

Rheumatic Fever and Rheumatic Heart Disease

Acute post-streptococcal inflammation → chronic valvular fibrosis

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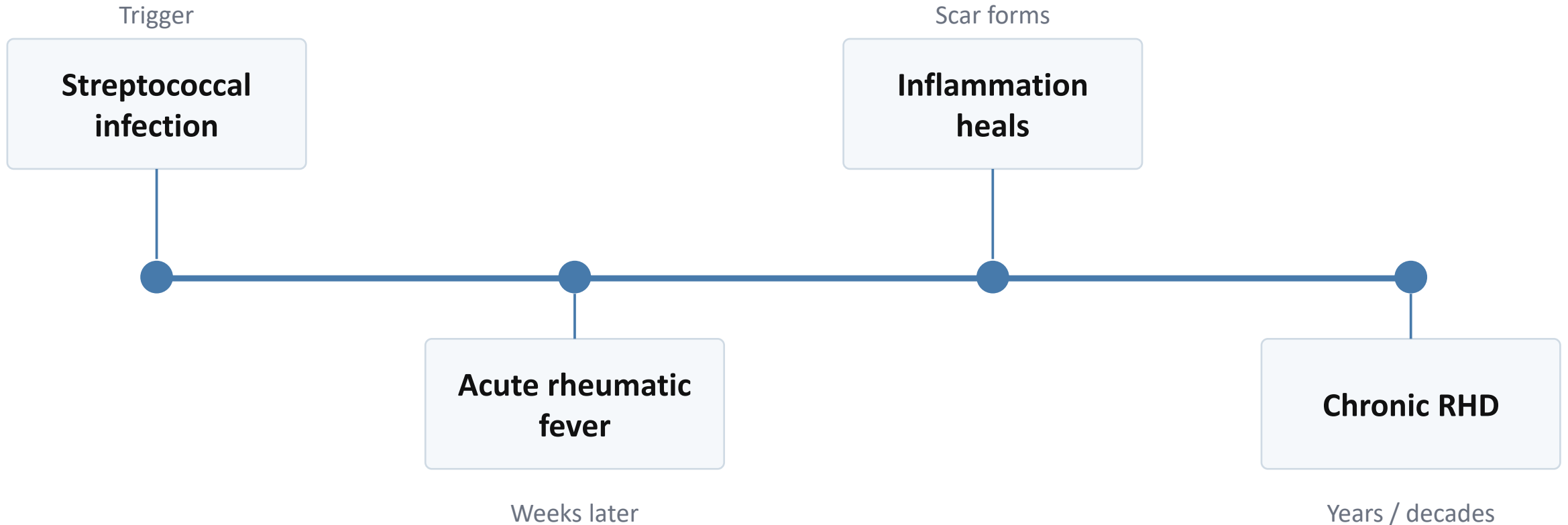
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Learning objectives

- Explain how immune cross-reactivity follows group A streptococcal infection.
- Recognize Aschoff bodies, rheumatic verrucae and chronic mitral distortion.
- Connect valve scarring to hemodynamic and thromboembolic sequelae.
- Apply the textbook description of clinical manifestations and Jones logic.

One disease process, two clinical time scales



An acute autoimmune illness can leave a delayed structural valve disease.

Schematic sequence; Intervals are not scaled

Rheumatic fever: Definition and trigger

- Acute, immunologically mediated multisystem inflammatory disease.
- Classically follows group A streptococcal pharyngitis.
- Occasionally follows streptococcal infection at other sites, including skin.
- Carditis is a major active manifestation and may progress to chronic RHD.

Chronic RHD: The structural endpoint

- Deforming fibrotic disease of cardiac valves is the defining lesion.
- Mitral valve is the dominant site of chronic involvement.
- Healed injury restricts opening, distorts closure or both.
- Clinical manifestations may not emerge until years after rheumatic fever.

Public health distribution

- RF and RHD have declined substantially in many regions.
- Improved sanitation and timely treatment of streptococcal pharyngitis contributed.
- RHD remains consequential in low-resource communities.
- Crowding and socioeconomic deprivation sustain ongoing disease burden.

Who develops acute RF?

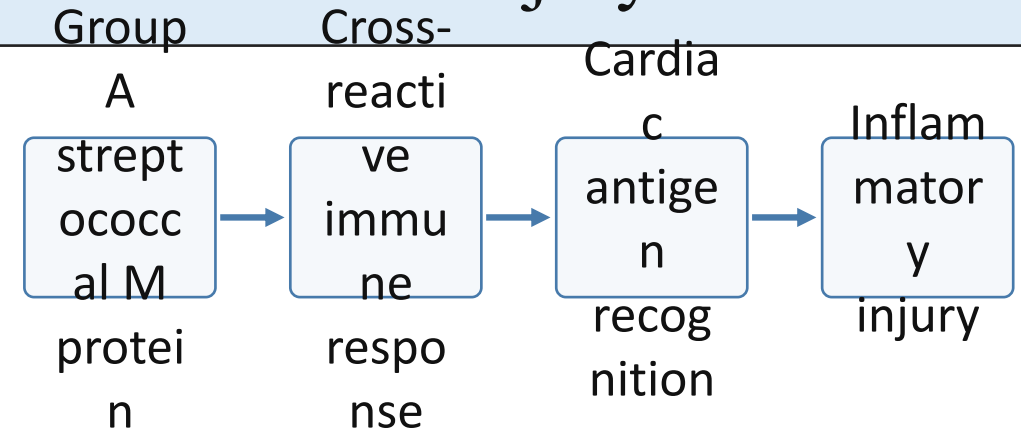
- First attacks occur most often at 5–15 years of age.
- Adult first presentations are possible.
- Only a minority develop RF after streptococcal infection.
- Approximately 0.3%–3% after infection.

