



OSTEOARTHRITIS

Cartilage degeneration, structural joint failure and clinicopathologic correlations

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Learning objectives

- Explain how normal cartilage composition supports motion and load bearing.
- Trace stress-driven matrix breakdown, cellular responses and disordered repair.
- Recognize early and late structural changes, radiographic signs and clinical patterns.
- Distinguish the typical osteoarthritis pattern from rheumatoid arthritis.

Osteoarthritis is structural failure of a synovial joint

Degeneration of articular cartilage



Progressive failure of joint architecture and function

Inflammation contributes secondarily rather than defining the primary lesion.

Normal joints balance mobility with stability

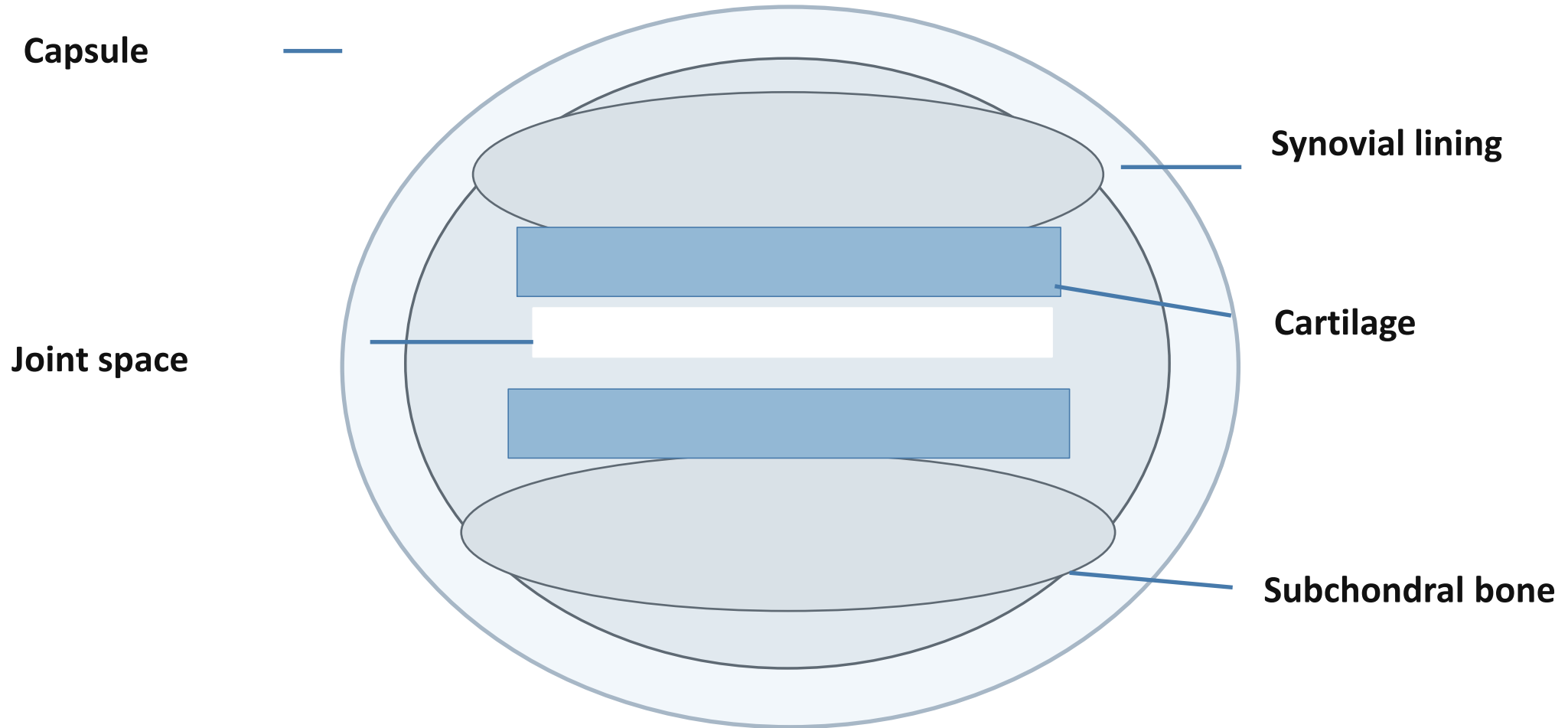
Solid (nonsynovial)

- No open joint cavity
- Connective tissue unites bones
- Little permitted motion

Synovial

- A joint space permits motion
- Capsule, synovium and ligaments
- Articular cartilage bears load

A synovial joint is a coupled tissue system



Synoviocytes support joint fluid physiology

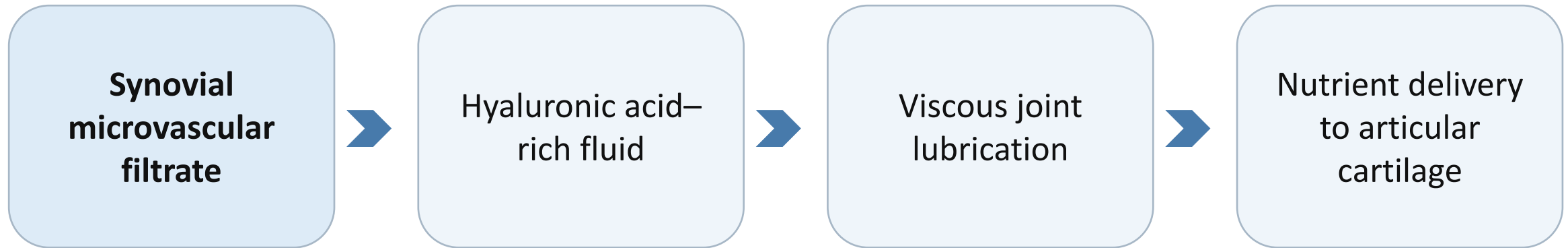
Type A synoviocytes

- Macrophage-like phenotype
- Specialized phagocytic function
- Part of synovial lining

Type B synoviocytes

- Fibroblast-like phenotype
- Produce hyaluronic acid
- Synthesize synovial proteins

Synovial fluid lubricates and nourishes cartilage



Synovium lacks a continuous basement membrane, permitting exchange with synovial fluid.

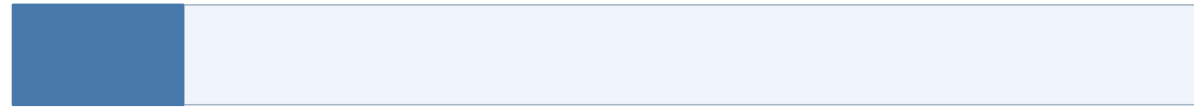
Articular cartilage has an unusual extracellular matrix

Water



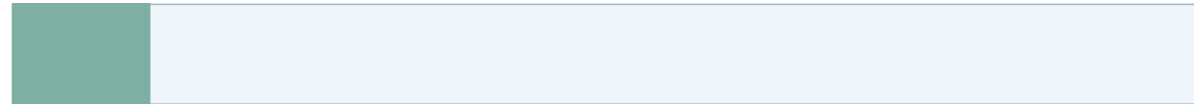
70%

Type II collagen



10%

Proteoglycans



8%

Proportions as stated for hyaline cartilage in the adjacent Robbins Joints section.

Collagen and proteoglycans provide complementary mechanics

Type II collagen

- Resists tensile stress
- Distributes/transmits joint loads
- Maintains a coherent fibrillar network

Water + proteoglycans

- Opposes compression
- Limits surface friction
- Retains interstitial water

Cartilage has limited direct vascular access

- Articular hyaline cartilage contains no blood vessels, lymphatics or nerves.
- The synovial fluid is an important route for cartilage nutrition.
- Cartilage function depends on the integrity of its extracellular matrix and chondrocytes.

