

Lyme Arthritis

An inflammatory joint manifestation of Borrelia infection

Organism • Immune response • Synovial morphology • Diagnostic reasoning

Dr Abu Suraih Sakhri

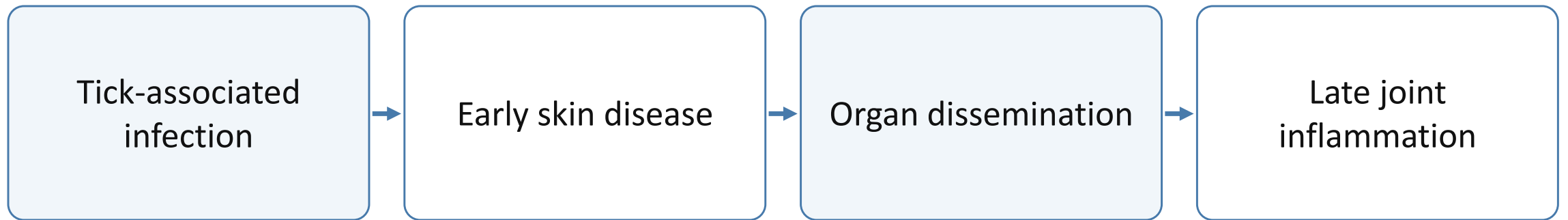
MBBS, MD (Pathology)

www.abusuraihsakhri.com

What this lecture should establish

- Link Ixodes-borne Borrelia infection to delayed joint disease
- Explain inflammatory mechanisms and synovial morphology
- Recognize the typical clinical joint pattern
- Interpret serology, synovial PCR, and persistent arthritis cautiously

Lyme arthritis is part of systemic infection



Joint disease is one manifestation of a multisystem, stage-dependent infection.

Infection and arthritis are not interchangeable

Lyme disease

Infection may produce skin, neurologic, cardiac, or musculoskeletal involvement.

Lyme arthritis

A late inflammatory joint manifestation with a characteristic large-joint pattern.

Borrelia burgdorferi is the principal US agent

ORGANISM

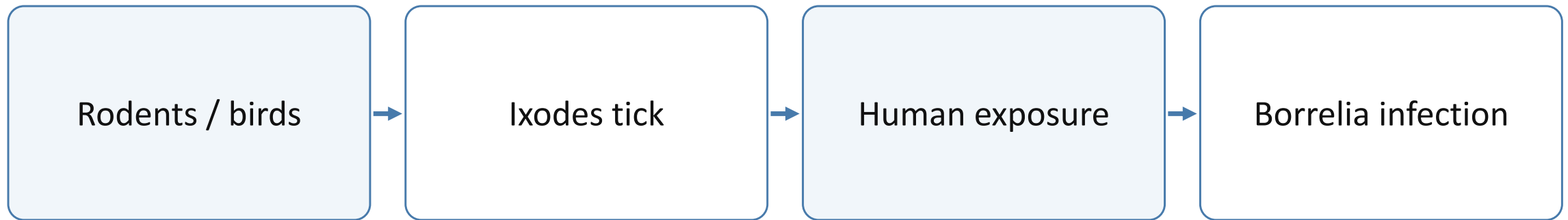
- Borrelia are slender, helical spirochetes.
- B. Burgdorferi is the major Lyme disease agent in the United States.
- The infectious organism initiates a host inflammatory response.
- The joint disease is not defined by direct visualization of bacteria.

Geographic species differ

Region	Lyme-associated species
United States	B. Burgdorferi
Europe and Asia	B. Burgdorferi, B. Afzelii, B. Garinii

These are textbook geographical associations, not an exhaustive species taxonomy.

Ixodes ticks connect animal reservoirs to humans



Rodents as reservoirs and birds particularly for B. Garinii.

Endemic settings guide suspicion

EPIDEMIOLOGIC CONTEXT

- US disease is concentrated in the Northeast and upper Midwest.
- Chapter 26 emphasizes New England and the mid-Atlantic region.
- The geographic distribution is expanding.
- Geographic exposure supports, but cannot by itself establish, the diagnosis.

Lyme disease has successive clinical phases

Early localized

Dermal infection; Erythema
migrans



Early disseminated

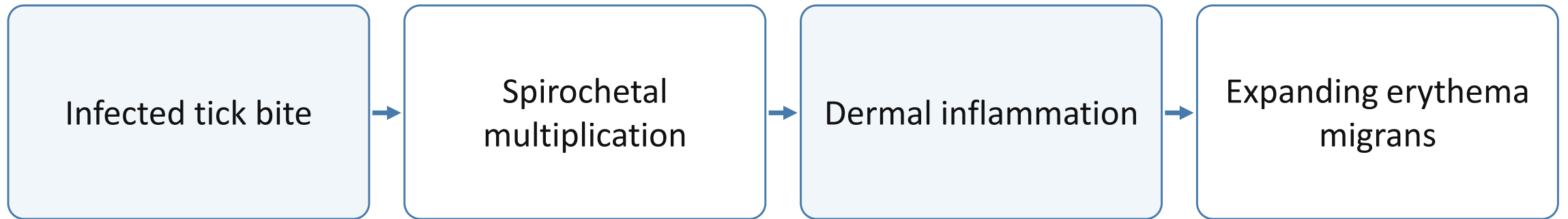
Secondary skin, neurologic,
cardiac, and
musculoskeletal
manifestations



