

Comparative Features of Osteoarthritis and Rheumatoid Arthritis

Pathogenesis • Morphology • Clinical discrimination

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Learning outcomes

By the end of this lecture, distinguish OA from RA by:

- Identifying the primary tissue and mechanism injured in each disorder.
- Relating cellular mechanisms to joint morphology and progression.
- Recognizing characteristic joint distribution, symptoms, and imaging.
- Explaining the value and limitations of RA serology and extra-articular disease.

The core differential: Six domains

Domain	Osteoarthritis	Rheumatoid arthritis
Primary driver	Biomechanical cartilage injury	Autoimmunity
Inflammation	Secondary / low grade	Primary / chronic synovitis
Pathology	Cartilage loss, osteophytes, cysts	Pannus, erosions, possible fusion
Serology	No characteristic autoantibodies	ACPA / rheumatoid factor
Extra-articular	Absent as an OA feature	May involve several organs

Different starting points converge on joint damage

Cartilage matrix injury



Chondrocyte response



Net matrix loss

OA: Wear-related stress and disordered repair initiate the process.

Autoimmune synovitis follows a different route

CD4+ T-cell response



Cytokine-driven synovitis



Pannus and erosions

RA: Immune inflammation is the primary engine of articular destruction.

What normally protects an articular surface?

Hyaline cartilage

- Type II collagen network resists tensile stress.
- Proteoglycans and water resist compression.

Chondrocytes

- Produce and renew cartilage matrix.
- Secrete remodeling enzymes and inhibitors.

Synovial environment

- Supports a mobile joint surface.
- Persistent synovial inflammation can destroy cartilage.

The primary lesion determines secondary changes

OSTEOARTHRITIS

- First major lesion: Articular cartilage matrix degeneration.
- Chondrocytes attempt repair, but matrix degradation exceeds synthesis.
- Subchondral bone responds to cartilage loss.

RHEUMATOID ARTHRITIS

- First major lesion: Persistent autoimmune synovitis.
- Hyperplastic synovium generates invasive pannus.
- Bone erosion follows inflammation and osteoclast activation.

Osteoarthritis is not primarily an autoimmune synovitis

Degeneration dominates even though inflammation is present.

- OA causes structural and functional failure of synovial joints.
- Biomechanical stress is the principal pathogenic mechanism.
- Inflammatory mediators can accelerate, but do not define, the primary lesion.
- Disease often develops insidiously as age-associated primary OA.

Primary and secondary osteoarthritis

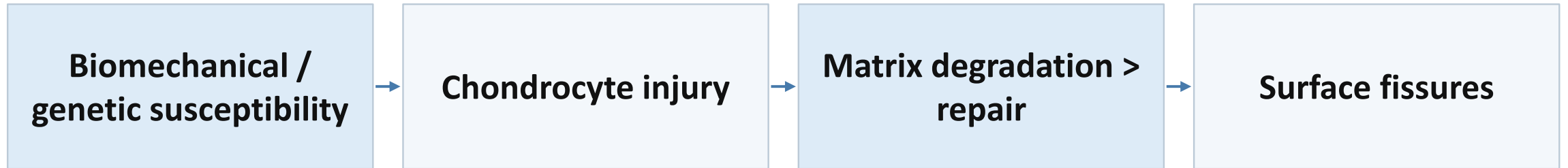
Primary OA

- Usually insidious without an identifiable initiating cause.
- Common after midlife; May affect few joints or be generalized.

Secondary OA

- Associated with predisposing joint deformity or earlier injury.
- Systemic factors named include diabetes, obesity, and ochronosis.

