NOTES
INFLAMMATORY ARTHRITIS

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Musculoskeletal disease subset; known immune component underlying disease
- Underlying trigger/cause not always understood

SIGNS & SYMPTOMS

- Painful, warm, stiff joints
- Variable extra-articular symptoms

DIAGNOSIS

LAB RESULTS

Synovial fluid analysis

- Cloudy yellow appearance
- White blood cell count (WBC) > 5,000
- Polymorphonuclear neutrophils (PMNs) < 25%

TREATMENT

MEDICATION

Anti-inflammatory medication

- Common NSAIDs
- Immunologically-targeted therapy
  - Anti-cytokine therapy (e.g. adalimumab)

ANKYLOSING SPONDYLITIS

osms.it/ankylosing-spondylitis

PATHOLOGY & CAUSES

- *Group:* seronegative spondyloarthritides
- *Characteristics:* articular cartilage destruction, bony joint fusion (ankylosis) → primarily spine, sacroiliac joints
- AKA rheumatoid spondylitis, Marie–Strümpell disease
- Autoimmune self-reactivity believed to underlie pathophysiology
  - Strong HLA-B27 association (MHC I serotype; positive in 90% of affected individuals)
  - *Relative risk for HLA-B27 individuals:* 100-200x
  - IL-23 receptor gene also implicated
  - Abnormal IL-23 cytokine regulation → naive CD4+ T cell → self-reactive Th17 cells
- Associated with Crohn's disease, ulcerative colitis

RISK FACTORS

- Biological sex
  - 3x ↑ individuals who are biologically male

COMPLICATIONS

- Aortic regurgitation
  - Aortic aneurysm → aortic valve annulus stretched → regurgitation
- Uveitis
- Enthesitis (tendinous insertion inflammation)
- Dactylitis ("sausage fingers")
- Decreased pulmonary function
- Thoracic-rib articulation spondylosis → ↓ chest wall expansion across respiratory cycle
- Secondary amyloidosis

SIGNS & SYMPTOMS

- Symptoms develop teens-20s
  - Lower back pain, spinal immobility
- Peripheral large joints (hips, knees, shoulders) involved in ⅓ of individuals
- Morning stiffness; improves throughout day, with exercise
- Untreated disease → extenuated kyphosis of spine

DIAGNOSIS

DIAGNOSTIC IMAGING

Lumbar spine radiograph

- Diagnostic → sacroileitis
- Progression of early findings
  - Subchondral erosions (pseudo-widening effect on X-ray) → sclerosis → sacroiliac joint fusion
- Late findings (10+ years of disease)
  - "Bamboo spine": prominent syndesmophytes (bony growth inside ligaments), diffuse calcification of paraspinal ligaments, spinal osteoporosis

LAB RESULTS

- ↑ erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) suggestive, not diagnostic
- ⊖ Rheumatoid factor (RF)

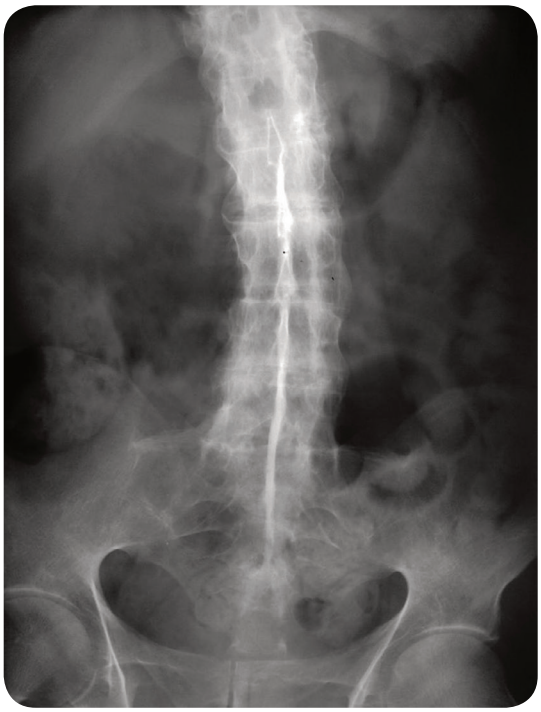

Figure 111.1 An X-ray image of demonstrating bamboo spine and the dagger sign in an individual with ankylosing spondylitis.