Chondrocytes maintain a regulated matrix equilibrium

Matrix production

Matrix turnover

Collagen II + proteoglycans



Remodeling enzymes + inhibitors

Healthy cartilage depends on coordinated synthesis and regulated breakdown.

Osteoarthritis is the most common joint disease

- The core pathology is degenerative rather than primarily autoimmune synovitis.
- Articular cartilage destruction initiates a cascade affecting bone and synovium.
- Structural changes culminate in impaired motion, pain and joint deformity.

The association with age is substantial

Steep age association

>50 years: Prevalence accelerates

>70 years: Approximately 40% affected

These are textbook population statements, not individual-risk predictions.

Primary osteoarthritis is usually insidious

- The more common form has no clearly identifiable initiating joint injury.
- It generally presents in later adulthood.
- Often only one or a few joints are involved; Generalized disease can occur.

Secondary osteoarthritis has a predisposing context

Altered geometry

Deformity changes joint mechanics

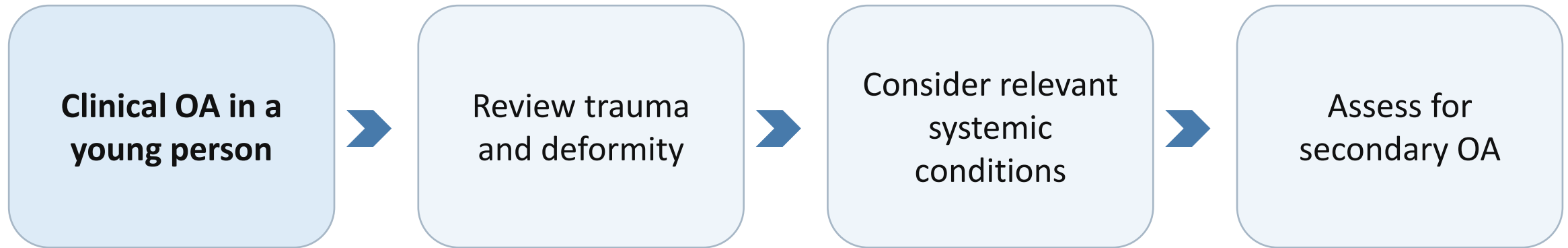
Prior damage

Previous articular injury

Systemic setting

Diabetes, obesity or
ochronosis

Young-onset osteoarthritis should prompt investigation



Age alone does not define the cause; Investigate the atypical presentation.

Primary and secondary disease share a final pathway

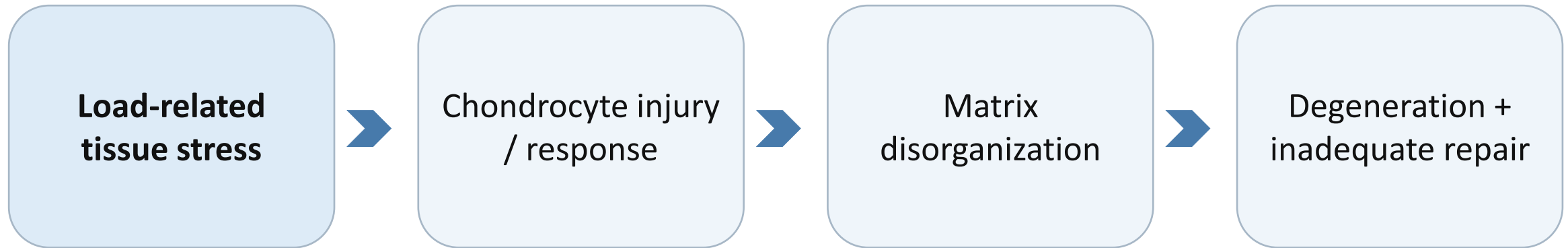
Primary OA

- Usually later onset
- No evident initiating cause
- Often oligoarticular

Secondary OA

- Often younger onset
- Recognizable predisposition
- Similar end-stage morphology

The pathogenic driver is biomechanical stress



The source identifies biomechanical stress as the principal pathogenic mechanism.

Genetic susceptibility can modify cartilage vulnerability

- Polymorphisms affecting matrix components may alter resistance to injury.
- Signaling-pathway variants may influence the chondrocyte response.
- Genetics is a predisposing contribution, not a single-gene explanation of most OA.

OA progresses when repair does not match matrix loss

Compensatory synthesis

Chondrocyte proliferation +
proteoglycans

Net degradation

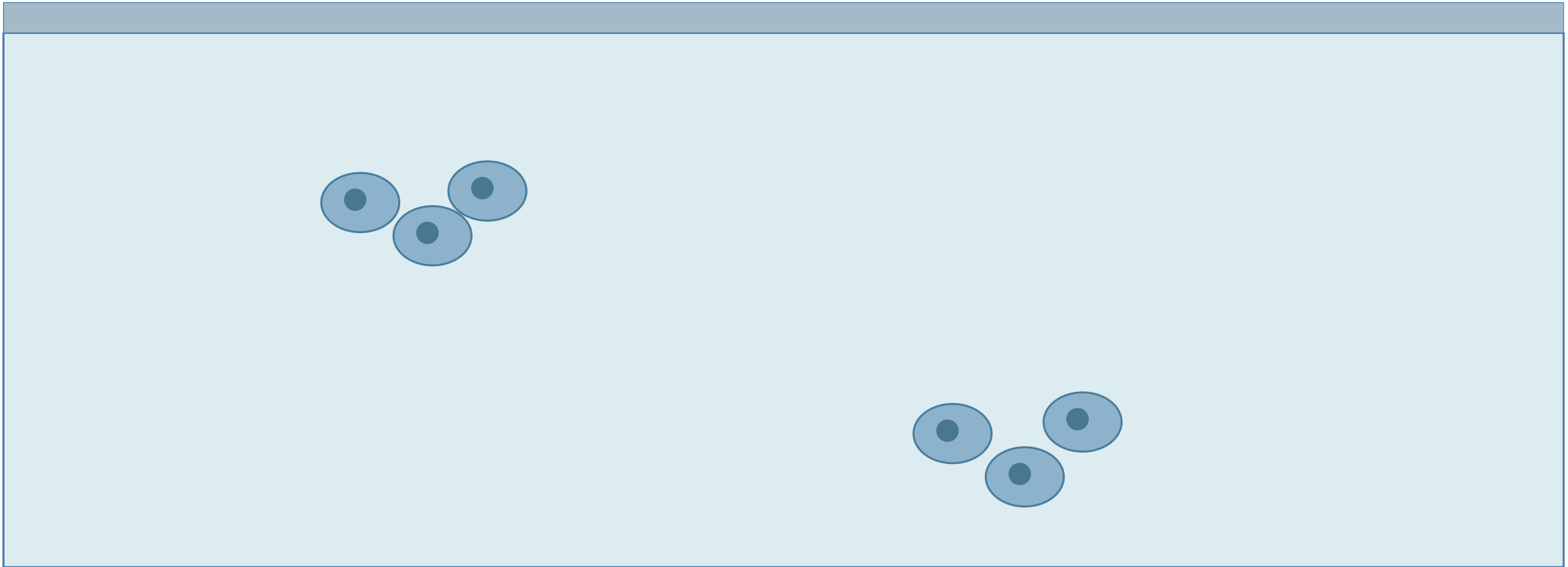
Matrix breakdown exceeds
replacement



Apparent early repair activity coexists with progressive matrix depletion.