Latency is a clue to pathogenesis

- RF typically appears around 10 days to 6 weeks after infection.
- The classic immunologic lag is about 2–3 weeks.
- By presentation, throat cultures may already be negative.
- The timing supports a delayed host immune response rather than direct invasion.

Immune cross-reactivity initiates tissue injury

- Streptococcal antigens share targets with host tissue.
- The surface M protein is a key antigen.
- Cardiac antigens may be recognized by the same response.
- Both humoral and cellular responses participate.

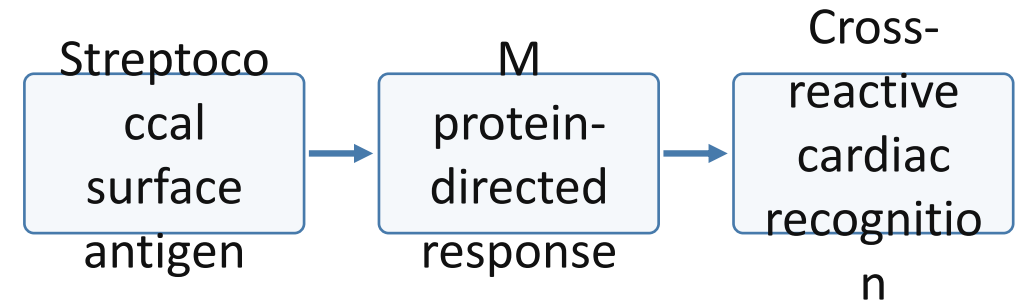


Cross-reaction, not myocardial colonization

Schematic

M protein provides the initiating antigen

- M protein is expressed on the bacterial surface.
- Antibodies and CD4⁺ T cells target its epitopes.
- Subsets of these responses recognize cardiac proteins.
- Predisposition influences which hosts mount damaging responses.



Cardiac targets of the immune response

Pericardium

Immune injury can produce pericardial inflammation.

Myocardium

Cellular inflammation and Aschoff bodies may develop.

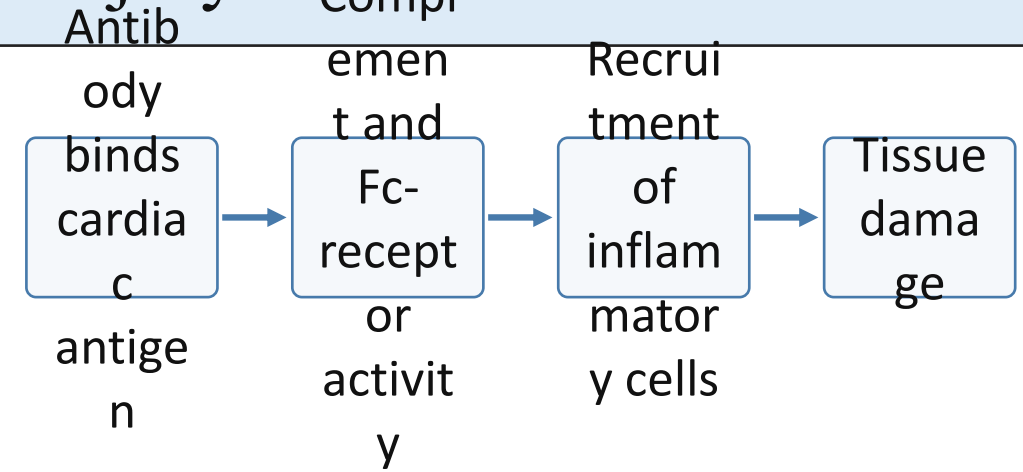
Valves

Endocardial and valvular injury can heal with scarring.

These compartments explain the pancarditis phenotype.

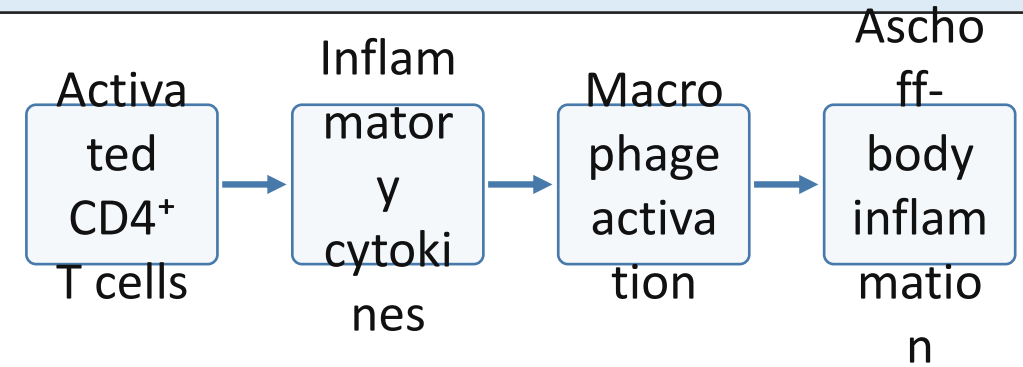
Antibody-mediated injury in R.F.

- Cross-reactive antibodies bind cardiac antigens.
- Complement activation amplifies local inflammation.
- Fc-receptor–bearing neutrophils and macrophages are recruited.
- Injury reflects host effector mechanisms.



