

# Cardiomyopathies

Definitions • etiologic framework • functional patterns

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# Learning objectives

- Define intrinsic myocardial dysfunction and distinguish primary from secondary disease.
- Classify cardiomyopathies by morphology and dominant functional defect.
- Associate etiologic categories with characteristic phenotypes and key mimics.
- Apply a cause-oriented framework to ambiguous cardiac presentations.

# Cardiomyopathy: The defining lesion

- A disease of heart muscle resulting from intrinsic myocardial dysfunction.
- The affected myocardium may show abnormal contractility, compliance, or both.
- Cardiomyopathy is an etiologic diagnosis—not merely an enlarged or poorly functioning heart.
- The same phenotype may arise through multiple biological mechanisms.

# Intrinsic disease versus secondary remodeling

## Intrinsic myocardial disorder

Heart muscle disease is the primary or systemic disease-related source of dysfunction.

Example: Genetic or toxic myocardial injury.

## Remodeling from another lesion

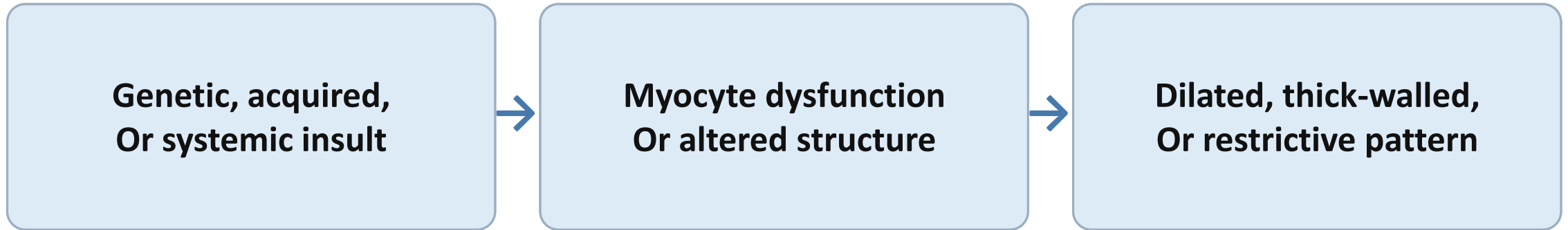
Myocardial change follows an extrinsic load or structural cardiac abnormality.

Example: Pressure overload from valve disease.

## Diagnostic boundary: Four major exclusions

- Coronary artery disease can cause myocardial dysfunction without constituting primary cardiomyopathy.
- Hypertension can lead to compensatory hypertrophy and subsequent failure.
- Valvular disease can impose chronic pressure or volume overload.
- Congenital structural heart disease may produce secondary ventricular dysfunction.

# Phenotype is not the same as cause



Identical morphologic appearances may have distinct causal pathways.

# Primary and secondary cardiomyopathy

## Primary

Principally confined to the heart muscle. Genetic disorders affecting myocardial proteins are representative examples.

## Secondary

Cardiac manifestation of a systemic disorder. Examples include sarcoidosis, iron overload, and muscular dystrophy.

## Primary does not necessarily mean inherited

- “Primary” describes where the disorder principally manifests.
- Genetic factors are prominent, but the classification is not simply genetic versus environmental.
- A clinically restricted heart-muscle phenotype does not establish one molecular etiology.
- Family and systemic evaluation help refine an initially descriptive label.