Early chondrocyte proliferation is reactive

Articular surface

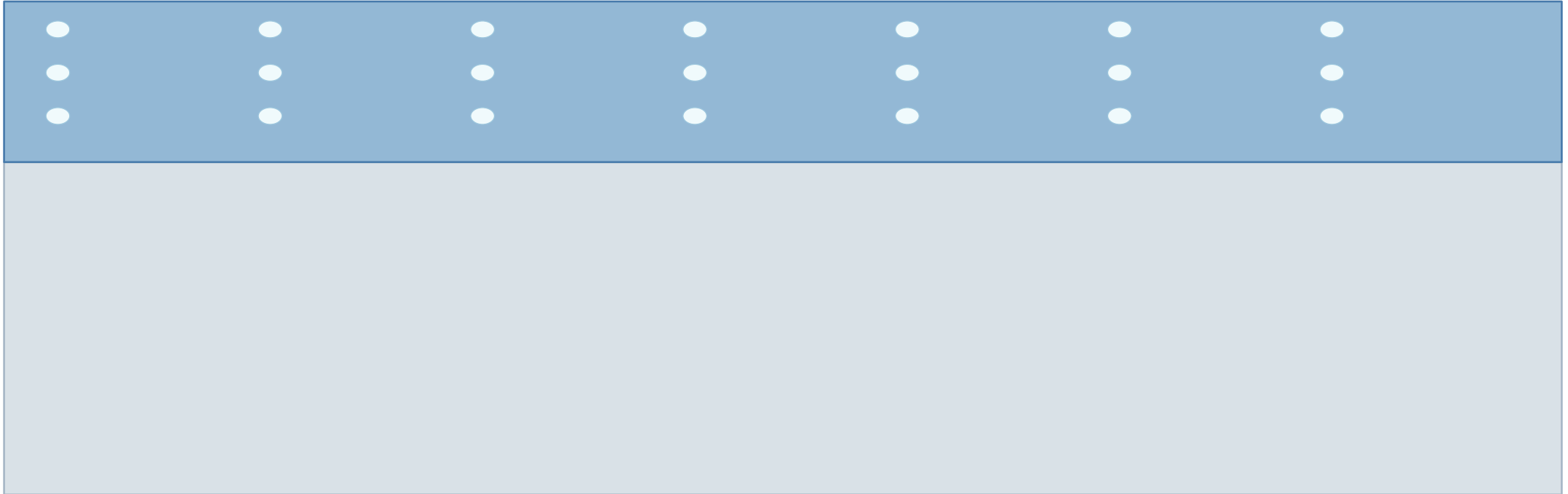


Chondrocyte clusters

Cell clusters are a morphological sign of the attempted response to matrix loss.

Cartilage water increases during early degeneration

Articular cartilage



Subchondral bone

Increased water accompanies disrupted matrix organization; It does not imply healthier cartilage.

Type II collagen forms the main fibrillar scaffold

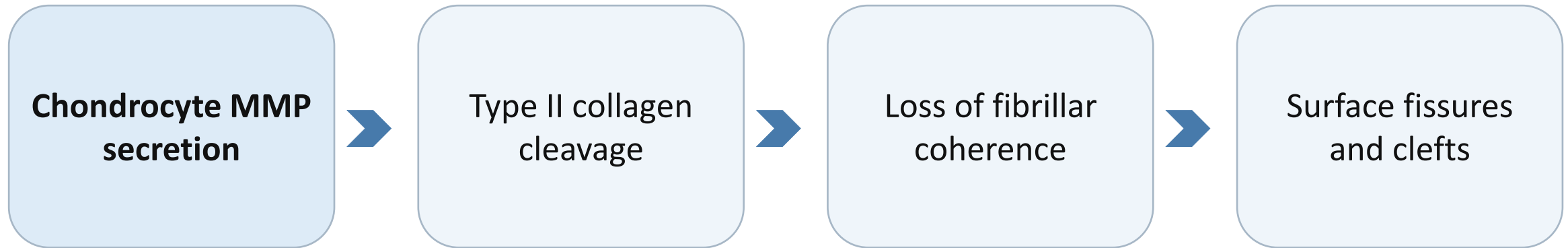
Articular cartilage



Subchondral bone

An intact network supports a mechanically coherent articular surface.

Matrix metalloproteinases dismantle collagen II



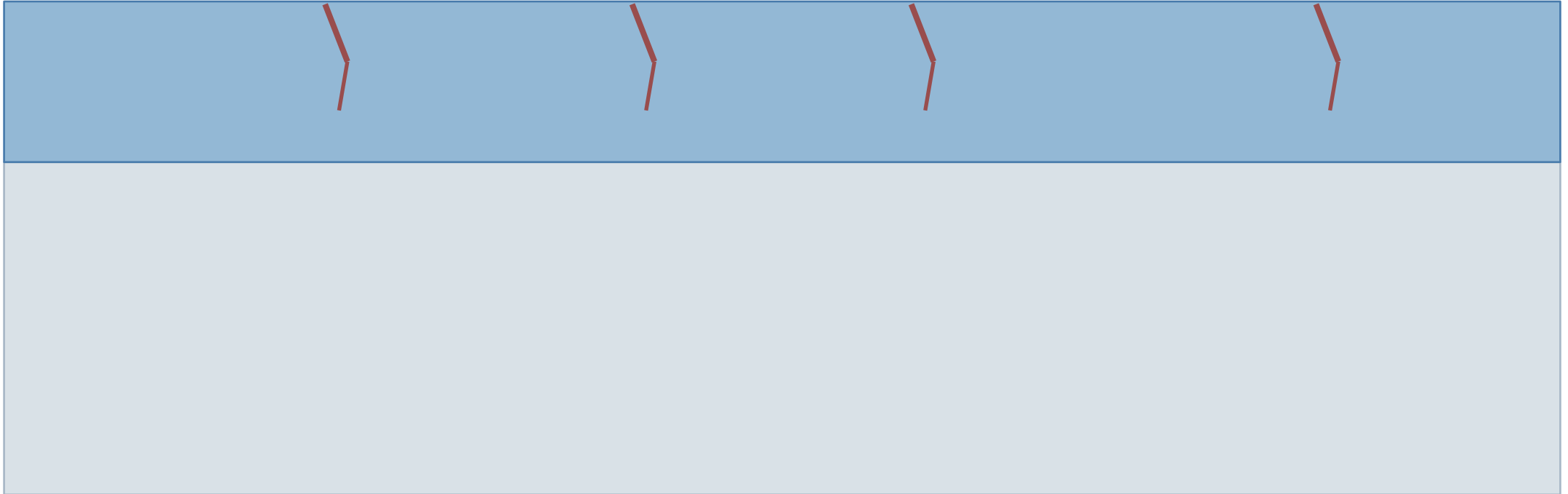
MMPs are degradative enzymes; Their effect exceeds matrix reconstruction in OA.

Proteoglycan depletion adds to matrix softening

- Chondrocytes continue to synthesize proteoglycans in early OA.
- Despite synthesis, proteoglycan degradation produces net matrix loss.
- Loss of collagen and proteoglycans together compromises articular surface integrity.

The cartilage surface breaks into fissures and clefts

Articular cartilage



Subchondral bone

Schematic illustration of focal surface fissuring; Not a histologic specimen.

