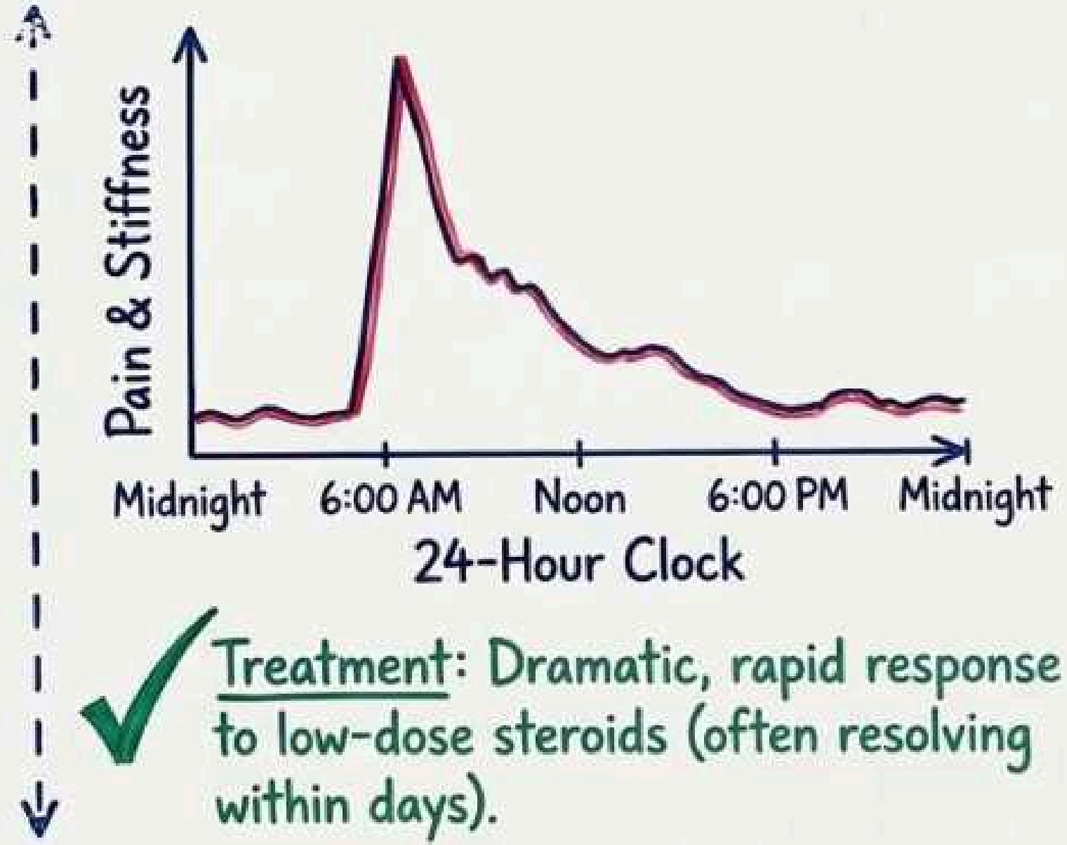
Polymyalgia Rheumatica (PMR)

¶ 5.6

Proximal Stiffness in the Elderly



- Demographics: Primarily affects individuals over 50.
- Symptoms: Marked pain and stiffness localized to shoulders and hips.
- Labs: Raised inflammatory markers.



