

Left-Sided Heart Failure

Mechanisms, cardiac and pulmonary morphology, clinical correlations

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Learning objectives

Etiology

Distinguish ischemic, pressure, valvular, and intrinsic myocardial substrates.

Mechanisms

Relate abnormal contraction or filling to pulmonary congestion and low output.

Morphology

Explain ventricular, atrial, interstitial pulmonary and alveolar alterations.

Clinical correlation

Connect symptoms, investigations and organ dysfunction to pathogenesis.

Heart failure: A functional definition

- The heart cannot provide enough perfusion to meet peripheral metabolic requirements.
- Inadequate forward flow is commonly accompanied by venous congestion.
- Clinical dysfunction may arise from impaired ejection, impaired filling, or both.
- The anatomic appearance alone does not establish functional severity.

Three connected consequences of left heart failure

Pulmonary backpressure

Passive congestion and edema

Intracardiac stasis

Atrial enlargement, fibrillation
and thrombus

Low forward perfusion

Renal and cerebral dysfunction

Parallel consequences of impaired left ventricular function

Four major etiologic groups

Ischemic heart disease

Infarction or ischemic myocardial damage undermines pump performance.

Systemic hypertension

Sustained pressure load induces hypertrophy and later dysfunction.

Aortic / mitral valve disease

Stenosis or regurgitation changes loading and chamber structure.

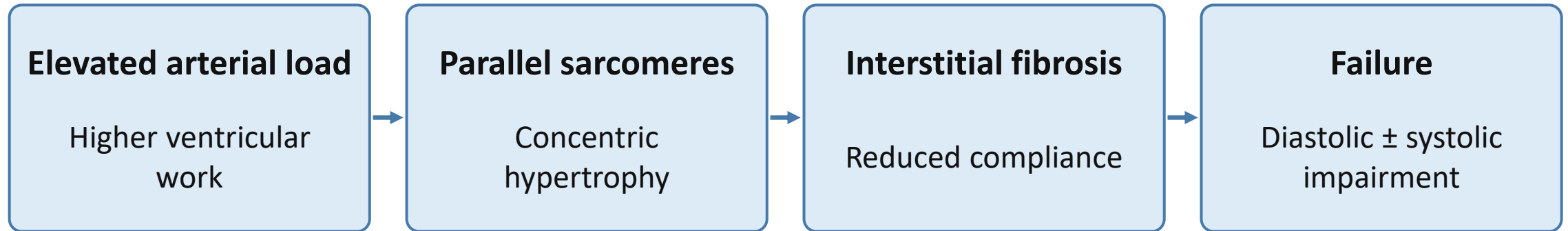
Primary myocardial disease

Intrinsic cardiomyopathic or infiltrative processes can impair contraction or filling.

Ischemic heart disease: Loss of effective myocardium

- Myocardial infarction removes contractile myocardium and produces regional dysfunction.
- Surviving myocardium carries greater mechanical work and undergoes compensatory hypertrophy.
- Chronic ischemic injury may coexist with fibrosis and impaired ventricular relaxation.
- Gross findings vary with infarct distribution and the surviving myocardial substrate.

Systemic hypertension: Pressure loading of the LV



Valvular disease imposes distinct loading patterns

Predominantly pressure overload

- Aortic stenosis increases outflow resistance.
- Parallel sarcomere addition expands myocyte cross-section.
- Wall thickening initially compensates for the high systolic workload.

Predominantly volume overload

- Aortic or mitral regurgitation increases chamber volume load.
- Serial sarcomere addition favors ventricular enlargement.
- Progressive dilation can coexist with greater total myocardial mass.

Intrinsic myocardial disease can impair either phase

- Primary myocardial pathology is a major Robbins etiologic category.
- Contractile derangement can produce systolic pump failure.
- Fibrosis and infiltrative disease can produce a stiff, poorly relaxing ventricle.
- Restrictive cardiomyopathy may present without the usual dilated or hypertrophied LV pattern.

Etiology and dominant mechanical consequence

Substrate	Initial mechanical disturbance	Possible phenotype
IHD / infarction	Loss of functioning myocardium	Reduced ejection; Remodeling
Systemic hypertension	Pressure overload	Hypertrophy; Stiffness
Aortic stenosis	LV outflow obstruction	Concentric wall thickening
Valve regurgitation	Volume overload	Chamber enlargement
Infiltrative myocardial disease	Reduced compliance	Impaired filling

Systolic and diastolic left-sided failure

Systolic failure (HFrEF)

Reduced ejection fraction reflects deranged ventricular contraction.

Diastolic failure (HFpEF)

Stiffness and impaired relaxation limit filling despite a relatively preserved ejection fraction.

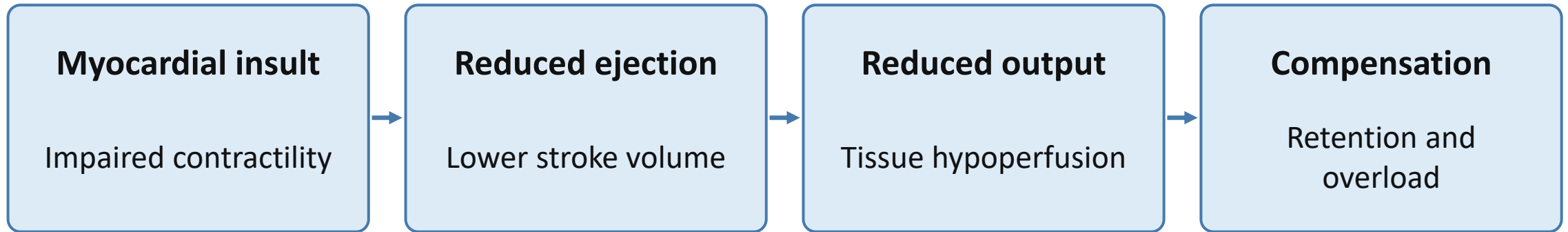
Shared downstream effect

Either mechanism can raise pulmonary filling pressure and cause congestion.

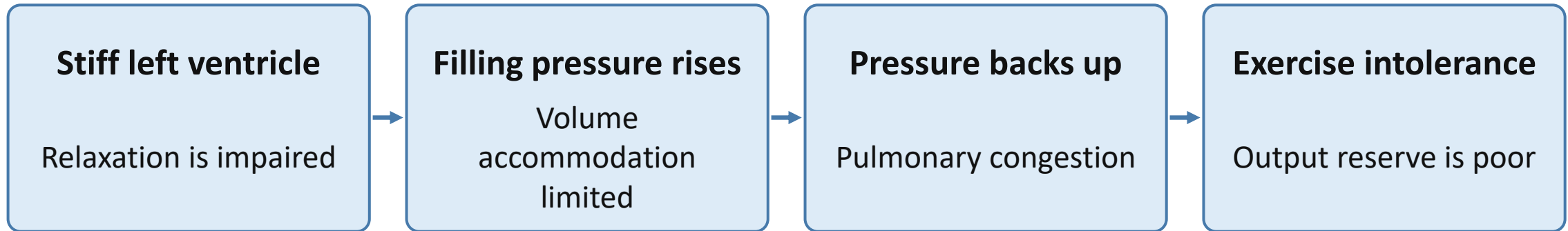
Clinical distinction

Ejection fraction describes a phenotype; The morphologic substrate still requires assessment.

