CARDIOMYOPATHIES

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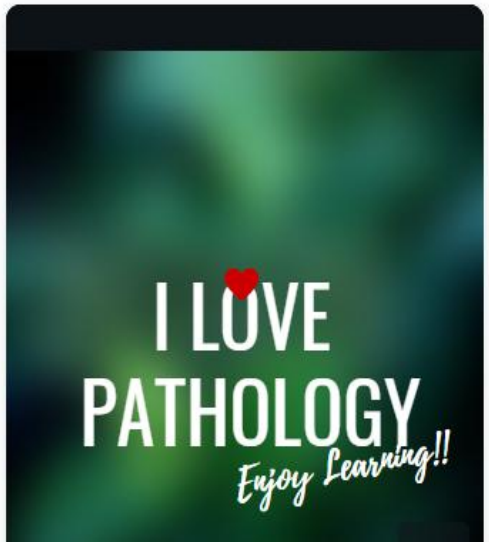
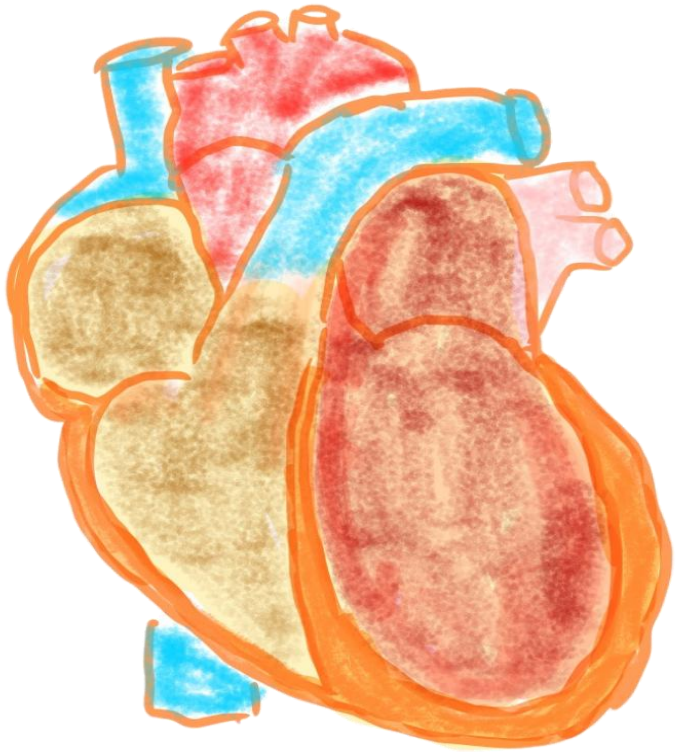


CARDIOMYOPATHIES



Heterogeneous group of diseases of the myocardium

associated with mechanical and/or electrical dysfunction

that ‘usually’ exhibit inappropriate ventricular hypertrophy or dilatation

and are due to a variety of causes that frequently are genetic

CARDIOMYOPATHIES

Primary

Involve predominantly the heart

- Genetic
- Acquired

Secondary

Myocardial involvement
As a part of systemic or multiorgan disorder

CARDIOMYOPATHIES

Recent advances reveal that many cardiomyopathies are caused by genetic mutations.

These **mutations** affect proteins involved in:

- Energy production
- Cardiac muscle contraction
- Cell-to-cell connections
- Cytoskeleton-ECM linkage

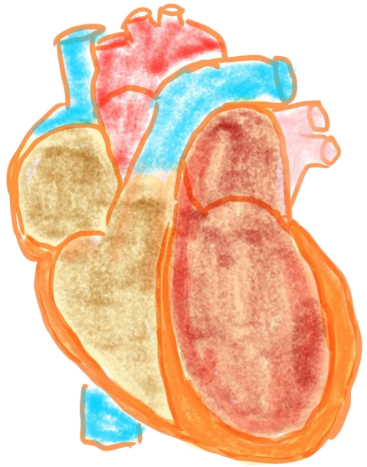
→ Abnormal heart contraction or relaxation

→ Disrupted ion transport, causing arrhythmias

CARDIOMYOPATHIES

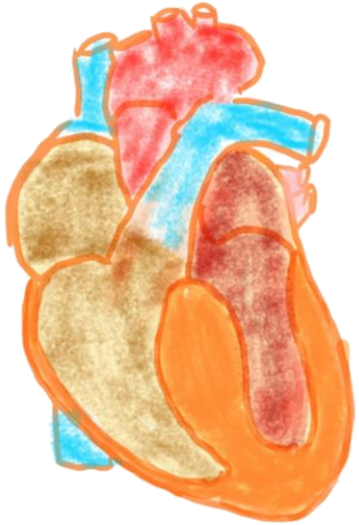
With three distinct pathological patterns

