

Infective Endocarditis

Etiology · pathogenesis · morphology · clinicopathologic diagnosis

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Define infective endocarditis and describe infected vegetations.
- Link microbial virulence and substrate to clinical tempo.
- Identify the major morphologic lesions and complications.
- Integrate cultures, imaging and clinical findings using Duke criteria.

Infective endocarditis: Core definition

- Microbial infection involves valve tissue or mural endocardium.
- Vegetations comprise thrombotic debris and microorganisms.
- Underlying cardiac tissue can be destructively involved.
- Although bacterial IE predominates, fungi and other microbes occur.

The principal anatomic targets

Native valves

Aortic and mitral valves are the most common sites.

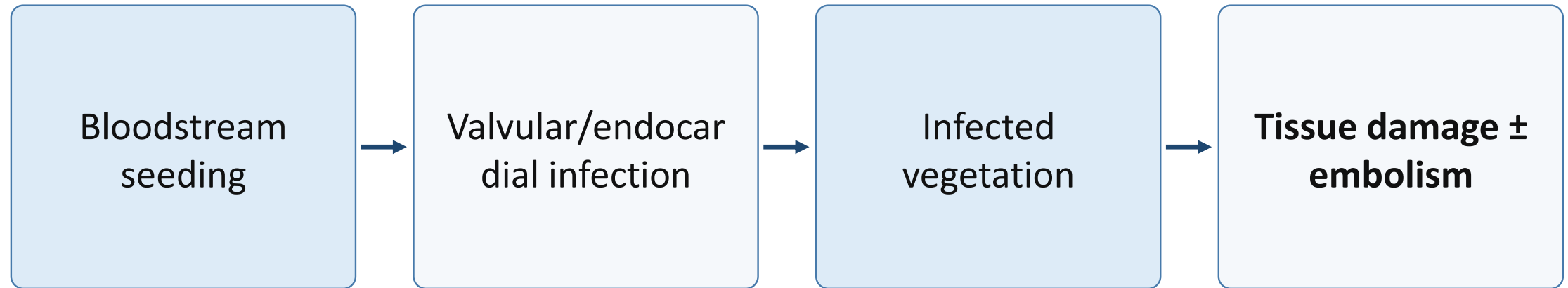
Right-sided valves

May be infected, particularly with injection drug use.

Mural endocardium

Infection is not strictly confined to valve leaflets.

Disease components are causally linked



Infection and thrombus formation interact; The vegetation is not a sterile clot.

Acute versus subacute: Traditional clinical pattern

Acute IE

- More virulent organisms, classically *S. Aureus*
- Can infect previously normal valves
- Rapid, destructive course

Subacute IE

- Less virulent organisms, often viridans streptococci
- Usually deformed valve substrate
- Indolent course over weeks to months

Acute and subacute form a continuum

- The distinction reflects tempo, virulence and often valve substrate.
- There is no absolute dividing line between the two forms.
- Cases with mixed features are recognized.
- Classify the actual clinical course rather than assuming an organism from tempo.

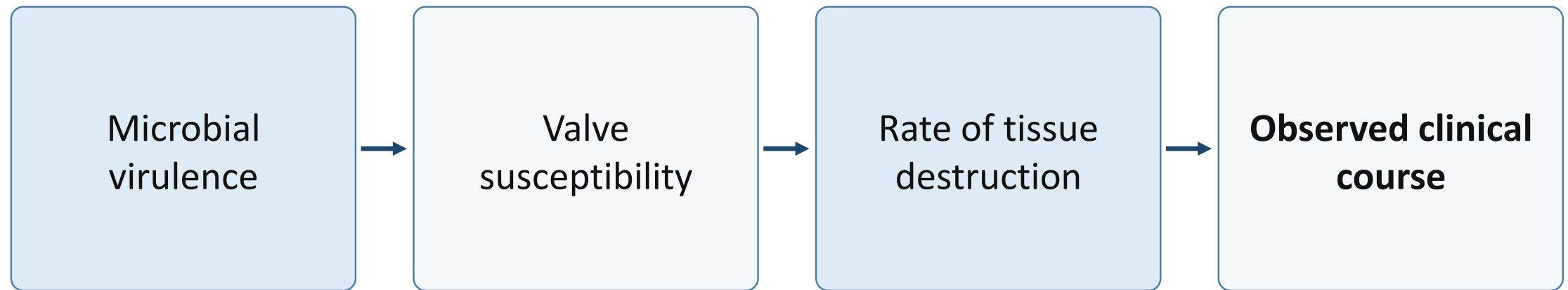
Acute IE: Rapid destruction

- Classically, *S. Aureus* can seed a previously normal valve.
- Vegetations and tissue damage may develop rapidly.
- Antibiotic therapy alone may not suffice in destructive cases.
- Surgery may become necessary; Morbidity can remain substantial.

Subacute IE: Persistent infection

- Often involves valves already abnormal or scarred.
- Viridans-group streptococci are the classic lower-virulence example.
- Progression may extend over weeks or months.
- Less destruction and a greater chance of medical cure are typical.

Clinical tempo is not just a clock



These determinants overlap; Presentation is variable.