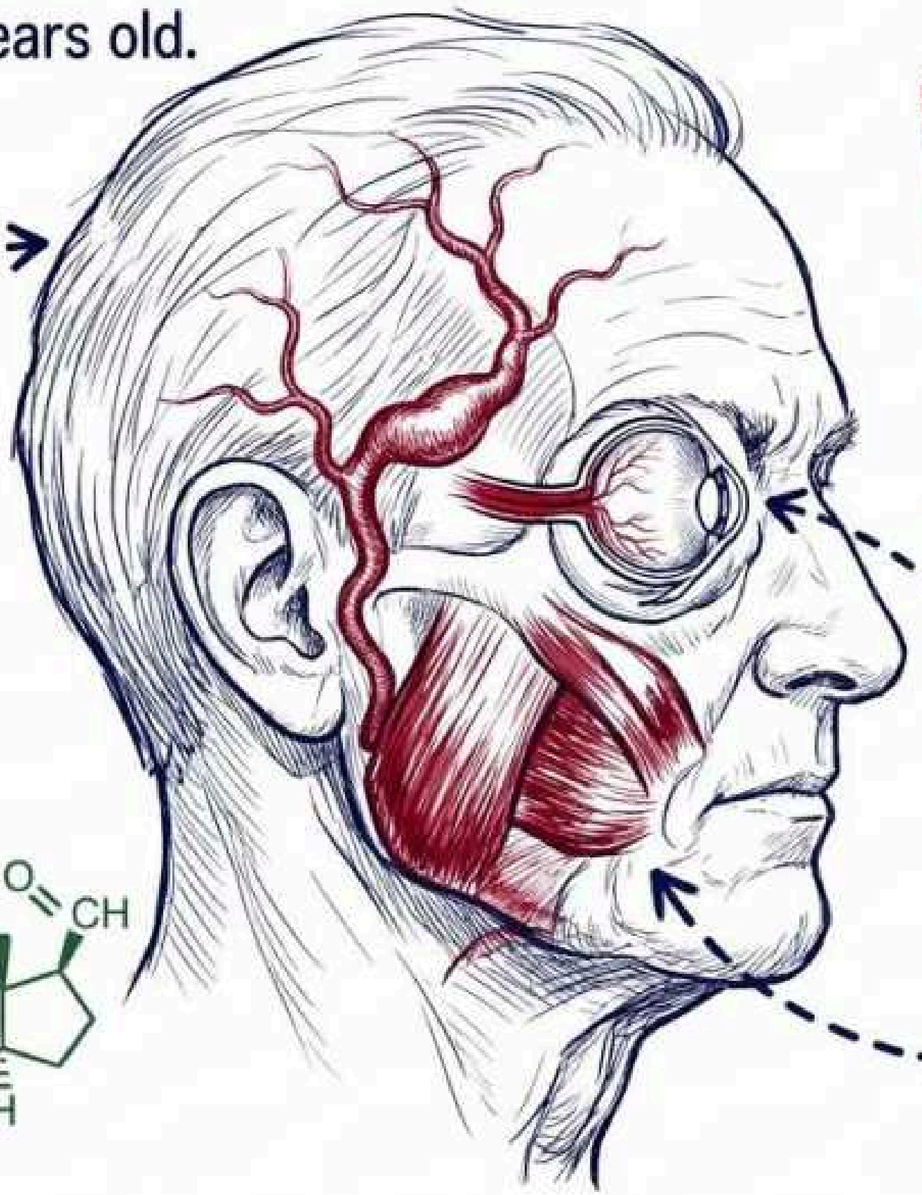
✓ Treatment: Dramatic, rapid response to low-dose steroids (often resolving within days).

Clinical Link: Closely associated with Giant Cell Arteritis (GCA) - inflammation of large arteries, especially of the head.

Giant Cell Arteritis (GCA)

Patient Profile: Individuals > 50 years old. Inflammation of large arteries, particularly of the head.

1. New-onset headache & scalp tenderness.



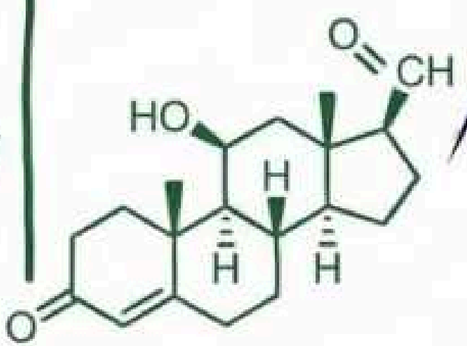
MEDICAL EMERGENCY

Inflammation of the **ophthalmic artery** can cause sudden, irreversible blindness.