T-cell–mediated injury in RF

- Cross-reactive CD4⁺ T lymphocytes recognize cardiac antigens.
- T-cell cytokines stimulate macrophage activation.
- Activated macrophages populate characteristic Aschoff lesions.
- Cell-mediated reactions coexist with antibody injury.



A combined immunologic lesion

Antibodies	CD4 ⁺ T cells	Outcome
Complement activation and Fc-receptor effector cells.	Cytokines and activation of tissue macrophages.	Inflammatory injury in cardiac layers; Subsequent healing.

Neither mechanism requires living streptococci in cardiac tissue.

Why direct infection is not the mechanism

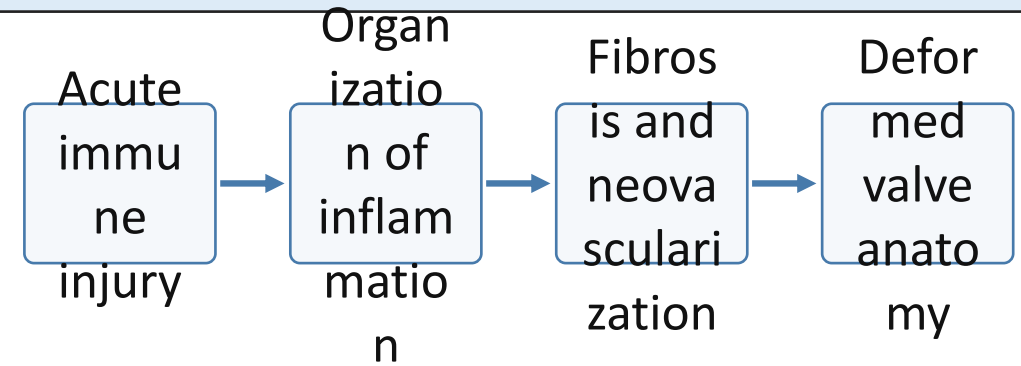
- Streptococci are absent from rheumatic cardiac lesions.
- RF appears after a latent period rather than contemporaneously with pharyngitis.
- Host-directed inflammation persists after the triggering infection resolves.
- Distinguish RF from infective endocarditis containing microorganisms.

Susceptibility is unequal across patients

- Most individuals with group A streptococcal infections do not develop RF.
- Intrinsic genetic susceptibility to cross-reactive responses.
- Genetic predisposition is an explanatory inference, not a single-gene diagnostic test.
- Exposure alone therefore cannot predict subsequent RF.

How an acute lesion becomes chronic RHD

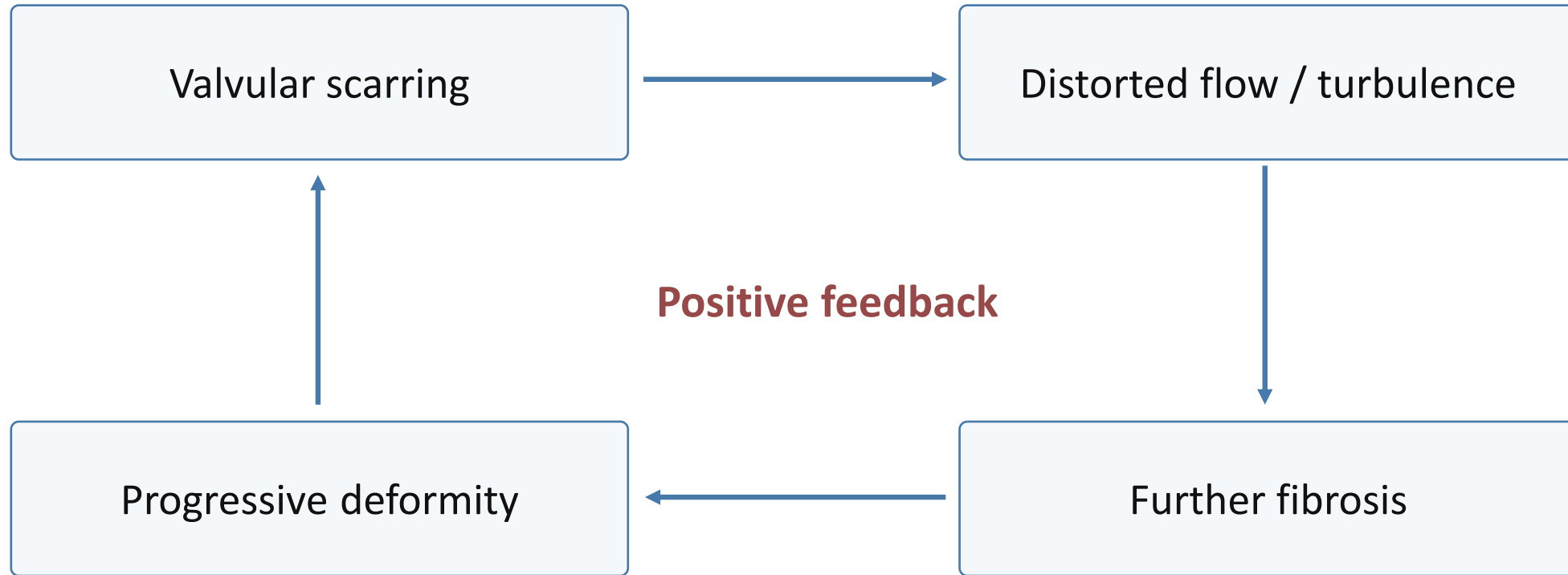
- Acute injury leads to inflammation and tissue damage.
- Organization and healing deposit fibrous tissue.
- Repeated attacks may produce cumulative deformity.
- The final clinical phenotype is dominated by valve fibrosis.