Acute and subacute IE: Morphology–tempo relationship

Feature	Acute pattern	Subacute pattern
Illustrative pathogen	Staphylococcus aureus	Viridans streptococci
Common substrate	May be normal	Frequently pre-damaged
Clinical onset	Abrupt, stormy	Insidious, prolonged
Valvular damage	Frequently severe	Usually less destructive
Repair response	Limited in rapidly destructive foci	Granulation and organization may occur

Valvular risk factors have changed

- Rheumatic valve scarring was historically the major substrate.
- As rheumatic disease declined, other structural lesions became prominent.
- Modern substrate includes degenerative disease, congenital anomalies and prostheses.
- Previous valve injury is common—but is not required for IE.

Predisposing cardiac abnormalities

Rheumatic scarring

A previously damaged valve provides susceptible tissue.

Mitral valve prolapse

One of the important contemporary structural substrates.

Calcific stenosis

Degenerative calcification is an antecedent valve lesion.

Bicuspid aortic valve

Susceptibility may occur with or without calcification.

Congenital defects

Altered cardiac structure increases risk.

Prosthetic valves

An implanted valve is a distinct infection substrate.

Pre-existing damage is not obligatory

- A previously abnormal valve can favor certain infections.
- Highly virulent microorganisms can invade apparently normal valves.
- *S. Aureus* exemplifies infection in either normal or deformed valves.
- Evaluate microbial virulence and the cardiac substrate together.

Microbiology follows ecological reservoirs

Oral flora

Viridans streptococci and
HACEK organisms.

Skin flora

Staphylococcus aureus; S.
Epidermidis in early
prosthetic infection.

Other agents

Enterococci, gram-negative
bacilli and fungi.

Viridans streptococci: Damaged native valves

- Members of normal oral flora.
- Especially important in IE of native valves that were previously abnormal.
- 50%–60% in that specific substrate category.
- A prototypic cause of subacute IE.

Staphylococcus aureus: Virulent infection

- Skin-associated organism with substantial invasive potential.
- Can infect valves that are healthy or already deformed.
- The major offender described in injection-associated IE.
- Associated with acute, tissue-destructive disease.

Injection drug use changes the risk profile

- Contaminated needles can directly introduce organisms into blood.
- *S. Aureus* is particularly important in this clinical setting.
- Right-sided valves may be infected.
- Valve location, exposure and organism offer mutually supporting clues.

HACEK organisms and other bacterial causes

- HACEK: Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella.
- This group as oral-cavity commensals.
- Enterococci are another recognized cause of IE.
- Gram-negative bacilli beyond HACEK are less common.

Fungal infective endocarditis

- Bacterial organisms account for most IE.
- Fungal infection is an established, less frequent alternative.
- The pathology remains an infected vegetation with destructive potential.
- Identification of the infecting organism is central to management.

Prosthetic valve infection: Timing and agents

Soon after implantation

- Roughly 1–2 months after valve surgery
- Skin-associated *S. Aureus* and *S. Epidermidis* predominate
- Implantation creates a distinct infection setting

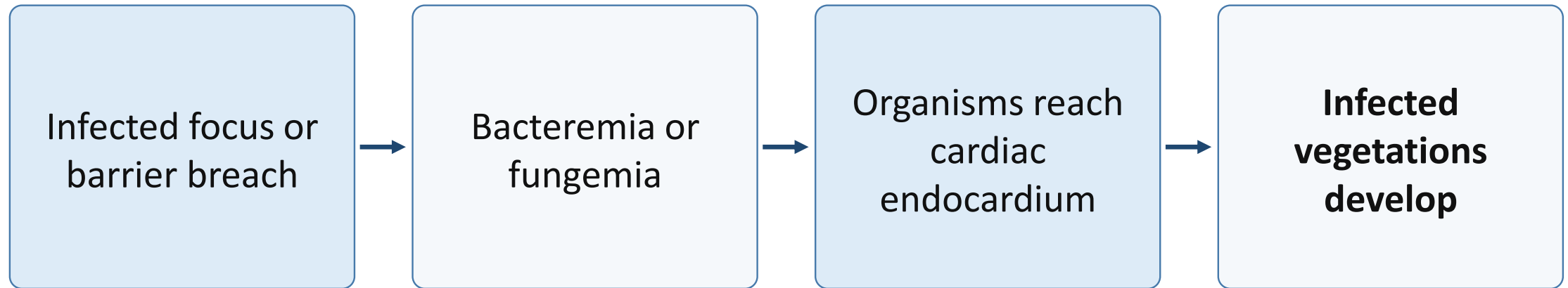
Late after implantation

- At least 1 year after surgery discussion
- Streptococci and *S. Aureus* are prominent
- Late infection differs from the perioperative pattern

Culture-negative endocarditis

- The textbook estimates approximately 10% of IE as culture-negative.
- Antibiotics given before cultures can suppress growth.
- Some causative organisms are difficult to recover.
- Organisms embedded in a vegetation may enter blood intermittently.

Bloodstream entry precedes valvular seeding



Potential entries: Oral cavity, gut, skin, procedures and contaminated injection equipment.

Potential sources of bloodstream seeding

- Overt infection at another anatomic site.
- Dental or surgical procedure-associated bloodstream exposure.
- Contaminated needles in injection drug use.
- Minor epithelial-barrier breaks in oral, gastrointestinal or cutaneous sites.

Two risk domains must be considered

- Microbial exposure: Organisms must enter the bloodstream.
- Cardiac susceptibility: Structural disease often increases risk.
- A sufficiently virulent organism may infect an intact valve.
- Absence of known heart disease does not exclude IE.

Three mechanistic consequences of vegetation formation

Persistent infection

Organisms remain within fibrin-rich infected material.

Mechanical disruption

Bulky lesions and invasion can impair leaflet function.