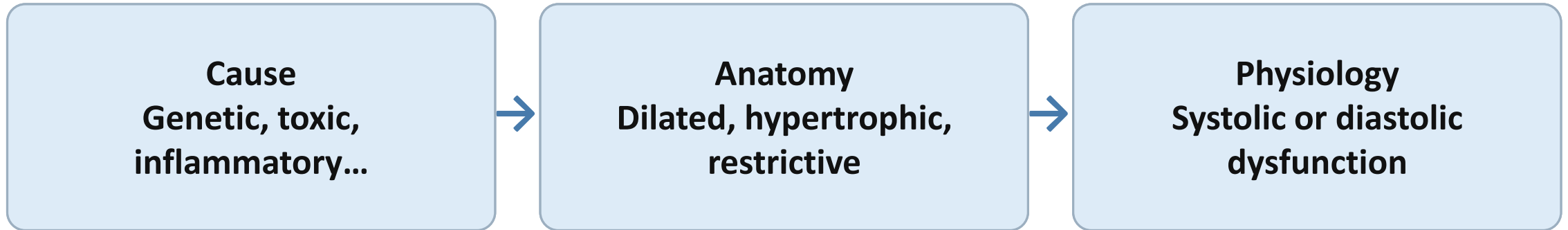
## Secondary cardiomyopathy: Systemic context

- The myocardial phenotype can reflect a broader metabolic, inflammatory, infiltrative, or neuromuscular illness.
- Cardiac involvement may dominate presentation even when the cause is extracardiac.
- Recognition of extracardiac clues can convert a nonspecific phenotype into a cause-specific diagnosis.
- Examples: Hemochromatosis, sarcoidosis, muscular dystrophy, storage disorders.

## “Idiopathic” is a status of knowledge

- Idiopathic cardiomyopathy means no cause has yet been established.
- It does not imply that no underlying mechanism exists.
- The source emphasizes that many previously unexplained cases now have identifiable genetic bases.
- Etiologic attribution can evolve with family evaluation and molecular investigation.

# Different classification axes answer different questions



A complete diagnosis should integrate cause, morphology, and function rather than select only one axis.

# The three major pathologic patterns

## Dilated

Enlarged ventricular chamber; Contractile impairment dominates.

## Hypertrophic

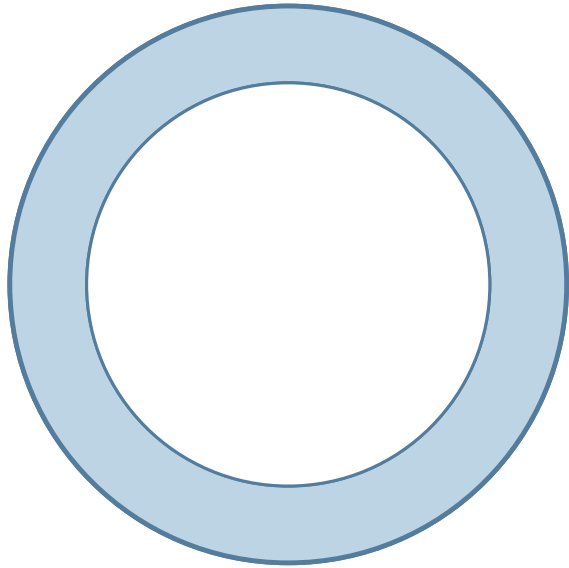
Excessive myocardial thickening; Impaired ventricular filling predominates.

## Restrictive

Reduced compliance without major chamber dilation; Impaired filling predominates.