Late disseminated

Chronic inflammatory
arthritis; Selected
neurologic manifestations

Early localized infection begins in the dermis

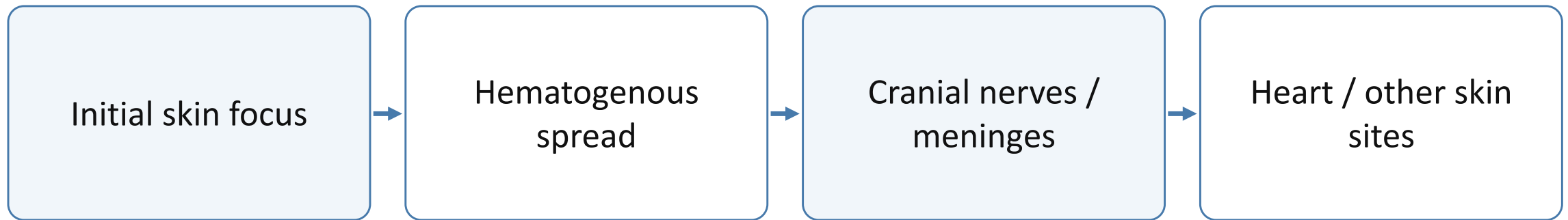


Erythema migrans is an early clinical clue

EARLY LOCALIZED STAGE

- An expanding erythematous lesion develops at the inoculation site.
- A pale center may occur; The appearance is not required to be target-shaped.
- Erythema migrans in approximately 80% of patients.
- Fever and lymphadenopathy may accompany the lesion.

Early dissemination involves several tissues



Joint or muscle pain may also occur during dissemination.

Migratory pain does not equal established arthritis

Early musculoskeletal manifestations

Migratory joint and muscle pain during dissemination.

Late inflammatory arthritis

Clinical episodes of synovitis that may last weeks to months.

Late disease may emerge months after exposure



Conceptual sequence; Timing is variable and is not a diagnostic clock.

Why early treatment changes arthritis frequency

Pattern	Clinical course
Treated earlier	Progression to arthritis is now uncommon account.
Without timely treatment	Migratory/persistent inflammatory arthritis becomes substantially more common.

Treated and untreated cohorts

<10%

Arthritis in current *Borrelia* infections, as described in Ch. 26

Up to 80%

Migratory arthritis with delayed/absent timely treatment

Textbook cohort-context estimates; They are not individual prognostic probabilities.

Large joints dominate the arthritis phenotype

01 **Knee**

02 Shoulder

03 Elbow

04 Ankle

Listed in descending order of frequency.

Knee involvement is the characteristic clue

CLINICAL PATTERN

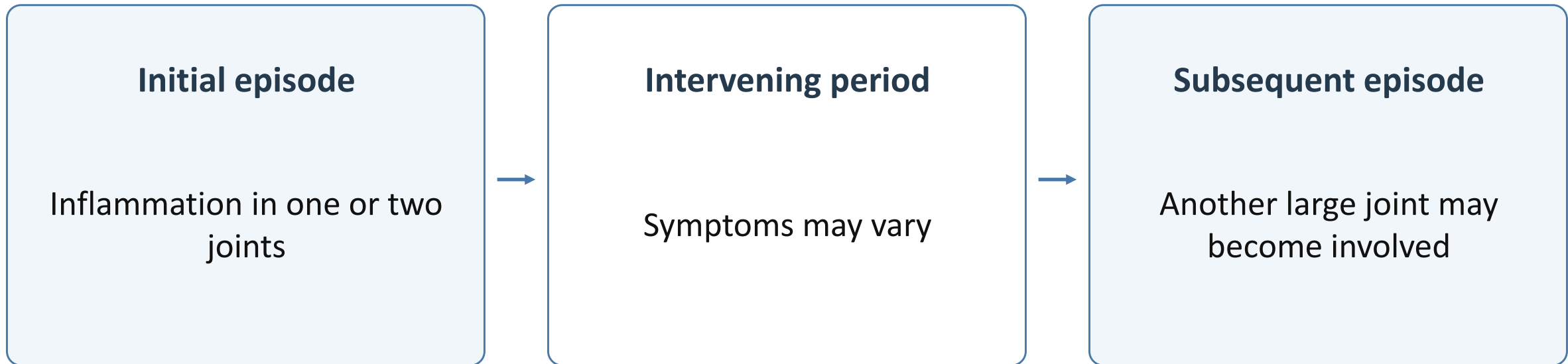
- Large-joint synovitis is typical.
- The knee is most frequently involved.
- A swollen knee after compatible exposure should trigger diagnostic consideration.
- The finding is suggestive, not pathognomonic.

Usually few joints are active at once

DISTRIBUTION

- Initial attacks often involve one or two joints.
- Joint disease can recur at another anatomical site.
- A limited joint count does not exclude a systemic infection.
- The pattern contrasts with a symmetric small-joint inflammatory polyarthrititis.

Arthritis can move between sites over time



The schematic indicates anatomical migration, not spread by direct contact between joints.

Individual attacks may last weeks to months

TEMPORAL PATTERN

- The initial episode can be prolonged.
- Attacks lasting weeks to months.
- Symptoms may recur or appear in different joints.
- Duration must be interpreted with clinical and laboratory evidence.