How cartilage injury becomes a persistent lesion



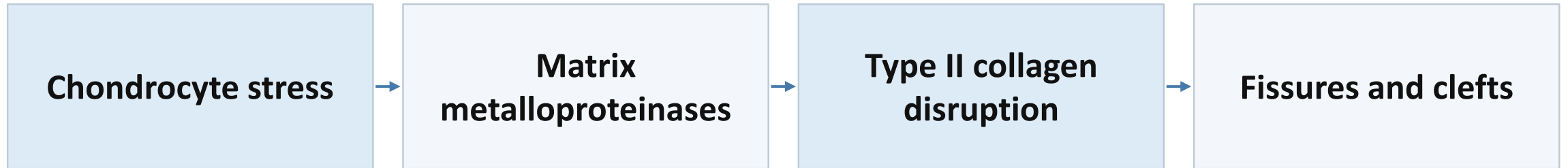
Cartilage loss is a failure of both extracellular matrix integrity and compensatory repair.

Early OA: Chondrocytes attempt repair

The early cellular response is active, not simply passive wear.

- Chondrocytes proliferate and form small clusters.
- Proteoglycan synthesis continues despite matrix damage.
- Cartilage water content increases.
- Catabolic degradation continues to exceed anabolic replacement.

OA matrix breakdown: Collagen and proteoglycans



Loss of the collagen network disrupts tensile integrity; Proteoglycan depletion contributes to surface failure.

Inflammation in OA: Contributor, not initiator

Synovial / chondrocyte signals

- IL-1, IL-6 and prostaglandins contribute to low-grade inflammation.
- Nitric oxide participates in tissue signaling.

Repair-associated signals

- TGF- β and bone morphogenetic proteins contribute to osteophyte development.
- TGF- β is also implicated in matrix metalloproteinase production.

OA morphology: A progressive sequence



Loose bodies, eburnation, cyst formation, and marginal osteophytes appear with progression.

OA: Superficial cartilage fibrillation

Histologic change reflects cleavage of the surface matrix.

- Fissures and clefts create a granular, softened articular surface.
- Chondrocyte clustering accompanies early cartilage degeneration.
- Progressive disruption ultimately removes full-thickness cartilage.
- The lesion begins in cartilage rather than invasive synovial pannus.

OA loose bodies arise from sloughed cartilage

Advanced articular cartilage may detach into the joint cavity.

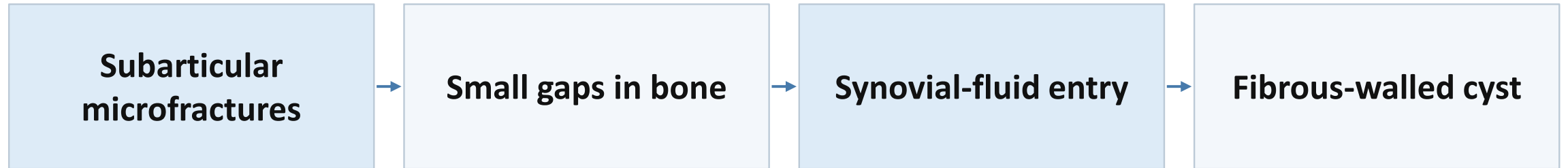
- Disrupted cartilage can separate as full-thickness fragments.
- Dislodged fragments become intra-articular loose bodies (“joint mice”).
- This finding belongs to advanced surface degeneration.
- It should not be mistaken for the immune pannus of RA.

OA eburnation is exposed, polished bone

Cartilage loss transfers friction to the subchondral surface.

- After total local cartilage loss, subchondral bone becomes the articular surface.
- Friction smooths and polishes exposed bone, yielding ivory-like eburnation.
- Subchondral sclerosis accompanies established radiographic OA.
- Eburnation is a bone response to absent cartilage, not synovial invasion.

How subchondral cysts form in OA



Fluid is forced into subchondral bone through a valve-like mechanism.

Osteophytes are marginal bony outgrowths

They represent a repair-associated response at joint margins.

- Mushroom-shaped bone projections form near articular edges.
- Initially capped by fibrocartilage and hyaline cartilage.
- Cartilage caps progressively ossify.
- TGF- β and bone morphogenetic proteins are implicated in their formation.