# Cardiomyopathy geometry: Three schematics

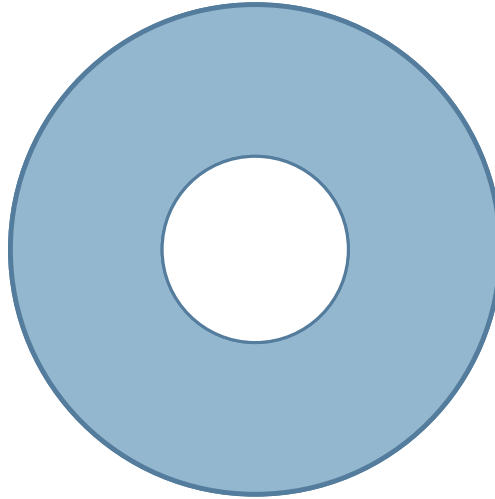
**Dilated**



**Large cavity**

Reduced contraction

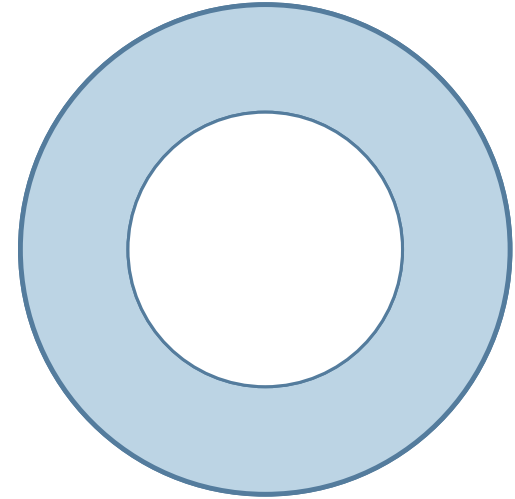
**Hypertrophic**



**Thick wall**

Reduced filling

**Restrictive**



**Near-normal chamber**

Stiff myocardium

Schematic LV short-axis cavity–wall relationships; Not a specimen or quantitative anatomy.

# Systolic and diastolic defects

## Systolic dysfunction

Ineffective ventricular contraction reduces emptying.

Best exemplified by the dilated pattern.

## Diastolic dysfunction

Reduced chamber compliance or cavity size impairs filling.

Typical of hypertrophic and restrictive patterns.

# Ejection fraction is a functional descriptor

- Left ventricular ejection fraction describes the fraction of end-diastolic volume ejected per beat.
- A reduced value supports depressed systolic performance.
- A preserved or increased value does not demonstrate normal relaxation or adequate filling.
- Interpret ejection fraction with the structural phenotype and clinical context.

## Functional patterns and textbook EF ranges

| Pattern             | LV ejection fraction | Dominant defect       |
|---------------------|----------------------|-----------------------|
| <b>Dilated</b>      | <40%                 | Reduced contractility |
| <b>Hypertrophic</b> | 50%–80%              | Reduced compliance    |
| <b>Restrictive</b>  | 35%–55%              | Reduced compliance    |

## Do not treat EF bands as diagnostic cutoffs

- The textbook gives approximate, phenotype-associated EF ranges—not exclusive diagnostic criteria.
- Hypertrophic and restrictive phenotypes may retain substantial systolic function.
- Clinical and morphologic patterns overlap; Ejection fraction alone cannot establish causation.
- The same patient may exhibit both filling and contraction abnormalities.

## Dilated cardiomyopathy dominates the group

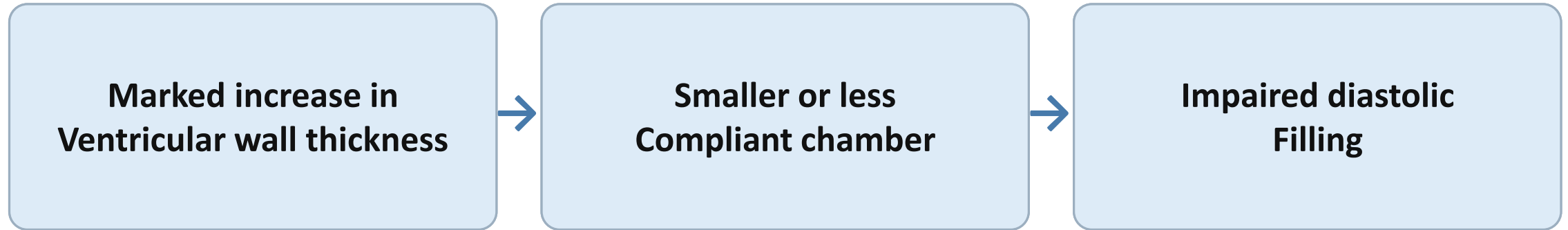
- The dilated pattern as the most frequent major cardiomyopathy category.
- It accounts for approximately 90% of cases classification.
- The dilated phenotype encompasses both genetic and acquired forms.
- This epidemiologic figure is textbook-specific and not a substitute for population-based contemporary estimates.