Several mediators amplify cartilage degradation

TGF- β

Induces MMP production in the source model

IL-1 and IL-6

Part of the cytokine milieu

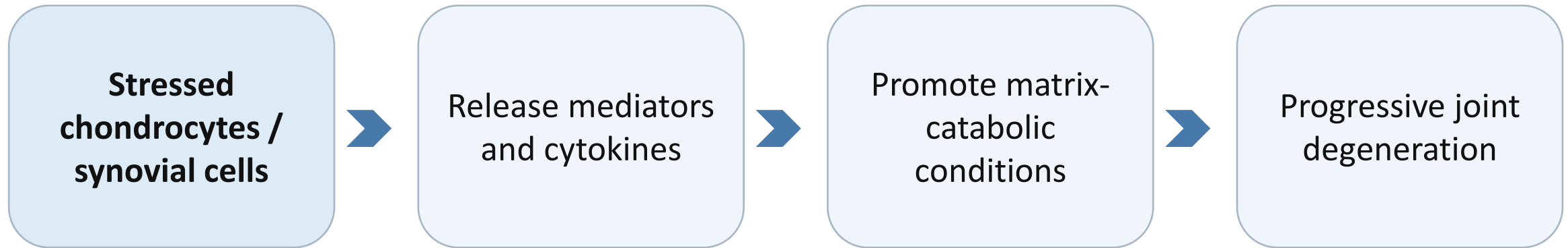
Prostaglandins

Diffusible contributors

Nitric oxide

Diffusible contributor

Synovial and cartilage cells communicate in OA



Mechanistic interpretation of the mediators identified.

Low-grade inflammation contributes to progression

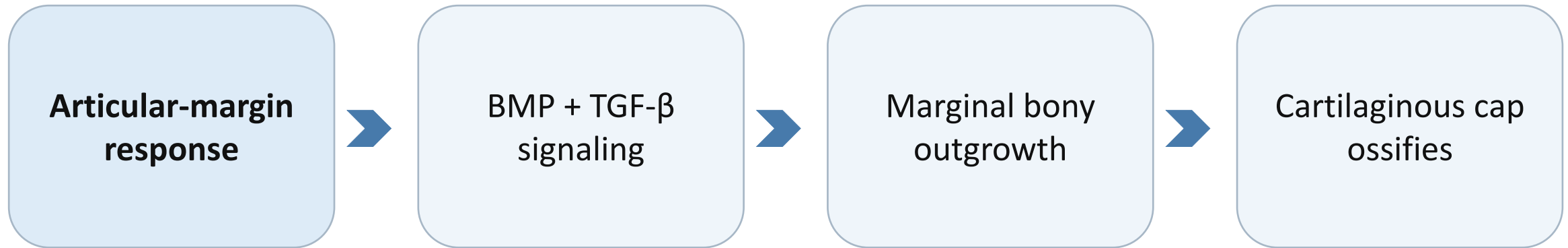
Dominant process

- Cartilage matrix degeneration
- Biomechanical stress
- Disordered repair

Secondary contribution

- Chronic low-level inflammation
- Locally generated mediators
- May amplify tissue damage

Osteophyte formation represents disordered repair



Bone morphogenetic proteins (BMPs) and TGF- β are implicated in osteophyte development.

TGF- β participates in more than one OA process

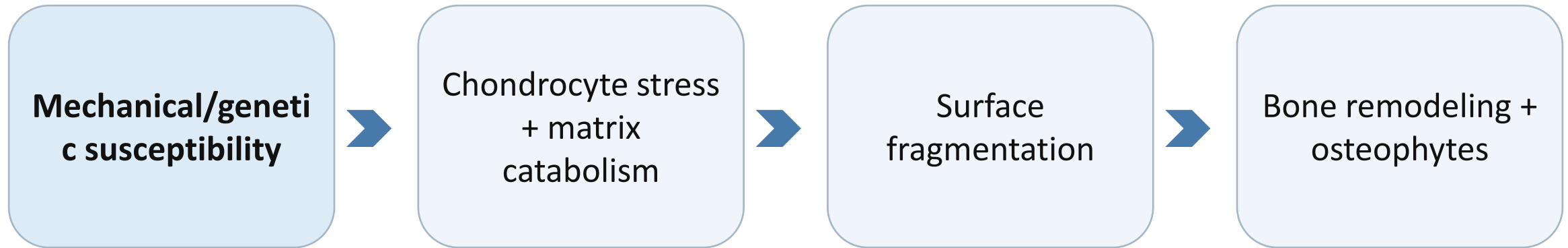
In cartilage matrix loss

- Associated with MMP induction
- Contributes to degradation
- Part of diffusible mediator network

At the joint margin

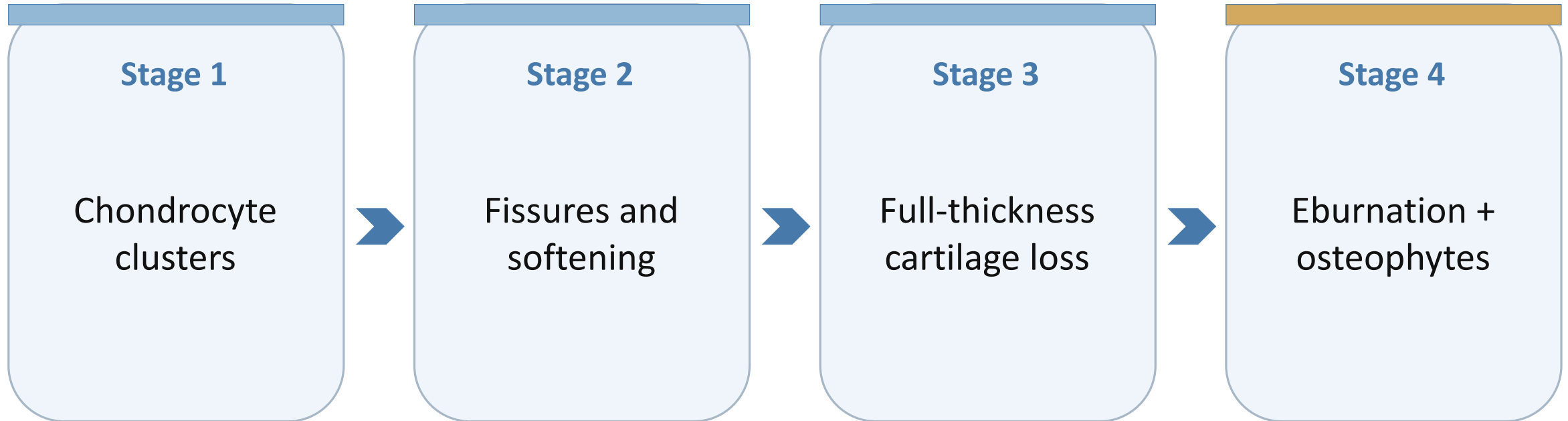
- Contributes to osteophyte genesis
- Acts with bone morphogenetic proteins
- Reflects aberrant bone/cartilage repair