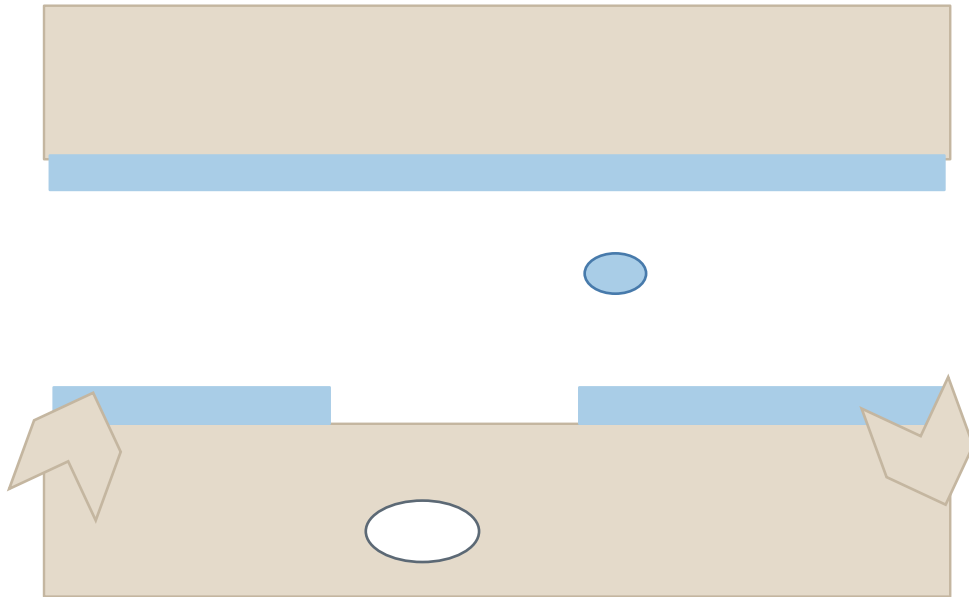
OA synovium is relatively quiet

Mild secondary inflammation contrasts with RA pannus.

- Usually only mild synovial congestion and fibrosis.
- Few infiltrating inflammatory cells are typical.
- Destructive lymphoplasmacytic synovitis is not the defining lesion.
- Absence of aggressive pannus helps explain why ankylosis is not characteristic.