# Dilated pattern: Morphology and mechanical deficit



The phenotype is the endpoint; Identifying an underlying injury or inherited mechanism remains essential.

# Hypertrophic pattern: Structure and filling



A thick wall is not by itself evidence of genetic hypertrophic cardiomyopathy: Pressure overload is a mimic.

## Restrictive pattern: Compliance is central



Systolic contraction can be relatively maintained despite substantial clinical disease.

# Why chamber size and function can diverge

## Large chamber, weak contraction

A dilated ventricle can have a large end-diastolic volume but still empty inefficiently.

Contractile dysfunction dominates.

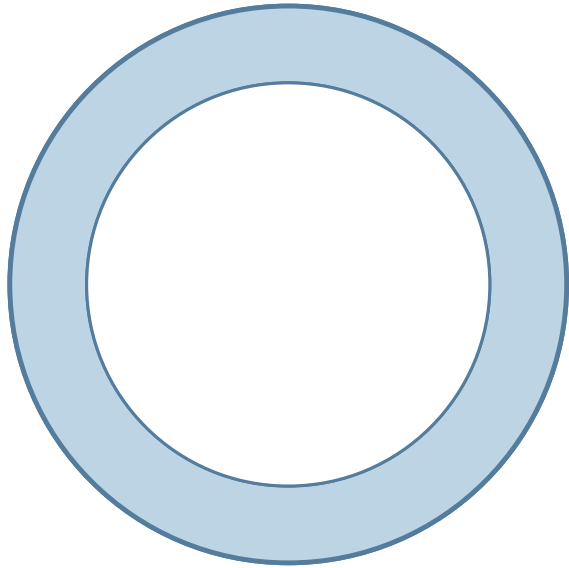
## Non-dilated chamber, poor filling

A thick or stiff ventricle may eject a relatively preserved fraction of a limited filled volume.

Diastolic dysfunction dominates.

# A first-pass differential begins with chamber geometry

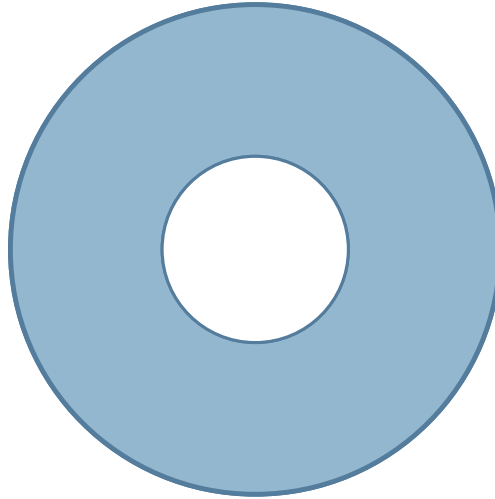
**Dilated**



**Large cavity**

Reduced contraction

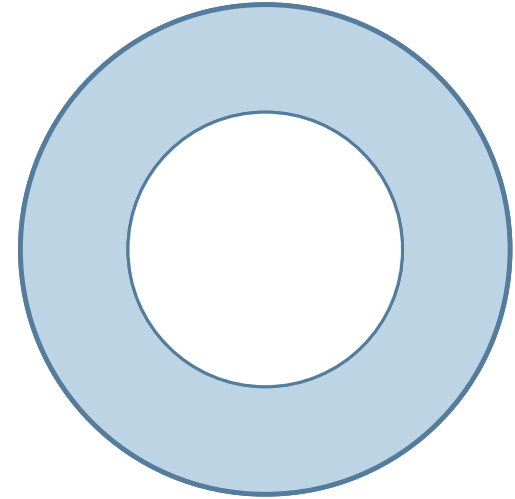
**Hypertrophic**



**Thick wall**

Reduced filling

**Restrictive**



**Near-normal chamber**

Stiff myocardium

Schematic LV short-axis cavity–wall relationships; Not a specimen or quantitative anatomy.