3. Visual disturbances.

2. Jaw claudication (pain when chewing).

Urgent Protocol: Initiate high-dose steroids immediately upon suspicion—do not wait for confirmatory tests.



Inflammatory Myopathies

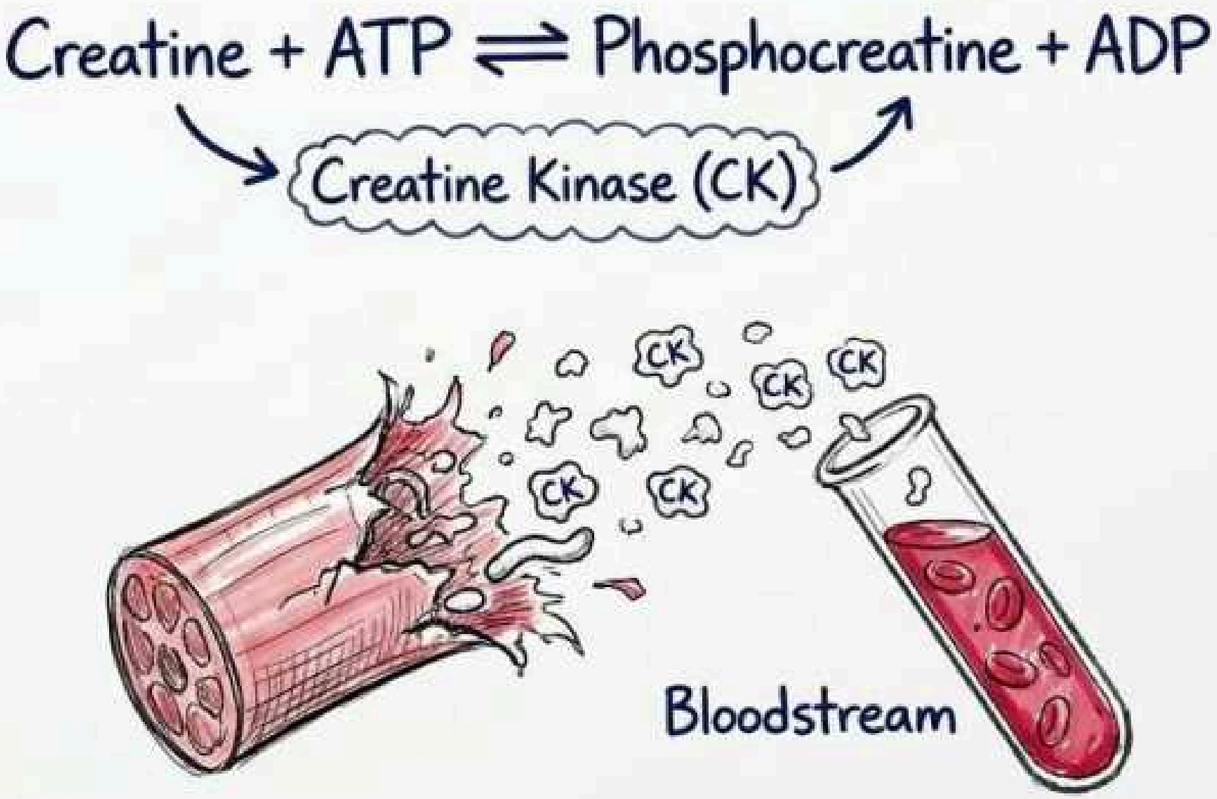
Autoimmune diseases of the muscle (Polymyositis & Dermatomyositis).



Presentation: Symmetrical weakness of proximal (trunk) muscles. Patients struggle to climb stairs or rise from chairs.