Symptom patterns change as infection evolves

Stage	Musculoskeletal presentation
Early disseminated	Migratory arthralgia and myalgia
Late disseminated	Arthritis of one or a few large joints
Late severe disease	Potential cartilage damage

Systemic history links an arthritic knee to Lyme

- A patient from an endemic region has recurrent swelling of a knee.
- Several months earlier, they recall an expanding erythematous rash.
- They have no evidence supplied here of an identified organism in joint fluid.

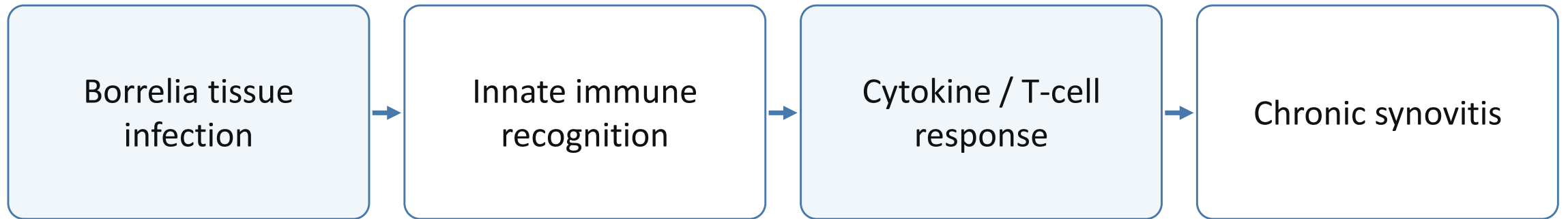
What elements raise suspicion for Lyme arthritis?

Case analysis: Combine pattern and exposure

CLINICOPATHOLOGIC REASONING

- Endemic geographic context increases pretest suspicion.
- A compatible earlier skin lesion places the joint disease in a systemic timeline.
- Recurrent large-joint synovitis matches the described phenotype.
- The diagnosis still requires appropriate testing and exclusion of alternatives.

The organism acts chiefly through host inflammation



The chapter does not attribute the tissue injury to *Borrelia* exotoxin or endotoxin.

Direct bacterial toxins are not the explanation

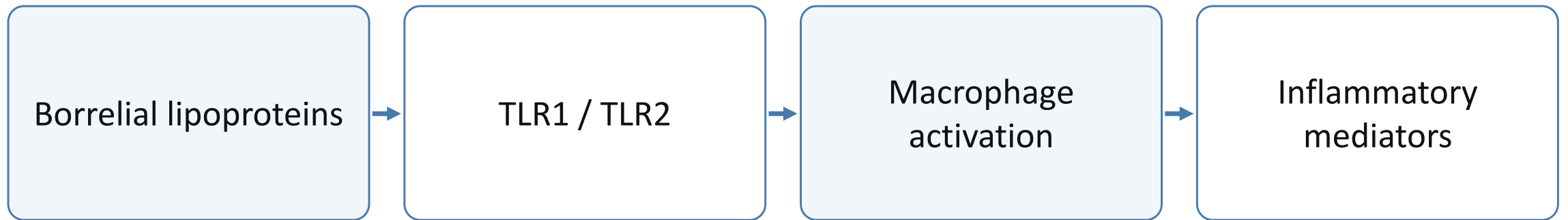
Not the stated mechanism

B. Burgdorferi is not described as producing damaging endotoxins or exotoxins.

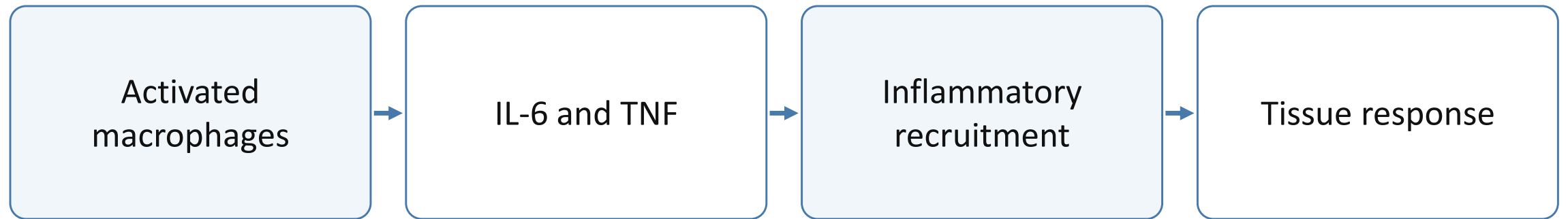
Dominant proposed mechanism

Inflammation produced by the host response to microbial antigens.

Borrelial lipoproteins activate innate sensors

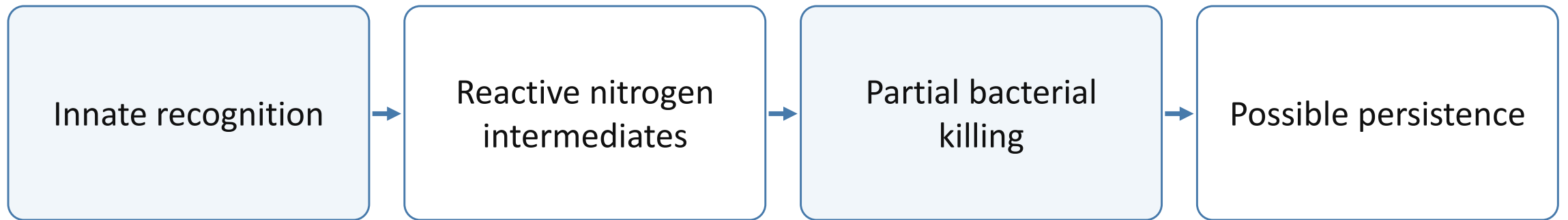


Macrophage cytokines amplify local inflammation



These molecules are mechanistic mediators, not diagnostic biomarkers in this source.