Reduced ejection fraction: The systolic pathway



Preserved ejection fraction does not exclude failure



Why exertion unmasks diastolic failure

- At rest, a stiff ventricle may maintain relatively preserved cardiac function.
- Increased peripheral metabolic demand requires an increase in cardiac output.
- Poor relaxation limits the ability to expand ventricular filling.
- Pressure may rise sharply and be transmitted backward to the lungs.

Compliance and backward pressure transfer

More compliant ventricle

- Accommodates diastolic inflow with smaller pressure change.
- Effective relaxation helps maintain ventricular filling.
- Pulmonary venous pressure remains less affected by a given filling demand.

Stiff ventricle

- Limited expansion makes filling pressure rise quickly.
- Pressure transmits to the left atrium and pulmonary veins.
- Dyspnea and pulmonary edema can occur despite preserved EF.

Substrates of diastolic failure

Hypertension

The commonest underlying cause.

Other associations

Diabetes, obesity and bilateral renal artery stenosis can contribute.

Myocardial disease

Fibrosis in IHD/cardiomyopathy, or cardiac amyloid infiltration, can impair relaxation.

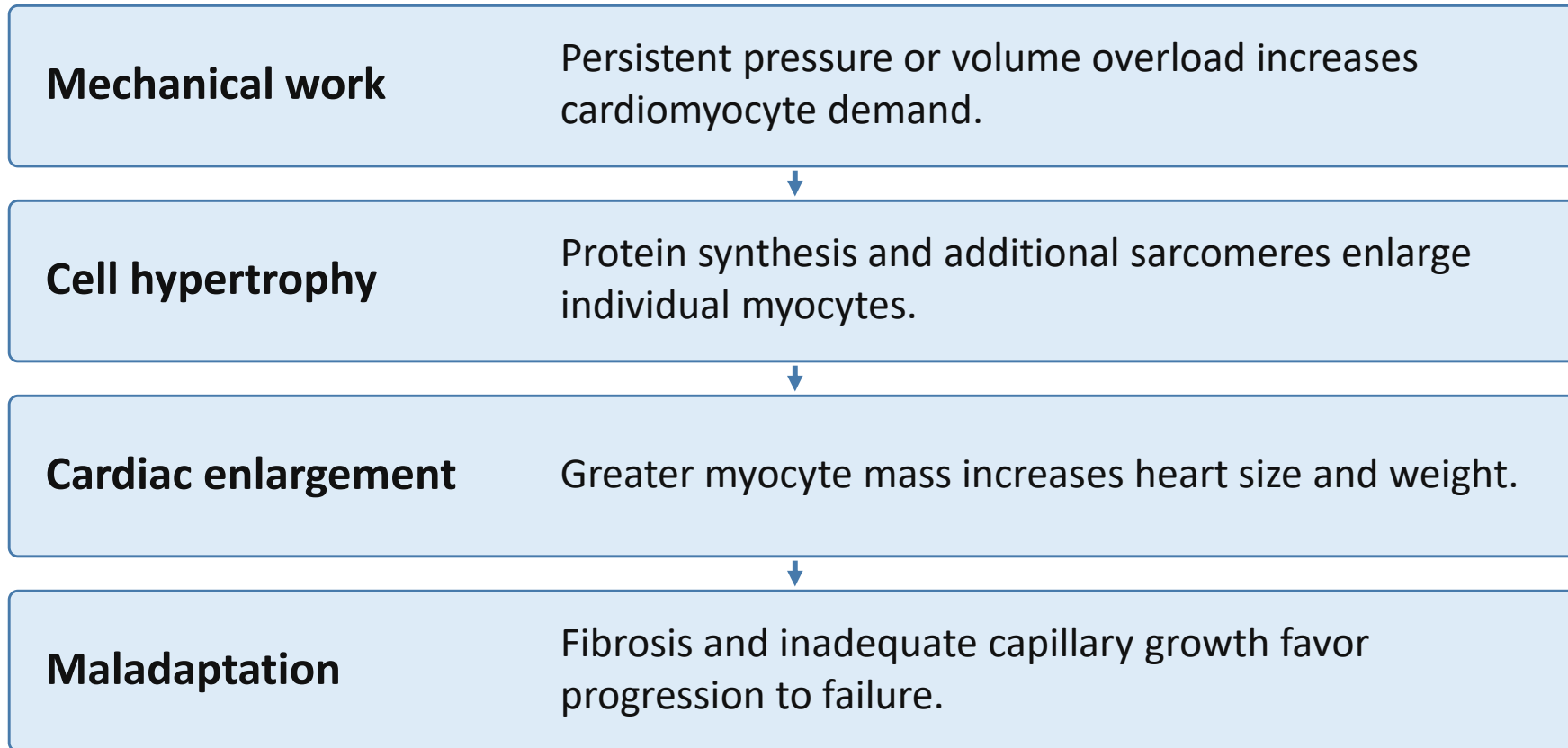
Older age

Fibrotic myocardial stiffening may contribute even without a recognized underlying disease.

A pericardial mimic of diastolic dysfunction

- Constrictive pericarditis limits the ability of the heart to fill.
- It can resemble intrinsic myocardial diastolic failure clinically.
- The constraining structure differs: Pericardium versus myocardium.
- Morphologic and echocardiographic evaluation is needed to distinguish mechanisms.

Remodeling begins as compensation



Pressure and volume overload: Sarcomere geometry

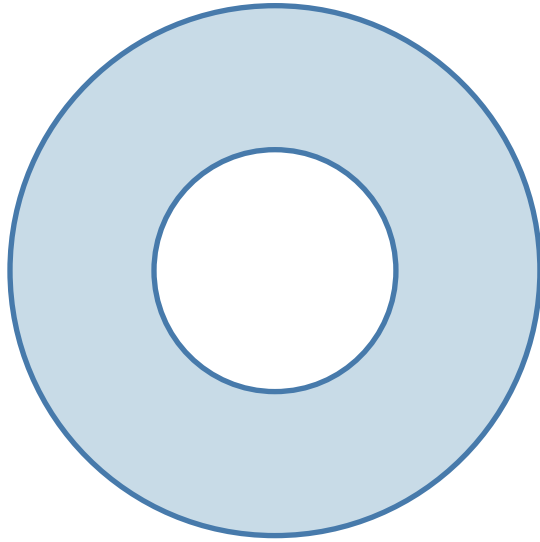
Pressure hypertrophy

- Sarcomeres added mainly in parallel.
- Myocytes gain cross-sectional area.
- Concentric wall thickening is characteristic.

Volume hypertrophy

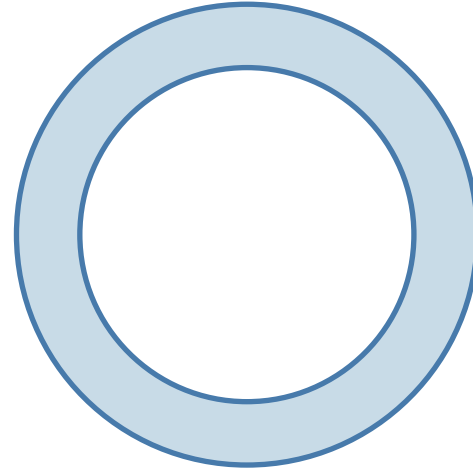
- Sarcomeres added mainly in series.
- Chamber dilation is prominent.
- Wall thickness can be high, normal or reduced.