## Atrial dilation can reveal impaired filling

- Restricted ventricular filling increases atrial pressure burden.
- The restrictive schematic highlights atrial dilation despite near-normal ventricular size.
- The hypertrophic pattern may also show left atrial enlargement.
- Atrial size complements ventricular wall and cavity observations.

# Overlap is an expected biological reality

- Clinical overlap among cardiomyopathy groups.
- Contractile impairment may coexist with abnormal relaxation or reduced compliance.
- The final phenotype need not reveal its initiating insult.
- Avoid interpreting the three-pattern schema as three mutually exclusive molecular diseases.

## Disease severity varies within each pattern

- The same morphologic category includes a spectrum of functional impairment.
- Structural change and clinical presentation are not necessarily proportional.
- Symptoms and risk may reflect cardiac rhythm as well as mechanical dysfunction.
- Classification organizes investigation; It does not replace individual assessment.

# Etiologic map: Seven broad categories

## **Injury / exposures**

Infection, toxins, drug effects, irradiation, inflammatory or immune injury.

## **Systemic disorders**

Metabolic disease, iron accumulation, infiltrative deposition, storage disorders.

## **Inherited disease**

Sarcomeric or structural-protein defects; Neuromuscular syndromes with cardiac involvement.

## Genetic causes: Beyond a single gene

- Genetic disorders may selectively disrupt myocardial fibers.
- The causal proteins and mechanisms differ between cardiomyopathy patterns.
- A familial phenotype does not necessarily predict one cardiac morphology.
- The expanding genetic basis is an important reason to revisit “idiopathic” cases.

# Cardiac-limited versus multisystem inheritance

## Predominantly cardiac

A heritable disorder can be expressed mainly as heart-muscle dysfunction.

The cardiac phenotype may drive family evaluation.

## Multisystem

Inherited skeletal muscle, metabolic, and storage disorders can include cardiomyopathy.

Extracardiac findings may identify the cause.

## Family history refines the etiologic hypothesis

- Multiple relatives with cardiomyopathy supports an inherited contribution.
- Family reports of unexplained sudden death or rhythm disease may be relevant.
- Variable expression can complicate simple affected/unaffected pedigree labels.
- Family information supplements—not substitutes for—clinical and structural assessment.

## Infectious mechanisms can injure myocardium

- Table 12.11 lists viruses, bacteria, fungi, protozoa, chlamydiae, and rickettsiae.
- Infectious myocarditis is a disease of the myocardium, not simply an extracardiac infection.
- Inflammatory injury may produce subsequent contractile dysfunction.
- Pathogen identification and inflammatory evidence require separate evaluation.

## Immune-mediated and inflammatory categories

- Myocarditis may be associated with several inflammatory mechanisms.
- Sarcoidosis can cause myocardial dysfunction within a multisystem disease.
- Posttransplant rejection is listed among immunologic cardiac muscle disorders.
- Myocardial inflammation should be interpreted in its cause and systemic context.

# Iron overload bridges metabolic and myocardial injury

- Hemochromatosis appears among metabolic causes of cardiomyopathy.
- Cardiac iron excess may be hereditary or related to repeated red-cell transfusion.
- Oxidative injury and interference with metal-dependent enzymes.
- Iron overload may generate a dilated functional phenotype.

## Storage and deposition diseases

- Table 12.11 includes glycogen storage disease, Fabry disease, and Hunter–Hurler syndrome.
- Amyloidosis is an important extracellular deposition disorder affecting myocardium.
- Different deposited or accumulated materials need not produce the same cardiac geometry.
- Systemic features may distinguish a deposition-related phenotype from primary myocardial disease.