Joint morphology: Two distinct mechanisms

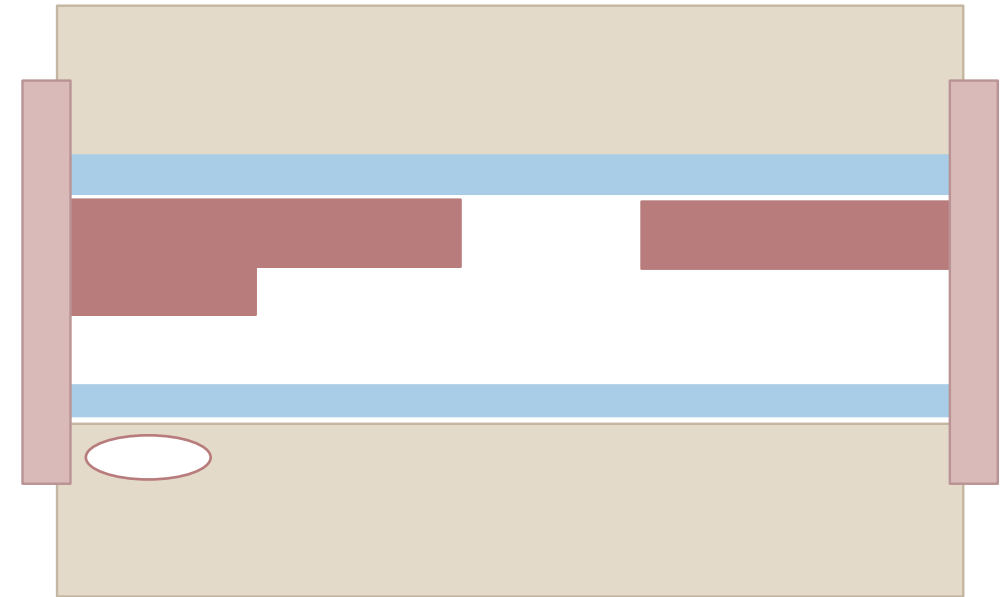
OSTEOARTHRITIS



Osteophytes

Cartilage loss / cyst

RHEUMATOID ARTHRITIS



Pannus

Bone erosion

Osteoarthritis: Structural changes and why they arise

Finding	Immediate lesion	Pathogenic explanation
Fibrillation	Surface clefts	Type II collagen / proteoglycan breakdown
Loose bodies	Detached cartilage	Full-thickness fragmentation
Eburnation	Polished subchondral bone	Cartilage loss exposes bone
Subchondral cysts	Fibrous-walled cavities	Fluid forced through bony defects
Osteophytes	Marginal bony projections	Abnormal reparative bone formation

OA radiographs show a characteristic bone–cartilage response

The advanced structural pattern often establishes the diagnosis.

- Joint-space narrowing reflects articular cartilage loss.
- Subchondral sclerosis marks a bone response to load.
- Osteophytes appear as peripheral bony projections.
- Subchondral cysts may accompany the typical pattern.

OA distribution: Load and local mechanics matter

Weight-bearing joints

- Knees and hips are common sites.
- Lower cervical and lumbar spinal levels may be affected.

Hand and foot joints

- Distal and proximal interphalangeal joints.
- First carpometacarpal and first tarsometatarsal joints.

Symptoms: OA pain differs from RA inflammation

OSTEOARTHRITIS

- Deep pain typically becomes worse during joint use.
- Stiffness on awakening usually improves with activity.
- Crepitus and limitation of motion may develop.

RHEUMATOID ARTHRITIS

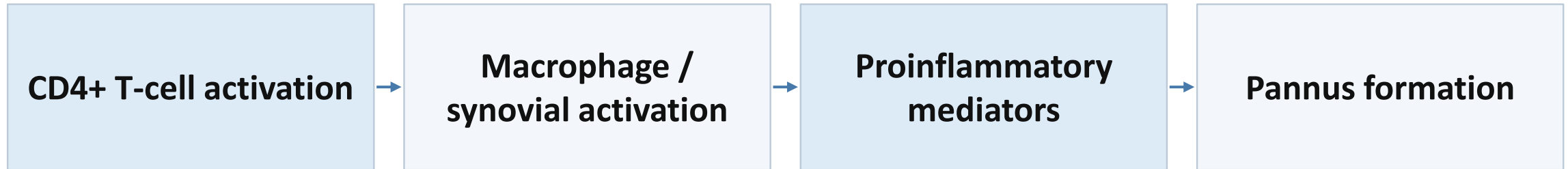
- Pain and stiffness are often worse on waking or after inactivity.
- Swelling, warmth, and inflammatory discomfort predominate.
- A chronic waxing-and-waning course may cause progressive limitation.

Rheumatoid arthritis is systemic autoimmunity

The primary lesion is a chronic nonsuppurative synovitis.

- RA produces proliferative inflammatory synovitis.
- Synovial inflammation destroys cartilage and periarticular bone.
- Progressive disease can produce fibrous and then bony ankylosis.
- Extra-articular lesions are possible in skin, lung, heart, and vessels.

RA pathogenesis: Adaptive immunity to synovial injury



The identity of the initiating joint antigen is not firmly established account.

RA effector mediators and their targets

TNF, IL-1, IL-6

- Macrophage-derived cytokines recruit and activate leukocytes.
- They promote synovial protease release and cartilage injury.

IL-17 and IFN- γ

- Th17-derived IL-17 recruits neutrophils / monocytes.
- Th1-derived IFN- γ activates macrophages and synovial cells.