OTHER DIAGNOSTICS

- Family history
- Physical examination
  - ↓ Spine flexion/extension and ↓ lateral range of motion

TREATMENT

MEDICATIONS

- NSAIDs (maximum daily dosing recommended)
  - First line for pain, stiffness
- TNF-alpha inhibitors
  - *Etanercept*: fusion protein (IgG1 Fc region, TNF alpha receptor); intercepts circulating TNF-alpha, competes with body's TNF alpha receptors
  - *Infliximab, adalimumab, certolizumab*: anti-TNF alpha monoclonal antibodies
  - *Sulfasalazine*: if TNF-alpha therapy ineffective; recommended for peripheral joint disease

Figure 111.2 The skeleton of an individual with ankylosing spondylitis. The lumbar and cervical spine have ossified completely and become fused.

OTHER INTERVENTIONS

- Exercise therapy
  - Home exercise therapy/formal physical therapy regimens
- Tobacco use cessation
- Heat, ice packs

GOUT

osms.it/gout

PATHOLOGY & CAUSES

- Episodic, arthritic disorder
- Monosodium urate crystallization in, around joint spaces; when left untreated, can manifest as tophi in chronic arthritic disorder
- *Monosodium urate (MSU):* purine and pyrimidine (nitrogen containing heterocycles; DNA components) → primary sources of uric acid; released when cells broken down
  - Limited solubility in plasma (only 6.8mg/dL)
  - Poorer solubility in joint space → lower temperature, synovial fluid composition favor precipitation
  - Sources of nidus (precipitates crystals) include collagen fibers, chondroitin sulfate, proteoglycans, cartilage fragments
  - Physiologic pH of 7.4 → uric acid loses cation, adds Na^+ → MSU crystals
- *Damage pathway:* MSU precipitate into joints → complement cascade activated, cytokines produced → leukocyte recruitment → macrophages phagocytose MSU → inflammasome activates caspase-1 → produce IL-1 and other proinflammatory cytokines → ↑ ↑ ↑ leukocyte recruitment, cytokine production
- Classification
  - 90% primary/idiopathic
  - 10% secondary

CAUSES

- ↑ production of uric acid, purines (most common)
- Diet high in red meat, shellfish, anchovies, organ meat
- ↑ cell turnover
- Cancer treatment → tumor lysis syndrome
- Polycythemia vera (5–10% develop gout)
- Lesch-Nyhan syndrome
  - Hypoxanthine guanine phosphoribosyl transferase (HGPRT) deficiency interrupts purine salvage pathway → ↑ degradation of purines → ↑ uric acid production
- Dehydration, alcoholic beverage consumption → ↓ clearance of uric acid
- Chronic kidney disease

RISK FACTORS

- Age
  - 20–30+ years of hyperuricemia → ↑ risk
- Biological sex (↑ individuals who are biologically male)
- Genetic
  - *HGPRT* (X-linked); *URAT1*, *GLUT9* (both involved in urate transport/homeostasis)
- Heavy alcohol consumption
- Obesity
- Drugs that ↓ urate excretion/↑ production (e.g. thiazides, aspirin)
- Glucose metabolization abnormalities (e.g. diabetes mellitus)
- Chronic lead toxicity → saturnine gout
  - Most common risk factor in U.S. is moonshine consumption → lead-lined stills

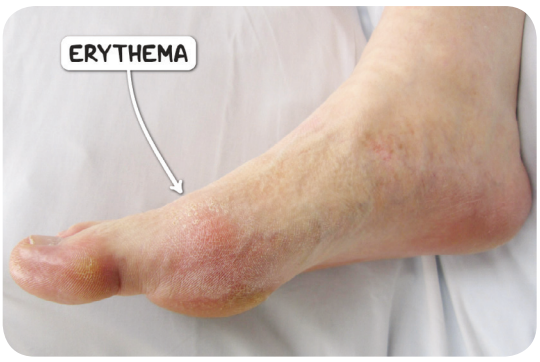

Figure 111.4 Gout of the great toe presenting as erythema of the overlying skin.