Repeat attacks compound valve injury

- After the initial episode, later streptococcal infections may reactivate RF.
- The same clinical manifestations may recur.
- Inflammatory episodes produce additive valve damage.
- Secondary prevention is conceptually important because injury is cumulative.

Valvular disease can amplify itself



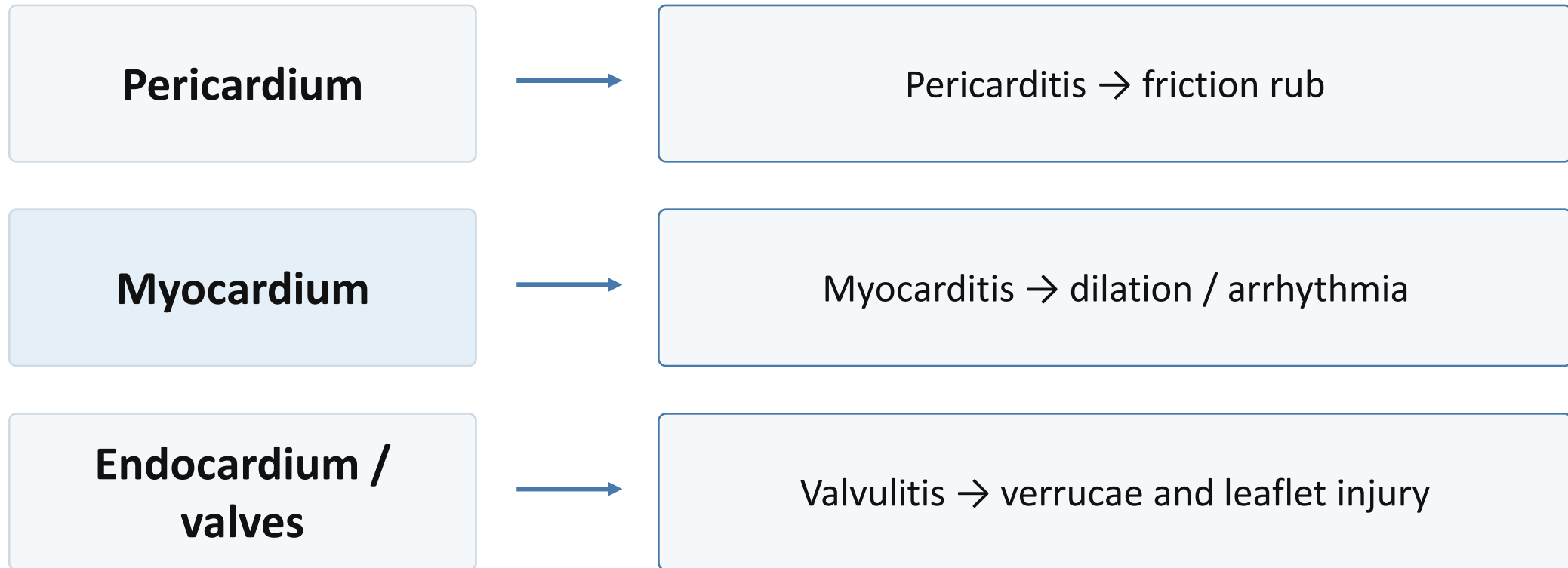
Schematic feedback loop

Acute RF is multisystem disease

- Migratory polyarthrititis of large joints.
- Carditis involving one or more cardiac layers.
- Subcutaneous nodules over extensor surfaces.
- Erythema marginatum: Circinate, irregular rash.
- Sydenham chorea: Rapid involuntary movements.

Acute carditis may affect all three layers

A tri-layer inflammatory process



Schematic: Three cardiac layers

Pericardial rheumatic inflammation

- Pericarditis is a manifestation of acute rheumatic carditis.
- Pericardial inflammation can produce a friction rub.
- It belongs to the acute inflammatory phase, not the defining chronic valve scar.
- Rheumatic carditis may involve other layers at the same time.

Myocardial rheumatic inflammation

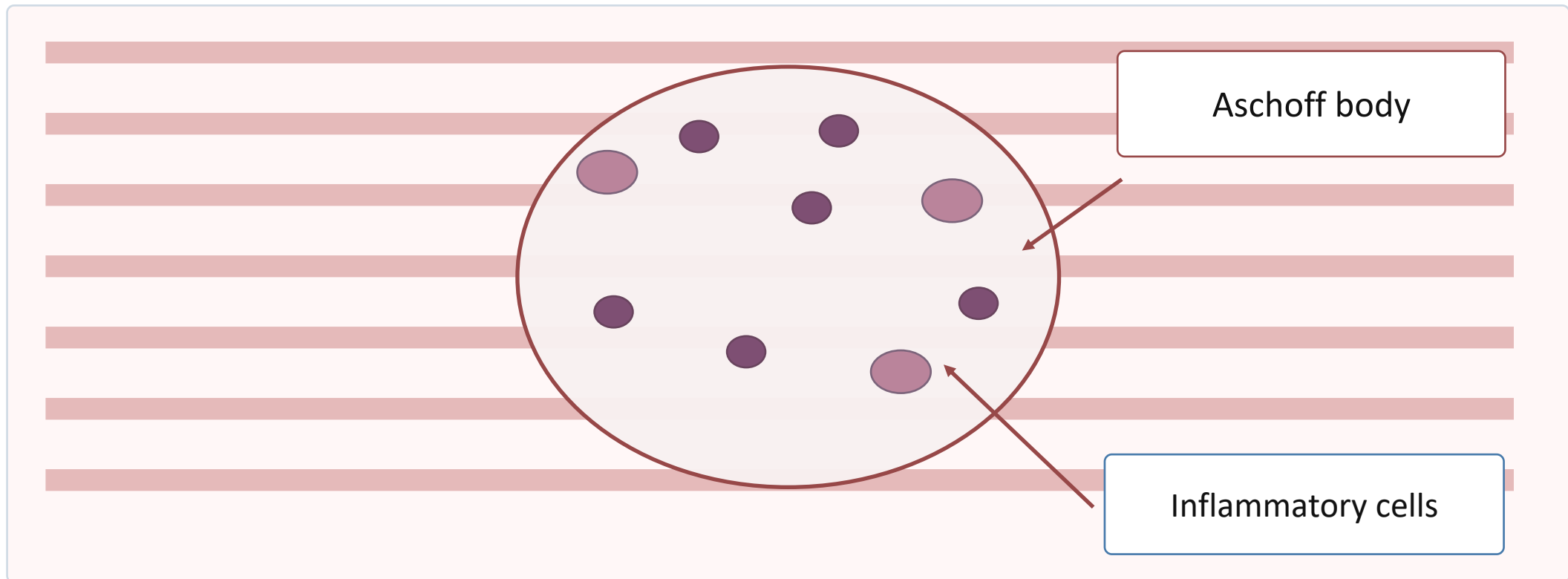
- Aschoff bodies can develop within the myocardium.
- Myocarditis may cause cardiac dilation.
- Dilation may lead to functional mitral insufficiency.
- Severe myocardial involvement can produce heart failure.