Innate killing can be incomplete



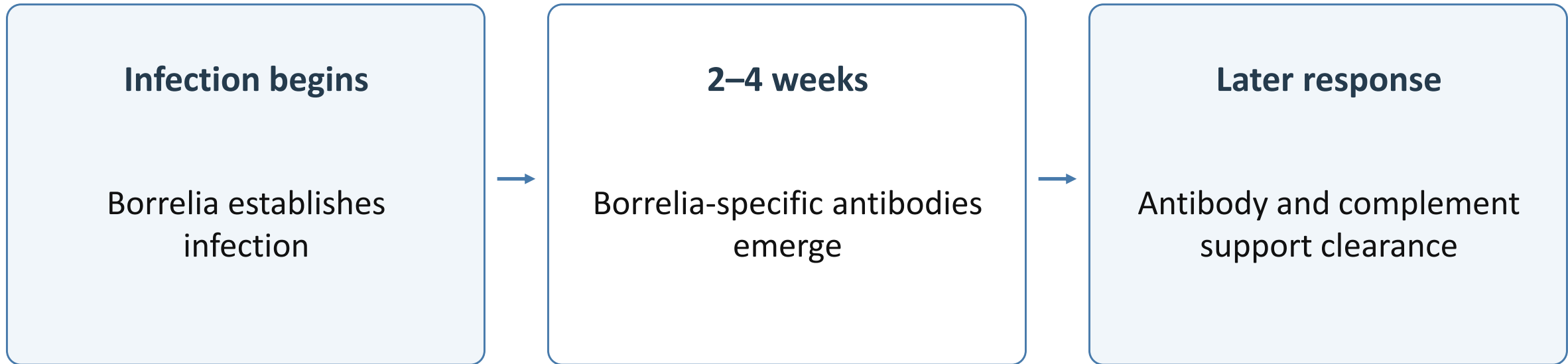
Innate responses often reduce but do not eliminate infection.

T cells contribute to inflammatory lesions

ADAPTIVE-CELL RESPONSE

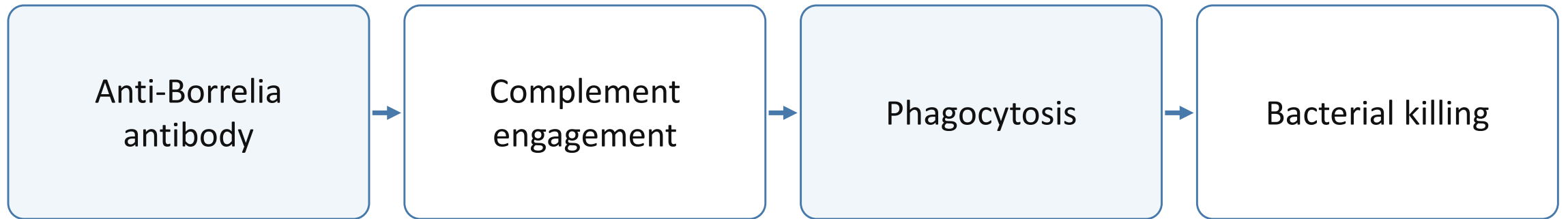
- The text implicates T cells and cytokines in lesion formation.
- CD4-positive T cells are prominent in affected synovium.
- The resulting lesion is chronic, cell-rich synovitis.
- Histology reflects immune activation rather than a toxin-mediated necrosis.

Specific antibody responses arise after infection



The 2–4-week interval is quoted as the textbook antibody-response timeline.

Antibody facilitates phagocytosis and killing



Immune evasion helps explain persistence

Antibody pressure

Host recognition targets expressed surface antigens.

Spirochetal evasion

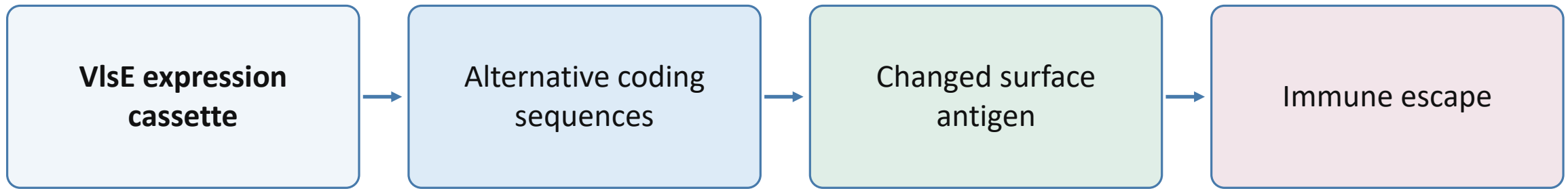
Antigenic variation and alteration of surface-protein expression reduce immune recognition.

Outer surface protein C changes during infection

OSPC

- Outer surface protein C supports establishment of infection.
- Its expression is not required for persistence.
- Downregulation is described as one way *Borrelia* evades antibody responses.
- Distinguish this mechanism from the separate VlsE antigenic-variation system.