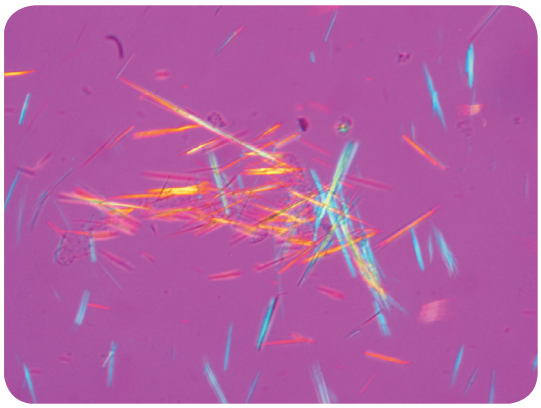

Figure 111.3 Urate crystals will display negative birefringence on polarised light microscopy.

COMPLICATIONS

- Gravel/stone passage → renal colic
- Renal failure → death in 20% individuals with chronic gout
- ↓ quality of life, generally not lifespan

SIGNS & SYMPTOMS

Acute, episodic arthritis

- Nocturnal onset
  - Awakening with complaints, e.g. "feeling like toe on fire"
- Most severe pain remits within first hours; pain can last days–weeks
- Painful, warm, erythematous, and swollen joint → ↓ range of motion → disability

First episode

- Commonly monoarticular; 50% of cases include first metatarsal joint (aka podagra)
- Asymptomatic period months–years → subsequent episodes (mono- or polyarticular)
  - 90% of other joints involved, progressively (ankle > heels > knees > wrists > fingers > elbows)
  - ↑ episodes, polyarticular effects without treatment

Chronic disease (tophaceous gout)

- On average, around 12 years after initial attack
- MSU deposition (joint spaces/affected cartilage)
- Painless, pedunculated mass; palpitation may discolor overlying skin
- Joint's range of motion sometimes limited
- Kidney complications take one of two forms
  - Symptoms of colicky flank pain, hematuria → uric acid nephrolithiasis
  - ↓ urine output, difficulty voiding → urate nephropathy

DIAGNOSIS

DIAGNOSTIC IMAGING

Radiographic/ultrasound/CT scan

- Joint destruction, bony erosions (rarely present on the first acute episode)
- Imaging findings become more likely with disease duration

X-ray

- Radiolucent uric acid nephrolithiasis

LAB RESULTS

Synovial fluid analysis

- MSUs in context of acute, arthritic episodes

Polarized light microscope

- Long, slender needle-shaped crystals in synovial fluid, neutrophil cytoplasm
  - Negatively birefringent; yellow under parallel light, blue under perpendicular light

OTHER DIAGNOSTICS

- Histological analysis of chronic tophaceous arthritis
  - Large aggregations of MSU surrounded by inflammatory reaction of foreign body giant cells
  - Hyperplastic, fibrotic, thickened synovium → pannus formation → destruction of underlying cartilage, juxta-articular bony erosions

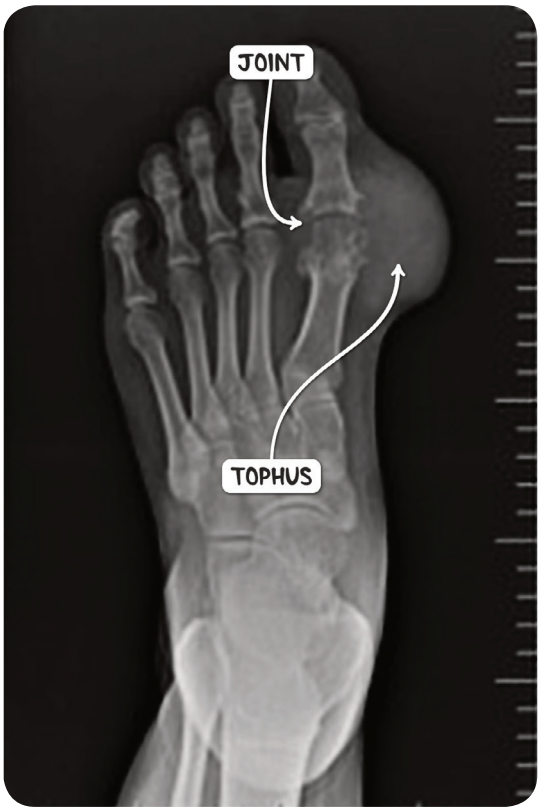

Figure 111.5 An X-ray image of the foot showing destruction of the first metatarsophalangeal joint by arthritis secondary to gout. There is an overlying gouty tophus.

