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Approach to Monoarthritis

Disclosures

- Nothing to disclose

Monoarthritis

“Inflammation of a single joint.”

Evaluation of Patients with Monoarthritis

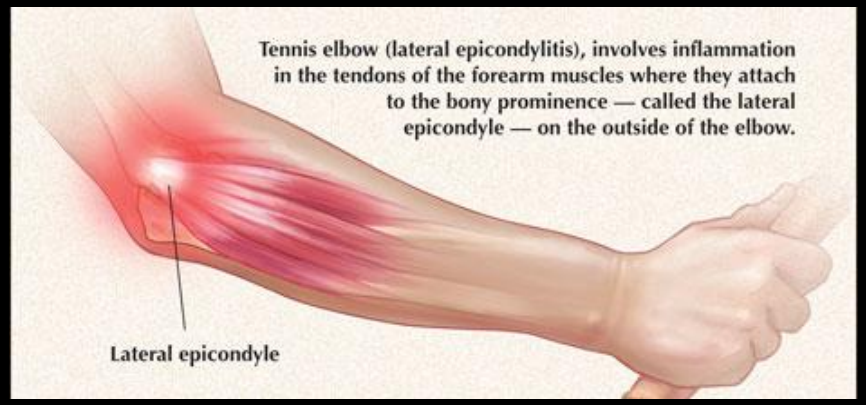
Case 1

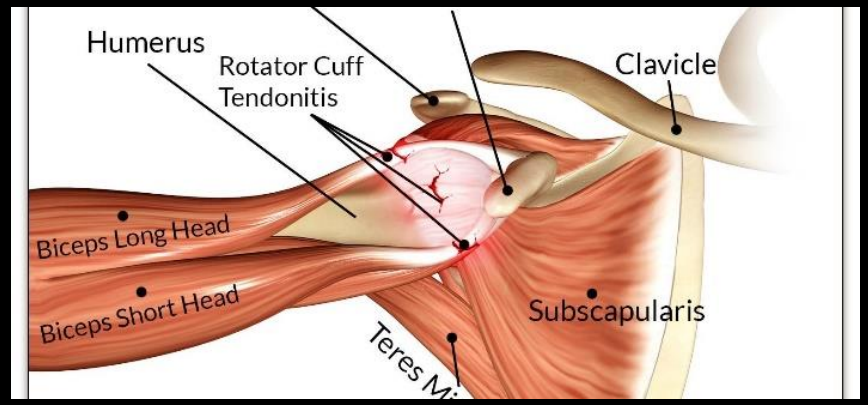
- 34 year old male
- Chief complaint: pain right ankle
- 4 days ago
  - Developed pain and swelling of his right ankle
  - Applied warm compress with no improvement
  - Difficulty ambulating
- PMH: Unremarkable except for a minor basketball injury 2-3 months ago (”na-*sprain* ako”)

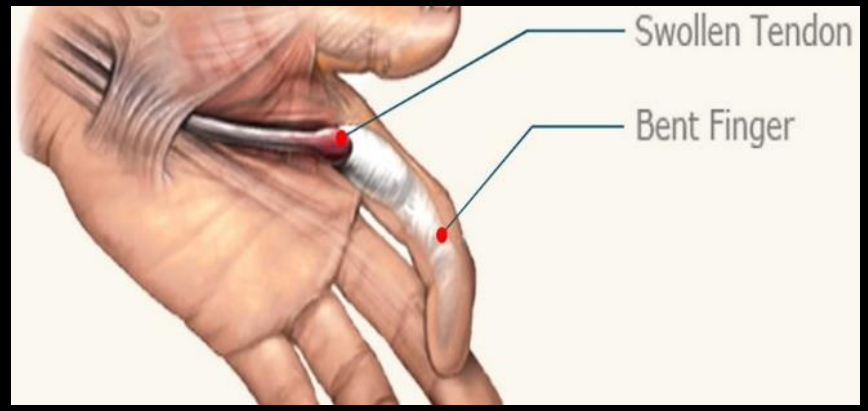
Is it *articular* or *non-articular?*

Non-articular musculoskeletal conditions

- Involve the periarticular structures: supportive extraarticular ligaments, tendons, bursae, muscle, fascia, bone, nerve, and overlying skin
- pain on active, but not passive (or assisted), range of motion
- focal tenderness in regions adjacent to articular structures
- radiate or be elicited with a specific movement
- seldom demonstrate swelling, crepitus, instability, or deformity of the joint itself







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Articular

- Involved structures: synovium, synovial fluid, articular cartilage, intraarticular ligaments, joint capsule, and juxtaarticular bone
- Deep or diffuse pain
- Pain or limited range of motion on active *and* passive movement
- Swelling from synovial proliferation, effusion, or bony enlargement
- Deformity
- Crepitations, instability, “locking”

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Is it *acute* or *chronic?*

Chronology of the complaint

- Duration:
  - Acute: < 6 weeks
  - Chronic: > 6 weeks
- Onset
  - Abrupt - gout, septic arthritis
  - Indolent - osteoarthritis, rheumatoid arthritis
- Evolution
  - Chronic - osteoarthritis
  - Migratory – rheumatic fever, gonococcal or viral arthritis
  - Intermittent – crystal arthropathies, Lyme arthritis
  - Additive – RA, psoriatic arthritis

Is it *inflammatory* or *non-inflammatory?*

Inflammatory	Non-inflammatory
Erythema Warmth Pain Swelling	Absence of cardinal signs of inflammation
Systemic symptoms (fatigue, fever, rash, weight loss)	Lack of systemic symptoms
Laboratory evidence of inflammation: Elevated erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP] thrombocytosis anemia of chronic disease hypoalbuminemia	Normal inflammatory markers
Prolonged morning stiffness	Intermittent stiffness (also known as gel phenomenon), < 60 minutes

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Clinical History

- Patient profile: age, sex, race

Age	Sex
Young: Reactive arthritis, SLE Middle age: gout, RA Older: Osteoarthritis	Male: Gout, SpA, AS Female: RA, SLE, OA

- Family medical history: gout, OA
- Precipitating events: trauma, antecedent/intercurrent infection,
- Past medical history/ co-morbidities: DM, renal disease, CA, osteoporosis
- Rheumatic review of systems: fever, rash, nail abnormalities, muscle pain, weakness, eye disease, and GI, GU, or nervous system involvement

Acute Monoarthritis

Sudden onset of monoarthritis in a synovial joint is a significant clinical event

TABLE 41-1 Causes of Acute Monoarticular Joint or Periarticular Pain*

Common Acute Monoarthritis
- Septic arthritis (nongonococcal, gonococcal)
- Crystal arthritis (gout, pseudogout)
- Reactive arthritides
- Lyme disease
- Plant thorn synovitis
- Other infections (mycobacterial, viral, soft tissue)

Trauma or Internal Derangement
- Loose bodies
- Stress fractures
- Ischemic necrosis
- Hemarthrosis

Existing Inflammatory Polyarthritis
- Psoriatic arthritis
- Enteropathic arthritis
- Rheumatoid arthritis/palindromic rheumatism
- Juvenile inflammatory arthritides

Non-Inflammatory Joint Disease
- Osteoarthritis
- Charcot's joints
- Storage diseases (hemochromatosis, ochronosis)

Synovial Disease
- Pigmented villonodular synovitis
- Lipoma arborescens
- Synovial osteochondromatosis
- Reflex sympathetic dystrophy
- Sarcoidosis
- Amyloid

Existing Systemic Disease
- Systemic lupus erythematosus
- Vasculitides (anti-neutrophil cytoplasmic antibody positive and negative)
- Henoch-Schönlein purpura
- Behçet's disease
- Bacterial endocarditis
- Familial Mediterranean fever
- Relapsing polychondritis

Bone Disease
- Paget's disease
- Osteomyelitis (Brodie's abscess)
- Osteogenic/osteoid tumors
- Metastatic disease
- Pulmonary hypertrophic osteoarthropathy

Soft Tissue Lesions

*This table shows the causes of inflammation in any one joint (monoarthritis) and pain around the joint that presents without inflammation (monoarthropathy).