Acute endocardial and valve injury

- Left-sided valves are commonly involved.
- Inflammation is associated with fibrinoid necrosis in cusps and chordae.
- Small, noninfective vegetations form at the closure lines.
- Healing contributes to fibrous valve distortion.

Aschoff bodies: Defining focal lesion

Interstitial inflammatory focus between myocardial fibers



Schematic only — not a histologic specimen

Aschoff-body cellular composition

- Focal cardiac inflammatory nodules in acute RF.
- Contain T lymphocytes and occasional plasma cells.
- Include large activated macrophages called Anitschkow cells.
- Characteristic cytologic appearance helps identify the lesion.

Anitschkow cells: Nuclear morphology

- Plump activated macrophages with abundant cytoplasm.
- Round-to-ovoid nuclei; Occasional binucleation.
- Condensed nuclear chromatin arranged in a slender, wavy central ribbon.
- The characteristic appearance is termed a “caterpillar cell.”

Read an Aschoff body systematically

Setting	Cellular milieu	Specific clue
Myocardium or other cardiac layers during active RF.	Lymphocytes, occasional plasma cells, activated macrophages.	Anitschkow macrophages with ribbonlike nuclear chromatin.

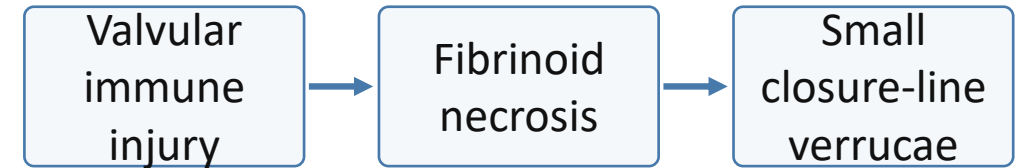
Lesion recognition requires tissue context, not a standalone cell.

Aschoff bodies are not a chronic requirement

- Aschoff bodies characterize active inflammatory rheumatic injury.
- They are rarely identified in late surgical or autopsy specimens.
- Decades may separate acute inflammation from chronic valve dysfunction.
- Absence of Aschoff bodies does not exclude chronic RHD.

Rheumatic verrucae: Morphology and site

- Small vegetations measure approximately 1–2 mm.
- Located along the line of valve closure.
- Overlie foci of fibrinoid necrosis.
- Characteristically belong to acute rheumatic valvulitis.



Location helps interpret vegetations

- RF: Small, warty vegetations along closure lines.
- Infective endocarditis: Often larger irregular destructive masses.
- RHD lesions are sterile despite being vegetative.
- Morphology must be interpreted together with the clinical setting.

MacCallum plaques: Endocardial response

- Irregular subendocardial thickening, usually in the left atrium.
- Occurs in the setting of rheumatic cardiac injury.
- Regurgitant jets may contribute to repeated endocardial trauma.
- Distinct from tiny verrucae directly on valve closure lines.

Acute valvular morphology: Three clues

Tissue injury

Fibrinoid necrosis of affected cusps and chords.

Surface lesion

Tiny verrucae located along valve closure lines.

Healing response

Organization of inflammation sets the stage for fibrosis.

Which valves are affected in chronic RHD?

Valve	Relative involvement	Interpretation
Mitral	Virtually always involved	Isolated in roughly two-thirds of cases
Aortic	May accompany mitral	Mitral + aortic in another ~25%
Tricuspid	Infrequent	Much less typical than left-sided valves
Pulmonary	Rare	Usually not the dominant valve lesion