VlsE variation creates shifting antigenic targets



One expressed VlsE antigenic variant is replaced by another: Antibody recognition can be evaded.

Two paths connect infection to lasting synovitis

Persistent infection-related immune activation

Ongoing interaction between
Borrelia antigens and host defenses.

Proposed postinfectious autoimmunity

Cross-reactive immune responses
continue after bacterial detection is
lost.

Autoimmune cross-reactivity remains a hypothesis

UNRESOLVED MECHANISM

- Molecular mimicry as a proposed mechanism.
- An antibody/T-cell response to outer surface protein A is implicated in the hypothesis.
- The corresponding self antigen(s) are unidentified in the excerpt.
- Do not teach cross-reactivity as a proven universal cause of persistent arthritis.

Lyme synovitis has a characteristic morphologic set

1

Lining-cell hyperplasia

2

Villous synovial hypertrophy

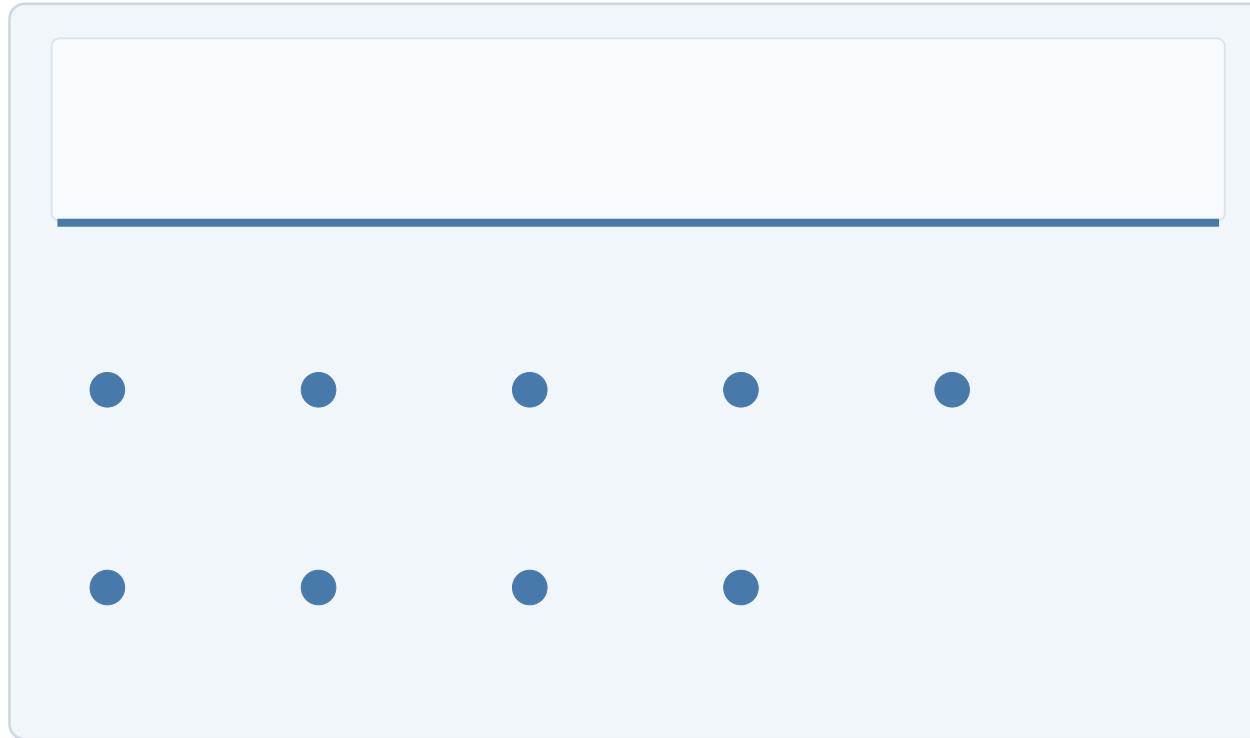
3

Mononuclear infiltrate

4

Vascular onion-skin thickening

Normal synovium provides a morphology baseline



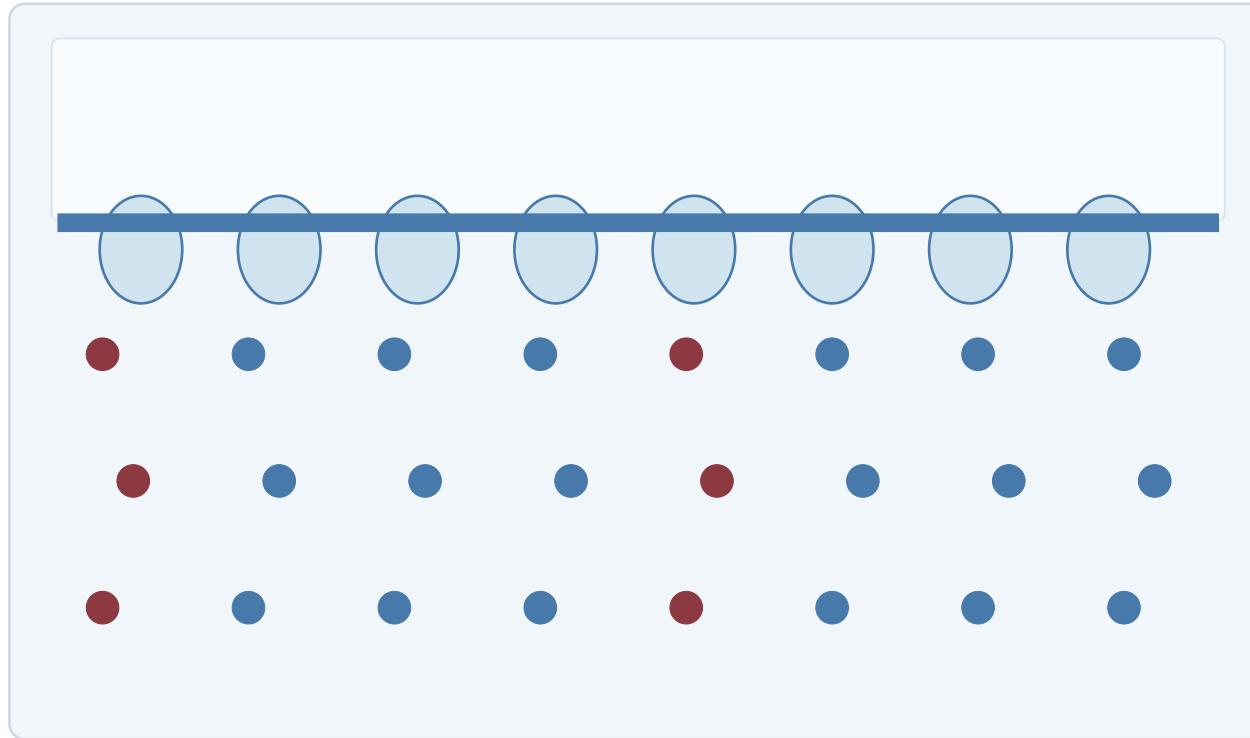
Thin synovial lining

Subsynovial stroma

Synovial vascular supply

Simplified schematic of synovial compartments; Not a tissue section.

Villous synovial hypertrophy increases surface folds