Dilated cardiomyopathy (DCM)

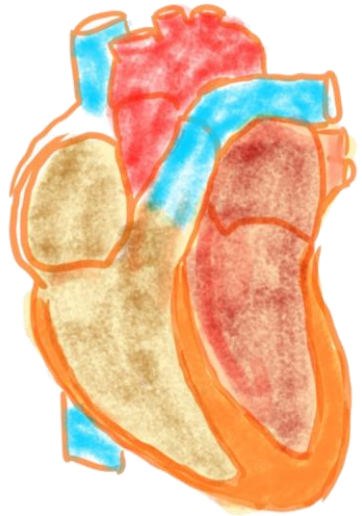


Most common

Hypertrophic cardiomyopathy



Restrictive cardiomyopathy



Least frequent

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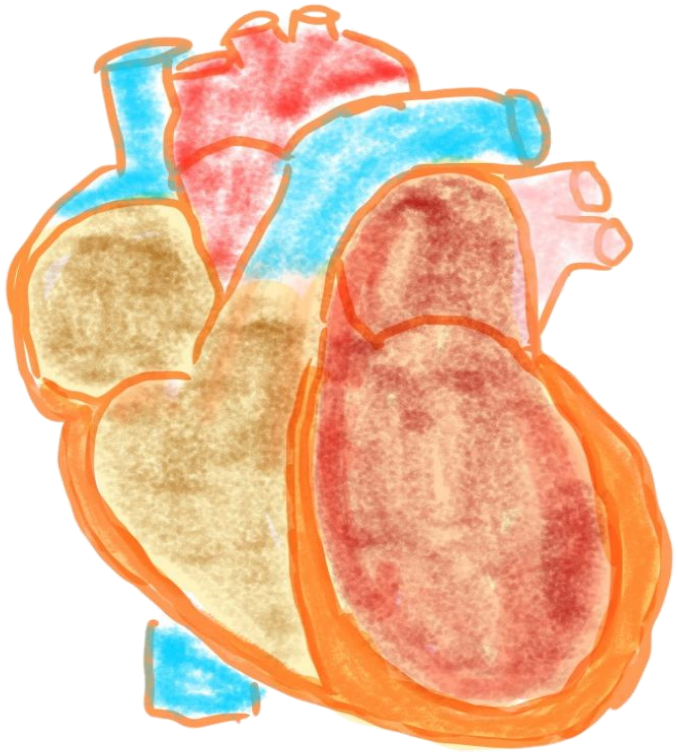
Dilated cardiomyopathy (DCM)

Characterized morphologically and functionally



By progressive cardiac dilation and contractile (systolic) dysfunction

usually with concomitant hypertrophy.

Diagnosis is made after ruling out:

Ischemic heart disease
Valvular disease
Hypertension
Congenital heart disease

If no cause is found → Primary/Idiopathic DCM

Genetic Causes of DCM- Role of Genetics in DCM

*~**50%** of DCM cases are familial*

Mutations affect:

Cytoskeleton
Sarcolemma
Nuclear envelope (e.g., lamin A/C)

Notable mutation: TTN (titin) truncation → 10–20% of cases

Inheritance patterns:

Mostly autosomal dominant with variable penetrance

Also X-linked, autosomal recessive, mitochondrial

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Dystrophin gene mutations → Can cause DCM as primary feature

May present with conduction abnormalities due to shared developmental origin

Other Contributing Factors to DCM

Myocarditis: Viral infections (e.g., coxsackie B) → inflammation → DCM

Alcohol & Toxins

Ethanol, acetaldehyde → direct toxicity
Thiamine deficiency → beriberi
Cobalt poisoning, cardiotoxic chemotherapy

Peripartum Cardiomyopathy:

Late pregnancy to postpartum

Related to antiangiogenic mediators (e.g., sFLT1, prolactin fragments)

Caused by genetic, hypertensive, metabolic or nutritional factors

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Iron Overload:

From hemochromatosis or repeated transfusions
Causes oxidative stress and enzyme dysfunction

Supraphysiologic Stress:

Persistent tachycardia, hyperthyroidism, fetal stress
Catecholamine excess → necrosis → DCM
Can result from pheochromocytoma, cocaine, dopamine

Takotsubo: Stress-Induced Cardiomyopathy

Triggered by emotional stress

Caused by catecholamine surge

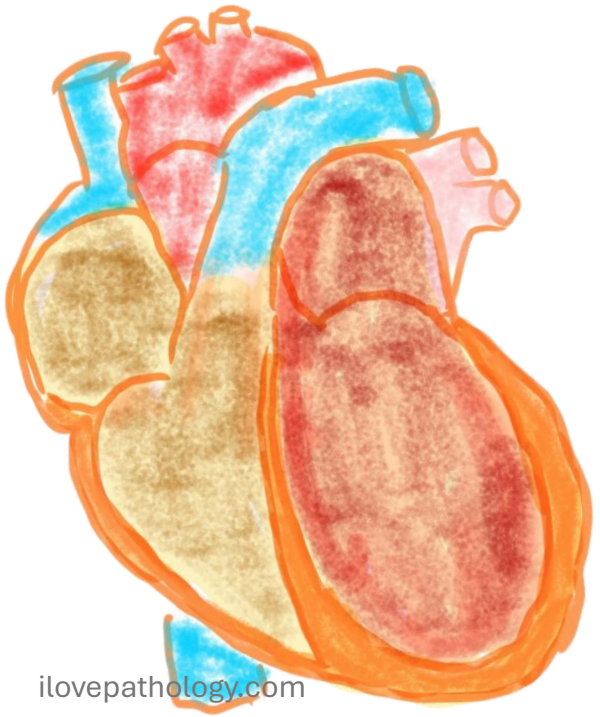
Sudden LV dysfunction, especially apex

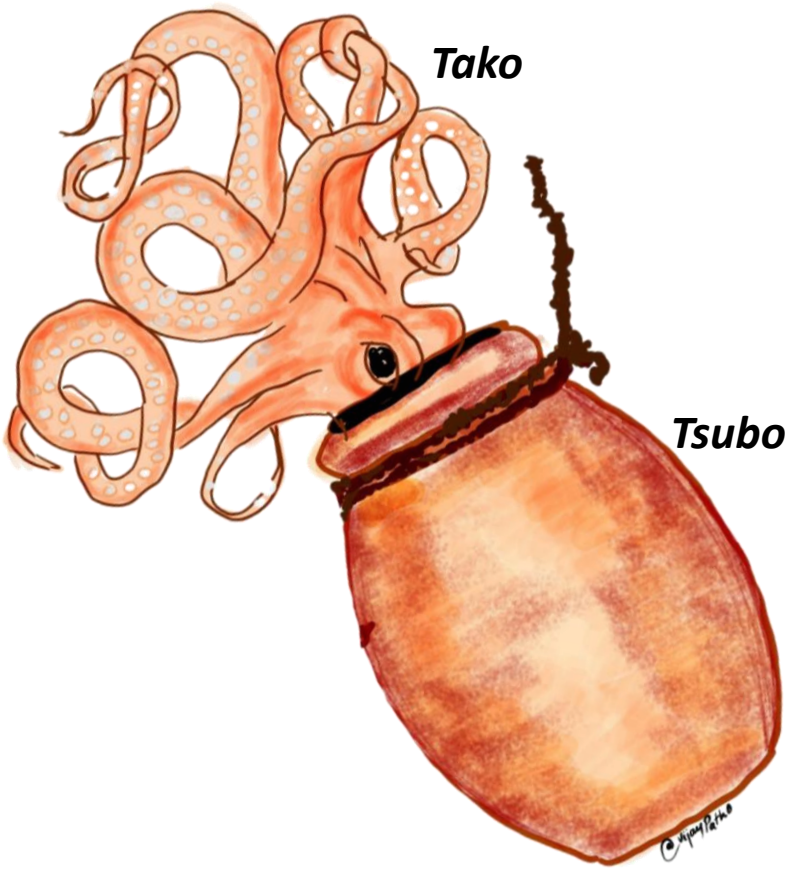
Mechanism:

Calcium overload
Focal coronary vasoconstriction

Called **"Broken Heart Syndrome"** 💔

Heart shape resembles **"Takotsubo"** pot (Japanese octopus trap)