Wall thickness is not equivalent to myocardial mass



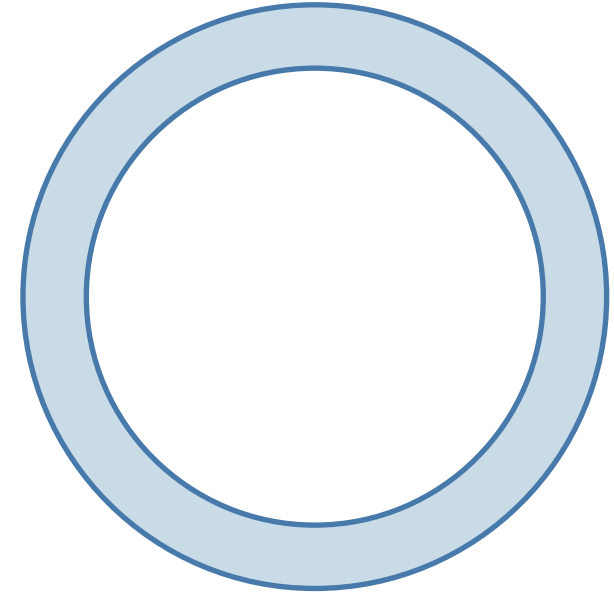
Pressure-loaded

Smaller cavity with thicker
relative wall



Reference

Reference cavity and wall
schematic



Dilated / hypertrophied

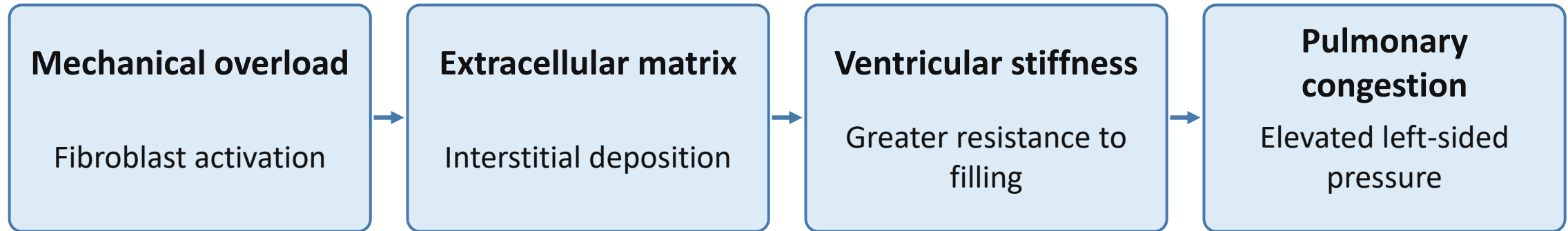
Larger chamber; Mass may rise
despite modest wall thickness

Simplified ventricular cross-sections; Schematic, not a specimen

Hypertrophy creates a supply–demand mismatch

- Hypertrophied myocytes enlarge without proportional increases in capillary density.
- A larger contractile mass increases myocardial oxygen and nutrient demand.
- Greater heart rate or inotropic state can further raise oxygen consumption.
- The remodeled myocardium is vulnerable to ischemic decompensation.

Interstitial fibrosis links remodeling to filling failure



Cellular remodeling extends beyond contractile size

Immediate-early genes

FOS, JUN, MYC and EGR1 in hypertrophic growth responses.

Fetal gene re-expression

Prolonged load is linked to fetal myosin forms, natriuretic peptides and collagen.

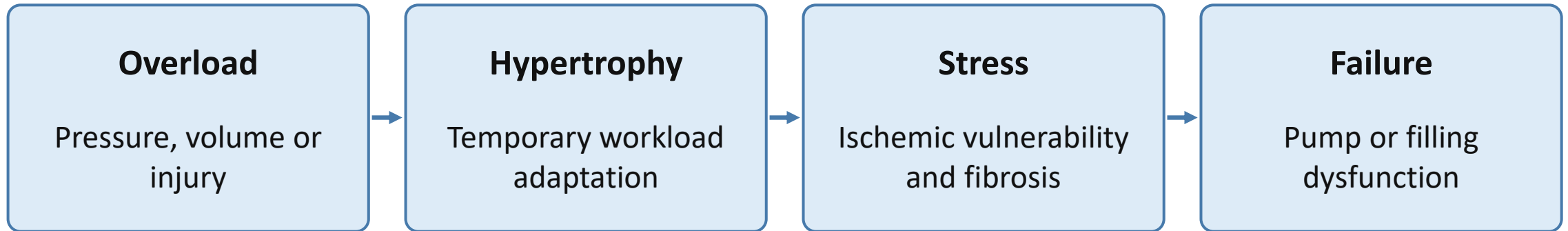
Myocyte nuclei

Enlarged or multiple nuclei may reflect increased DNA ploidy without cell division.

Stromal response

Nonmyocyte cells contribute fibrosis and remodeling.

Adaptation can become a self-amplifying burden



Regional injury versus diffuse mechanical burden

Myocardial infarction

- Loss of muscle produces regional dysfunction.
- Surviving myocardium hypertrophies under increased work.
- Scars and viable regions can coexist.

Valvular overload

- Pressure or volume burdens myocardium more globally.
- Remodeling may affect the entire LV.
- Resulting architecture depends on load and disease course.

Gross pathology must be interpreted in context

- The failing LV may contain an infarct, diseased valves, or intrinsic myopathy.
- Severe hypertrophy, dilation, or both are common but not universal.
- The usual LV response depends strongly on the initiating pathologic process.
- Cardiac size and wall thickness do not alone define functional severity.

The usual left ventricular phenotype

Hypertrophy

The left ventricle is usually hypertrophied in left-sided failure.

Dilation

Dilation is frequent and can be massive in advanced disease.

Geometry

The chamber may enlarge even when wall thickness seems unimpressive.

Interpretation

Consider load pattern, infarction and primary myocardial disorders.

Two important exceptions to the usual LV pattern

Mitral stenosis

- Left atrial inflow obstruction can cause pulmonary congestion.
- The LV need not develop the common hypertrophied, dilated morphology.
- Interpret the valve lesion before inferring LV structural change.

Unusual restrictive cardiomyopathies

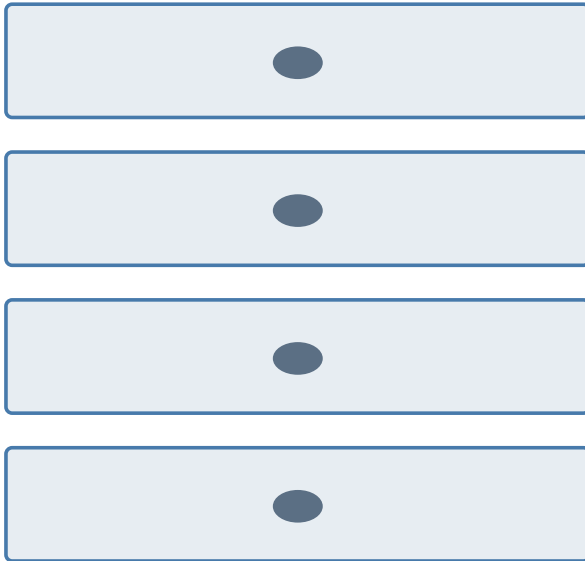
- Impaired filling may occur without marked LV dilation.
- Stiff myocardial tissue can produce pulmonary backpressure.
- Preserved size is not proof of preserved diastolic function.