If acute and focal or monoarticular…

Consider ”Red Flag” Conditions
<u>Septic arthritis</u>
Gout
Fracture
Vascular ischemia
Acute carpal tunnel syndrome

- Most critical diagnosis to consider is INFECTION
- Acute monoarthritis presentations (i.e., those that develop suddenly) are usually related to trauma
- Monoarthritis presentations that develop during a 1 to 2 day perio are usually inflammation- or infection-related.

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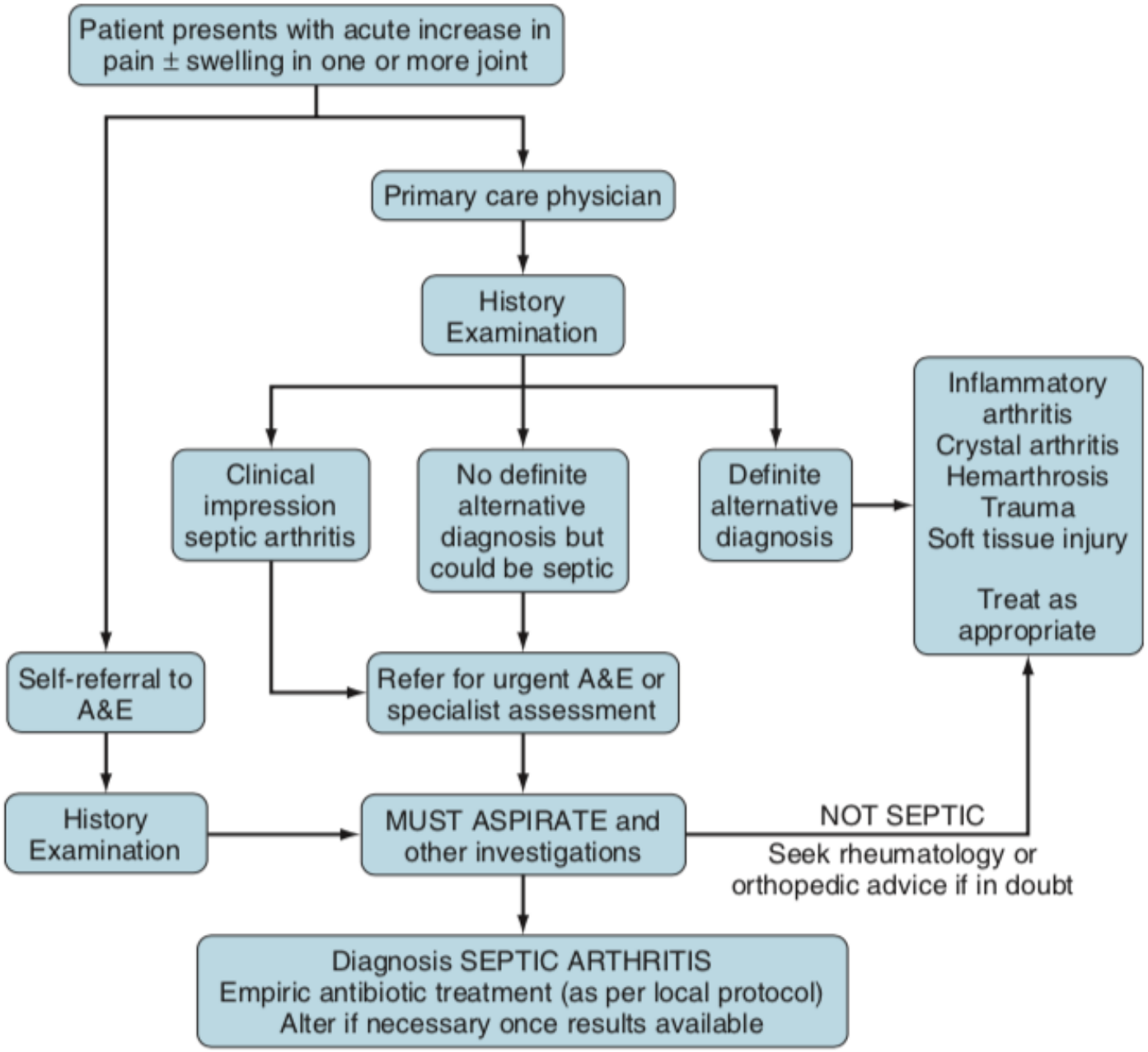

Figure 41-1 Algorithm for assessing patients with acute monoarthritis. A&E, Accident and emergency department (or emergency room).

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Investigations

- Most useful test in acute monoarthritis is examination of ***synovial fluid***
- Normal synovial fluid:
  - clear or a pale straw color
  - viscous, primarily because of the high levels of hyaluronate ***(+ string sign/test)***

Figure 11-7. String test showing normal synovial fluid viscosity.

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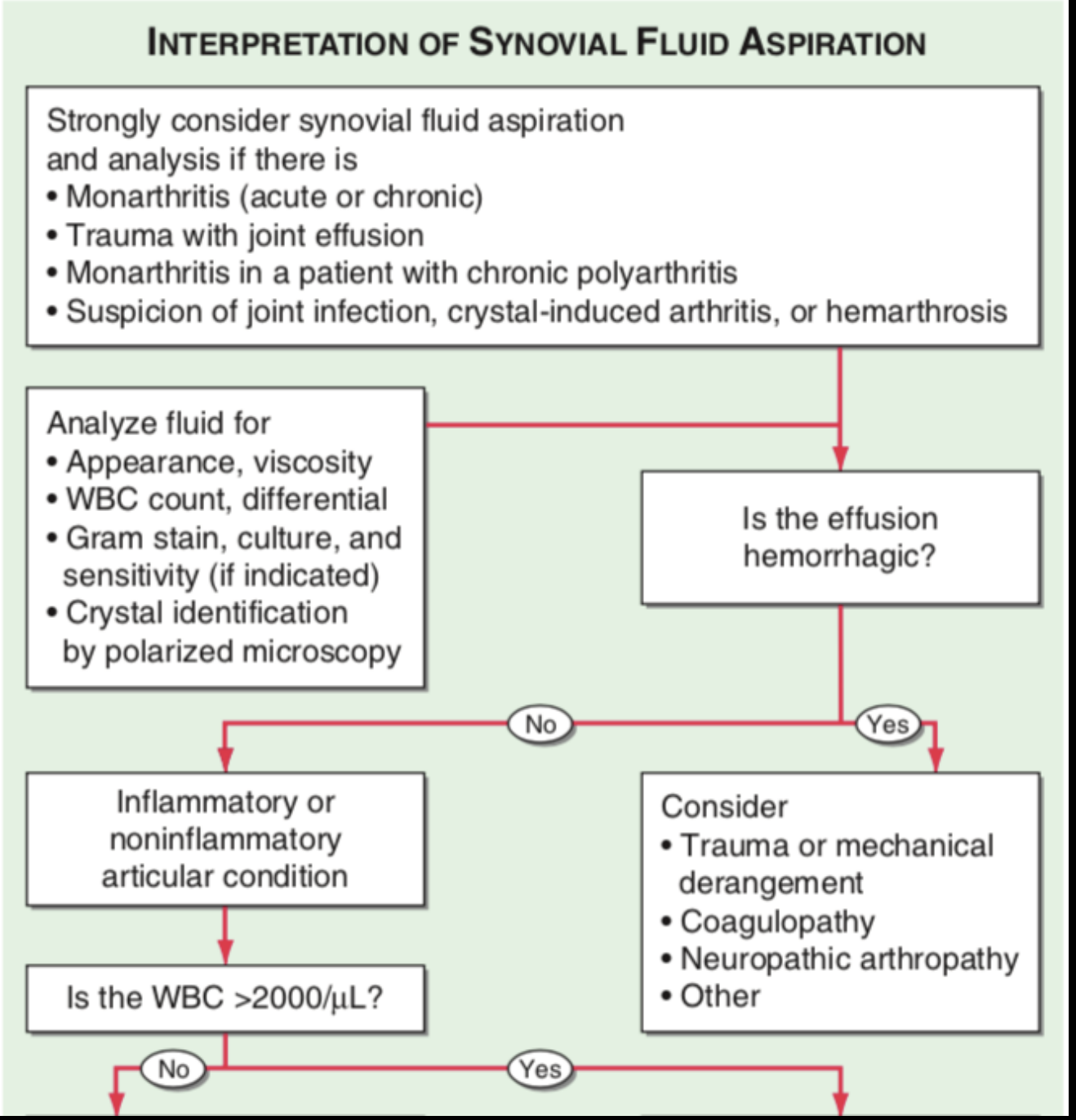