Emboolic shedding

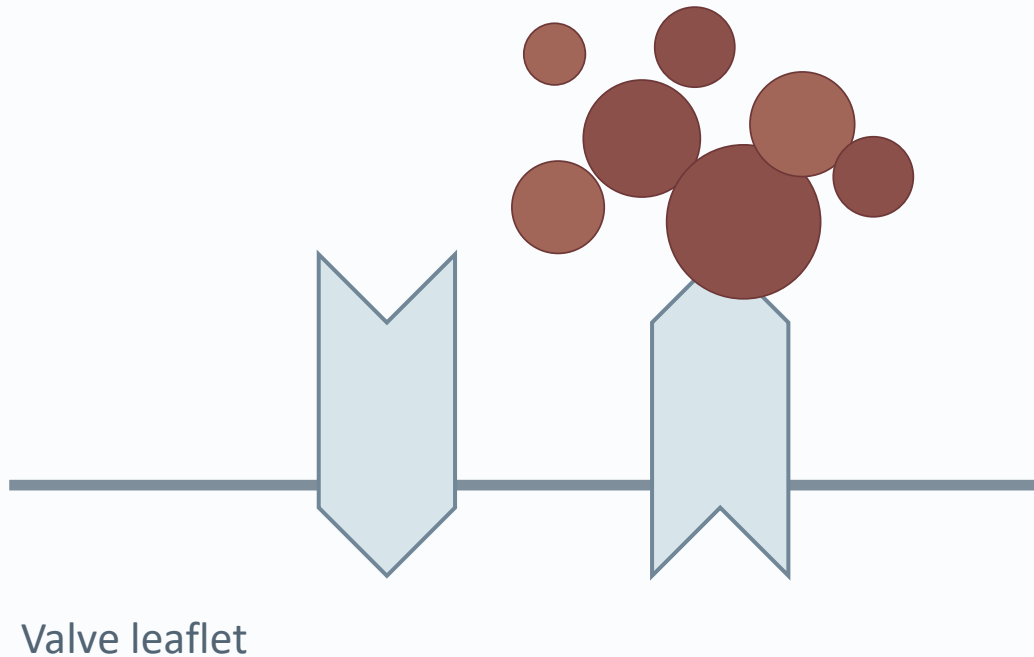
Friable fragments break away into the circulation.

The term “vegetation” needs qualification

- A vegetation is a mass on a valvular/endocardial surface.
- In IE it contains organisms and an inflammatory component.
- Noninfected vegetations also occur in other diseases.
- Morphology, microbiology and clinical context establish the distinction.

Gross hallmark: A bulky, friable vegetation

Friable infected vegetation



Interpretation

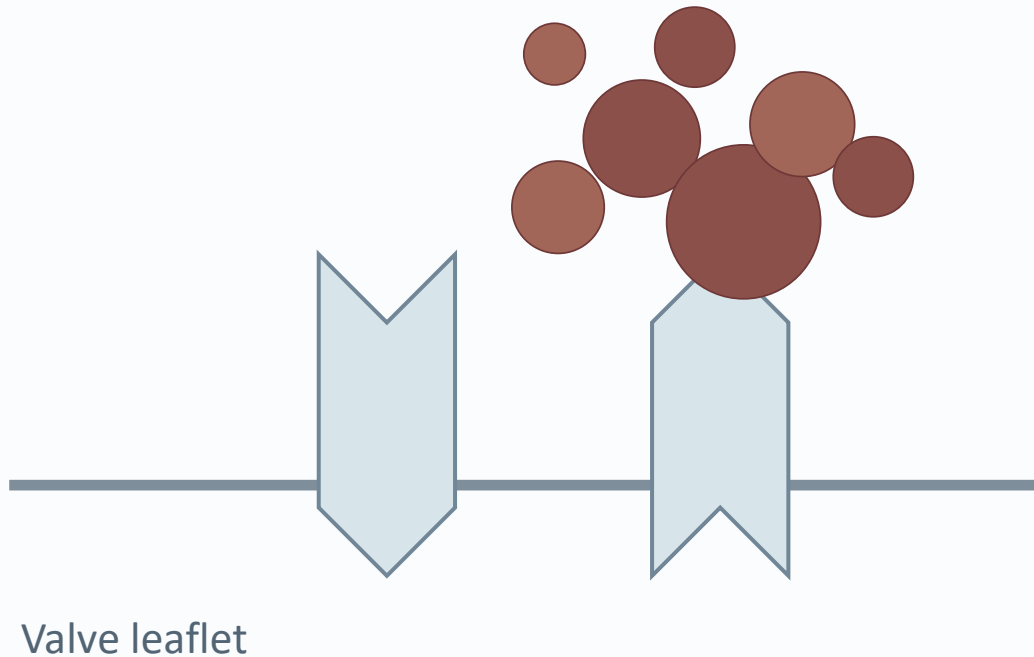
- Irregular mass on the valve surface.
- Fibrin, inflammation and organisms are present.
- The lesion may erode or destroy underlying tissue.

Aortic and mitral valve predominance

- These are the commonest sites account.
- One or several vegetations can occur on a leaflet.
- More than one valve may be infected.
- Morphologic location must be interpreted with clinical exposure.