Microscopic findings in failing myocardium

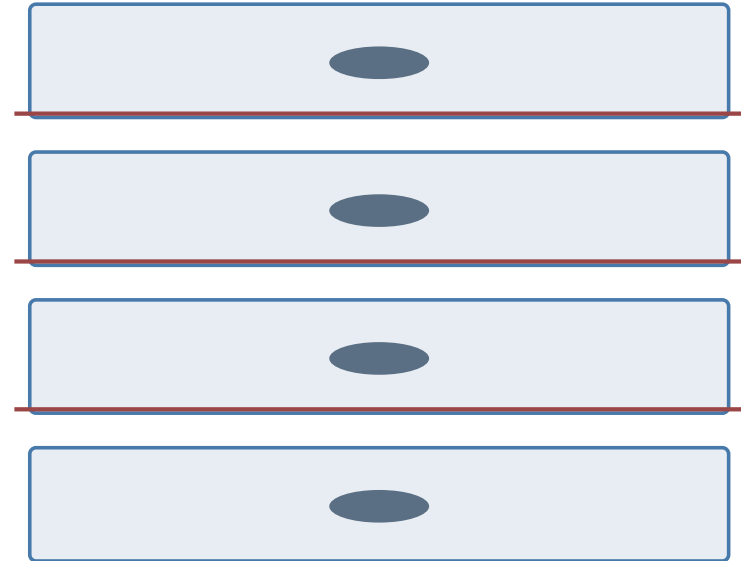
- Myocyte hypertrophy is a frequent but nonspecific microscopic alteration.
- Interstitial fibrosis varies in extent between causes and disease courses.
- Myocyte nuclei may appear enlarged in hypertrophic remodeling.
- Microscopy must be integrated with gross and clinical etiology.

Myocyte enlargement and interstitial fibrosis

Reference myocardium



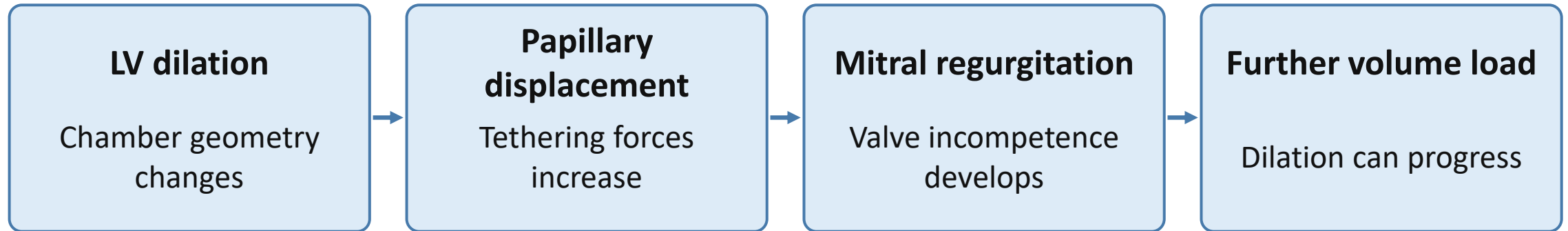
Hypertrophy



Myocyte enlargement, larger nuclei and interstitial fibrosis (red lines)

Original editable schematic; Not a photomicrograph

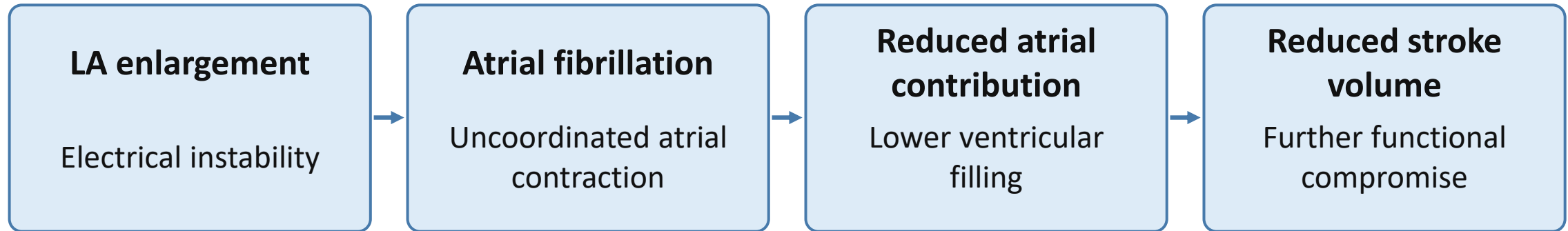
Ventricular dilation can worsen mitral competence



Why the left atrium enlarges

- Diastolic dysfunction elevates pressures transmitted to the left atrium.
- LV dilation with mitral incompetence adds atrial pressure and volume load.
- Secondary atrial dilation increases the susceptibility to atrial fibrillation.
- The atrial structural response has clinical thromboembolic implications.

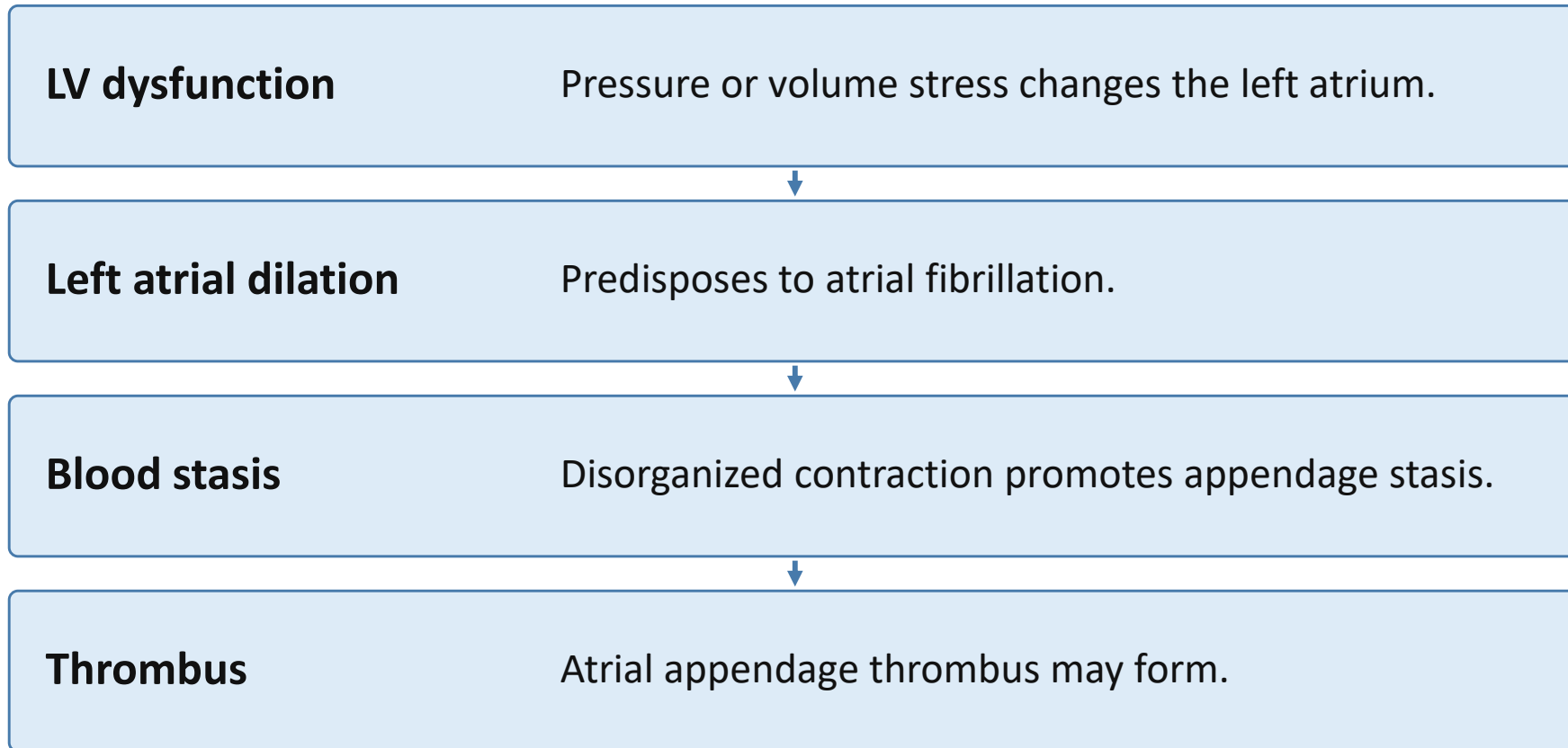
Atrial fibrillation compounds cardiac dysfunction