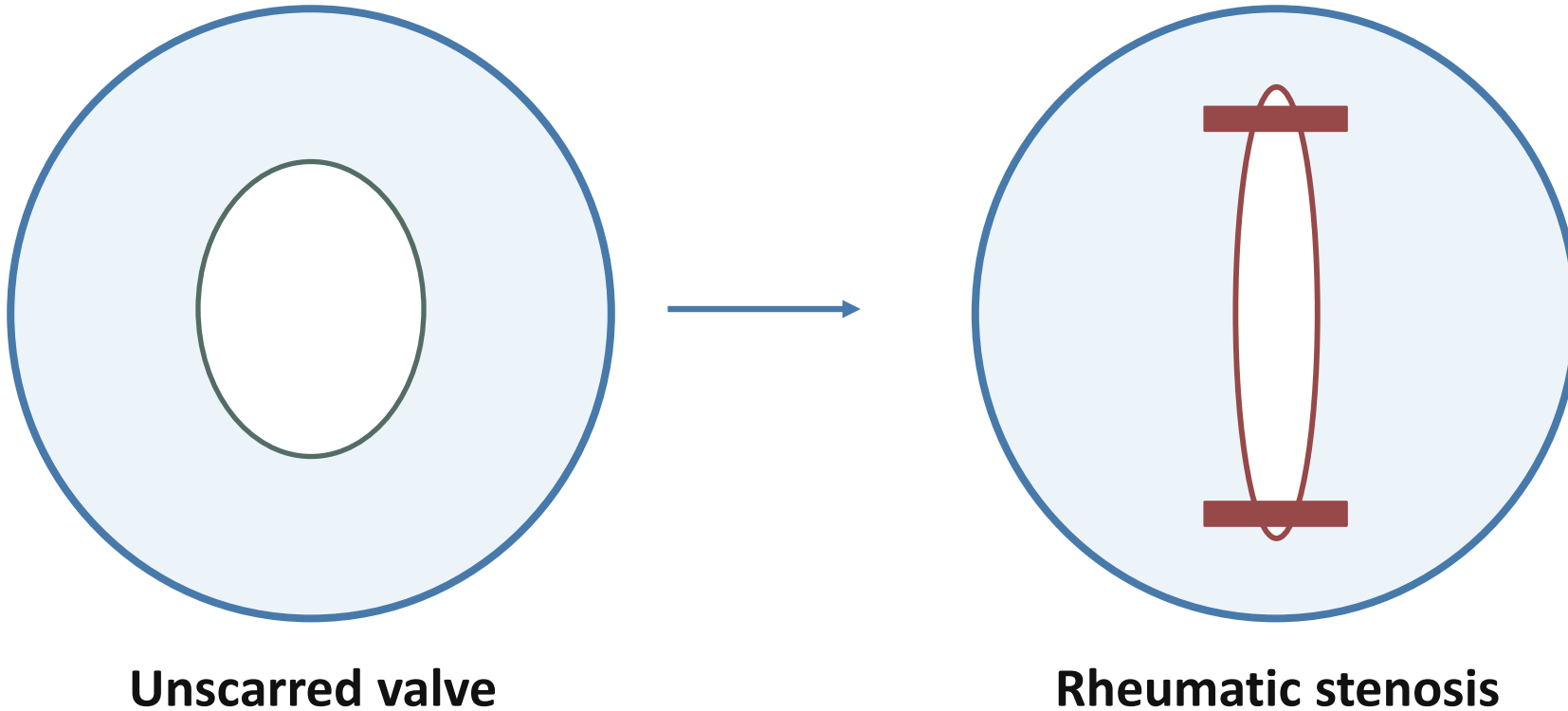
The mitral valve is the signature chronic target.

Chronic rheumatic mitral valve: Triad

- Diffuse leaflet thickening with distortion.
- Fusion and shortening of the commissures.
- Thickened, shortened and fused chordae tendineae.
- These are consequences of recurrent or healed inflammation.

Commissural fusion narrows the mitral orifice

Schematic: Progressively restricted valve opening.



Simplified en-face valve schematic — not a specimen

Commissural fusion has a mechanical consequence

- Bridging fibrosis fixes opposing leaflet margins together.
- The valve cannot open fully during diastole.
- Progressive restriction produces a stenotic mitral orifice.
- Calcification may supervene on chronically scarred commissures.

Chordal thickening adds valve distortion

- Rheumatic inflammation involves tendinous cords as well as cusps.
- Healing causes chordal thickening, shortening and fusion.
- The mobile support apparatus becomes tethered and rigid.
- Combined chordal and leaflet lesions impair normal valve mechanics.

“Fish-mouth” mitral stenosis

- Commissural fibrosis and calcification leave an elongated restricted aperture.
- The narrowed opening is conventionally called fish-mouth or buttonhole stenosis.
- It reflects fixed mechanical narrowing, not an acute transient spasm.
- Gross inspection should evaluate leaflets, commissures and chordae.

Microscopic chronic valve remodeling

- Organization of earlier inflammation results in scarring.
- Transmural fibrosis obliterates normal leaflet architecture.
- Post-inflammatory neovascularization may be conspicuous.
- These changes help distinguish longstanding remodeling from acute valvulitis.

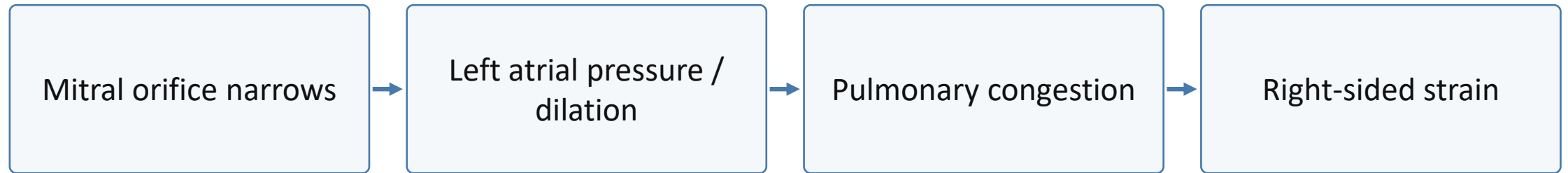
From acute to chronic: Lesion correspondence

Acute	Repair	Chronic
Aschoff bodies, fibrinoid injury and verrucae.	Organization of inflammatory injury and fibrous healing.	Commissural fusion, rigid leaflets and thickened chordae.