# Infiltrative disease and myocardial stiffness

- Sarcoidosis and carcinomatosis are listed among infiltrative etiologies.
- Radiation-related fibrosis can alter myocardial compliance.
- The resulting phenotype may be restrictive, but the mechanism is not uniform across causes.
- Etiologic diagnosis therefore requires more than documenting impaired filling.

## Toxins: A mechanistically diverse group

- Alcohol, cobalt, catecholamines, carbon monoxide, lithium, hydrocarbons, and arsenic.
- Several cytotoxic medications are also listed as myocardial toxins.
- Toxic exposures may produce myocardial dysfunction without a distinctive gross pattern.
- Exposure history can be decisive when the structural phenotype is nonspecific.

## Antineoplastic therapy belongs in the history

- The table includes doxorubicin, daunorubicin, and cyclophosphamide.
- Therapy-related myocardial dysfunction must be considered in the appropriate exposure context.
- A phenotype alone does not attribute damage to a specific chemotherapy agent.
- Do not infer drug-specific risk or dose thresholds from the introductory textbook table.

## Nutritional and metabolic contributors

- Table 12.11 lists protein deficiency, thiamine deficiency, and other avitaminoses.
- Nutrient-related myocardial dysfunction can accompany systemic illness or substance misuse.
- The etiologic task is to establish the relevant nutritional disturbance.
- An apparent idiopathic phenotype may become explainable after targeted history and testing.

# Endocrine and electrolyte disturbances

- Hyperthyroidism and hypothyroidism are listed metabolic conditions.
- Both hyperkalemia and hypokalemia are included among possible myocardial disorders.
- Their influence on cardiac function is context-dependent and does not establish a single fixed phenotype.
- Consider reversible systemic disturbances before applying an unexplained label.

# Neuromuscular disease points beyond the heart

- Muscular dystrophy is an explicit systemic cause of cardiomyopathy.
- Friedreich ataxia and congenital atrophies are also listed.
- Neurologic or skeletal-muscle signs can redirect the etiologic workup.
- Cardiac and extracardiac phenotypes should be interpreted together.

# One phenotype can arise from multiple causes

| <b>Dilated pattern</b>       | <b>Hypertrophic pattern</b> | <b>Restrictive pattern</b> |
|------------------------------|-----------------------------|----------------------------|
| <b>Genetic disorders</b>     | Genetic disorders           | Amyloidosis                |
| <b>Alcohol / myocarditis</b> | Storage disorders           | Radiation fibrosis         |
| <b>Anthracyclines</b>        | Friedreich ataxia           | Idiopathic                 |
| <b>Iron overload</b>         | Infant of diabetic mother   | —                          |

## Cause-to-pattern mapping is many-to-many

- A cause such as a systemic metabolic disorder can produce more than one expression of disease.
- A morphologic pattern often has multiple unrelated etiologies.
- A population category cannot be applied as a certain individual-level diagnosis.
- Keep the cause and observed phenotype as distinct statements in the final diagnosis.

# Cardiomyopathy mimics: Recognize the competitor

## **Pressure overload**

Hypertension or aortic stenosis may produce substantial hypertrophy.

## **Volume overload**

Valve defects and congenital abnormalities can produce chamber enlargement.

## **Ischemic injury**

Coronary disease may produce regional injury, remodeling, and reduced systolic function.

# A dilated ventricle is not automatically DCM

## **Dilated cardiomyopathy phenotype**

Intrinsic heart-muscle dysfunction can cause progressive ventricular dilation and poor contraction.

## **Secondary dilation**

Ischemic, hypertensive, valvular, or congenital disease may produce an enlarged dysfunctional heart.

# A thick ventricle is not automatically HCM

## **Hypertrophic cardiomyopathy**

Primary myocardial disease with pronounced hypertrophy and impaired filling.

## **Pressure-overload hypertrophy**

Longstanding hypertension or aortic stenosis may also yield increased wall thickness.