Pathogenesis integrates cartilage, cells and bone



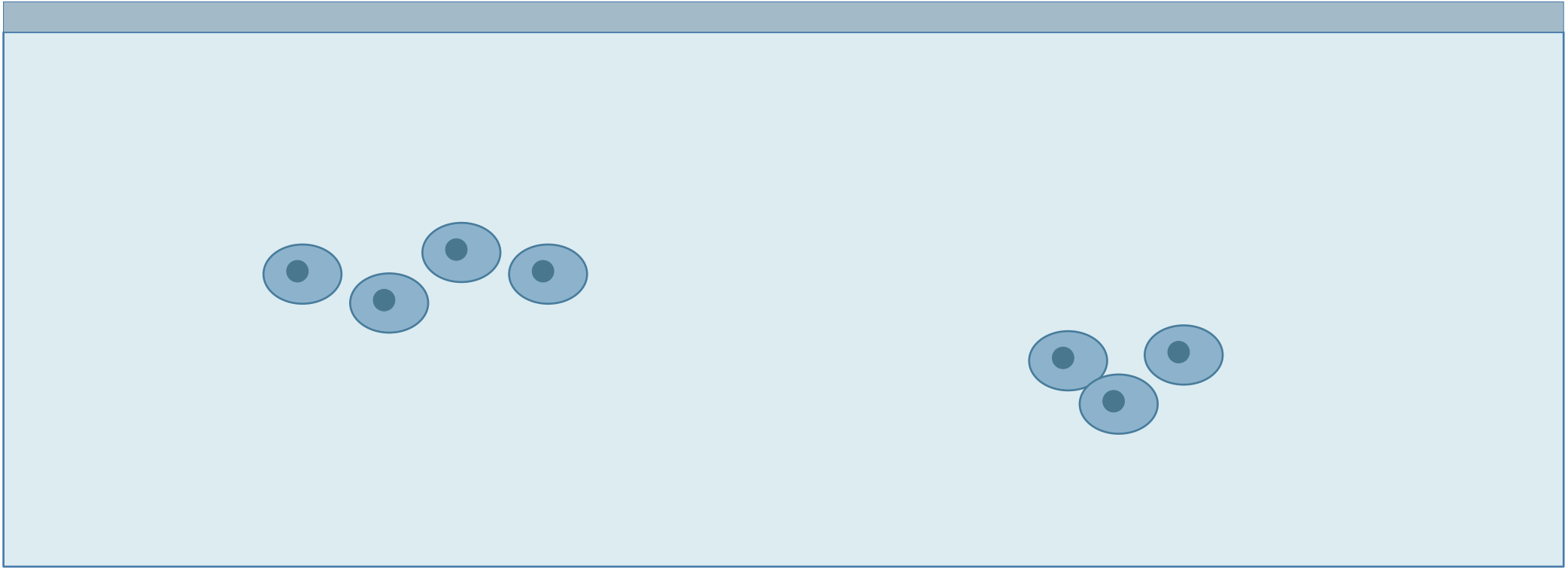
The joint changes as an interconnected organ, not just a layer of cartilage.

OA morphology changes along a recognizable sequence



Cell clusters are an early microscopic change

Articular surface



Chondrocyte clusters

Reactive chondrocytes form multicellular groups within cartilage.

A fibrillated surface becomes granular and soft

Articular cartilage

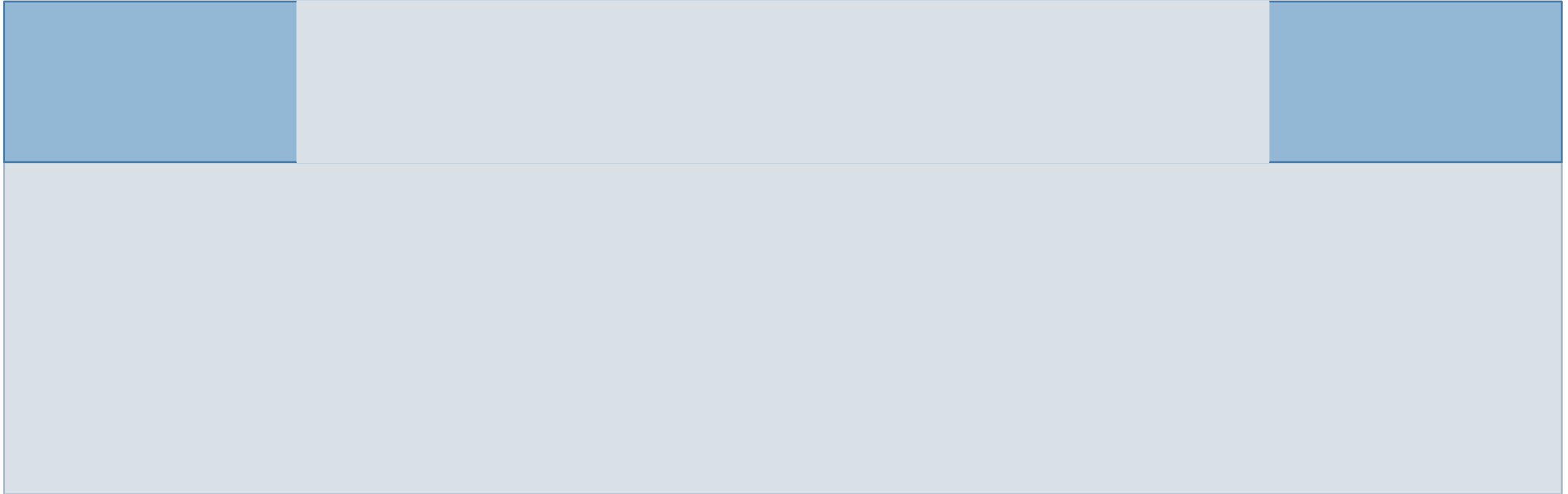


Subchondral bone

Breakdown of type II collagen and proteoglycans precedes gross surface disruption.

Advanced OA exposes subchondral bone

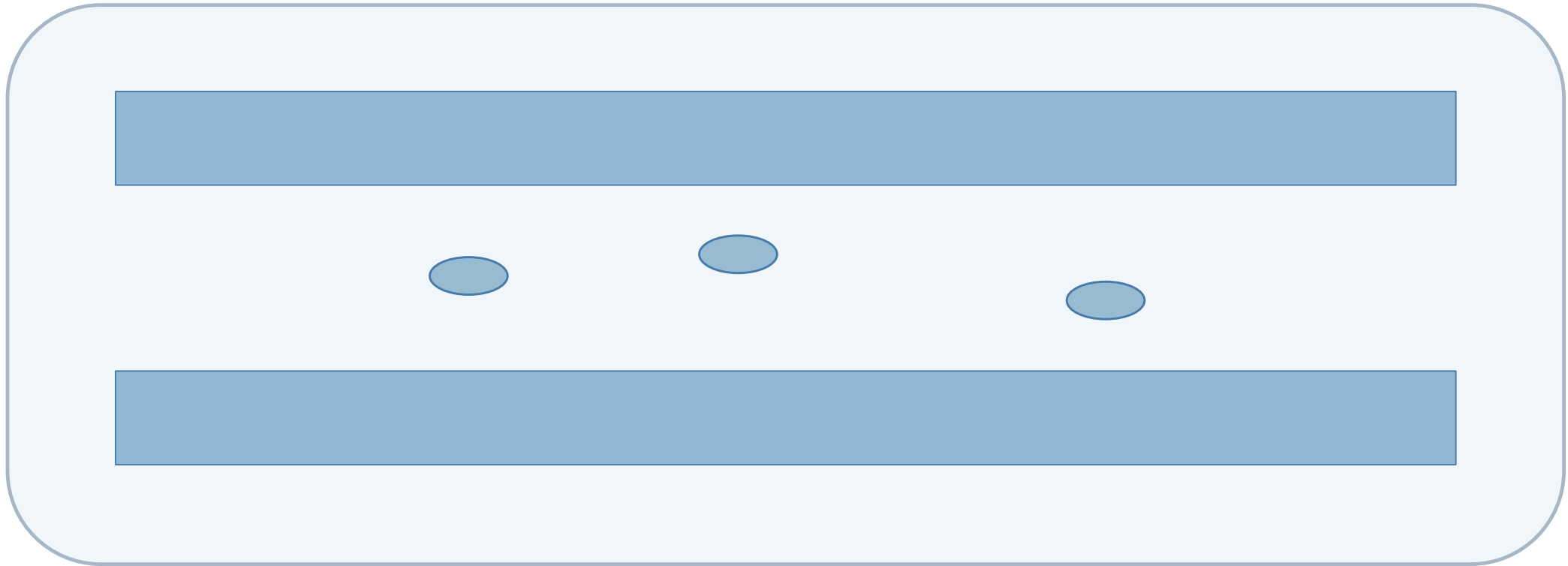
Articular cartilage



Subchondral bone

Loss of full-thickness articular cartilage brings opposing bony surfaces into contact.