Villous projection

Thickened synovial lining

Inflammatory stromal cells

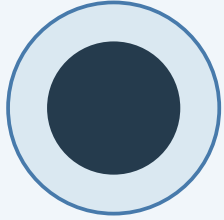
Schematic tissue architecture, not a specimen.

Synoviocyte hyperplasia thickens the lining

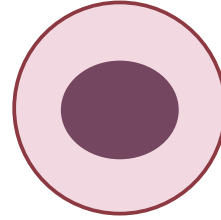
LINING RESPONSE

- Reactive hyperplasia produces additional synovial lining cells.
- The lining becomes conspicuous and enlarged.
- It coexists with villous changes and chronic inflammation.
- It is not specific for Lyme arthritis in isolation.

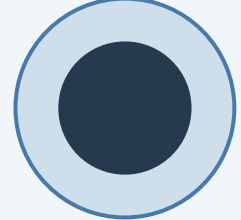
The infiltrate is predominantly mononuclear



Lymphocytes



Plasma cells



CD4-positive T cells

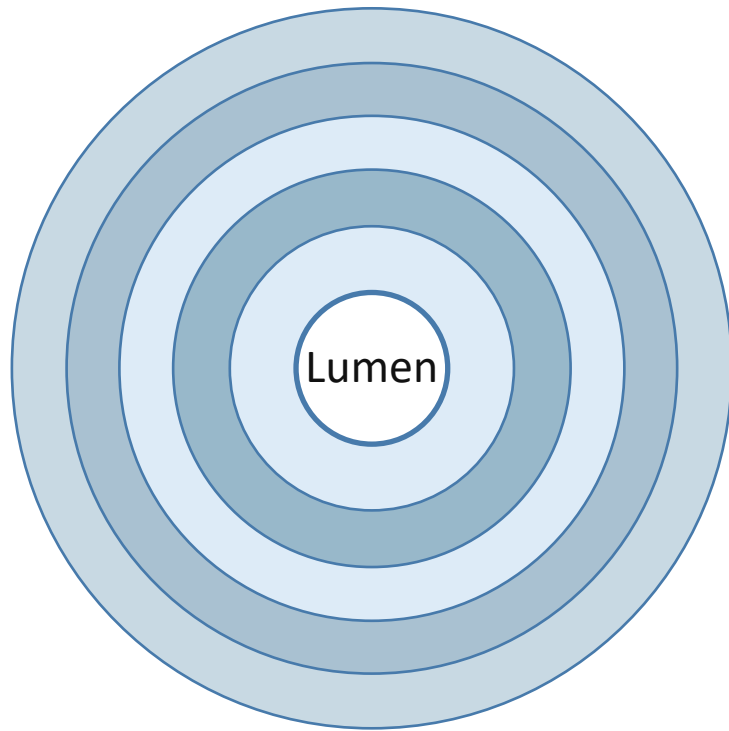
Conceptual cell roster; No microscopic identification is implied.

Fibrin accompanies the chronic synovitis

MATRIX CHANGE

- The joint-section morphology includes fibrin deposition.
- It accompanies synovial hyperplasia and inflammatory infiltrates.
- The finding belongs to the combined pattern of synovial inflammation.
- Fibrin alone cannot identify Borrelia infection.

Obliterative endarteritis is a distinctive clue



Concentric vascular wall thickening

Narrowed arteriolar lumen

Onion-skin-like pattern

Schematic of reported arteriolar lesion; Not histology.