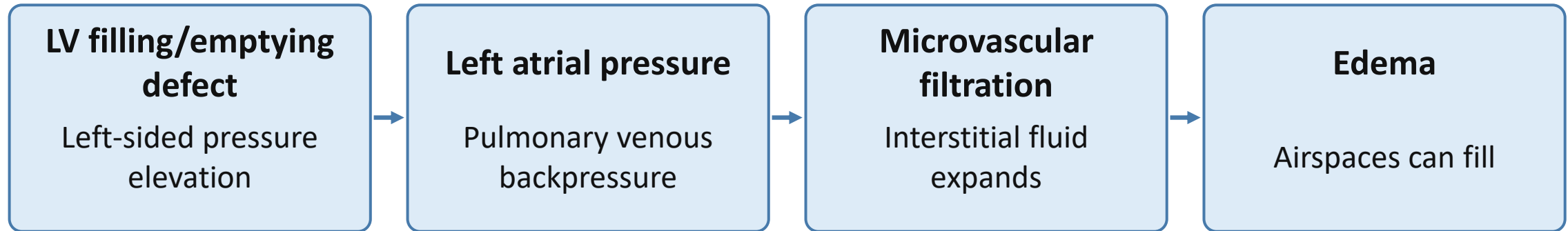
Stasis favors left atrial appendage thrombus

- Atrial fibrillation predisposes to uncoordinated atrial contraction and blood stasis.
- Stasis is especially important in the left atrial appendage.
- The atrial appendage is a common site for thrombus formation.
- An intracardiac thrombus represents an additional complication beyond pulmonary edema.

Cardiac consequences form a connected chain



Backward failure culminates in pulmonary edema



Pulmonary congestion reflects venous backpressure

- Blood backs up in the pulmonary circulation when the left heart fails.
- Elevated hydrostatic forces promote movement of fluid from vessels into lung tissue.
- Pulmonary congestion may occur with systolic or diastolic failure.
- Fluid accumulation ultimately compromises gas exchange and causes breathlessness.

Earliest pulmonary edema: Interstitial fluid

- The first changes include perivascular and interstitial edema.
- Interlobular septa are particularly involved in this early stage.
- Alveolar airspaces may not yet be filled with fluid.
- This step precedes more extensive edema of alveolar structures.

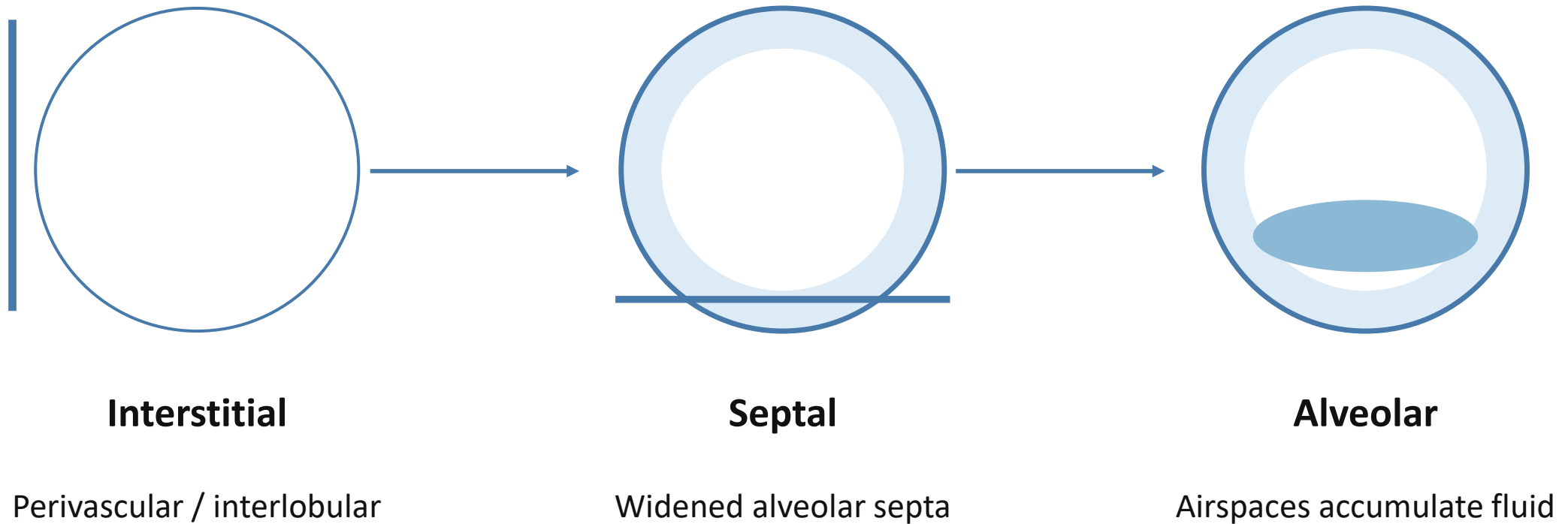
Progression to edematous alveolar septa

- Fluid extends through the pulmonary interstitium.
- Alveolar septa become progressively widened by edema.
- Widened septa alter the interface between pulmonary capillaries and air.
- Further progression permits edema fluid to enter alveolar spaces.

Alveolar edema is the severe pulmonary stage

- Edema fluid accumulates within alveolar airspaces.
- Fluid-filled alveoli contribute to impaired ventilation and dyspnea.
- Extravasated red blood cells and plasma proteins may also enter airspaces.
- Alveolar macrophages subsequently clear red cells and proteins.

Morphologic sequence of pulmonary edema



Schematic: Fluid distribution, not actual histology

Gross lung morphology in left-sided failure

Weight

Pulmonary congestion and edema yield heavy lungs.

Moisture

Edema produces characteristically wet lung tissue.

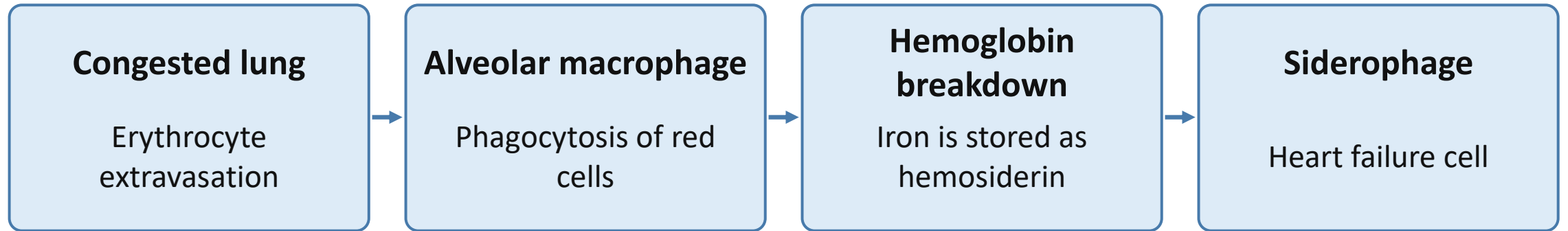
Distribution

Fluid accumulates in perivascular, interstitial and ultimately alveolar compartments.