RANKL explains inflammatory bone erosion

Activated T cells



RANKL expression



Osteoclast activation



Bone resorption

RA marginal erosions are immunologically driven; OA osteophytes reflect abnormal repair.

Citrullination creates important RA autoantigens

Post-translational protein modification can generate recognized epitopes.

- Arginine residues are converted to citrulline in certain proteins.
- Joint-associated targets include fibrinogen, type II collagen, α -enolase, and vimentin.
- Anti-citrullinated peptide antibodies (ACPA) recognize modified epitopes.
- Antibody responses complement, rather than replace, T-cell-driven inflammation.

ACPA is diagnostically useful, not universal

A positive result adds evidence for RA in the proper clinical setting.

- ACPA is detected in serum in up to about 70% of cases.
- ACPA can coexist with synovial lymphoid follicles and plasma cells.
- Absence of ACPA does not exclude RA.
- The initiating pathogenic antigen(s) remain incompletely defined.

Rheumatoid factor identifies a distinct autoantibody response

Rheumatoid factor is not synonymous with ACPA.

- Rheumatoid factor refers to autoantibodies directed against the Fc region of IgG.
- IgM and IgA rheumatoid factors in many RA patients.
- Rheumatoid factor is neither obligatory nor completely disease-specific.
- Autoantibody results should be interpreted with the joint phenotype.

Why genetic and environmental factors matter in RA

Inherited susceptibility

- HLA-DR4 is associated particularly with ACPA-positive RA.
- Genetic predisposition influences disease development and persistence.

Potential triggers

- Smoking and infection, including periodontitis, are proposed contributors.
- They may facilitate citrullination; Precise triggers are uncertain.

RA synovium changes its gross architecture

Inflamed synovium no longer remains thin and smooth.

- Synovium becomes edematous, thickened, and hyperplastic.
- Delicate and bulbous villous projections emerge.
- Increased vascularity develops with angiogenesis.
- The expanding tissue forms the substrate for invasive pannus.

RA synovitis contains an organized immune infiltrate

Histology demonstrates chronic immune-mediated inflammation.

- Synoviocyte proliferation and hyperplasia.
- CD4+ helper T cells, B cells, plasma cells, dendritic cells, and macrophages.
- Lymphoid follicles may form within the synovium.
- Fibrin-rich surface exudates may contain neutrophils.

RA: Pannus is an invasive lesion, not just swelling

Components

- Edematous hyperplastic synovium and inflammatory cells.
- Granulation tissue and proliferating fibroblasts.

Destructive effects

- Spreads onto the cartilage surface.
- Erodes cartilage and allows inflammatory tissue to extend toward bone.

From proliferative synovitis to joint destruction

Synovial hyperplasia



Inflammatory pannus



Cartilage erosion



Joint-space loss

Persistent inflammatory granulation tissue invades cartilage rather than merely responding to its disappearance.

RA progression: Erosion to ankylosis



Fibrous fusion may eventually ossify; OA does not typically produce joint fusion.

Subchondral pathology in OA and RA

OSTEOARTHRITIS

- Eburnation and sclerosis are consequences of cartilage loss.
- Subchondral cysts arise through bony gaps and fluid entry.
- Marginal osteophytes add bone.

RHEUMATOID ARTHRITIS

- Osteoclast-driven resorption produces erosions.
- Pannus directly penetrates cartilage and bone.
- Ankylosis may ultimately fuse joint surfaces.

Rheumatoid nodules show a necrobiotic architecture

These extra-articular lesions are a pathologic clue to RA.

- Usually firm, nontender subcutaneous masses at pressure sites.
- Central fibrinoid necrosis is a defining microscopic feature.
- A rim of activated macrophages surrounds the necrotic center.
- Lymphocytes and plasma cells populate the surrounding tissue.

Extra-articular RA can involve several organ systems

RA is not confined to synovial joints.