Why vegetation friability matters

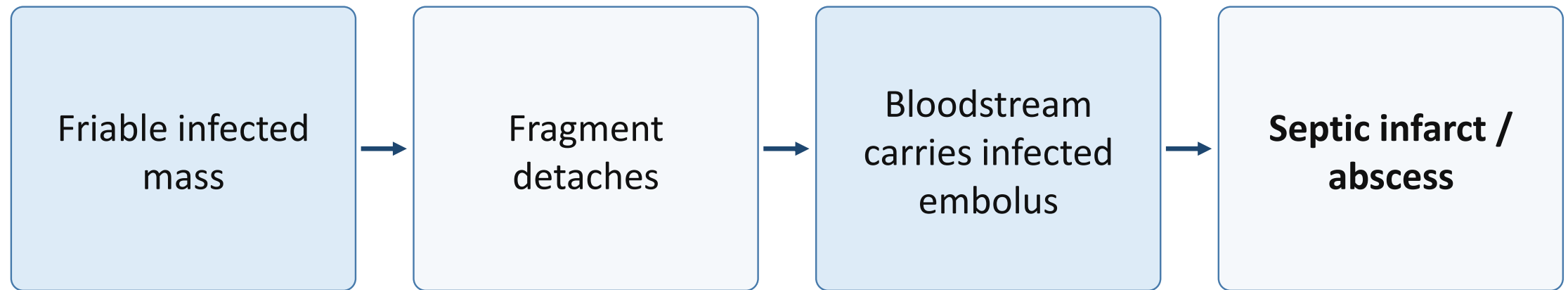
Friable infected vegetation



Interpretation

- Loose infected fragments can detach.
- Embolic fragments may seed infection distally.
- Septic infarcts and abscesses may follow.

Vegetation to septic embolus

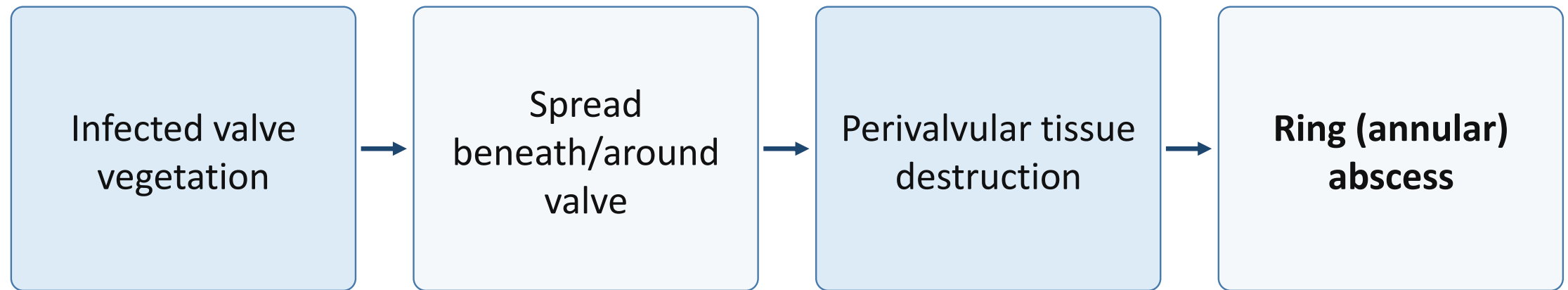


The infected character of the embolic fragment changes its downstream consequences.

Valvular injury: More than surface thrombus

- IE may erode valve cusps and adjoining tissue.
- Destruction can create a new valvular defect.
- The resultant turbulent flow or regurgitation may generate a murmur.
- Tissue invasion differentiates destructive IE from bland sterile deposits.

How a ring abscess develops



Ring abscess with acute S. Aureus infection of a bicuspid aortic valve.

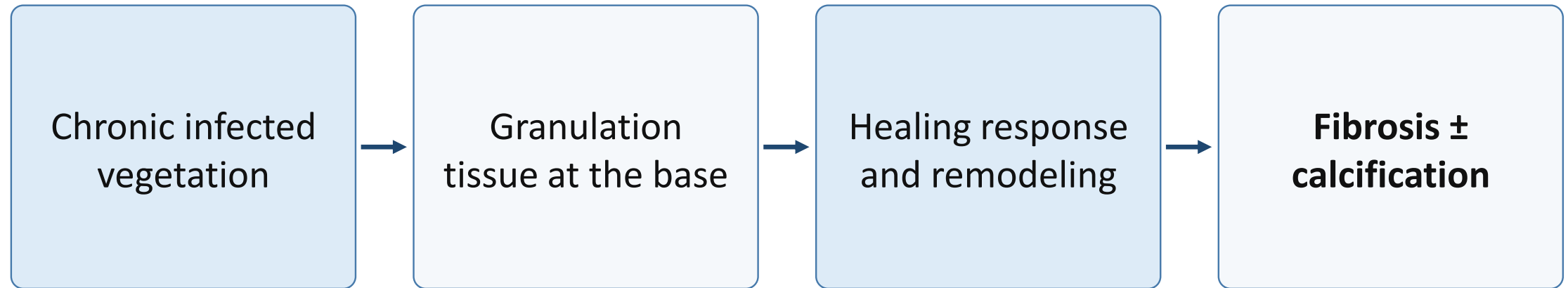
Perivalvular infection is a high-risk feature

- Extension can invade the underlying myocardium.
- Annular (“ring”) abscess is a characteristic severe lesion.
- Arrhythmia may suggest spread into myocardium/conduction structures.
- Local anatomic destruction may prompt surgical intervention.

The basic microscopic constituents

- Fibrin is a major structural component of the vegetation.
- Inflammatory cells are admixed with infected material.
- Bacteria or other causative organisms may be embedded.
- The histologic diagnosis depends on infection-related findings in context.