Interpretation

Gross pulmonary findings indicate congestion; Cardiac disease establishes its cause.

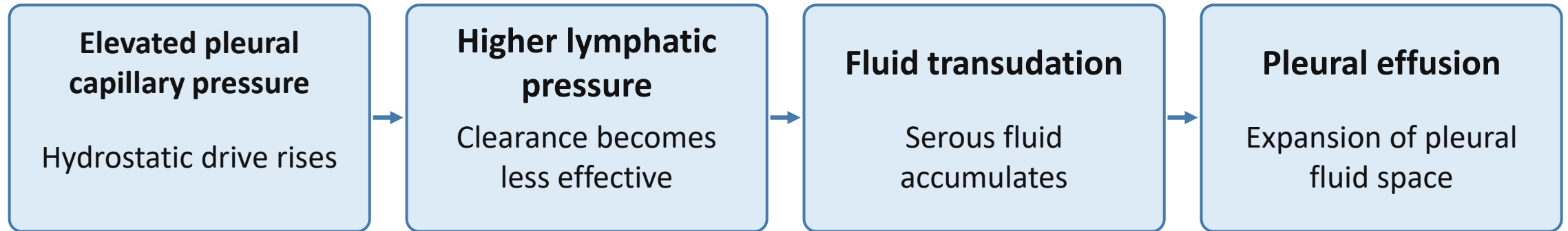
Red cells and iron lead to heart failure cells



Heart failure cells signify previous bleeding

- Alveolar macrophages ingest red cells that have escaped into edematous alveoli.
- Iron derived from digested erythrocytes accumulates as hemosiderin.
- Hemosiderin-laden macrophages are termed “heart failure cells.”
- They are evidence of prior episodes of pulmonary edema rather than a specific myocardial etiology.

Why pleural effusions occur



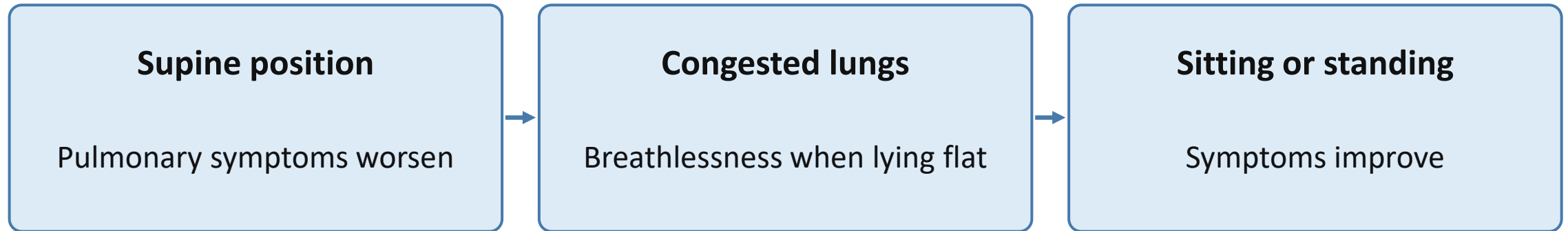
Compare fluid compartments affected by congestion

Compartment	Structural change	Clinical / morphologic relevance
Pulmonary interstitium	Perivascular and interlobular edema	Early congestion
Alveolar septa	Progressive septal widening	More extensive tissue edema
Alveolar airspaces	Intraluminal fluid; RBCs; Macrophages	Advanced edema; Heart failure cells
Pleural cavity	Serous transudative effusion	Fluid outside the lung parenchyma

Exertional cough and dyspnea may be the first symptoms

- Early pulmonary congestion commonly causes cough and breathlessness on exertion.
- Exercise increases demand on a ventricle with limited cardiac reserve.
- The pulmonary fluid burden may worsen as ventricular dysfunction advances.
- Absence of resting dyspnea does not exclude early left-sided failure.

Orthopnea: A positional consequence of congestion



Paroxysmal nocturnal dyspnea

Timing

A severe episode of breathlessness typically occurs during the night.

Experience

Patients may awaken with an intense sensation of suffocation.

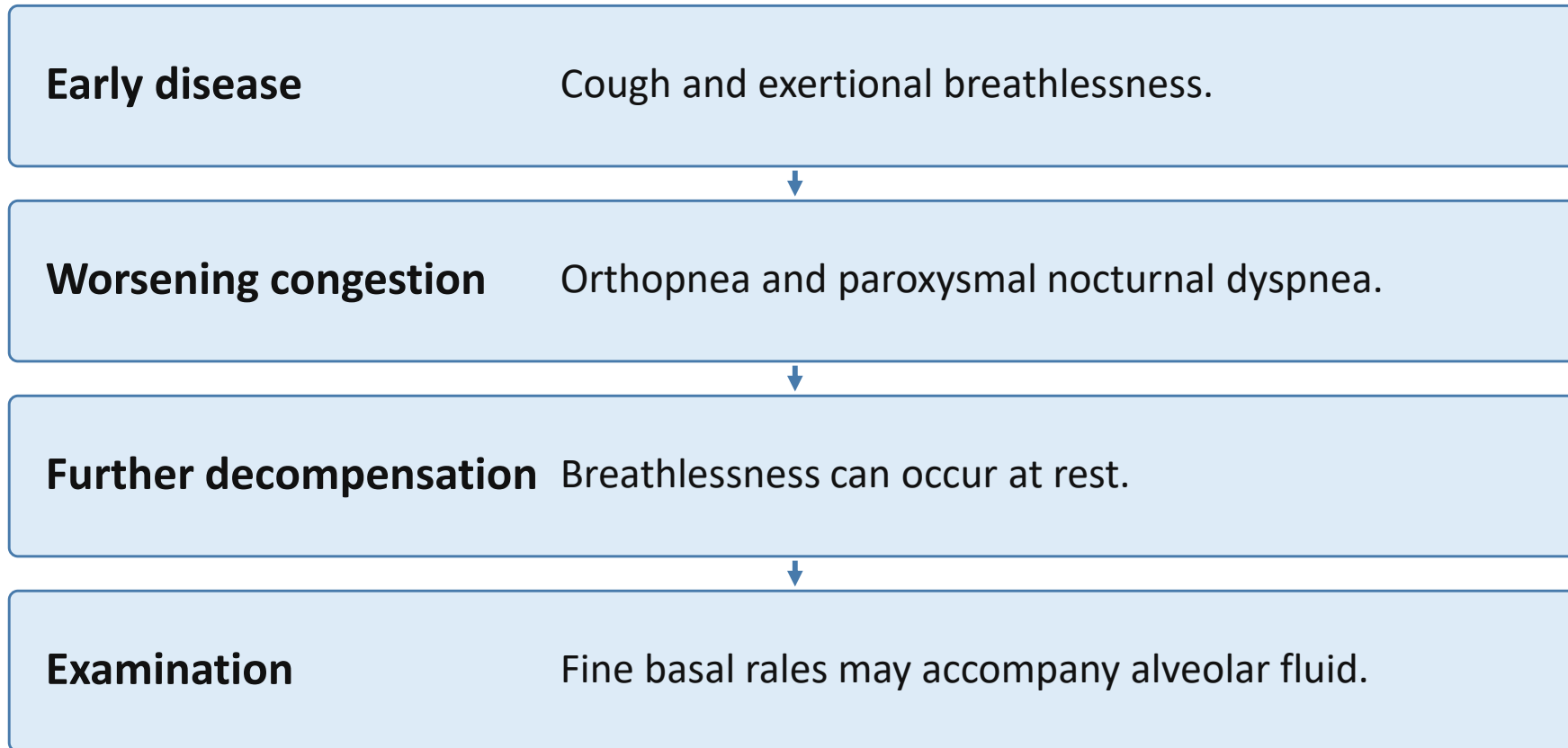
Underlying problem

Worsening pulmonary edema produces the respiratory symptoms.