Detached cartilage produces intra-articular loose bodies

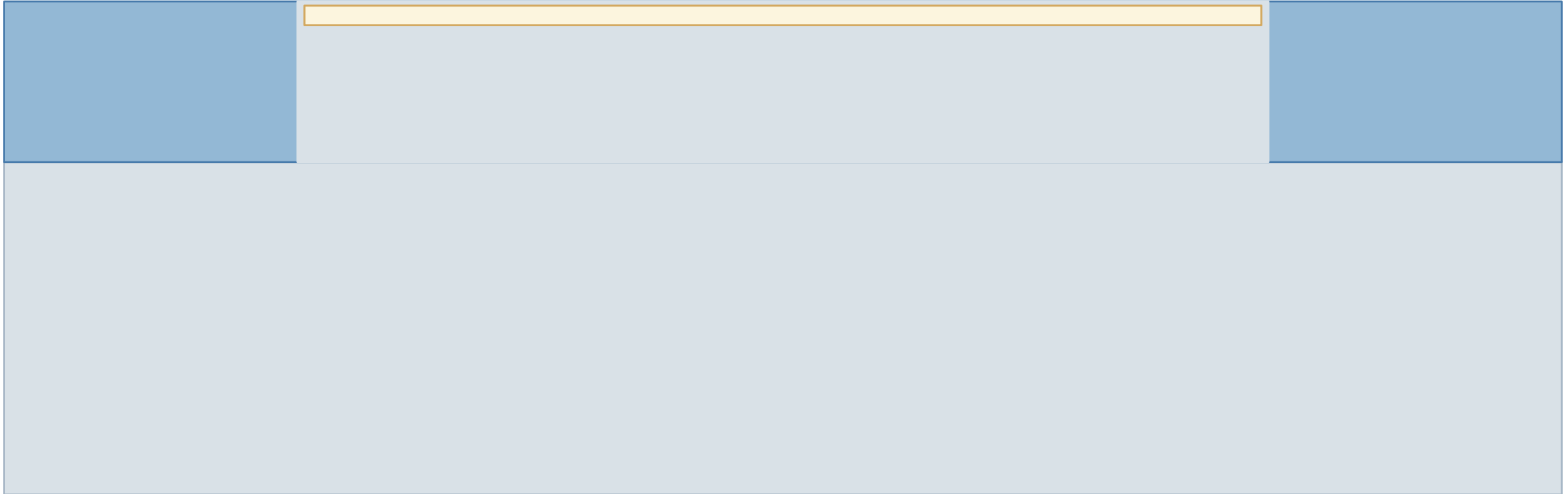


Detached cartilage fragments inside joint space

Full-thickness cartilage fragments can slough and move freely in the joint (“joint mice”).

Eburnation is polished exposed subchondral bone

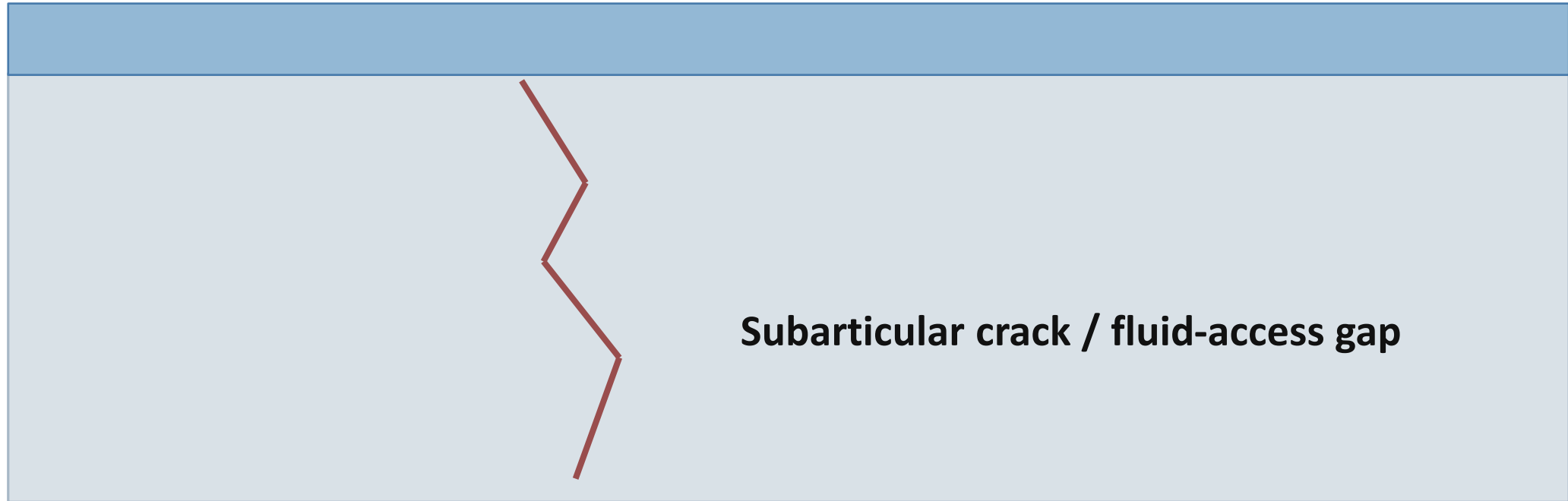
Articular cartilage



Subchondral bone

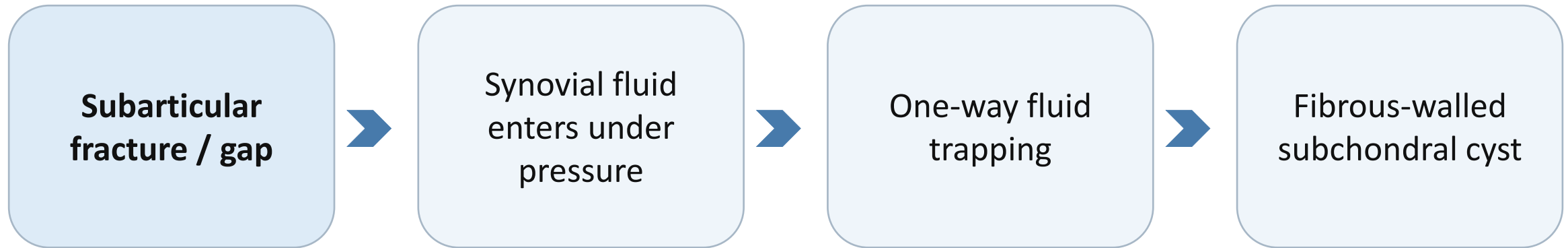
Repeated contact burnishes exposed bone to an ivory-like articular surface.