Subacute vegetation may show organization



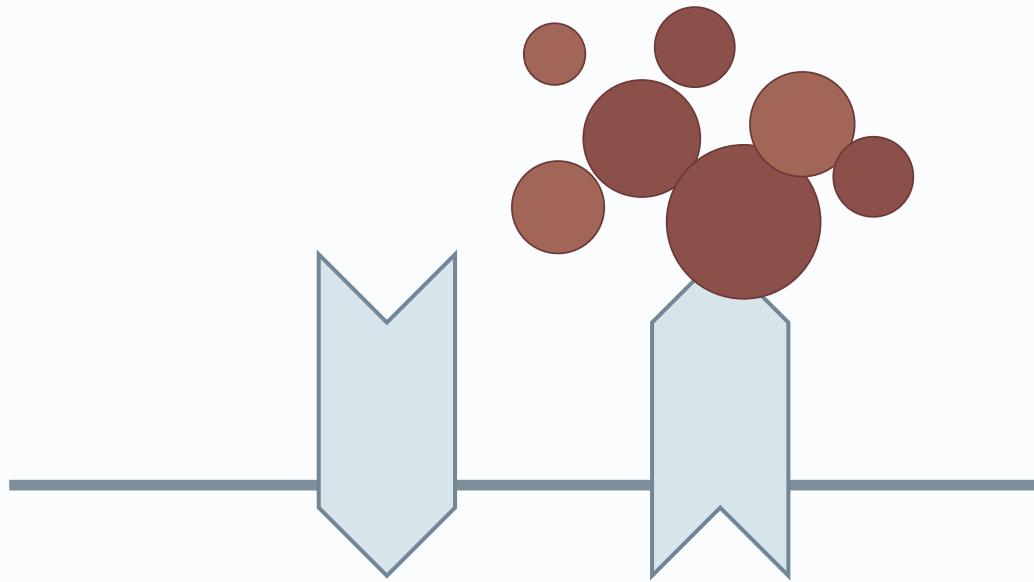
Chronic inflammatory cells can accompany the later organization of subacute lesions.

Acute and subacute morphology can overlap

- Acute vegetations are often more destructive.
- Subacute lesions tend to preserve more valve substance.
- Granulation tissue favors an evolving healing response.
- A single histologic feature cannot rigidly define clinical tempo.

Infected versus sterile vegetation

Friable infected vegetation



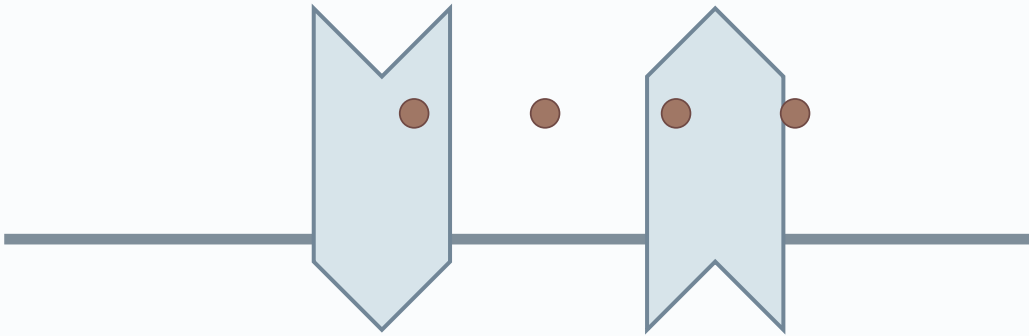
Valve leaflet

Interpretation

- IE vegetation is bulky, friable and infected.
- A sterile thrombus need not destroy the valve.
- Gross appearance alone is not sufficient for final classification.

Rheumatic endocarditis: Closure-line verrucae

Small verrucae at closure line

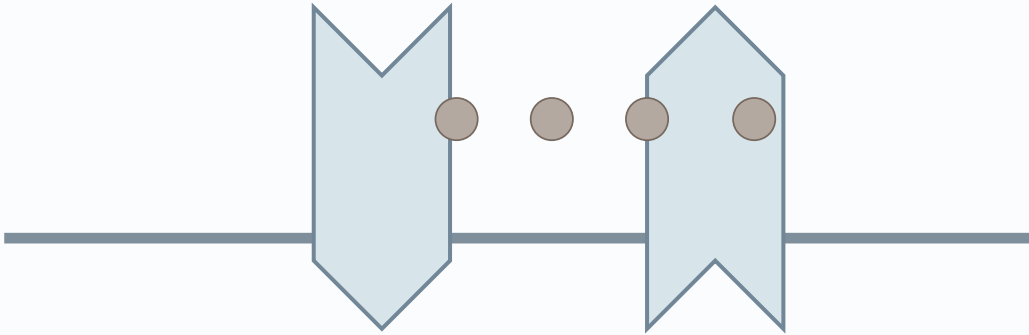


Interpretation

- Small, warty lesions follow the line of closure.
- They occur during the rheumatic fever phase.
- Distribution and size differ from typical bulky IE.

Nonbacterial thrombotic endocarditis

Small, bland, non-destructive thrombi



Interpretation

- Typical sterile vegetations are small and bland.
- Usually located along the line of valve closure.
- Their local effect is generally nondestructive.