Context

Often signifies progression beyond uncomplicated exertional dyspnea.

Clinical progression of pulmonary symptoms



Basal rales arise from edematous alveoli

- Fine rales are characteristically heard at the lung bases.
- In the Robbins account, edematous alveoli snap open during inspiration.
- This links an auscultatory finding directly to alveolar fluid accumulation.
- Rales are a manifestation of pulmonary congestion, not proof of one specific cause.

S3 and S4 reflect different loading states

Third heart sound (S3)

- Associated with ventricular volume overload.
- Can accompany enlargement and impaired systolic function.
- Interpret along with chamber size and LV performance.

Fourth heart sound (S4)

- Associated with increased myocardial stiffness.
- Suggests impaired ventricular compliance.
- Fits a diastolic dysfunction phenotype.

Cardiac examination and imaging clues

Cardiomegaly

An enlarged cardiac silhouette may be apparent on imaging.

Tachycardia

A common compensatory manifestation of LV failure.

Ventricular sounds

S3 may reflect volume overload; S4 suggests increased stiffness.

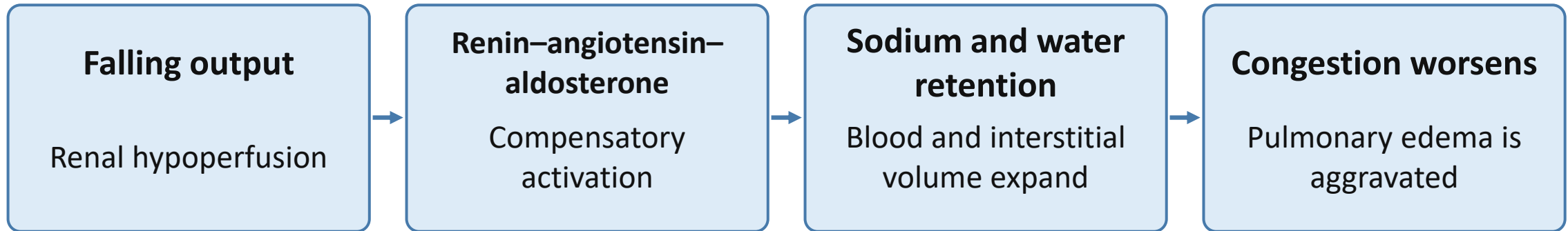
Valve effects

Progressive ventricular enlargement can cause secondary mitral regurgitation.

Link clinical findings to pathology

Finding	Pathologic mechanism	Interpretation
Exertional dyspnea	Pulmonary congestion	Early reduced reserve
Orthopnea / PND	Progressive pulmonary edema	More symptomatic congestion
Basal fine rales	Opening of edematous alveoli	Alveolar fluid
S3	Ventricular volume overload	Loading abnormality
S4	Myocardial stiffness	Impaired compliance

Reduced renal perfusion recruits compensatory pathways



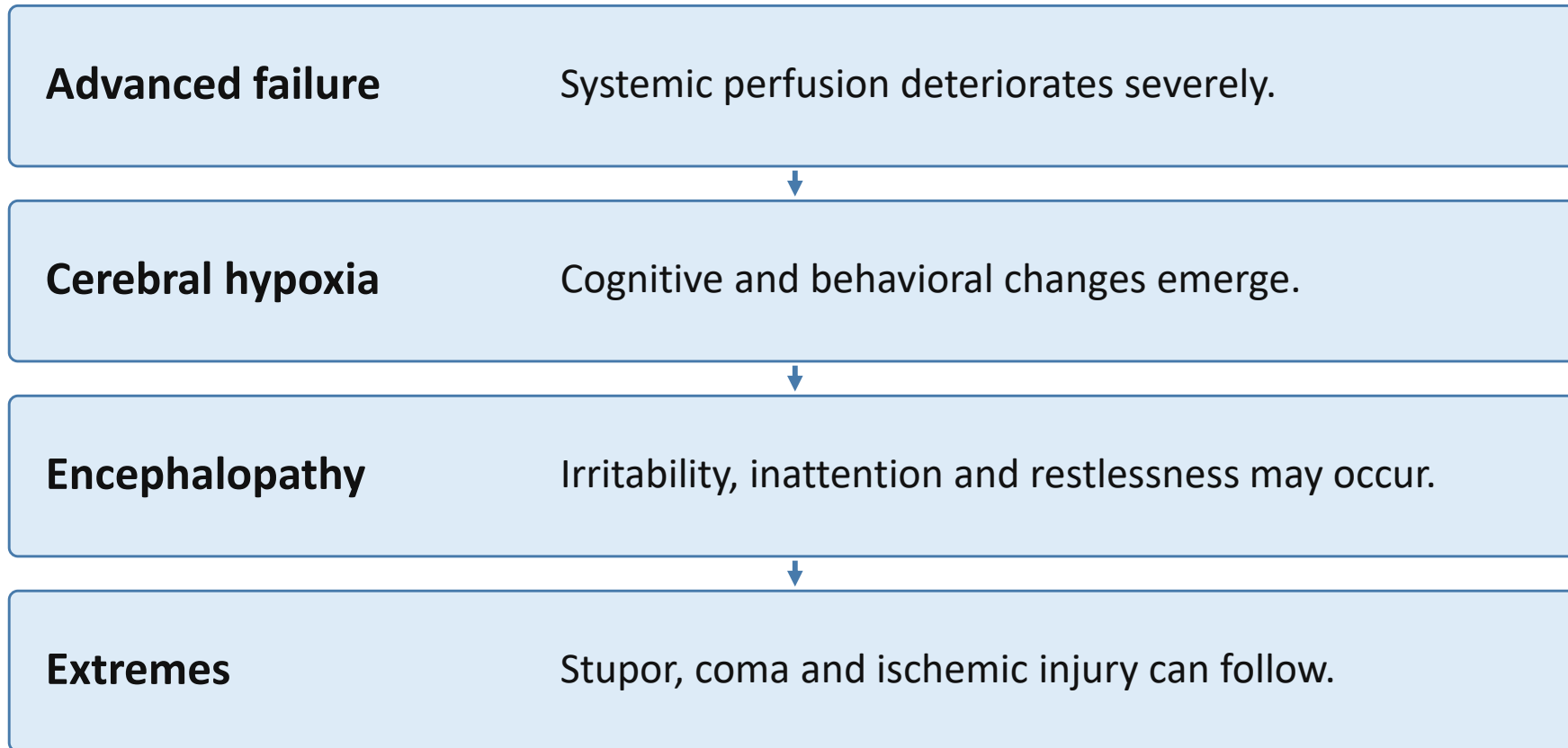
Renin–angiotensin activation can become maladaptive

- The kidney responds to diminished perfusion as if the circulation were underfilled.
- Salt and water retention expands intravascular and interstitial fluid volumes.
- Additional volume increases the burden on the failing left heart.
- Pulmonary congestion can therefore worsen despite an initially compensatory response.