Onion-skin arteriolar walls require contextual reading

VASCULAR PATHOLOGY

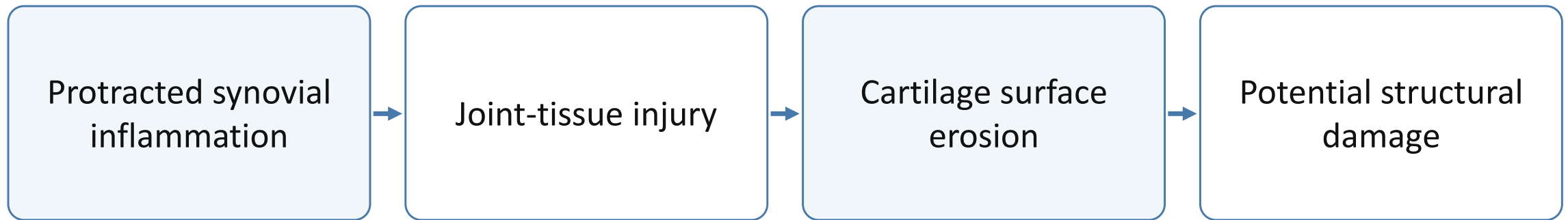
- Concentric thickening of arteriolar walls.
- The lumen may be compromised by obliterative endarteritis.
- Comparable concentric vascular lesions can occur in other disorders.
- Interpret vascular morphology with the complete synovial picture.

Early morphology can resemble rheumatoid synovitis

Finding	Lyme arthritis	Rheumatoid arthritis
Synovial lining	Hyperplasia	Hyperplasia may occur
Infiltrate	Mononuclear; CD4 T cells prominent	Chronic inflammatory cells
Arterioles	Onion-skin–like thickening noted	Not the defining RA lesion

Comparison is conceptual; No single feature independently establishes disease identity.

Late disease can erode cartilage



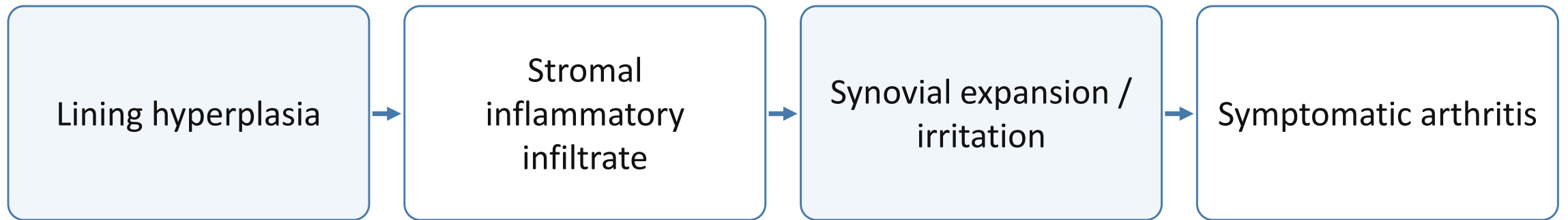
Extensive large-joint cartilage erosion in late disease.

Severe cases can mimic rheumatoid arthritis

PITFALL

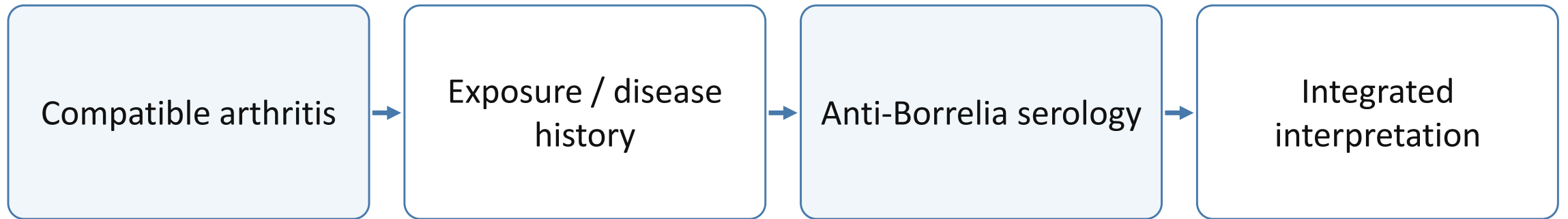
- The histopathologic resemblance may be striking.
- Synovial hypertrophy and mononuclear inflammation overlap.
- The disease context and joint distribution help separate diagnoses.
- Morphology alone should not be assigned etiologic specificity it lacks.

Clinical swelling is the tissue-level outcome



This is an explanatory synthesis of the described morphological pattern.

Diagnosis integrates phenotype and laboratory evidence



Anti-Borrelia serology is the principal test

DIAGNOSTIC PRINCIPLE

- Diagnosis is usually serologic.
- The test detects the host antibody response to Borrelia.
- A positive antibody result requires compatible clinical interpretation.
- The excerpt does not specify a contemporary testing algorithm.

PCR detects Borrelia DNA in synovial fluid

≈70%

Synovial-fluid PCR detection described for patients with Lyme arthritis

Not stand-alone

The textbook nevertheless presents serology as the usual diagnostic basis

PCR performance is source-specific and should not be generalized to every specimen or population.

A negative PCR is not an absolute exclusion

What PCR measures

Nucleic acid from *Borrelia* in the tested joint sample.

What it cannot by itself resolve

The entire clinical state, including immune-driven inflammation or test limitations.

Interpretive teaching inference; Synovial PCR is an adjunct, not the source-preferred stand-alone diagnostic test.