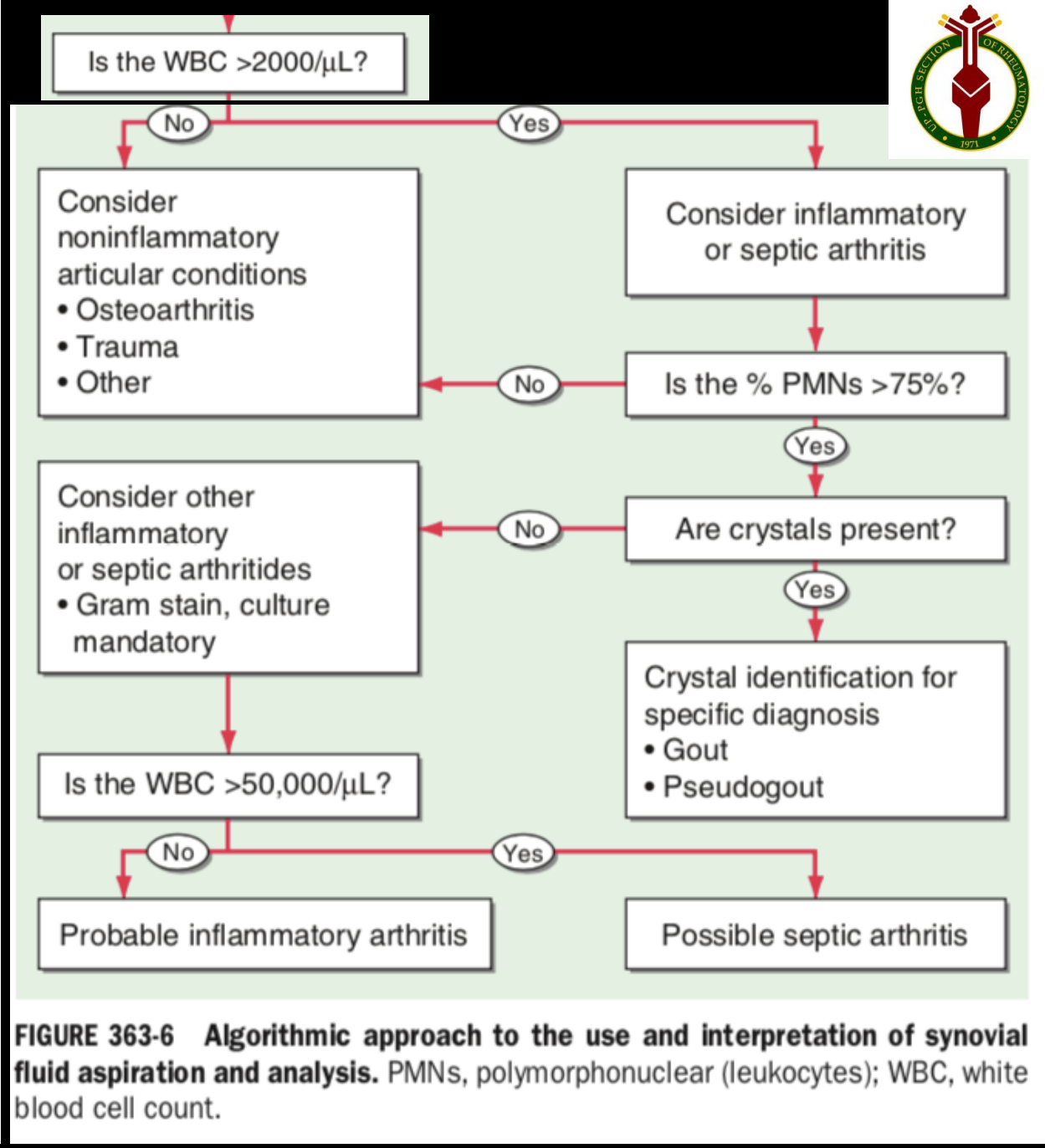

FIGURE 363-6 Algorithmic approach to the use and interpretation of synovial fluid aspiration and analysis. PMNs, polymorphonuclear (leukocytes); WBC, white blood cell count.

Measure	Normal	Noninflammatory	Inflammatory	Septic	Hemorrhagic
Volume, ml	<3.5	Often >3.5	Often >3.5	Often >3.5	Usually >3.5
Clarity	Transparent	Transparent	Translucent-opaque	Opaque	Bloody
Color	Clear	Yellow	Yellow to clear	Yellow/green	Red
Viscosity	High	High	Low	Variable	Variable
WBC/mm3	<200	0-2,000	2,000-100,000	15,000->100,000	200-2000
% PMN	<25	<25	>50	>75%	50-75
Culture	Negative	Negative	Negative	Often positive	Negative

Investigations

- Complete blood count
  - Inflammatory: elevated WBC, anemia
- ESR, CRP
  - Inflammatory: elevated
  - Non-inflammatory: normal for age
- Uric acid
  - Elevated in gout
- Blood cultures are mandatory in patients with suspected septic arthritis and should *precede* antibiotic prescription
- Others if indicated: Viral screening (IgG and IgM antibodies), antistreptolysin-O test (ASOT), Lyme serolog, autoantibody tests (RF, anti-CCP), HLA, thyroid function

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Imaging

- Plain radiographs:
  - tissue swelling
  - calcium in periarticular tissues
  - fractures
  - local bone disease
  - loose bodies
  - destructive changes in long-standing arthritides
- CT scanning
  - better identifies fractures, bone diseases, and intra-abdominal and chest pathology
  - useful when magnetic resonance imaging (MRI) is contraindicated
  - can show osteomyelitis in addition to acute inflammation