- Skin: Rheumatoid nodules.
- Blood vessels: Leukocytoclastic vasculitis in severe disease.
- Pleura, lung, and pericardium may be affected.
- Ocular disease can include uveitis and keratoconjunctivitis.

Joint distribution provides an early diagnostic clue

OSTEOARTHRITIS

- Knees, hips, spine, DIP / PIP, and thumb-base joints are common.
- Often one or a few joints, although generalized OA occurs.
- Prominent distal interphalangeal osteophytes can form Heberden nodes.

RHEUMATOID ARTHRITIS

- Usually begins in small joints of hands and feet.
- Often symmetric and eventually polyarticular.
- MCP and PIP involvement is characteristic in the hands.

Joint symptoms reflect the underlying lesion

OSTEOARTHRITIS

- Mechanical pain with joint use.
- Brief stiffness that tends to improve after movement.
- Crepitus / restricted range of motion with degeneration.
- Significant systemic autoimmune manifestations are not typical.

RHEUMATOID ARTHRITIS

- Morning / post-rest inflammatory stiffness.
- Swollen, warm, painful joints.
- Fatigue and malaise may precede arthritis.
- Chronic relapsing inflammation can produce deformities.

The hand is a high-yield OA–RA discriminator

Specific joint groups matter more than a generic “hand arthritis” label.

- OA frequently affects distal interphalangeal joints and first carpometacarpal joints.
- Heberden nodes reflect distal interphalangeal osteophytes.
- RA typically involves metacarpophalangeal and proximal interphalangeal joints.
- RA hand deformities may include ulnar deviation and flexion–hyperextension.

Comparison of imaging patterns

Domain	Osteoarthritis	Rheumatoid arthritis
Joint space	Narrowing from cartilage loss	Narrowing after cartilage destruction
Bone margin	Marginal osteophytes	Periarticular erosions
Bone density	Subchondral sclerosis	Juxta-articular osteopenia
Other signs	Subchondral cysts / eburnation	Deformity and possible ankylosis

A radiograph measures structure, not symptom severity

OA structural severity is not a direct pain scale.

- Radiographic OA can be diagnostic when characteristic advanced changes are present.
- The extent of radiographic OA does not correlate tightly with pain and disability.
- Clinical limitation still requires direct functional assessment.
- For inflammatory RA, erosions and osteopenia indicate a different mechanism.

Serologic evaluation separates immune disease from degeneration

OSTEOARTHRITIS

- There is no characteristic OA autoantibody panel.
- Laboratory serology is not the defining basis of OA diagnosis.
- Typical advanced imaging may obviate biopsy.

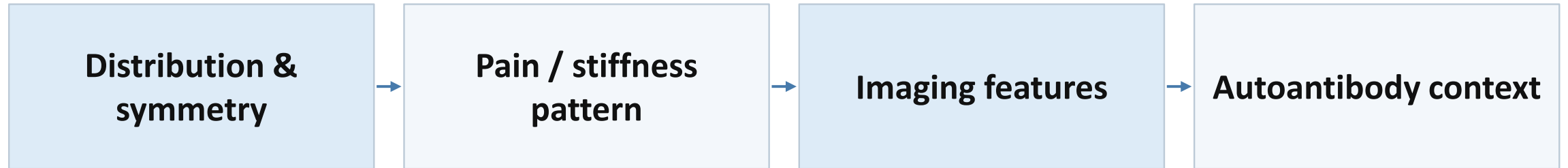
RHEUMATOID ARTHRITIS

- ACPA and rheumatoid factor support RA diagnosis.
- Seronegativity is possible; Roughly one-fifth.
- Clinical pattern and radiography remain important; Biopsy is rarely required.