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MACROSCOPY

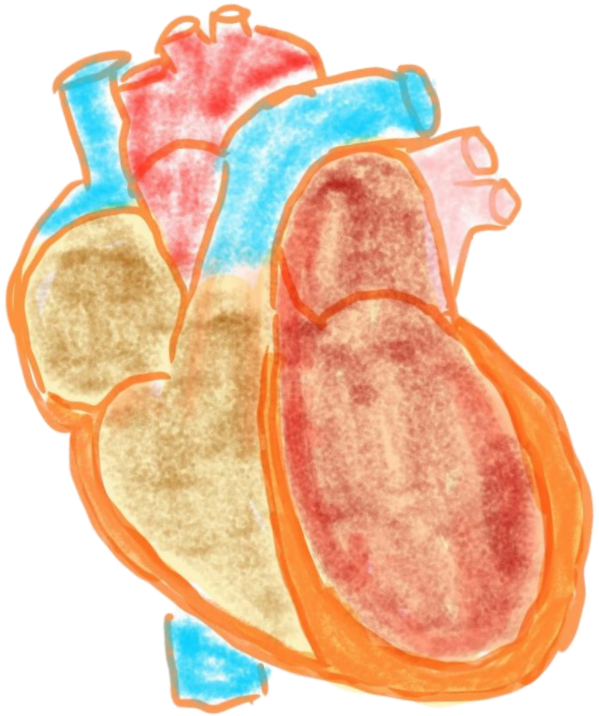
Heart is **enlarged, heavy, and flabby**

Weighs 2–3 times normal

Dilation affects all chambers

Mural thrombi may form due to blood stasis

Risk of thromboembolism



Note that there should be **NO** primary valvular alterations

*If mitral/tricuspid regurgitation is present**, it is functional** (due to chamber dilation)*

MICROSCOPY

Histologic findings are **nonspecific**

Morphologic changes do not always match clinical severity

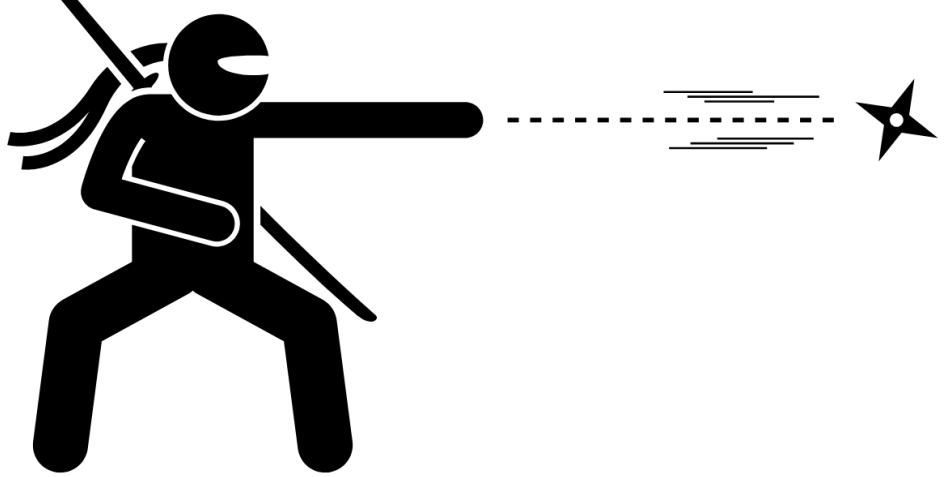
Interstitial and endocardial fibrosis (variable)

Subendocardial scars from prior ischemia

Hypertrophied muscle cells with enlarged nuclei

Some myocytes may be stretched or irregular

MICROSCOPY



In TTN-truncation DCM:

Myocytes show hyperchromatic, distorted nuclei

Appear as **"Ninja star"-** like shapes

these can be a nonspecific finding,

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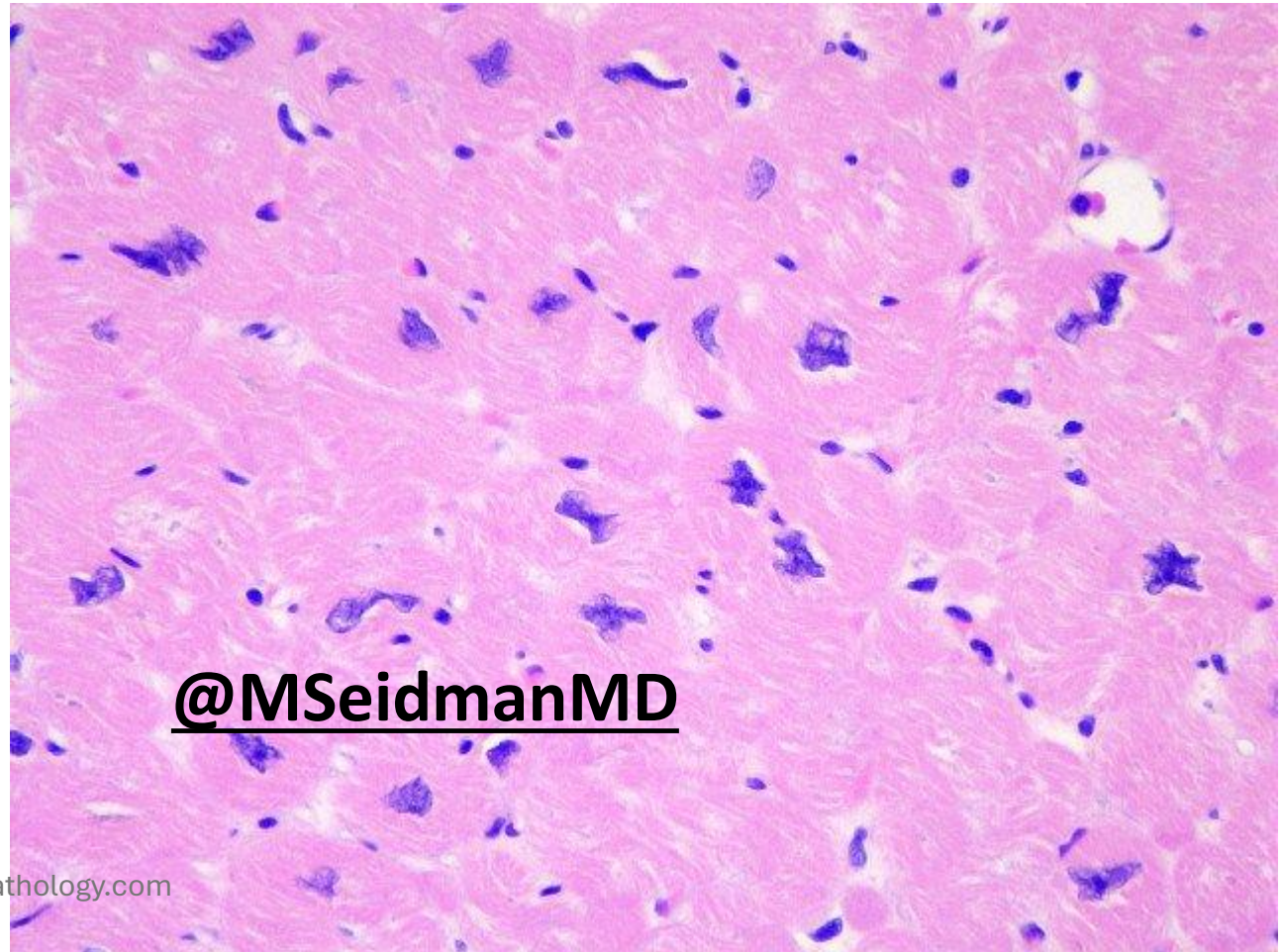
If ≥5% of myocytes show this → suggestive of titin mutation



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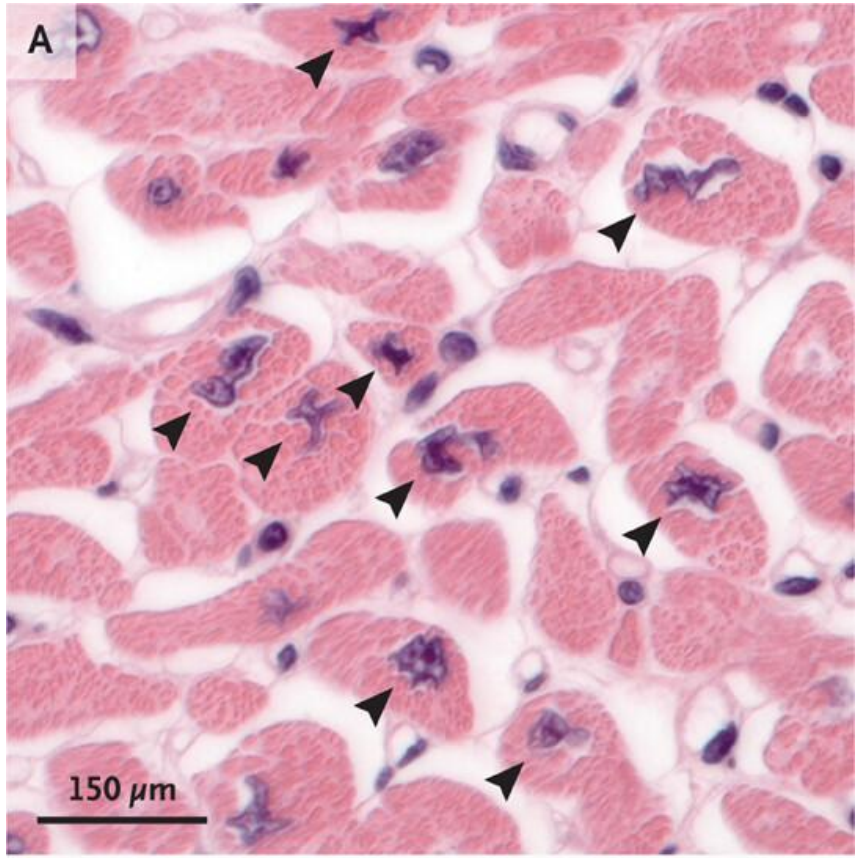