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Imaging

- Ultrasound:
  - quick, efficient, inexpensive
  - equally effective versus MRI and clinical examination in detecting synovitis[5] and soft tissue damage
  - In acute monoarthritis: can identify loculated synovial fluid for aspiration and/or injection
- MRI
  - best technique for soft tissue imaging
  - can diagnose internal ligament damage and tendon enthesitis
  - most effective in identifying avascular necrosis of bone
  - useful when identifying the extent of inflammation in acute monoarthritis and sub-clinical joint involvement

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Specific Diagnoses

Septic (bacterial) arthritis

- presence of bacteria in synovial fluid is a medical emer- gency as the mortality rate is between 7% and 15%
- Large limb joints are most frequently involved,
- Usually associated with underlying OA or inflammatory arthropathies, especially RA
- Increases risk for septic arthritis:
  - joint surgery, including arthroplasty and intra-articular injection
  - if with distant infections
  - underlying disease affecting the immune response
  - taking drugs that impair immune function
  - elderly

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Septic (bacterial) arthritis

- acute, painful, swollen monoarthritis
- more than 10% of patients with native joint infections are seen with polyarticular infection
- fever >50% of cases
- sweats/rigors ~30%
- High ESR, CRP, WBC count (35% normal WBC)
- Blood cultures may be positive when synovial fluid culture is negative
- Synovial fluid: cloudy with a high WCC (>50,000)
  - Gram stain should be performed
  - Culture is mandatory but detects the organism in only approximately 50% of cases
- Organisms: *Staphylococcus aureus* and *Staphylococcus epidermidis*, streptococci, and Gram-negative bacteria, increasing prevalence of methicillin-resistant *S. aureus*

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Septic arthritis:

- very early: normal x-rays but changes can occur rapidly
  - joint-space narrowing
  - loss of continuity of the white cortica line
  - marginal erosions
  - superimposed osteomyelitis: periosteal reaction, bone destruction, and sequestrum formation
- MRI: changes within 12 hours
  - Synovial enhancement + joint effusion highest correlation septic joint
  - Bone erosions, bone marrow edema, cartilage loss, and erosion enhancement

Gonococcal Arthritis

- consequence of bacteremia arising from gonococcal infection or from asymptomatic gonococcal mucosal colonization of the urethra, cervix, or pharynx
- Septic arthritis is present in about 50% of cases, usually monoarticular
- only 25% of synovial fluid samples from the septic joint are Gram stain positive for *N. gonorrhoeae*.
- Bacterial culture is gold standard
- nucleic acid hybridization assays and nucleic acid amplification tests (NAATs) allow rapid diagnosis and non-invasive sampling
- Treat with cephalosporin-based regimen + treatment for concomitant *Chlamydia trachomatis*

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Treatment

- First priority is to aspirate the joint and examine the fluid, treatment is then started without further delay
- General measures:
  - Analgesics
  - IV fluid
  - Immobilize the joint
  - Antibiotics: most guidelines recommend 2 to 6 weeks for native joints
  - Aspiration to dryness
  - Refer to Orthopedics

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Gram stain	**Antimicrobial** (Dose adjust for renal function)
Gram-positive cocci	Vancomycin 15–20 mg/kg (actual body weight) administered IV q 8–12 h
Gram-negative cocci (concern for *Neisseria*)	Ceftriaxone 1 g IV q 24 h + azithromycin 1 g PO x 1 (or doxycycline 100 mg PO BID × 7 days)
Gram-negative rods	Ceftazidime 2 grams IV q 8 h, cefepime 2 grams IV q 8–12 h, piperacillin/tazobactam 4.5 g IV q 6 h, or a carbapenem (imipenem 500 mg IV q 6 h, meropenem 1 g IV q 8 h, doripenem 500 mg IV q 8 h)
	B-lactam allergy:
	Aztreonam 2 g IV q 8 h or fluoroquinolone (ciprofloxacin 400 mg IV q 12 h or levofloxacin 750 mg IV q 24 h)
Gram-stain negative	Concern for STD associated: ceftriaxone 1 g IV q 24 h + azithromycin 1 g PO × 1 day (or doxycycline 100 mg PO BID × 7 days)
	No STD risk:
	Vancomycin 15–20 mg/kg IV q 8–12 h + ceftriaxone 1 g IV q 24 h or vancomycin 15–20 mg/kg IV q 8–12 h plus cefepime 2 g IV q 8–12 h (for elderly, immunocompromised, healthcare-associated)

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Gout and other Crystal-Associated Arthropathies

- different microcrystals can induce acute or chronic arthritis or periarthritis:
  - monosodium urate (MSU)
  - calcium pyrophosphate (CPP)
  - calcium apatite (apatite)
  - calcium oxalate (CaOx)
- often similar clinical presentations
- synovial fluid analysis is needed to distinguish the type of crystal involved
  - Polarized light microscopy alone can identify most typical crystals except apatite
- synovial fluid characteristics in crystal-associated diseases are nonspecific, and synovial fluid can be inflammatory or noninflammatory apart from identification of microcrystalline materials

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TABLE 365-1 Musculoskeletal Manifestations of Crystal-Induced Arthritis	
Acute mono- or polyarthritis	Destructive arthropathies
Bursitis	Chronic inflammatory arthritis
Tendinitis	Spinal arthritis
Enthesitis	Peculiar type of osteoarthritis
Tophaceous deposits	Carpal tunnel syndrome

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Gout

- metabolic disease
- middle-aged to elderly men and *postmenopausal* women
  - Women represent only 5–20% of all patients with gout
- Risk factors:
  - Obesity
  - Hypertension
  - Renal insufficiency
  - Hypertriglyceridemia and hypercholesterolemia
  - Hyperuricemia
  - Diabetes
  - Early menopause
- Precipitating events: dietary excess, trauma, surgery, excessive ethanol ingestion, hypouricemic therapy, and serious medical illnesses (eg. myocardial infarction, stroke)