- Histological analysis of gouty nephropathy
  - MSU (with/without tophi) deposits in medullary interstitium/tubules

TREATMENT

MEDICATIONS

Acute flare therapy

- Anti-inflammatory treatment ASAP within acute flare → rapid, complete resolution faster
- Glucocorticoids (oral and/or intra-articular injections)
- NSAIDs (i.e. naproxen, indomethacin)
- Colchicine (inhibits leukocyte migration)
- Biologic agents (IL-1 inhibitors)

Management and prevention

- Limit medications that alter urate balance (e.g. thiazides, aspirin)
- Initiate medications that ↓ uric acid levels
- Xanthine oxidase (XO) inhibitors (allopurinol, febuxostat)
  - *Mechanism of action:* directly inhibits enzyme → urate production, stimulates purine base reutilization → ↓ ↓ ↓ urate concentration
- Uricosuric medications (probenecid)
  - ↑ urate excretion at kidney
- Uricase medications (rasburicase)
  - Mimic enzyme that catalyzes urate conversion → allantoin (more soluble purine degradation product); enzyme absent in humans

OTHER INTERVENTIONS

- Benefit largely due to ↓ development/worsening of obesity, cardiovascular disease, diabetes mellitus
- Diet modification
  - Limit/avoid soda, red meat, seafood
- Alcohol moderation
- ↑ physical activity

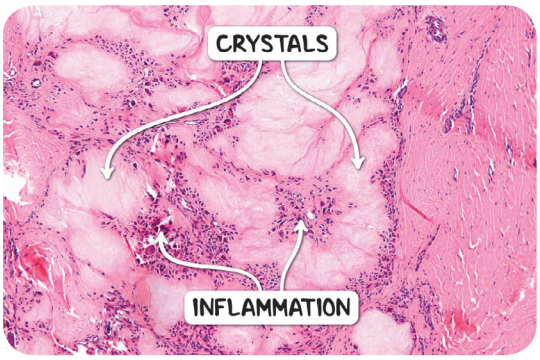

Figure 111.6 The histological appearance of a gouty tophus. There is a large aggregate of urate crystals which is associated with granulomatous inflammation.

JUVENILE IDIOPATHIC ARTHRITIS

osms.it/juvenile-idiopathic-arthritis

PATHOLOGY & CAUSES

- Arthritic symptoms of unknown etiology; present < 16 years old for ≥ six weeks
- Unknown pathophysiology; appears related to TH1 and TH17 cells → cell mediators
  - IL-1, IL-17, TNF-gamma

RISK FACTORS

- HLA and PTPN22 variants

COMPLICATIONS

- 10% develop disability in adulthood

SIGNS & SYMPTOMS

- Arthritis
  - Oligo- or polyarticular involvement; large joints affected > small
- Rheumatoid nodules, factor usually absent

DIAGNOSIS

LAB RESULTS

- Antinuclear antibodies may be ⊕ or ⊖

TREATMENT

- Similar to rheumatoid arthritis
- Some success with IL-6 R antibody biologic disease-modifying antirheumatic drug (DMARD)

PSEUDOGOUT

osms.it/pseudogout

PATHOLOGY & CAUSES

- Calcium pyrophosphate (CPP) crystal depositions in articular cartilage
- AKA chondrocalcinosis
- Unlike gout, hyperuricemia
  - No known direct substance concentration → ↑ crystal formation
- Pathway of joint inflammation, destruction similar to gout
  - Articular cartilage proteoglycans degraded, serve as nidus for crystal formation around chondrocytes
  - CPP crystals precipitate around chondrocytes → complement cascade activated, cytokines produced → leukocyte recruitment → macrophages phagocytose MSU (inflammasome activates caspase-1) → produce IL-1, other proinflammatory cytokines → further leukocyte recruitment, cytokine production