Prerenal azotemia reflects severe hypoperfusion

- Progressively reduced renal blood flow can impair nitrogenous waste excretion.
- The resulting azotemia is described as prerenal in the Robbins account.
- This consequence indicates inadequate forward perfusion as well as congestion.
- It is distinct from the direct pulmonary manifestations of backward failure.

Severe cerebral hypoperfusion is a late consequence



Forward failure and backward failure affect different organs

Dominant mechanism	Target compartment	Representative consequence
Backward congestion	Pulmonary microcirculation	Interstitial / alveolar edema
Backward congestion	Pleural capillaries and lymphatics	Serous pleural effusions
Cardiac stasis	Left atrium / appendage	Atrial thrombus
Forward hypoperfusion	Kidney	RAAS activation; Prerenal azotemia
Forward hypoperfusion	Brain	Hypoxic encephalopathy

Echocardiography interrogates multiple mechanisms

Ejection fraction

Measures systolic performance and helps identify reduced-EF failure.

Wall motion

Displays regional dysfunction potentially associated with infarction or ischemia.

Valve function

Assesses stenosis or regurgitation and their loading consequences.

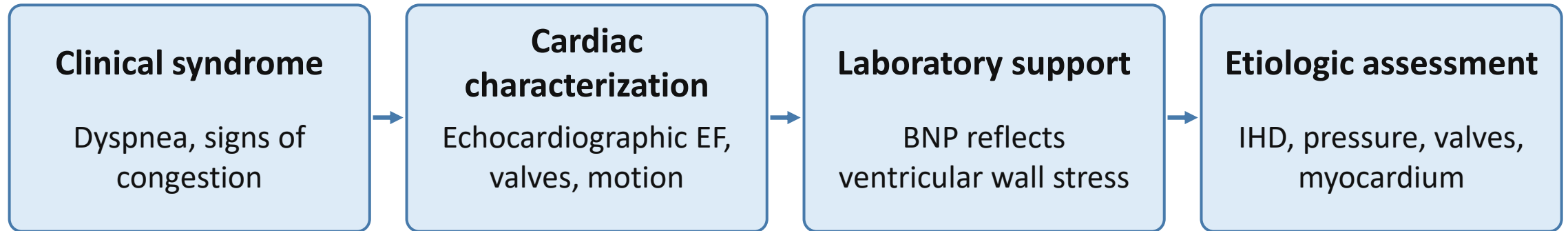
Thrombus / structure

Can identify chamber changes and possible mural thrombus.

BNP provides complementary evidence of heart failure

- Ventricular cardiomyocytes release B-type natriuretic peptide in response to wall stress.
- BNP can support quantitative assessment of clinical heart failure.
- A low BNP value has high negative predictive value for heart failure in the Robbins account.
- BNP should be interpreted alongside history, examination and cardiac imaging.

Integrating a suspected left-sided failure presentation



Left-sided and right-sided failure: Predominant effects

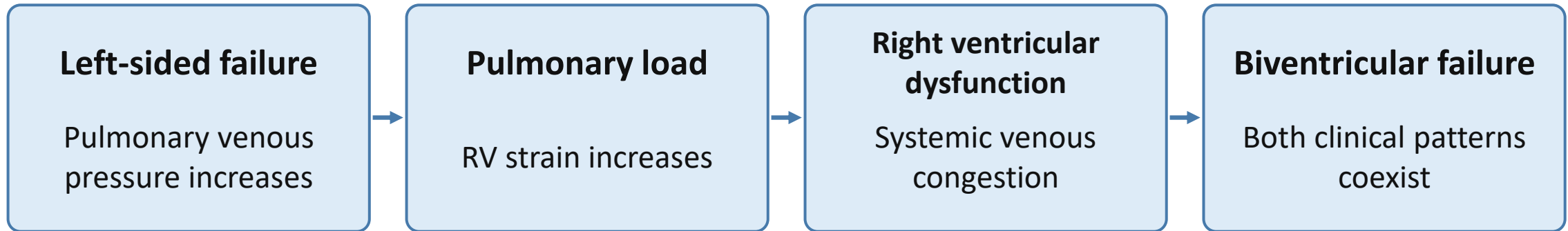
Left-sided failure

- Pulmonary congestion and edema predominate.
- Left atrial stasis and systemic underperfusion may coexist.
- Common causes: IHD, HTN, valve and myocardial disease.

Right-sided failure

- Systemic and portal venous congestion predominate.
- Dependent edema and visceral congestion are typical.
- Often occurs secondary to longstanding left-sided failure.

Chronic left-sided failure may evolve into biventricular failure



Case study: Breathlessness after myocardial infarction

A patient with established ischemic heart disease develops exertional dyspnea, later orthopnea, cardiomegaly and an S3. Imaging suggests an enlarged left ventricle.

Discussion prompts

- Which functional phenotype is plausible?
- Explain why the lungs become edematous.
- What additional atrial complication may arise?

Case interpretation: Ischemic LV dysfunction

Mechanism

Infarcted myocardium can impair contraction and promote LV enlargement.

Congestion

Raised left-sided pressures cause pulmonary edema and orthopnea.

Complication

Atrial dilation can predispose to fibrillation and thrombus.

Case study: Preserved EF with pulmonary symptoms

An older patient with longstanding systemic hypertension experiences marked dyspnea during activity and cannot lie flat comfortably. Echocardiography shows preserved ejection fraction, and the LV is thick-walled.

Discussion prompts

- Explain how a preserved EF can coexist with failure.
- Identify the likely loading substrate.
- Why might an S4 be present?

Case interpretation: Impaired ventricular relaxation

Mechanism

Pressure overload and interstitial fibrosis may produce LV stiffness.

Hemodynamics

Filling pressure can rise and transmit to pulmonary veins.

Examination

S4 is associated with increased myocardial stiffness.

Case study: Hemosiderin-containing alveolar macrophages

A lung tissue specimen from a patient with chronic cardiac decompensation contains pigment-bearing macrophages in alveolar spaces. The lungs are described as heavy and wet.

Discussion prompts

- What does the macrophage pigment represent?
- Reconstruct the sequence that generated it.
- Does this finding identify a specific cardiac etiology?

Case interpretation: Heart failure cells

Pigment

Hemosiderin is stored iron from phagocytosed extravasated red cells.

Sequence

Congestion → alveolar bleeding → macrophage uptake → hemosiderin.

Meaning

Previous pulmonary edema is supported; The exact cardiac cause is not established.

Integrated pathology synthesis

Causes

IHD, hypertension, aortic or mitral disease, and myocardial disorders are dominant substrates.

Heart

LV hypertrophy or dilation, nonspecific fibrosis, atrial enlargement and possible thrombus.

Lungs

Interstitial then alveolar edema, heart failure cells and serous pleural effusions.

Systemic effects

Low output promotes RAAS retention, azotemia and, when severe, cerebral dysfunction.

Primary reference

Robbins, Cotran & Kumar

Pathologic Basis of Disease · 11th edition (2026)

Left-Sided Heart Failure and adjacent Heart Failure material

All explanatory drawings are original editable schematics; no reproduced clinical or histologic specimens.