⚠ Dermatomyositis Specifics: Also includes cutaneous (skin) involvement.
Critical Red Flag: In adults, it is associated with an underlying malignancy. A comprehensive search for cancer is advised.

Biomarker Mechanism:



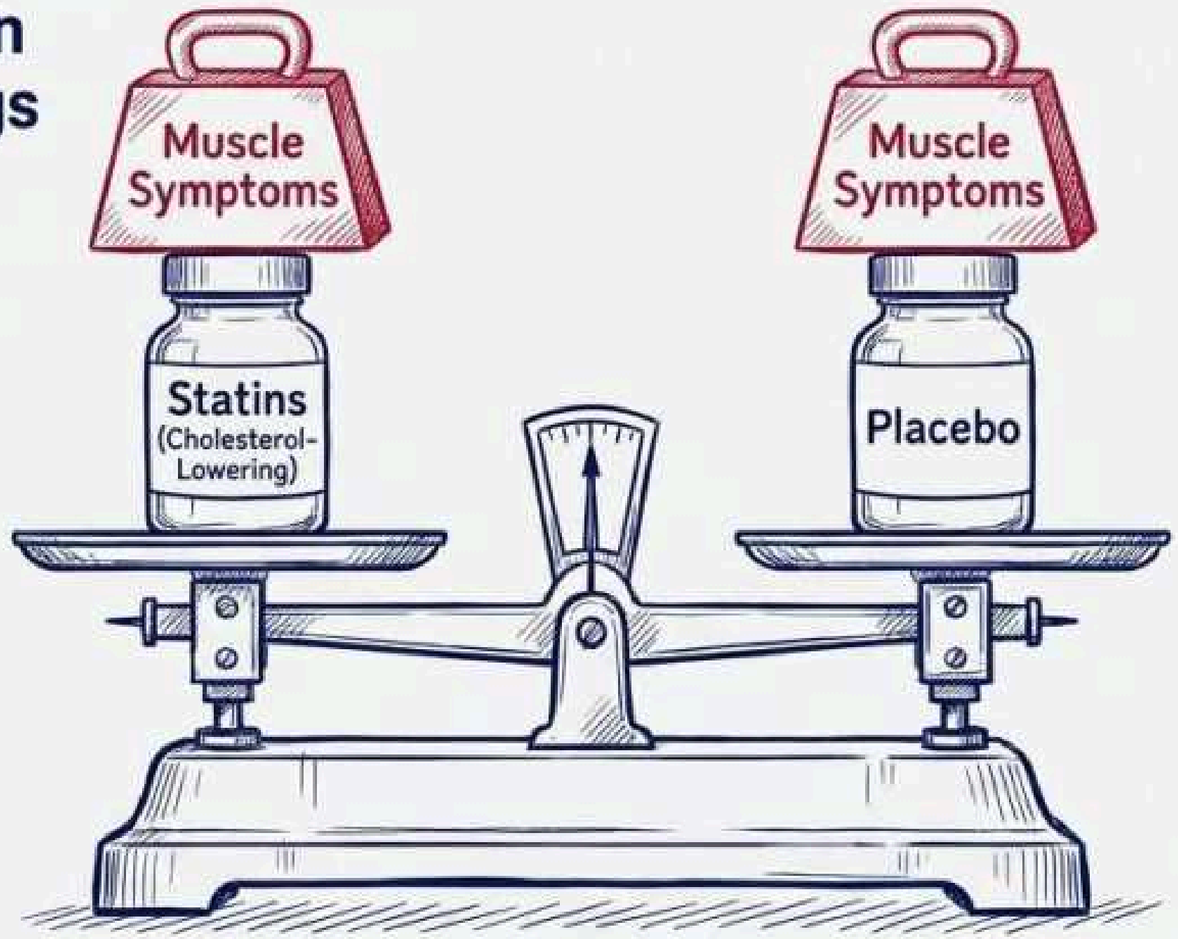
Raised levels of the muscle enzyme Creatine Kinase (CK) in the blood indicate active muscle damage.