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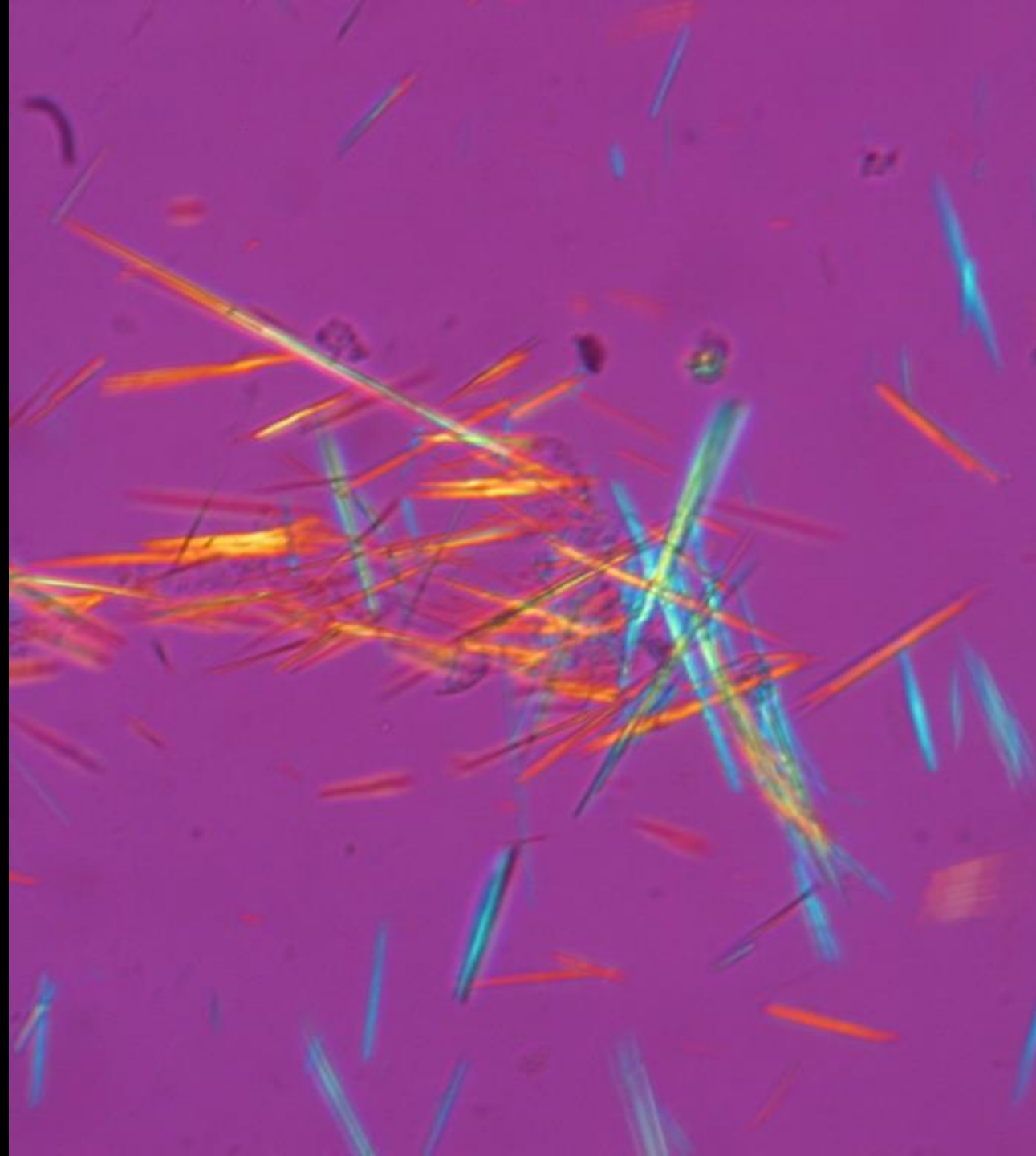
Clinical Features

- Acute arthritis is the most common early clinical manifestation
- Polyarticular flares can occur in subsequent episodes
  - *Podagra:* first metatarsophalangeal joint monoarthritis
  - Lower limbs (tarsal joints, ankles, and knees)
  - Finger joints and upper extremities involved in elderly or if with advanced disease
- first episode of acute gouty arthritis frequently begins at night
- dramatic joint pain and swelling: rapidly become warm, red, and tender,
- clinical appearance that often mimics that of cellulitis
- Early attacks tend to subside spontaneously within 3–10 days with *no residual symptoms*
- Intervals until the next episode vary in length

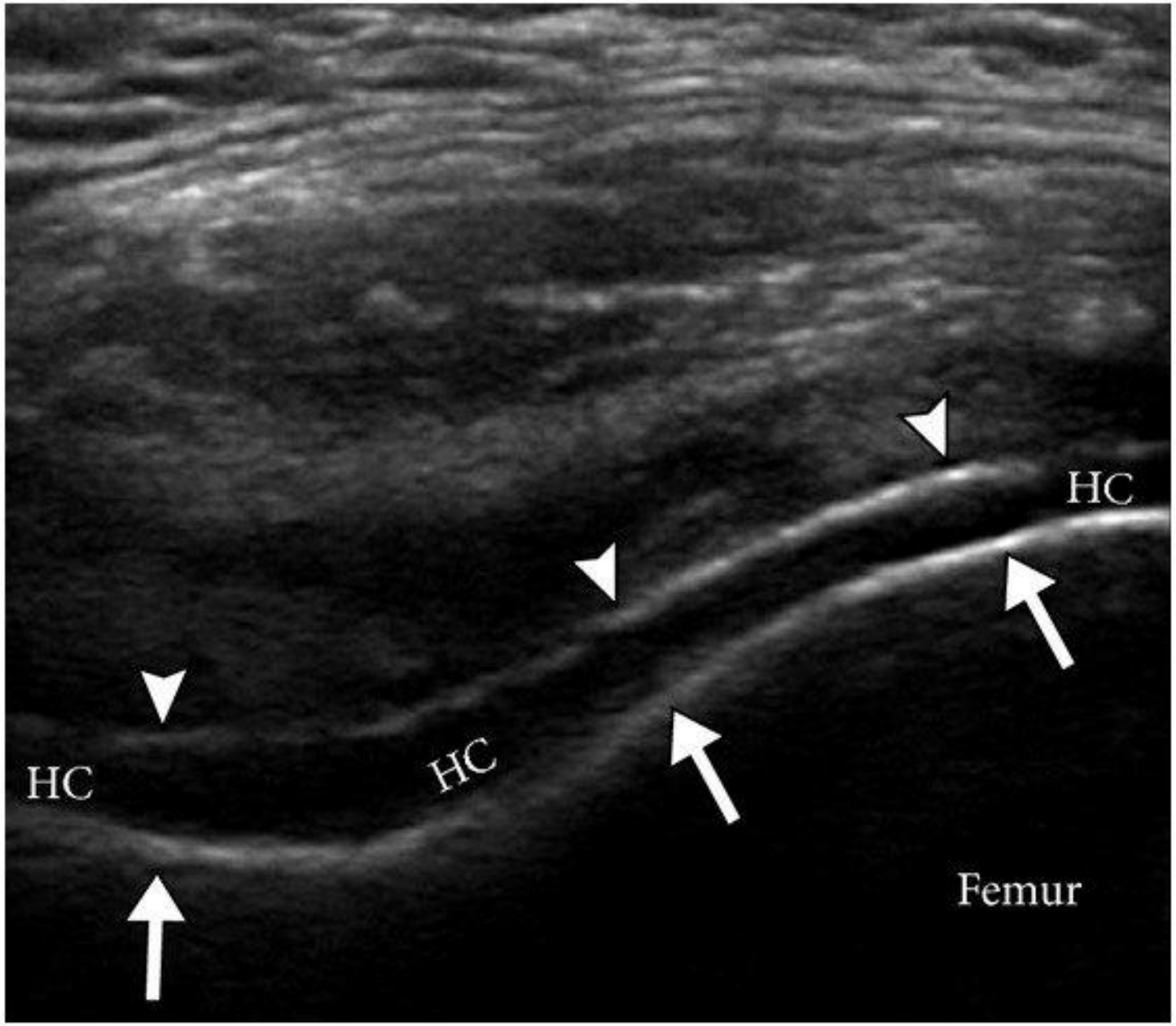
Diagnosis

- Presumptive diagnosis ideally should be confirmed by needle aspiration of acutely or chronically involved joints or tophaceous deposits
  - Needle-shaped MSU crystals
  - Brightly birefringent with negative elongation with polarized light
- Synovial fluid:
  - 2000 to 60,000/µL WBC
  - May be cloudy
  - If large amount of crystals, can be chalky/ pasty
- Serum uric acid levels can be normal or low at the time of an acute attack