CAUSES

- Sporadic (idiopathic)
- Hereditary
  - Autosomal dominant version → early manifestation, more severe symptoms
  - Also associated with osteoarthritis
  - Mutations in pyrophosphate transport channel
- Secondary to previous joint damage, hyperparathyroidism, hemochromatosis, hypothyroidism, ochronosis, diabetes

RISK FACTORS

- Age
  - Usually affects individuals > 50 years; by > 85 years → 30–60% prevalence
- ↓ magnesium levels

COMPLICATIONS

- Significant joint damage
  - ≤ 50% of individuals

SIGNS & SYMPTOMS

- Episodic joint pain
  - Knee most commonly affected; followed by wrists → elbows → shoulders → ankles
- Duration of several days–weeks
- Oligo- or polyarticular
- Frequently asymptomatic

DIAGNOSIS

OTHER DIAGNOSTICS

Histological analysis

- Gross
  - Chalky, white, friable
- Microscopic
  - Aggregates stain as blue/purple, oval
- Crystals
  - Rhomboid, ⊕ birefringent
- Crystallization first develops in articular cartilage, menisci, intervertebral discs

Physical examination

- Acutely painful, inflamed joint; commonly knee

TREATMENT

MEDICATIONS

Acute flares

- NSAIDs
- Colchicine
- Glucocorticoids

Management and prevention

- Colchicine

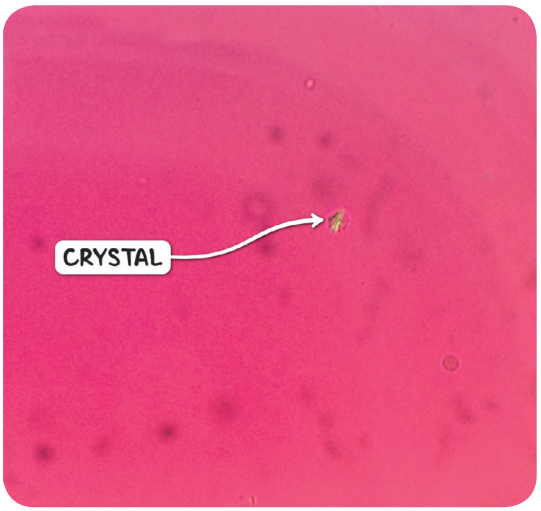

Figure 111.7 A calcium pyrophospahte crystal in joint fluid aspirated from the knee of an individual with pseudogout.

OTHER INTERVENTIONS

- Treat underlying disorder (if known)
- Symptomatic therapy similar to gout treatment

GOUT VS. PSEUDOGOUT

	GOUT	PSEUDOGOUT
CRYSTALS	Monosodium urate (MSU)	Calcium pyrophosphate (CPP)
CRYSTAL HISTOLOGY	Needle-shaped; ⊖birefringent	Rhomboid; ⊕birefringent
AGE OF ONSET (YEARS)	May be young, largely RF*-dependent	50+
MOST COMMONLY AFFECTED JOINT	1st MTP* joint	Knee

*RF - risk factor, MTP - metatarsophalangeal joint

PSORIATIC ARTHRITIS

osms.it/psoriatic-arthritis

PATHOLOGY & CAUSES

- *Group:* seronegative spondyloarthritides
- Associated with psoriasis
- Affects peripheral, axial joints; ligaments, tendons (entheses)
- Abnormal T cell response to unknown culprit antigen
  - T_H1, T_H17 cells thought responsible → stimulate activated $CD8^+$ T cells → cytokine, growth factor environment change/destroy local tissue
  - Implicated synovial cell mediators: IL-1, IL-6, TNF-alpha, IL-8
  - Synovial fibroblasts interact with immune response → secreting IL-1beta, IL-6, and platelet-derived growth factors (PDGF)
  - Affected synovia marked with increased vascularity → ↑ leukocytic entryways

TYPES

- *Mild:* one joint involved/responds to NSAIDs
- *Moderate-severe:* NSAID-resistant
- *Severe:* polyarticular, erosive; functional limitation