Statins & Muscle Aches

The Nocebo Effect in Lipid-Lowering Drugs

The Clinical Reality:

- Statins commonly cause reported muscle aches, but serious structural muscle damage is rare.



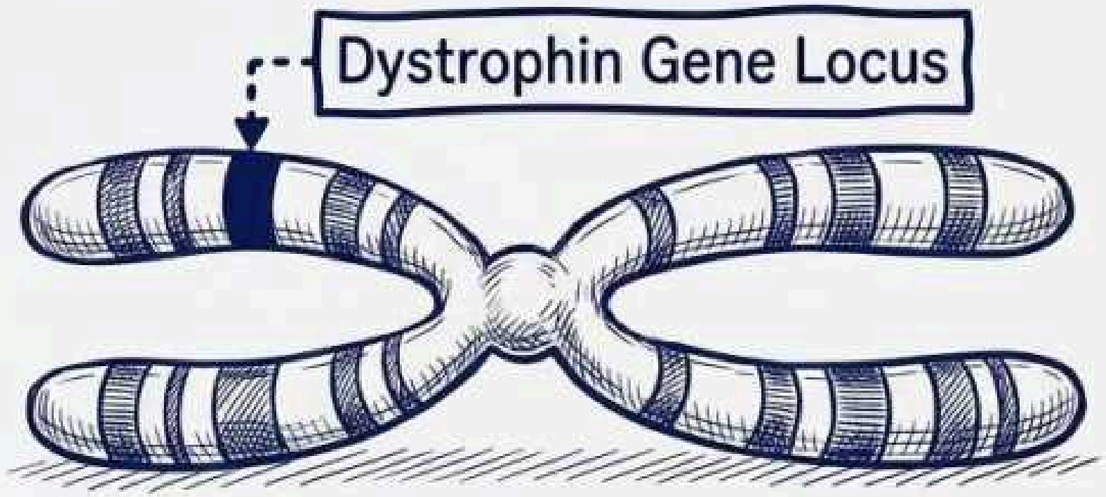
The Trial Data:

- Rigorous placebo-controlled trials reveal that most muscle symptoms reported by people taking statins occur at identical rates with placebos.

Key Takeaway: Essential context for patients to prevent unnecessary discontinuation of life-saving cardiovascular drugs that protect heart function.

Inherited Muscle Diseases

Muscular Dystrophies: The Genetic Basis of Weakness



Duchenne Muscular Dystrophy (DMD):

- Genetics: Caused by mutations in the dystrophin gene on the X chromosome.
- Presentation: Affects boys, causing progressive muscle weakness from early childhood.

Gene Discovered

1986

One of the first disease genes identified via positional cloning (as described in Medicine 503 B).

Management & Future

Present

Steroids are used to slow disease progression, while advanced gene-based treatments are actively in development.

Lecture Synthesis

Summary of Connective Tissue & Muscle Pathologies

Multi-Organ Autoimmune

Conditions:

- Lupus
- Sjögren's
- Systemic Sclerosis
- Vasculitis

Core Theme: Systemic reach, antibody-driven, severe internal organ risk.

The Older Adult

Conditions:

- Polymyalgia Rheumatica
- Giant Cell Arteritis

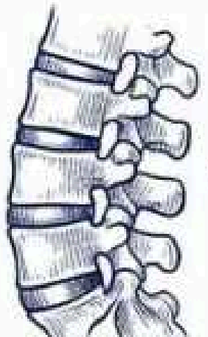
Core Theme: Highly steroid-responsive. GCA is a critical sight-threatening visual emergency.

Muscle Weakness

Etiologies:

- Autoimmune (Myopathies)
- Drug-related (Statins/Placebo)
- Inherited (DMD)

Core Theme: Proximal weakness driven by entirely distinct pathophysiologies.



Next Lecture:
Back pain, fractures, and injuries.