Subarticular microfractures alter the bone compartment



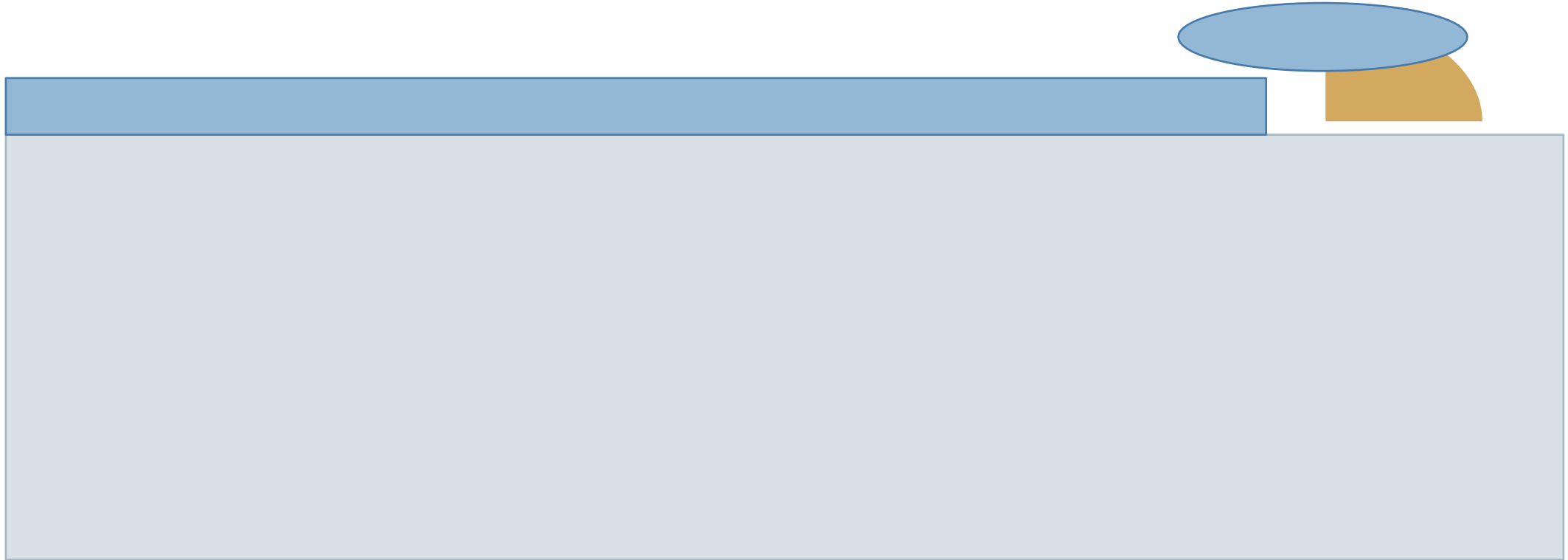
Small fractures produce gaps beneath the damaged articular surface.

Subchondral cysts arise by a valve-like process



The “ball-valve” mechanism is described in the Robbins morphology section.

Osteophytes are marginal bony outgrowths



Marginal bone outgrowth

Mushroom-shaped peripheral outgrowths develop a fibrocartilage/hyaline-cartilage cap that ossifies.

OA synovitis is usually limited

- Synovium may show mild congestion and fibrosis.
- Few inflammatory cells are usually present.
- This relatively modest synovial reaction contrasts with the dominant inflammatory synovitis of RA.

Structural changes generate the classic imaging triad

Joint-space loss

Reflects reduced cartilage thickness

Subchondral sclerosis

Denser bone beneath the joint

Marginal osteophytes

Peripheral bony outgrowths

Radiographs reflect more than cartilage degeneration

Cartilage compartment

- Narrowing of joint space
- Loss of effective bearing surface
- Surface fragmentation

Subchondral / marginal bone

- Increased bone density
- Marginal bony proliferation
- Secondary bone remodeling

Typical advanced radiographs usually avoid the need for biopsy

- Joint-space narrowing, subchondral sclerosis and osteophytes form a characteristic combination.
- These advanced imaging findings are sufficiently diagnostic.
- Tissue biopsy is therefore not routinely required for a typical presentation.

Pain is characteristically aggravated by use

- Deep joint pain usually increases with mechanical activity.
- Morning stiffness generally improves with movement.
- Clinical examination also detects crepitus and restricted range of motion.

Morning stiffness and pain follow a mechanical pattern

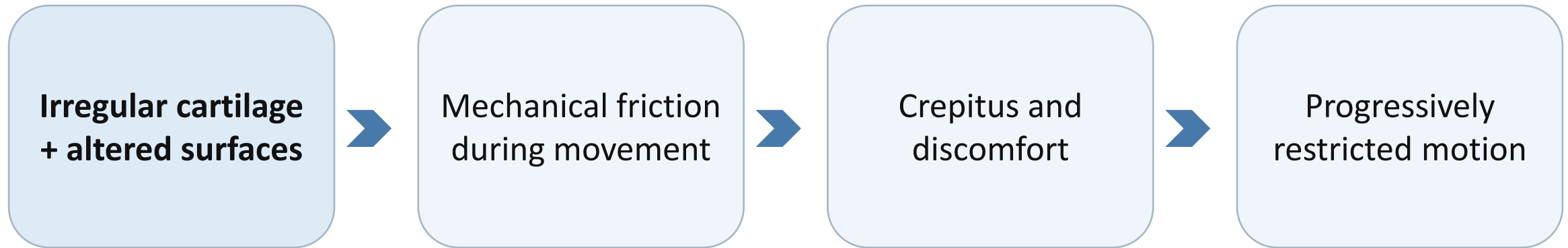
After inactivity

- Stiffness may be evident on waking
- Movement tends to ease stiffness
- Chronic OA does not require marked synovitis

With use

- Deep joint pain is provoked
- Load-bearing movement is limited
- Function may decline

Crepitus and reduced motion reflect articular damage



Clinicopathologic interpretation of the source clinical and morphology descriptions.