CAUSES

- Local trauma induces dysregulated immune response → local tissue destruction
  - AKA Koebner phenomenon
- 10% of psoriatic individuals develop arthritis symptoms

RISK FACTORS

- HLA-B27
- HLA-Cw6
- Obesity
- Associated diseases
  - Myopathy, enteropathy, AIDS
- Age: 30 50 years old

SIGNS & SYMPTOMS

- Predominantly peripheral arthritis of hands, feet
- Distal interphalangeal (DIP) joint first affected, asymmetrically distributed in > 50% of individuals
- Sacroiliac joint affected in 20% of individuals
- Degree of joint involvement may be mild/progress → severe, disfiguring disease as in rheumatoid arthritis (RA)

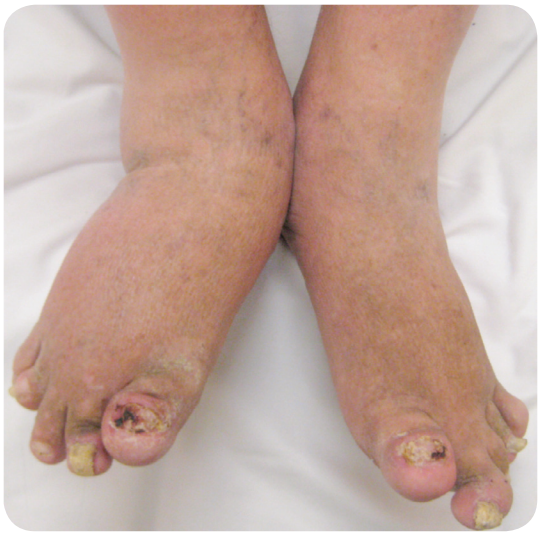

Figure 111.8 The feet of an individual with psoriatic arthritis. There is inflammation of the ankle and the interphalangeal joints as well as psoriatic nail changes.

DIAGNOSIS

DIAGNOSTIC IMAGING

- Characteristic "pencil-in-cup" malformation at DIP joint

OTHER DIAGNOSTICS

Histological analysis

- Similar to RA, but symptoms not as severe, remissions more frequent, joint destruction less frequent

History

- 40% of affected individuals have first-degree relative with psoriatic arthritis

Physical examination

- Integument examination consistent with psoriasis
- Papules, plaques with silver scales on extensor surfaces (fingers, knees, elbows)
- Commonly affects scalp, nails ("nail pitting")
- Musculoskeletal examination consistent with arthritis
- Asymmetric involvement of both peripheral, axial joints
- Commonly affects DIP joints under skin manifestations

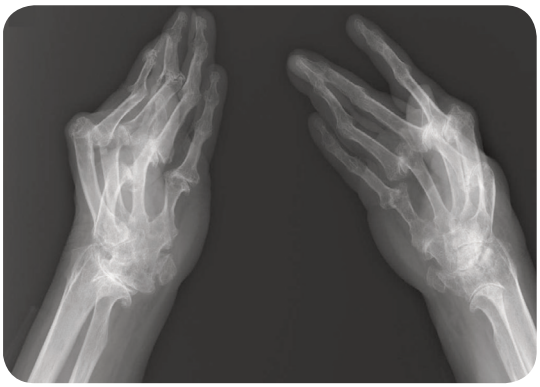

Figure 111.9 An X-ray image of the hands of an individual with long-standing psoriatic arthritis which has progressed to arthritis mutilans. Telescoping of the phalangeal joints is visible.

TREATMENT

MEDICATIONS

Mild disease

- NSAIDs

Moderate-severe disease

- Conventional (DMARD) therapy
- Methotrexate (MTX; co-treat with daily folic acid), leflunomide (does not also target skin disease)
  - Both require eliminating alcohol intake

Severe disease

- 'Biologic' DMARD (e.g. TNF inhibitor)
- Etanercept, adalimumab, infliximab, certolizumab
  - All require latent TB screening before initiation therapy initiation
- Anti-IL-17 'biologic' (e.g. secukinumab, ixekizumab, brodalumab)