Imaging

- Ultrasound may aid earlier diagnosis
  - double contour sign overlying the articular cartilage
- Radiographic changes in advanced disease:
  - cystic changes
  - well-defined erosions with sclerotic margins (often with overhanging bony edges)
  - soft tissue masses



Treatment

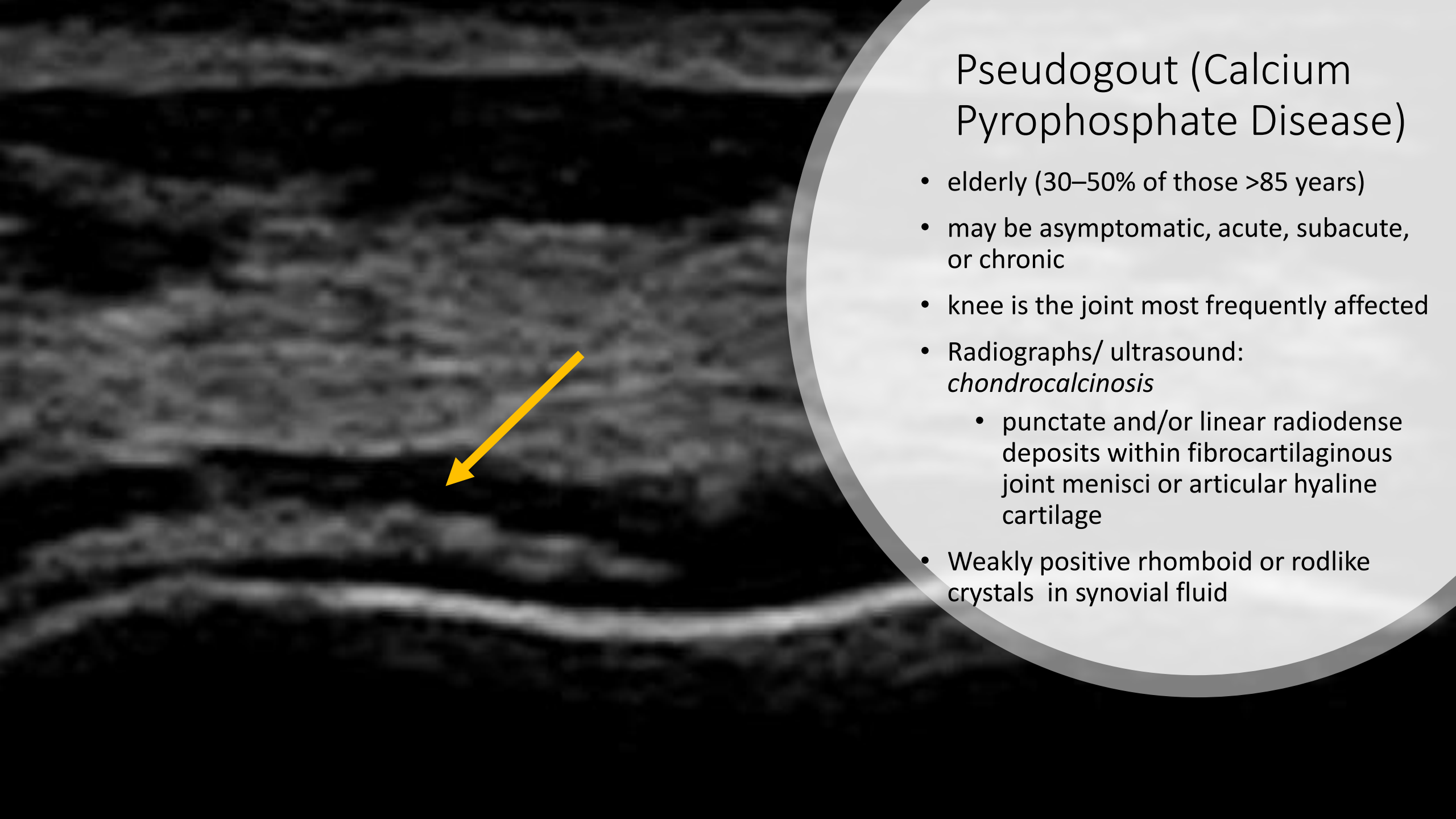
Acute Treatment: Goal is to STOP THE ACUTE ATTACK

- NSAIDs
- Colchicine: 0.5mg 3x a day
- Corticosteroid (systemic or intra-articular)
  - prednisone 30–50 mg/d then tapered

Chronic treatment: PREVENTION OF ATTACKS

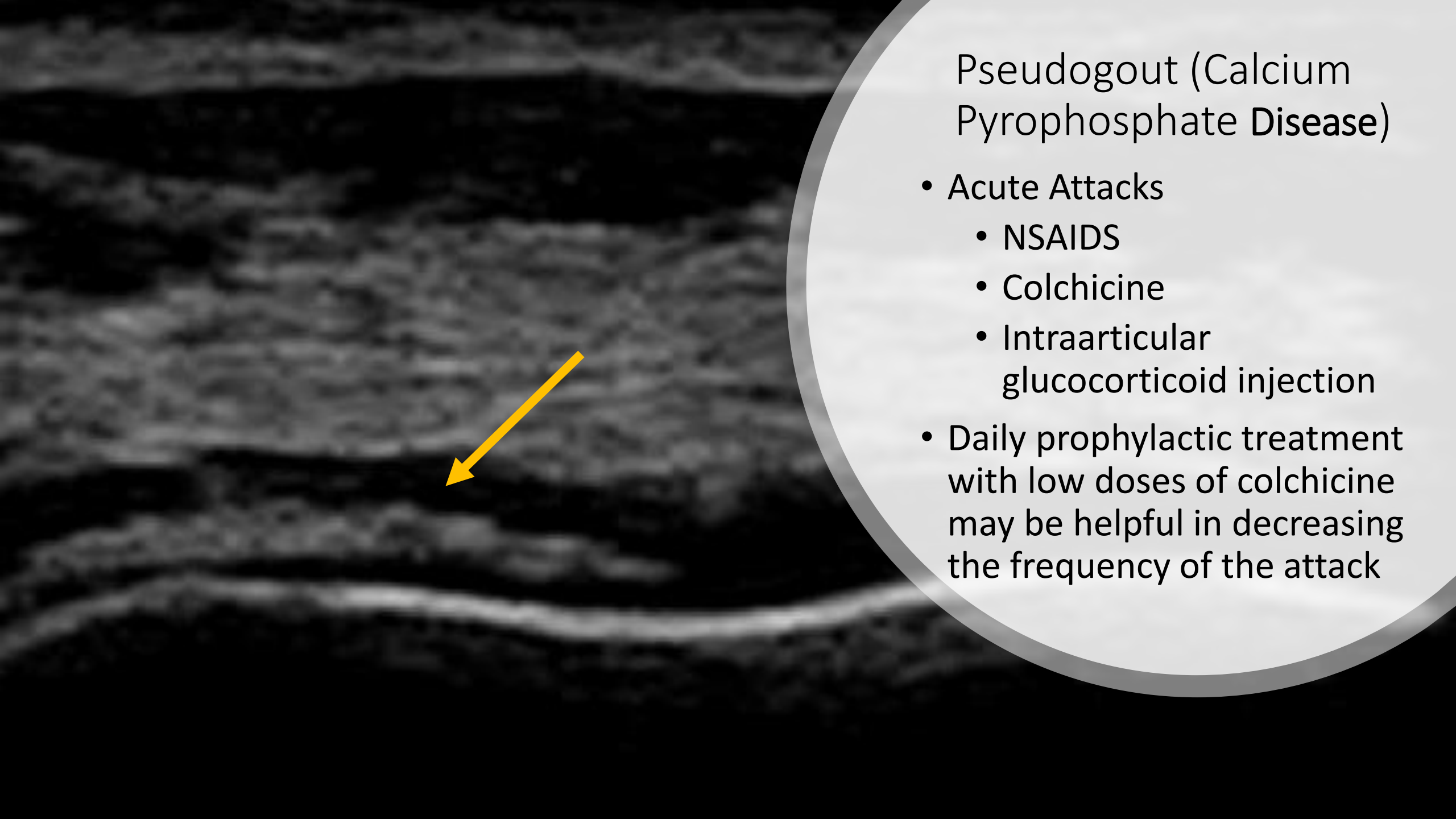
- Modify risk factors: hypertension, obesity, diabetes
- Lower uric acid levels: Allopurinol, Febuxostat