NBTE: Histology and embolic hazard

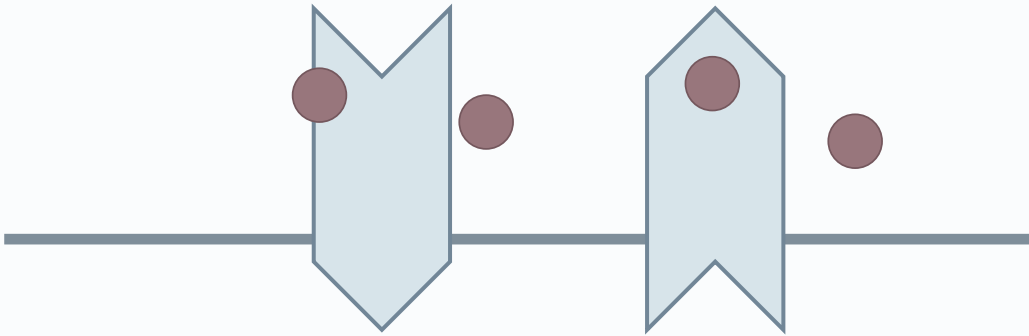
- Sterile thrombi measure approximately 1–5 mm.
- Vegetations are bland and loosely attached.
- They elicit little or no inflammatory reaction.
- Embolization can cause major infarcts despite minimal valve injury.

NBTE: Hypercoagulable substrate

- Occurs in debilitated states, including malignancy or sepsis.
- Associated with chronic disseminated intravascular coagulation.
- Mucinous adenocarcinomas can generate a procoagulant milieu.
- Damaged valves are not a prerequisite.

Libman–Sacks vegetations: Distinct distribution

Vegetations on either leaflet surface



Interpretation

- Sterile small-to-medium lesions in systemic lupus.
- Can occur on either or both valve surfaces.
- May extend to chordae or chamber endocardium.

Libman–Sacks: Immune-mediated valvulitis

- Immune-complex deposition activates complement.
- Fc-receptor–bearing inflammatory cells are recruited.
- Valvulitis and fibrinoid necrosis are characteristic.
- Persistent injury can cause scarring and leaflet fusion.

Four vegetative patterns: Key discriminators

Pattern	Infection?	Typical distribution	Principal tissue effect
Infective	Yes	Bulky irregular mass; may extend to chordae	Potential tissue destruction
Rheumatic	No infection in verrucae	Small closure-line warts	Rheumatic valvulitis/scarring
NBTE	Sterile	Small closure-line thrombi	Minimal local reaction; emboli possible
Libman–Sacks	Sterile	Either or both valve surfaces	Valvulitis, fibrinoid necrosis

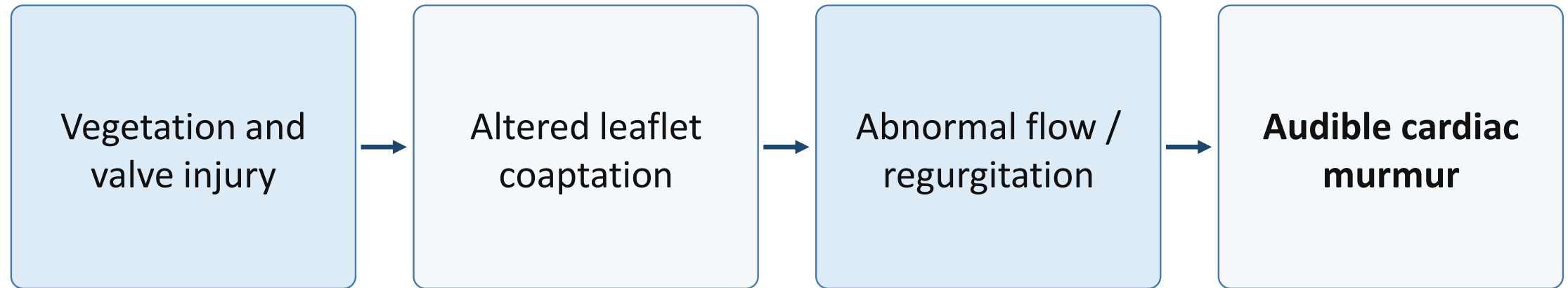
Acute presentation is often systemic

- Fever may develop rapidly with chills.
- Weakness and lassitude accompany the febrile illness.
- A fulminant course should raise concern for virulent infection.
- The pattern reflects systemic infection plus cardiac involvement.

Older patients may have muted findings

- Fever is the most consistent sign but may be low-grade or absent.
- Fatigue and weight loss may dominate.
- A nonspecific “flu-like” illness can obscure diagnosis.
- Absence of a dramatic fever does not exclude IE.

How a murmur can arise in IE



Some murmurs predate infection because structural disease was already present.

A murmur is useful but not absolute

- Most patients with left-sided IE have a murmur.
- Some murmurs reflect new valve injury.
- Others arise from a pre-existing valve abnormality.
- Murmur interpretation requires previous cardiac history.

Three clinical consequence domains

Cardiac

Valve damage, ring abscess
and arrhythmia.

Embolic/infectious

Septic emboli, distant
abscesses and sepsis.

Immune-mediated

Immune-complex
glomerulonephritis.

Classical peripheral signs: Now less frequent

- Improved diagnosis and treatment reduced prolonged untreated disease.
- Splinter hemorrhages may reflect microembolic events.
- Janeway lesions involve palms or soles.
- Osler nodes and Roth spots are other historical diagnostic clues.

Janeway lesions: Vascular phenomenon

- Typically erythematous or hemorrhagic lesions.
- Nontender macules on palms or soles.
- The textbook associates these with septic embolic events.
- Duke criteria list them among vascular phenomena.