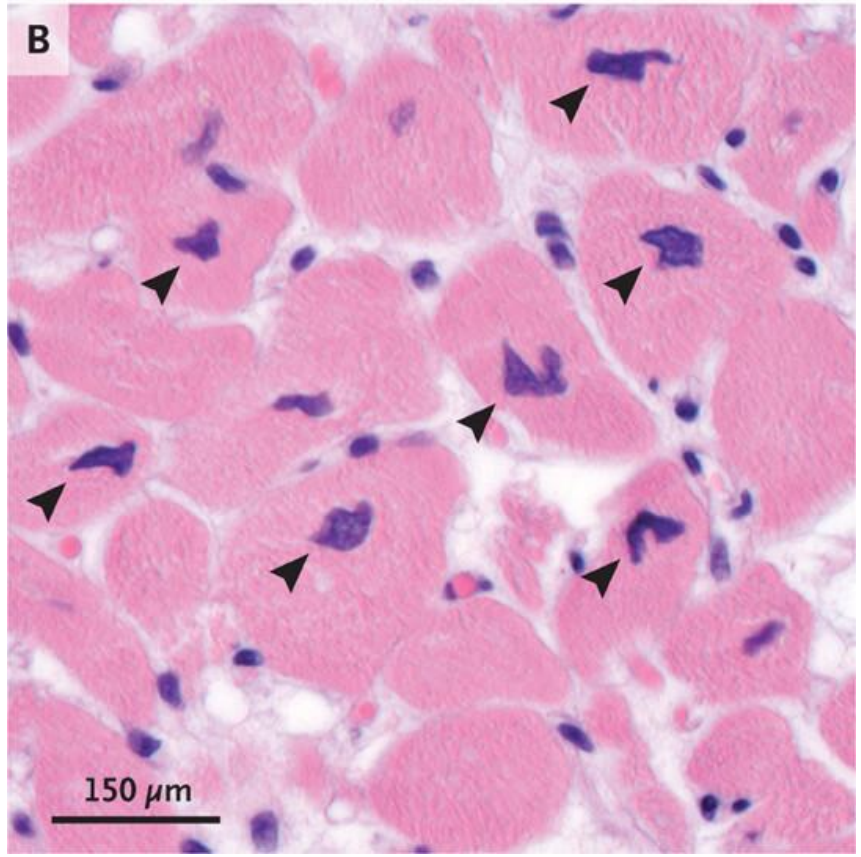

Truncations of Titin Causing Dilated Cardiomyopathy

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CLINICAL FEATURES AND PROGNOSIS

Core issue: **Ineffective contraction**

Ejection fraction <25% (Normal: 50–65%)

Typical age: 20 to 50 years, but can occur in children

Symptoms of congestive heart failure (CHF):

Shortness of breath, Fatigue,
Reduced exercise tolerance

Common findings:

Secondary mitral regurgitation
Arrhythmias, Thromboembolism from intracardiac thrombi

CLINICAL FEATURES AND PROGNOSIS

Outcomes:

Death often from progressive failure or arrhythmia

High mortality (10–50% per year)

Treatment:

Some improve with drugs or biventricular pacing

Cardiac transplant for advanced cases

Ventricular assist devices (VADs)

Can lead to long-term improvement in some patients

THANKS FOR WATCHING