DEPENDS ON : number of acute attacks (2 or more)
serum uric acid > 9.0mg/dL (535umol/L)
uric acid stones or tophi



Pseudogout (Calcium Pyrophosphate Disease)

- elderly (30–50% of those >85 years)
- may be asymptomatic, acute, subacute, or chronic
- knee is the joint most frequently affected
- Radiographs/ ultrasound: *chondrocalcinosis*
  - punctate and/or linear radiodense deposits within fibrocartilaginous joint menisci or articular hyaline cartilage
- Weakly positive rhomboid or rodlike crystals in synovial fluid



Pseudogout (Calcium Pyrophosphate **Disease**)

- Acute Attacks
  - NSAIDS
  - Colchicine
  - Intraarticular glucocorticoid injection
- Daily prophylactic treatment with low doses of colchicine may be helpful in decreasing the frequency of the attack

Chronic Monoarthritis

Osteoarthritis

- the most common type of arthritis
- leading cause of disability in the elderly
- prevalence of OA rises strikingly with age, highly prevalent in those aged >60
- more common in women than in men
- Risk factors: age, genetics, obesity

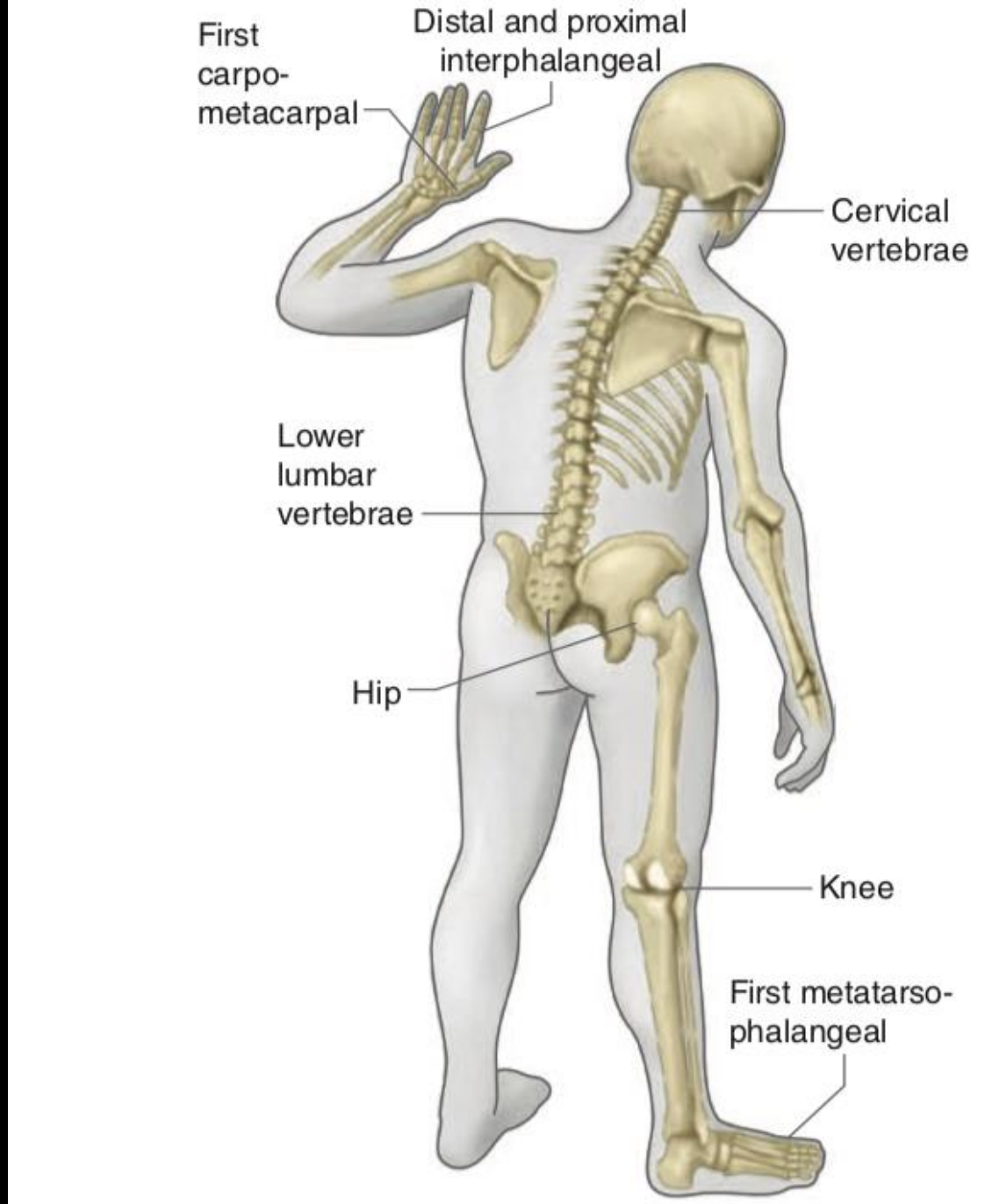


FIGURE 364-1 Joints commonly affected by osteoarthritis.

Osteoarthritis

- In early disease, pain is episodic, triggered by activity
  - either during or just after joint use and then gradually resolves
- Pain becomes continuous as disease progresses
- Stiffness of the affected joint may be prominent, usually brief (<30 min)
- OA is the most common cause of chronic knee pain in persons aged >45
- Bony swelling/ enlargement
- Crepitus
- Deformity

Osteoarthritis

- No blood tests are routinely indicated for workup of patients with OA *unless* symptoms and signs suggest inflammatory arthritis
- Synovial fluid:
  - Clear/ straw-colored
  - Positive string sign (normal)
  - If white count is >1000/µL, inflammatory arthritis or gout or pseudogout is likely
- X-rays are ONLY indicated when joint pain and physical findings are not typical of OA or if pain persists after inauguration of treatment effective for OA
  - correlate poorly with the presence and severity of pain

Disease Management

• OA is a condition which progresses slowly over a period of many years and **cannot be cured**

• Treatment is directed at decreasing the symptoms of the condition, and slowing the progress of the condition

•Functional treatment goals:
- •Limit pain
- •Increase range of motion and muscle strength
- •Improve functionality