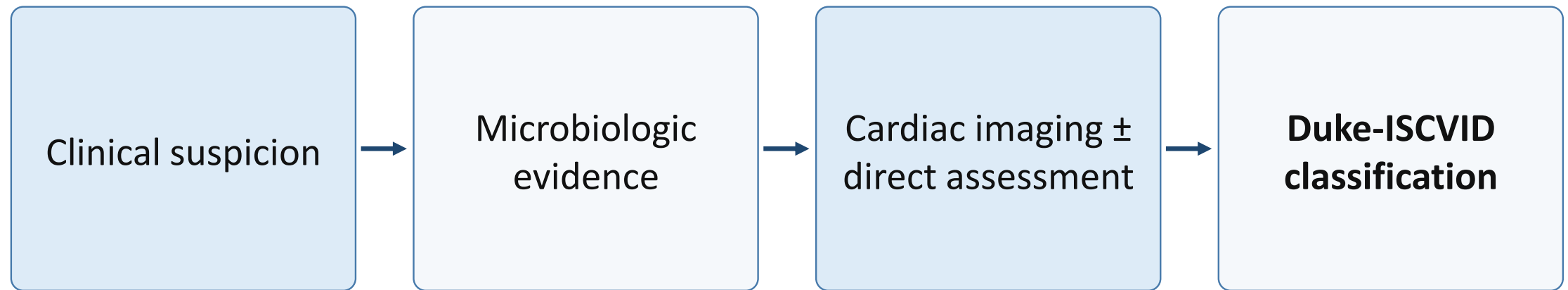
Osler nodes and Roth spots: Immune clues

- Osler nodes are tender nodules, usually at finger pulp.
- Roth spots are retinal hemorrhages with pale centers.
- These are listed among Duke immunologic phenomena.
- Do not assume their absence excludes IE.

Splinter hemorrhages: Contextual clue

- Linear subungual hemorrhages can accompany microembolic disease.
- Historically associated with long-standing IE.
- They are not specific on their own.
- Interpret peripheral signs alongside cultures and cardiac findings.

Diagnosis integrates independent evidence



Source table: 2023 Duke-ISCVID criteria, reproduced 11e.

Pathologic diagnosis: Organism in relevant tissue

- Demonstration may be by culture or histologic examination.
- Relevant material includes valve vegetation or an embolized fragment.
- Explanted prosthetic valves/sewing rings and device material also qualify.
- Pathologic evidence is distinct from clinical criteria.

Clinical Duke categories: Source table

- Clinical diagnostic combinations: 2 major criteria; Or
- 1 major plus 3 minor criteria; Or
- 5 minor criteria.
- These are the positive combinations printed Table 12.9.

Major microbiologic criteria

- Characteristic organisms identified by blood culture.
- Nucleic acid–based assays or immunofluorescence may contribute.
- Persistently positive results for unusual organisms also feature.
- Exact microbial interpretation depends on the criterion wording.

Major imaging and operative criteria

- Imaging can demonstrate a valve- or implant-related oscillating mass.
- Abscess or partial separation of an artificial valve are major findings.
- New valve regurgitation detected by imaging is included.
- Direct inspection during cardiac surgery can provide a major criterion.

Duke minor criteria: Host context and fever

- A predisposition can be heart lesion, prosthetic valve or intracardiac device.
- Injection drug use is an additional predisposing context.
- Fever is a minor clinical criterion.
- Risk factors support interpretation; They do not independently prove IE.

Duke minor criteria: Vascular phenomena

- Major arterial embolism or septic pulmonary infarct.
- Mycotic aneurysm or intracranial hemorrhage.
- Conjunctival hemorrhages and Janeway lesions.
- These link cardiac infection to vascular consequences.

Duke minor criteria: Immune and laboratory findings

- Immune findings: Glomerulonephritis, Osler nodes, Roth spots.
- Rheumatoid factor is included as an immune phenomenon.
- A single culture positive for an unusual organism may count as minor microbiologic evidence.
- Categories should not be double-counted as independent major findings.

Three diagnostic evidence streams

Cultures / assays

Identify the microorganism and establish microbiologic evidence.

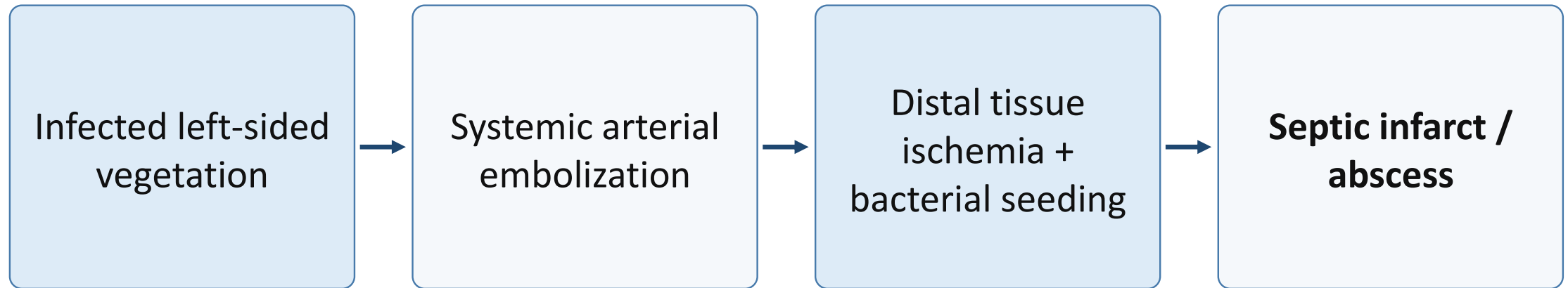
Cardiac imaging

Detect vegetations, abscess, dehiscence and new regurgitation.