# Restricted filling is not always restrictive CM

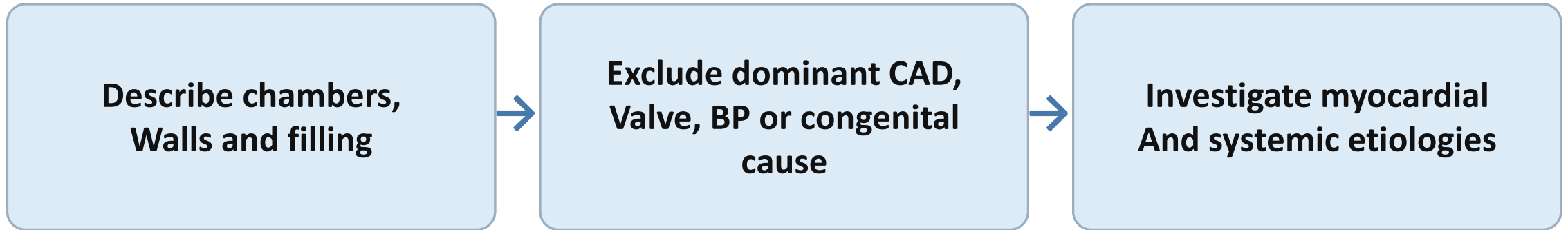
## Myocardial restriction

A stiff myocardium reduces ventricular compliance and limits filling.

## Constrictive pericarditis

A pericardial mechanical constraint may mimic restriction without an intrinsic myocardial cause.

# Reason through the phenotype before the label



A defensible diagnosis distinguishes what the heart looks like from why it became abnormal.

# Heart failure is a consequence, not the etiology

- Impaired contractility can lead to reduced forward ejection.
- Impaired compliance can raise filling pressures despite relatively preserved ejection fraction.
- Both physiologic routes may produce clinical heart-failure syndromes.
- Describing heart failure alone does not identify the causative cardiomyopathy.

# Electrical and mechanical disease intersect

- Arrhythmogenic cardiomyopathy within the dilated-pattern discussion.
- Myocardial and conduction abnormalities may overlap.
- Rhythm disturbance does not itself define the same mechanism as impaired contraction.
- An electrical presentation can warrant evaluation for structural myocardial disease.

## Why morphology alone has limits

- An enlarged ventricle describes a structural endpoint shared by multiple causes.
- Fibrosis or myocyte hypertrophy may represent nonspecific responses to myocardial injury.
- A deposition or inflammatory lesion may be more etiologically informative when present.
- Combine morphology with exposure, systemic, functional, and family information.

# An integrated assessment uses three evidence streams

## Phenotype

Ventricular size, thickness, contraction, compliance and atrial geometry.

## Etiology

Genetics, inflammatory / systemic disease, toxin or treatment exposures.

## Competing causes

Coronary disease, hypertension, valve disease, congenital abnormality; Pericardial constriction where relevant.

## A cause-oriented history changes the differential

- Family cardiac disease or sudden death suggests possible inherited susceptibility.
- Medication, alcohol, occupational, or environmental exposures may implicate toxicity.
- Neuromuscular, inflammatory, infiltrative, and metabolic histories support secondary forms.
- A negative initial history does not establish idiopathic disease conclusively.

## Structural assessment must answer focused questions

- Is the ventricle dilated, thick-walled, or approximately normal in size?
- Is impaired contraction or impaired filling the dominant defect?
- Are the atria enlarged in a pattern compatible with filling pressure elevation?
- Could an extrinsic pressure, volume, ischemic, or pericardial problem explain the findings?

## An etiologic diagnosis can remain provisional

- A patient may satisfy a recognizable cardiomyopathy phenotype before its cause is known.
- “Idiopathic” should be qualified by the evaluation undertaken and available evidence.
- Some inherited and acquired mechanisms yield indistinguishable late morphologies.
- Diagnostic revision is appropriate when new evidence emerges.