TABLE 364-1 Pharmacologic Treatment for Osteoarthritis

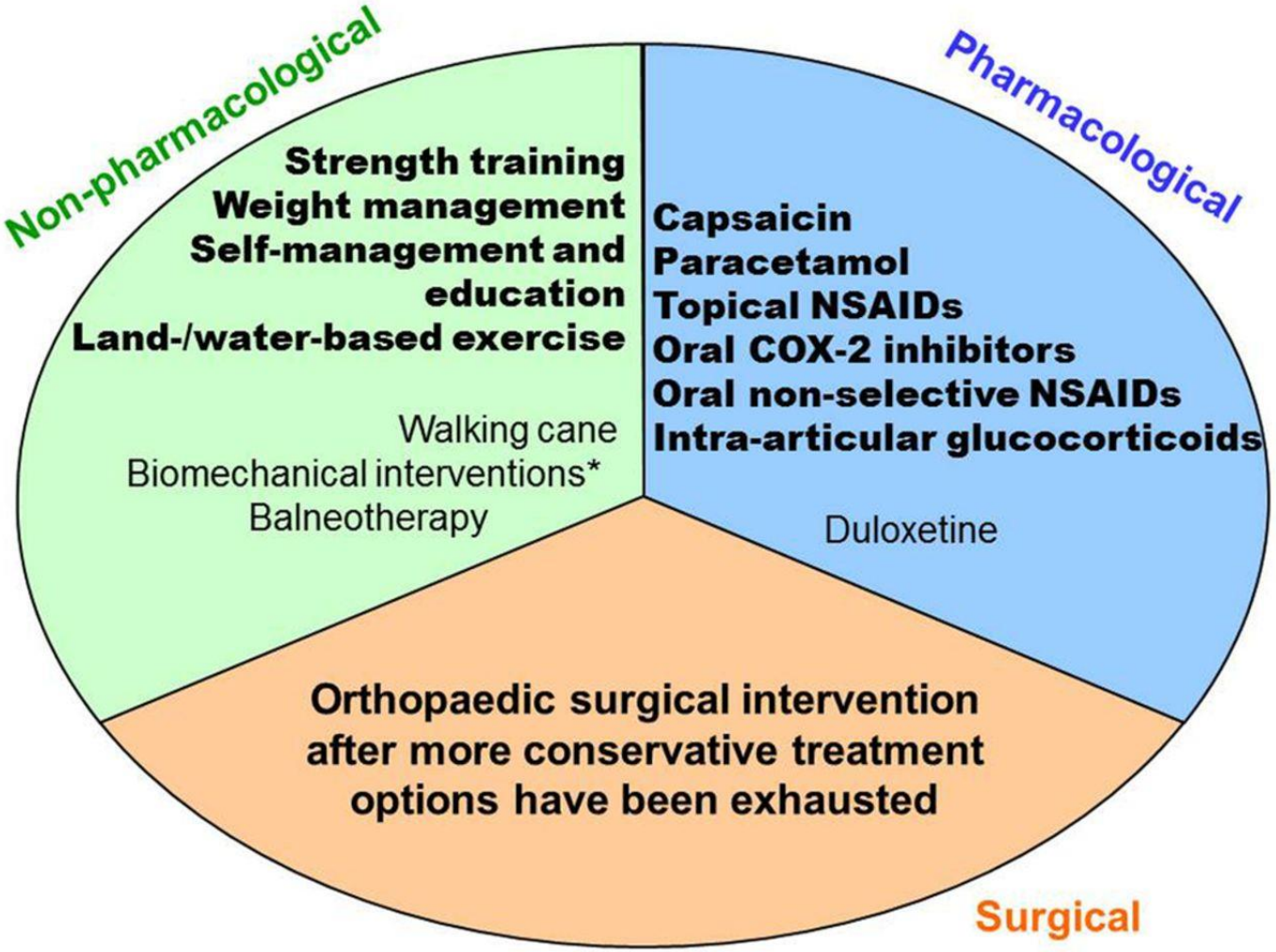
TREATMENT	DOSAGE	COMMENTS
Acetaminophen	Up to 1 g tid	Prolongs half-life of warfarin. Make sure patient is not taking other treatments containing acetaminophen to avoid hepatic toxicity.
Oral NSAIDs and COX-2 inhibitors		Take with food. Increased risk of myocardial infarction and stroke for some NSAIDs and especially COX-2 inhibitors. High rates of gastrointestinal side effects, including ulcers and bleeding, occur. Patients at high risk for gastrointestinal side effects should also take either a proton pump inhibitor or misoprostol.[a] There is an increase in gastrointestinal side effects or bleeding when taken with acetylsalicylic acid. Can also cause edema and renal insufficiency.
Naproxen	375–500 mg bid	
Salsalate	1500 mg bid	
Ibuprofen	600–800 mg 3–4 times a day	
Celecoxib	100–200 mg qd	
Topical NSAIDs		Rub onto joint. Few systemic side effects. Skin irritation common.
Diclofenac Na 1% gel	4 g qid (for knees, hands)	
Opiates	Various	Common side effects include dizziness, sedation, nausea or vomiting, dry mouth, constipation, urinary retention, and pruritus. Respiratory and central nervous system depression can occur.
Capsaicin	0.025–0.075% cream 3–4 times a day	Can irritate mucous membranes.
Intraarticular injections		
Steroids		
Hyaluronans	Varies from 3 to 5 weekly injections depending on preparation	Mild to moderate pain at injection site. Controversy exists regarding efficacy.

[a]Patients at high risk include those with previous gastrointestinal events, persons ≥60 years, and persons taking glucocorticoids. Trials have shown the efficacy of proton pump inhibitors and misoprostol in the prevention of ulcers and bleeding. Misoprostol is associated with a high rate of diarrhea and cramping; therefore, proton pump inhibitors are more widely used to reduce NSAID-related gastrointestinal symptoms.

Abbreviations: COX-2, cyclooxygenase-2; NSAIDs, nonsteroidal anti-inflammatory drugs.

Source: Adapted from DT Felson: N Engl J Med 354:841, 2006.

Treatments considered 'Appropriate' in at least one of the four subphenotypes of knee osteoarthritis.12 Quality of evidence is indicated by: bold=good; not bold=fair.



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Tuberculous Arthritis

- most common presentation is chronic granulomatous inflammatory monoarthritis
- involves the large weight-bearing joints (hips, knees, ankles)
- Progressive monoarticular swelling and pain dev over months to years
- Synovial fluid: cell count of 20,000/µL, ~50% neutrophils
  - AFB positive in < 1/3 of cases, cultures are positive in 80%
- Synovial tissue biopsy culture positive in ~90% of cases
  - granulomatous inflammation
- NAA methods shorten the diagnosis time to 1 or 2 days
- Radiographs: peripheral erosions at the points of synovial attachment, periarticular osteopenia, and eventually joint-space narrowing

Case 1

- 34 year old male
- Chief complaint: pain right ankle
- 4 days ago
  - Developed pain and swelling of his right ankle
  - Applied warm compress with no improvement
  - Difficulty ambulating
- PMH: Unremarkable except for a minor basketball injury 2-3 months ago (”na-*sprain* ako”)

Case 1

- Denies fever, rash, or other symptoms
- Had *isaw* the night before
- Older brother and father both have gout
- 2 years ago, had an episode of pain and swelling involving the left big toe that lasted 2-3 days and resolved spontaneously
- Physical examination:
  - Warmth, redness, swelling
  - LOM both active and passive

- Articular or non-articular?
- Inflammatory or non-inflammatory?
- Acute or chronic?

Thank you!