Clinical context

Assess fever, substrate, vascular events and immune phenomena.

Systemic consequences of left-sided IE

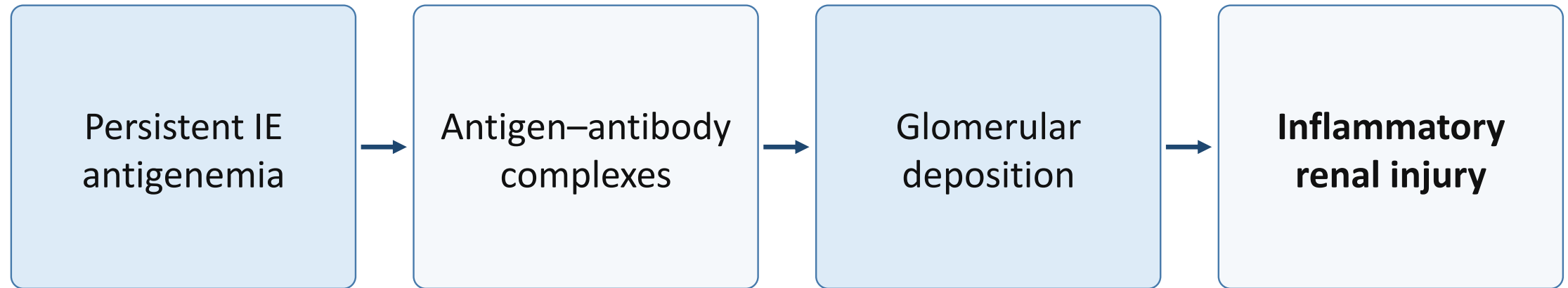


The destination organ depends on the vascular distribution of the embolus.

Septic infarcts and mycotic aneurysms

- Embolic material may contain viable organisms.
- Secondary infection can form an abscess at the embolization site.
- An infected vessel wall can develop a mycotic aneurysm.
- “Mycotic” in this context does not necessarily mean fungal.

Immune-complex glomerulonephritis



This is immune-mediated injury, distinct from a septic renal embolus.

Cardiac invasion can disturb conduction

- Annular infection may extend into myocardial tissue.
- Conduction structures may be involved by adjacent inflammation.
- New arrhythmias can be a warning sign of extension.
- An arrhythmia does not specify the lesion, but raises concern.

Adverse features in the clinical course

- Sepsis indicates serious systemic infection.
- Arrhythmia may reflect local myocardial/conduction invasion.
- Systemic embolization can produce organ injury.
- These features are described as especially unfavorable.

Principles of treatment and prognosis

- Untreated IE is usually fatal.
- Prolonged effective antimicrobial therapy is central.
- Valve replacement may be necessary for destructive disease.
- Prosthetic-valve IE has particularly challenging outcomes.

Case application: Acute destructive IE

Clinical vignette

- Acute fever and chills; New murmur.
- No documented prior valve disease.
- Blood cultures grow *Staphylococcus aureus*.
- Cardiac imaging demonstrates a destructive vegetation.

Question: Which features point toward the acute pattern?

Case reasoning: Acute destructive pattern

- Rapid onset supports the acute clinical tempo.
- *S. Aureus* can invade previously normal valves.
- Destructive valvular morphology strengthens the pattern.
- Major microbiology and imaging findings also support the IE diagnosis.

Case application: Persistent febrile illness

Clinical vignette

- Weeks of fatigue and intermittent low-grade fever.
- A pre-existing structurally abnormal valve.
- Blood cultures identify viridans streptococci.
- Imaging reveals a valve vegetation.

Question: Why is a subacute pattern more plausible?

Case reasoning: Subacute infection

- Prolonged, insidious symptoms favor the subacute spectrum.
- The damaged native valve is a typical substrate.
- Viridans organisms are a textbook etiologic example.
- Subacute morphology may show organization at the lesion base.

Case application: Vegetation without infection

Pathology vignette

- An individual with mucinous adenocarcinoma develops emboli.
- Valve shows small, bland, sterile thrombi at the closure line.
- No destructive valvulitis is identified.

Question: Which noninfected form best fits?

Case reasoning: Nonbacterial thrombotic endocarditis

- Hypercoagulability in malignancy favors NBTE.
- Small closure-line sterile thrombi are the typical morphology.
- Major systemic emboli may occur without valve destruction.
- Do not mistake sterile vegetation for infective endocarditis.

Integrated synthesis: Three decisive questions

- Is the lesion infected or sterile?
- How virulent is the organism, and what valve substrate exists?
- Is there local destruction, septic embolization or immune injury?
- Do microbiology and cardiac imaging support the clinical diagnosis?

References and source limitations

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026), ch. 12, pp. 511–514.
- Diagnostic clinical criteria: Robbins Table 12.9, adapted from the 2023 Duke-ISCVID criteria (Fowler et al., Clin Infect Dis. 2023;77:518–526).
- All valve drawings and flow diagrams are original, editable explanatory schematics—not photographs of pathology specimens.
- Original textbook figure images and chapter PDF were not provided; figure-specific visual verification was therefore not performed.