The lesion changes in character as the inflammatory episode heals.

Mitral stenosis: Atrial-to-pulmonary consequences

Consequence of mitral outflow obstruction



Schematic causal pathway

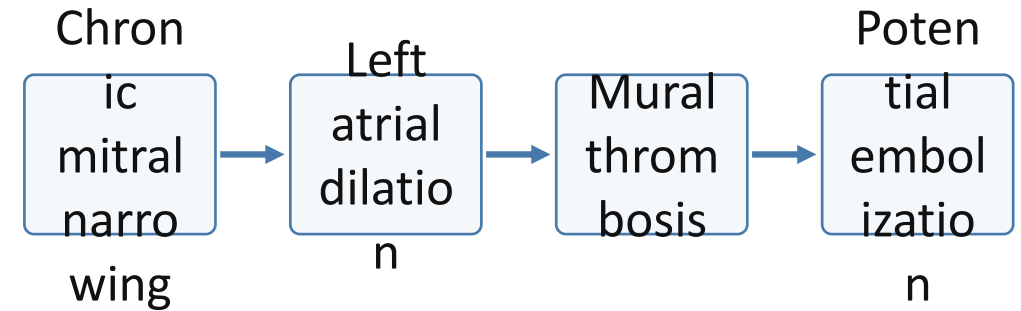
Isolated pure mitral stenosis generally leaves the left ventricle largely unaffected.

Left atrial remodeling in mitral stenosis

- Fixed obstruction chronically elevates the pressure burden upstream.
- The left atrium progressively dilates with tight mitral stenosis.
- A dilated atrium is susceptible to rhythm disturbance.
- Its cavity may contain mural thrombi.

Why atrial thrombi matter

- Left atrial dilation favors intracavitary stasis.
- Mural thrombi may form in advanced rheumatic mitral stenosis.
- Embolic fragments can enter the systemic circulation.
- Thromboembolism is an important chronic RHD complication.



Pulmonary consequences of mitral stenosis

- Persistent left atrial outflow obstruction causes pulmonary congestion.
- Long-standing congestive changes affect vessels and lung parenchyma.
- Sustained pulmonary vascular loading may follow.
- These changes contribute to right ventricular hypertrophy.

Right ventricular adaptation

- Pulmonary vascular consequences transmit pressure load to the right heart.
- Right ventricular hypertrophy may develop over time.
- The change is secondary to left-sided valvular disease.
- Thus a mitral lesion can ultimately produce right-heart pathology.

Why the left ventricle may be preserved

- Pure isolated mitral stenosis obstructs flow before blood reaches the left ventricle.
- The main pressure burden lies upstream in the left atrium and lungs.
- The LV is largely unaffected in isolated pure stenosis.
- Associated regurgitation or other lesions alter this expectation.

Migratory polyarthrititis is a clinical pattern

- Typically affects large joints sequentially.
- One joint becomes painful and swollen, then another is involved.
- Each episode may last days before spontaneous resolution.
- It ordinarily leaves no residual joint disability.

Other major RF manifestations

Skin

Erythema marginatum:
Irregular circinate rash.

Subcutaneous tissue

Nodules over extensor
surfaces of the extremities.

Nervous system

Sydenham chorea:
Involuntary rapid
movements.

How acute carditis presents

- Pericardial friction rub suggests pericardial inflammation.
- Tachycardia and arrhythmias reflect cardiac involvement.
- Myocardial dilation can cause functional mitral insufficiency.
- Fulminant cardiac inflammation may culminate in heart failure.

Carditis and arthritis dominate presentations

- Carditis and arthritis as predominant manifestations.
- Joint involvement is reported more commonly in adults than children.
- Joint disease is usually transient; Valvular injury can be permanent.
- This divergence explains the long-term importance of cardiac disease.

Streptococcal evidence may be serologic

- The preceding pharyngeal infection may have resolved before clinical RF.
- Throat culture can therefore be negative when RF develops.
- Antibodies to streptococcal products may remain measurable.
- Antistreptolysin O and anti-DNase B responses.

Jones criteria: Textbook diagnostic logic

- Begin with evidence of antecedent group A streptococcal infection.
- Classical rule: Two major manifestations, or one major plus two minor.
- Minor findings are nonspecific and include fever, arthralgia and acute-phase reactants.
- The criteria are evolving and are applied differently across risk settings.

Major and minor manifestations in the source

Major manifestations	Minor examples
Carditis	Fever
Migratory polyarthrititis	Arthralgia
Subcutaneous nodules	Elevated acute-phase reactants
Erythema marginatum	Other Jones elements not reproduced here
Sydenham chorea	Risk-adjusted rules require current guideline reference

This is a textbook teaching summary, not a current diagnostic checklist.

Diagnostic caution: Risk matters

- Jones criteria evolve over time.
- Low-risk and high-risk settings do not use identical applications.
- Do not apply a simplified classroom list as an exhaustive clinical algorithm.
- In actual practice, consult the current locally adopted diagnostic criteria.

Acute rheumatic versus infective endocarditis

Feature	Rheumatic valvulitis	Infective endocarditis
Mechanism	Cross-reactive host immunity	Microbial infection of endocardium
Vegetations	Small; Line of closure	Typically bulky and irregular
Organisms in lesion	Absent	May be present in vegetation
Tissue effects	Fibrinoid injury; Later fibrosis	Potentially destructive infection

Vegetation size and distribution support, but do not replace, clinicopathologic diagnosis.