Hips and knees are common OA sites

Hip

Weight-bearing synovial
joint

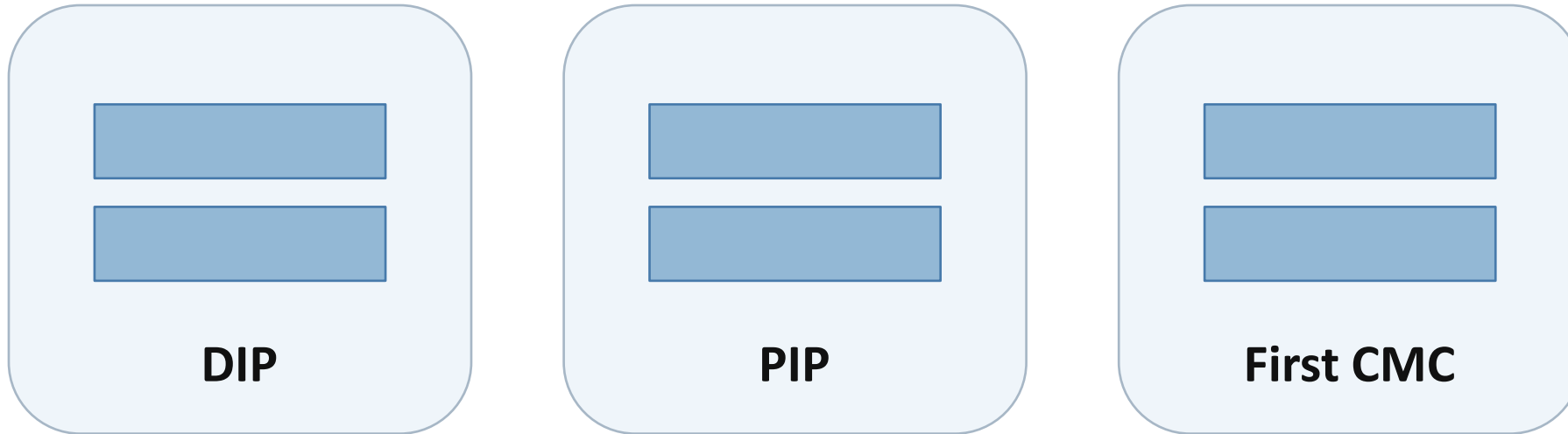
Knee

Weight-bearing synovial
joint

Spine

Cervical and lower lumbar
levels

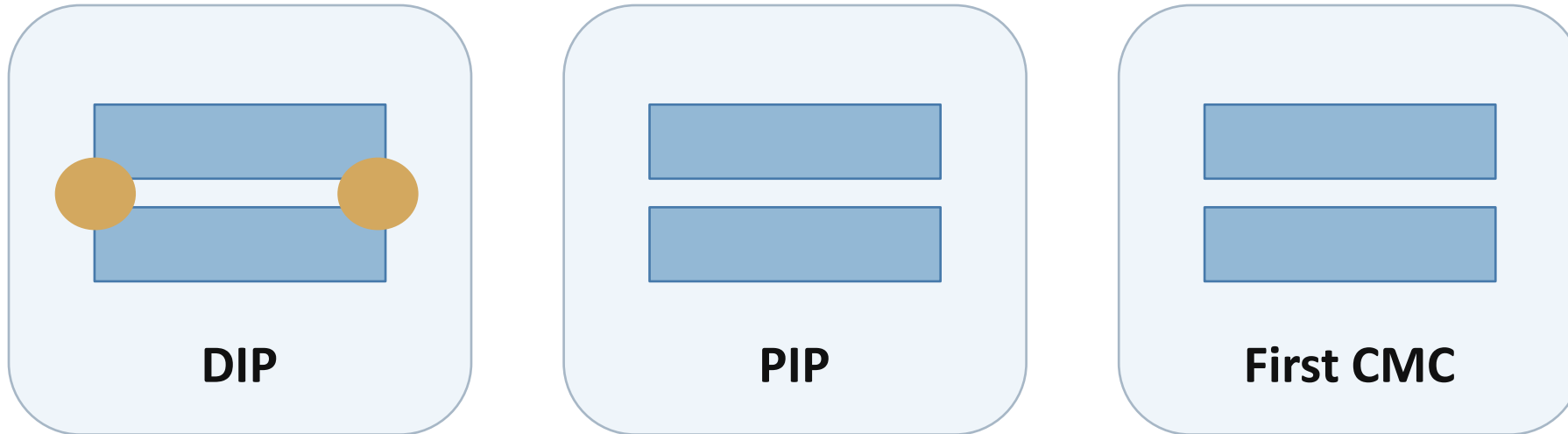
Hand OA has a recognizable distribution



Illustrative joint groups, not a scaled anatomical drawing

Frequently involved joints: Distal and proximal interphalangeal joints, and first carpometacarpal joint.

Heberden nodes are distal interphalangeal osteophytes



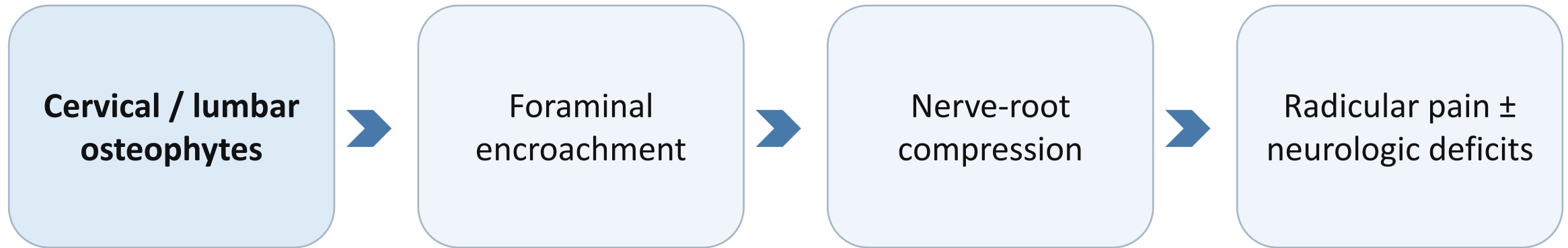
DIP marginal osteophytes appear as palpable nodes

Prominent osteophytes at the DIP joints; The source notes they are common in females.

OA can involve the first tarsometatarsal joint

- Lower-limb disease extends beyond the hip and knee.
- The first tarsometatarsal joint is among the described typical sites.
- Overall joint distribution and use-related symptoms reinforce the clinical pattern.

Spinal osteophytes can narrow neural foramina



Associated findings may include muscle spasm and atrophy.

Joint deformity occurs without true joint fusion

OA structural outcome

- Osteophytes and deformity
- Movement may become limited
- Joint fusion is not characteristic

RA contrast

- Destructive proliferative synovitis
- Progressive cartilage damage
- Some cases progress to ankylosis

Radiographic severity and symptoms may diverge

Severe imaging change $\neq$ severe pain in every patient



Structural grade alone cannot determine individual disability

This imperfect correlation is explicitly noted in the source.

OA and RA differ fundamentally in the initiating lesion

Osteoarthritis

- Degenerative cartilage failure
- Biomechanical stress dominant
- Often one or few joints

Rheumatoid arthritis

- Autoimmune synovitis
- Immune-mediated tissue destruction
- Inflammatory joint phenotype

Clinical patterns help separate OA from RA

OA pattern

- Pain worsens with use
- Stiffness improves with activity
- DIP joints can be involved

RA pattern

- Symptoms often worse after inactivity
- Inflammatory warmth and swelling
- DIP involvement relatively unusual

Treatment addresses function and symptoms

Symptoms

Pain management + anti-inflammatory drugs

Local inflammation

Intra-articular corticosteroid injection

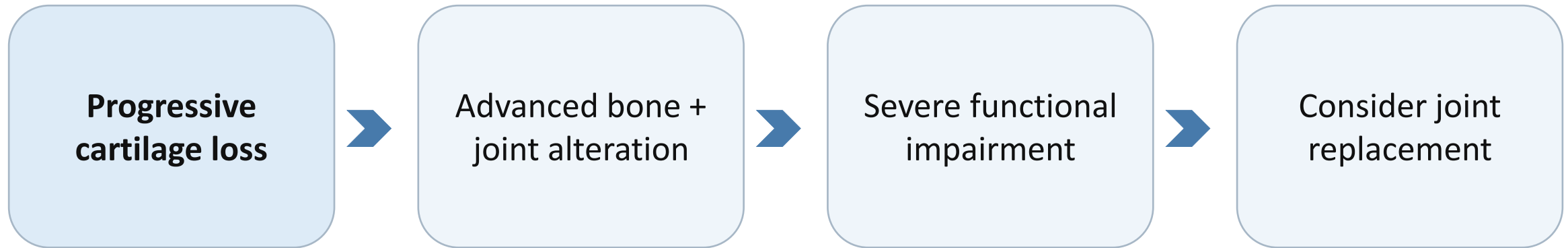
Mechanical burden

Activity modification

Severe joint failure

Arthroplasty

A structurally failed joint may require arthroplasty



Arthroplasty among options in severe cases, without detailing surgical criteria.

Application: Older adult with mechanical knee pain

A 68-year-old has gradually progressive knee pain with use, brief stiffness improving with movement, and crepitus. Radiography shows osteophytes, joint-space loss and sclerosis.

- Which joint tissue is primarily damaged?
- Which three changes establish the characteristic radiographic pattern?
- Is biopsy ordinarily needed?

Application: Investigate osteoarthritis in a younger adult

A 35-year-old with chronic pain in one knee has a prior major articular injury and degenerative radiographic changes.

- Why does this presentation suggest secondary OA?
- Which historical feature provides the leading predisposition?
- What final tissue pathway is shared with primary OA?

Pathology synthesis: A four-compartment disease

Cartilage

Matrix loss, fissures, fragmentation

Subchondral bone

Eburnation, microfractures, cysts

Joint margins

Osteophyte formation

Synovium

Usually mild secondary changes

Five findings that define the OA phenotype

- Primary matrix degeneration with imbalance between breakdown and repair.
- Early chondrocyte proliferation and superficial fissuring.
- Late cartilage loss, eburnation, cysts and osteophytes.
- Mechanical pain with characteristic age and joint distribution.
- Joint-space narrowing, subchondral sclerosis and marginal osteophytes on radiography.

Source and interpretive boundaries

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Osteoarthritis and adjacent Joints/Arthritis sections.

Mechanism figures and clinical correlations are original, editable teaching schematics reconstructed from the supplied text.

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