## Case 1: Marked dilation and poor contraction

A patient has a globally enlarged ventricular chamber and markedly reduced contractile function. No cause has yet been established.

- Which functional pattern is most compatible?
- What competing disease categories must be assessed?

## Case 1: Identify phenotype, then exclude mimics

- The dominant pattern is dilated with systolic dysfunction.
- Assess ischemic, hypertensive, valvular, and congenital explanations before labeling primary DCM.
- Then consider genetic disease, myocardial inflammation, iron excess, alcohol or medication toxicity.
- Unknown cause after evaluation may justify a provisional idiopathic designation.

## Case 2: Thick ventricle with impaired relaxation

Imaging shows increased left ventricular wall thickness and reduced diastolic filling without major ventricular cavity dilation.

- Which cardiomyopathy pattern is suggested?
- Why must blood pressure and valve history be reviewed?

## Case 2: Hypertrophy has competing explanations

- The appearance is compatible with a hypertrophic functional pattern.
- Hypertensive heart disease and aortic stenosis can mimic this geometry.
- An intrinsic cardiomyopathy requires evidence beyond increased wall thickness alone.
- An etiologic label should integrate clinical and familial information.

## Case 3: Stiff chambers and atrial enlargement

The ventricles are not substantially dilated, but filling is restricted and both atria are enlarged. A systemic disorder is suspected.

- Which functional pattern is plausible?
- What two broad etiologic and mimicking categories are relevant?

## Case 3: Separate myocardial from pericardial causes

- The dominant physiology suggests restrictive cardiomyopathy.
- Infiltrative / deposition disorders, including amyloidosis, are important etiologic possibilities.
- Pericardial constriction can mimic a restrictive functional presentation.
- Structural myocardial evidence and clinical context are needed for attribution.

## Case 4: Systolic failure after drug exposure

A patient has newly recognized global myocardial dysfunction and a history of treatment with a potentially cardiotoxic antineoplastic drug.

- Which etiologic category is raised?
- Does that exposure prove drug-induced cardiomyopathy?

## Case 4: Exposure is a clue, not proof

- Medication-associated toxicity is a plausible acquired cause.
- Anthracyclines and cyclophosphamide among potential myocardial toxins.
- Temporal association and phenotype require interpretation alongside alternative causes.
- The introductory source does not provide agent-specific causal thresholds.

# Three-pattern rapid differential

| Question       | Dilated              | Hypertrophic            | Restrictive               |
|----------------|----------------------|-------------------------|---------------------------|
| Chamber cavity | Increased            | Usually not dilated     | Usually not dilated       |
| Wall change    | Variable hypertrophy | Marked hypertrophy      | Often subtle              |
| Main defect    | Systolic             | Diastolic               | Diastolic                 |
| Key mimic      | CAD / valves         | Hypertension / stenosis | Constrictive pericarditis |

## Four errors that lead to misclassification

- Equating reduced ejection fraction with every cardiomyopathy.
- Calling any thick-walled heart genetic hypertrophic cardiomyopathy.
- Calling ventricular enlargement primary dilated cardiomyopathy before excluding competitors.
- Ignoring systemic etiologies when the heart is the dominant presenting organ.

## Integrative conclusions

- Cardiomyopathy denotes intrinsic myocardial dysfunction and requires etiologic context.
- The three major patterns organize dominant geometry and contractile/filling physiology.
- Most patterns have multiple possible causes; Primary and systemic disorders can converge phenotypically.
- Exclude common nonmyopathic mimics before labeling an unexplained phenotype idiopathic.

## Primary textbook reference

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026).
- Chapter 12, The Heart: “Cardiomyopathies” introductory section.
- Classification and causes interpreted from Tables 12.10 and 12.11.
- Morphologic pattern comparisons based on the discussion accompanying Figure 12.28.