Late presentation: Years after RF

- Chronic valvular symptoms can appear years or decades after acute RF.
- The manifestations depend on the valves involved.
- Valve lesions may lead to murmurs, dilation, hypertrophy and heart failure.
- Historical RF may no longer be clinically apparent at presentation.

Atrial fibrillation links valve and embolic disease

- Atrial fibrillation is particularly important in rheumatic mitral stenosis.
- Chronically enlarged atria are vulnerable to rhythm disturbance.
- Atrial arrhythmia and mural thrombosis can coexist.
- Clinical morbidity can therefore extend beyond the valve opening itself.

RHD predisposes to later infective endocarditis

- Chronically scarred valves are abnormal endocardial substrates.
- Infective endocarditis as a chronic RHD complication.
- Superimposed infection is distinct from the initial sterile RF mechanism.
- New infective lesions should not be interpreted simply as RF recurrence.

Long-term outcome is heterogeneous

- Severity differs with affected valves and degree of deformity.
- Arrhythmias, embolic events and heart failure alter the course.
- Repeated inflammation can drive cumulative valve damage.
- Valve repair or replacement has improved prognosis in suitable patients.

Case 1 — delayed systemic illness

A school-age child develops fever and sequential swelling of large joints several weeks after sore throat.

- Which immune sequence connects the two illnesses?
- Which cardiac finding would be important to look for?
- Why might the throat culture already be negative?

Answer: Cross-reactive post-streptococcal immunity; Assess for carditis.

Case 2 — ventricular inflammation

A patient with active RF develops tachycardia, an enlarged heart and functional mitral insufficiency.

- Which heart layer is producing the major dysfunction?
- What focal inflammatory lesion may be present?
- What macrophage nuclear pattern characterizes that lesion?

Answer: Myocarditis; Aschoff bodies containing Anitschkow cells.

Case 3 — chronic valvular sequelae

An adult with a remote history of RF develops mitral stenosis, left atrial dilation and an atrial arrhythmia.

- Which structural valve lesions are expected?
- Why may left atrial thrombus develop?
- What right-sided cardiac consequence may follow?

Answer: Fused commissures/chordae; Stasis and embolism; Eventual RV hypertrophy.

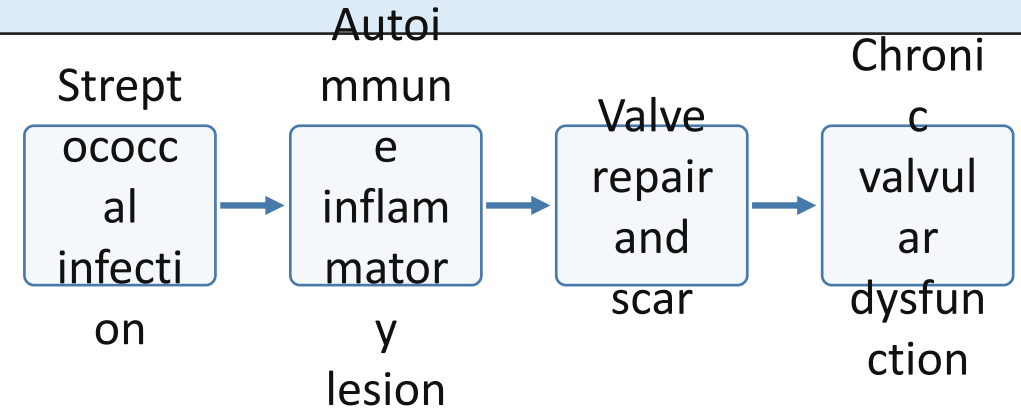
Acute RF versus chronic RHD

Feature	Acute RF	Chronic RHD
Primary biology	Cross-reactive inflammation	Fibrotic repair and distortion
Characteristic heart lesion	Aschoff bodies; Verrucae	Commissural / chordal fusion
Typical time relation	Weeks after infection	Often years to decades later
Predominant hazard	Active carditis	Stenosis, AF, embolism, failure

Both phases are manifestations of the same post-streptococcal disease process.

Mechanism-to-morphology synthesis

- Initiating pathogen is group A streptococcus.
- Cross-reactive host immunity creates acute injury.
- Aschoff bodies and tiny closure-line verrucae signify active disease.
- Healing and recurrent inflammation produce distorted, stenotic valves.



Five morphological points to retain

- Aschoff bodies are focal inflammatory cardiac lesions of active RF.
- Anitschkow macrophages show wavy “caterpillar” nuclear chromatin.
- Verrucae are tiny closure-line vegetations in rheumatic valvulitis.
- Chronic mitral disease fuses commissures and chordae and thickens leaflets.
- Fibrosis and neovascularization obliterate normal valve architecture.

Five clinical links to retain

- Antecedent streptococcal infection precedes an immune-mediated syndrome.
- Migratory large-joint arthritis may resolve without deformity.
- Carditis can generate lasting valvular lesions.
- Mitral obstruction promotes atrial dilation, thrombosis and lung congestion.
- Chronic RHD may present decades after the initial febrile episode.

Reference and source boundaries

Primary textbook

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026). Chapter 12, “The Heart.”

Visual provenance

Mechanism, valve and histology diagrams are original editable schematics, not diagnostic photographs or reproduced textbook figures.

The brief Jones summary follows the textbook wording; verify current risk-stratified criteria before clinical use.