Why similar-looking symptoms may have different causes

Finding	OA interpretation	RA interpretation
Joint pain	Articular cartilage loss / altered load	Active synovial inflammation
Stiffness	Mechanical stiffness, improves with activity	Inflammatory stiffness after rest
Swelling	Bony enlargement / secondary changes	Synovial thickening and inflammation
Reduced motion	Cartilage depletion / osteophytes	Pannus, erosions, eventual fusion

A defensible clinical comparison workflow



Interpret these domains together; No isolated symptom or serologic test should replace clinicopathologic correlation.

When the pattern is atypical, reconsider the differential

The textbook contrasts OA and RA; Not all arthritis is either one.

- Young-onset OA merits assessment for a predisposing abnormality.
- RA may lack rheumatoid factor and ACPA.
- Joint distribution and inflammatory signs may overlap in practice.
- Crystal, infectious, and other immune-mediated arthritides form separate categories.

Therapeutic goals follow the pathogenesis

OSTEOARTHRITIS

- Reduce pain and preserve joint function.
- Modify mechanical load and activities.
- In severe structural disease, arthroplasty may be considered.
- Anti-inflammatory approaches can be used for symptoms.

RHEUMATOID ARTHRITIS

- Suppress immune inflammation and prevent progressive destruction.
- Methotrexate and other immunosuppressants.
- TNF antagonists and other immune-targeting biologics are described.
- Disease control may require sustained therapy.

Immunosuppression adds a risk absent from mechanical OA care

Pathway-directed RA treatment has clinically relevant tradeoffs.

- TNF plays a central role in sustained synovial inflammation.
- Anti-TNF treatment reduces inflammation but is not curative.
- Long-term anti-TNF therapy predisposes to opportunistic infections.
- Robbins specifically highlights reactivation or infection involving *Mycobacterium tuberculosis*.

Case A: Activity-related knee pain

A 68-year-old has slowly progressive knee discomfort worsened by walking, crepitus, and radiographs showing osteophytes with subchondral sclerosis.

Which process best explains the radiographic pattern?

OA — cartilage loss with load-related subchondral bone remodeling.

Case B: Inflammatory small-joint arthritis

A patient has symmetric painful swelling of metacarpophalangeal and proximal interphalangeal joints, marked stiffness on waking, and periarticular erosions.

What lesion principally drives the cartilage destruction?

RA — inflammatory synovial pannus invading the articular surface.

Case C: Negative serology does not close the diagnosis

A patient has symmetric warm small-joint swelling and erosive inflammatory changes, but both rheumatoid factor and ACPA tests are negative.

Does negative serology exclude rheumatoid arthritis?

No — seronegative RA exists; Interpret clinical and imaging evidence.

High-yield final comparison

Diagnostic axis	Osteoarthritis	Rheumatoid arthritis
Pathogenesis	Cartilage degeneration / failed repair	Autoimmune inflammatory synovitis
Inflammation	Secondary, usually limited	Primary and prominent
Tissue result	Fissures, eburnation, osteophytes	Pannus, erosions, ankylosis
Distribution	Weight-bearing, DIP / thumb base	Symmetric small joints, MCP / PIP
Clinical timing	Use-related pain	Morning or post-rest symptoms
Serology / systemic	No characteristic autoantibodies	ACPA / RF; extra-articular lesions

Morphology explains the entire differential

Use causal reasoning rather than memorizing disconnected features.

- OA: Matrix failure → fissures → cartilage loss → sclerosis, cysts, and osteophytes.
- RA: Autoimmunity → chronic synovitis → pannus → cartilage and bone erosion.
- OA is predominantly a degenerative joint disease; RA is systemic immune-mediated disease.
- Distribution, inflammatory symptoms, radiology, and serology form a coherent diagnostic pattern.

Sources and source-fidelity boundaries

Primary source

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026), Chapter 26 — Joints: Osteoarthritis and Rheumatoid Arthritis.

Comparative source

Table 26.5: primary lesion, inflammation, distribution, pathology, antibodies, and organ involvement. Figure 26.37: morphology labels.

Original teaching schematics are not photomicrographs or reproduced textbook figures.