Consider alternative causes of monoarthritis

Disorder	Distinguishing contextual clue
Acute bacterial septic arthritis	Abrupt painful swollen joint; Organism may be demonstrated in aspirate
Mycobacterial arthritis	Indolent, often destructive, granulomatous process
Lyme arthritis	Endemic exposure; Episodic large-joint synovitis; Serology

Acute septic arthritis requires prompt clinical assessment; Do not defer evaluation based on presumed Lyme disease.

Viral arthritis can have a different time course

Viral arthritis

Chapter 26 describes acute-to-subacute joint disease with several viral infections.

Lyme arthritis

The source emphasizes prolonged/recurrent large-joint inflammatory attacks.

Neither duration nor distribution alone is definitive.

Rheumatoid arthritis is a major pathologic mimic

Feature	Lyme arthritis	Rheumatoid arthritis
Pattern	One or a few large joints	Often begins in small joints of the hands
Mechanism	Infection-associated immune response	Autoimmune synovial inflammation
Microscopy	Chronic synovitis; Vascular onion-skin change	Inflammatory pannus / destructive synovitis

Osteoarthritis has a different primary lesion

Feature	Lyme arthritis	Osteoarthritis
Primary problem	Inflammatory synovitis	Mechanical cartilage degeneration
Joint disease	Episodic large-joint swelling	Degenerative weight-bearing joint changes
Morphology	Cell-rich chronic synovitis	Cartilage fibrillation; Osteophytes; Sclerosis

Synovial biopsy is pattern recognition, not proof

PATHOLOGY REPORTING

- Identify lining hyperplasia and chronic mononuclear infiltrates.
- Look for fibrin and onion-skin arteriolar lesions.
- Recognize overlap with rheumatoid and other chronic synovitides.
- Use the clinical and laboratory framework to support etiology.

Antibiotics are effective in most Lyme arthritis

≈90%

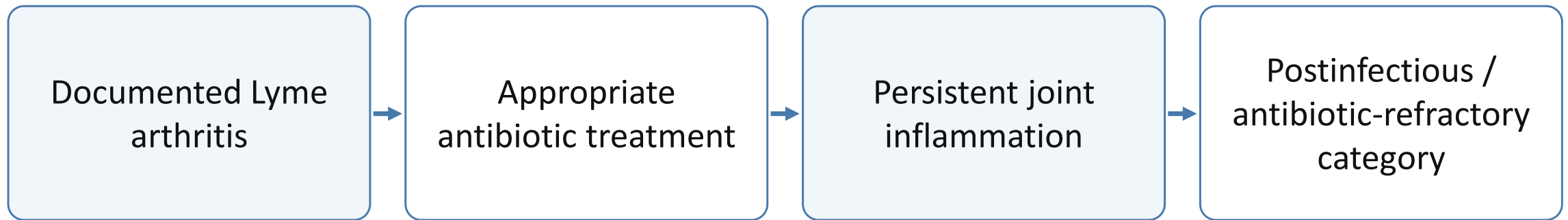
Curative treatment response to antibiotics
active against *Borrelia*, per Robbins

Residual cases

Persistent joint inflammation is described as
uncommon

The textbook section does not provide drug regimens or treatment durations.

Postinfectious arthritis may persist after therapy



These labels for an uncommon persistence scenario.

Post-treatment synovial PCR is often negative

POSTINFECTIOUS DISEASE

- The text notes that *Borrelia* frequently cannot be detected in these cases.
- Negative detection may persist even with PCR.
- Persistent arthritis therefore does not automatically demonstrate ongoing detectable infection.
- The proposed immune mechanism remains incompletely defined.

Separate observation from the proposed explanation

Status	What can be said
Observed	Some arthritis persists after antibiotics; PCR is often negative.
Proposed mechanism	Cross-reactive immune responses to OspA and unknown self-antigens.
Not established by excerpt	An obligatory autoimmune pathway for all persistent arthritis.

Persistent swelling is a diagnostic reasoning problem

- A person with previously diagnosed Lyme arthritis received antibiotic treatment.
- The knee remains inflamed despite completion of therapy.
- Repeat synovial-fluid PCR does not detect *Borrelia* DNA.

What can and cannot be inferred from this pattern?

Case analysis: Postinfectious is not a synonym for active infection

INTERPRETIVE DISCIPLINE

- Persistent clinical synovitis is the observation.
- The negative PCR reduces evidence for detectable organisms in the sampled joint.
- An immune-mediated explanation in some cases.
- Neither a pathogen-free state nor active infection is proven by symptoms alone.

Pathology–clinical integration: Four checkpoints

- Is the joint distribution consistent with large-joint Lyme arthritis?
- Does the exposure and systemic disease chronology fit?
- Are Borrelia antibodies and other findings interpreted appropriately?
- Could another cause of arthritis explain the presentation?

Five defining facts to retain

- Ixodes-transmitted *Borrelia* initiates the disease.
- Early systemic infection can precede delayed synovitis.
- One or a few large joints—especially the knee—are typically involved.
- Synovitis includes lining hyperplasia, mononuclear cells, and arteriolar change.
- Serology is central; PCR and post-treatment persistence require interpretation.

Sources and image integrity

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 26: Lyme Arthritis, pp. 1093–1094.

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 8: Lyme Disease, pp. 344–345.

Constructed illustrations are editable conceptual diagrams, not patient specimens or reproduced histology.