OTHER INTERVENTIONS

- Exercise, physical therapy, occupational therapy
- Weight reduction

REACTIVE ARTHRITIS

osms.it/reactive-arthritis

PATHOLOGY & CAUSES

- *Group:* seronegative spondyloarthritides
- Characterized by triad
  - Arthritis, nongonococcal urethritis/cervicitis, conjunctivitis
- AKA Reiter syndrome
- *Hypothesis:* autoimmune reaction to prior infection of GU/GI system
- *Genitourinary triggers:* urethritis/cervicitis
  - *Common pathogen:* *Chlamydia trachomatis*
- *Gastrointestinal triggers:* diarrheal illness
  - *Common pathogens:* *Shigella*, *Salmonella paratyphi*, *Yersinia enterocolitica*, *Campylobacter jejuni*
- RF
- HIV ⊕
- HLA-B27 ⊕ (80+% of affected individuals)

COMPLICATIONS

- Digital tendon sheath synovitis → dactylitis ("sausage" finger/toe)
- Tendoligamentous insertion sites ossification → calcaneal spurs, bony outgrowths
- Severe spinal disease; becomes indistinguishable from ankylosing spondylitis
- Extra-articular involvement
  - Inflammatory balanitis, conjunctivitis, cardiac conduction abnormalities, aortic regurgitation

SIGNS & SYMPTOMS

Arthritic symptoms

- Develop several weeks post-initial infection
- Common, early symptoms
  - Joint stiffness, low back pain
- Days later
  - Painful joints, effusion, lack of mobility
- Most asymmetrically affected joints
  - Ankles, knees, feet; upper extremity involvement less common

Other symptoms

- Fever, malaise, weight loss, fatigue
- Symptoms' severity waxes, wanes; usually lasts 1.5–6 months
- Recurrent arthritic episodes, tendonitis, lumbosacral pain in 50% of individuals
- Keratoderma blennorhagicum
  - Vesiculopustular, waxy lesions on the soles or palms

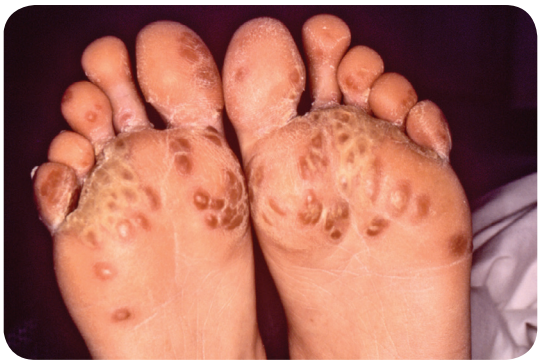

Figure 111.10 Keratoderma blennorhagicum on the feet of an individual with reactive arthritis.

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Involved joint
  - No specific diagnostic changes
- Negative for stress fractures, other forms of arthritis

LAB RESULTS

Synovial fluid analysis

- Absence of joint space infection, crystals

Cultures

- May be helpful if GI/GU symptoms ongoing → identify well-associated bacteria

OTHER DIAGNOSTICS

History

- Preceding illness, rapid-onset arthritis/systemic symptoms
- Arthritic presentation often too late for stool/urine culture (for GU/GI trigger)

Physical examination

- Lower extremity joint involvement as above

TREATMENT

MEDICATIONS

- NSAIDs
- Glucocorticoids; intra-articular, systemic formulation available
- Resistant/chronic (> six months) disease
  - DMARD (e.g. sulfasalazine, MTX, azathioprine)
- Antibiotics not recommended
  - *Exception:* triggering disease process (GI/GU diarrhea/urethritis/cervicitis) ongoing
- Skin involvement (if present) → topical salicylates

OTHER INTERVENTIONS

- Conjunctivitis (if present) → ophthalmology referral

RHEUMATOID ARTHRITIS

osms.it/rheumatoid-arthritis

PATHOLOGY & CAUSES

- Systemic, chronic, autoimmune inflammatory disorder involving joint synovium
- May progress to disfigurement → cartilaginous, bony damage over time
- Dual hit hypothesis (genetics and environment)
  - *Genetics:* HLA-DR1 or DR4 genetic predisposition → thought to underlie the immune pathogenesis pathway below
  - *Environment:* cigarette smoke, pathogen (i.e. gut bacteria) → may contribute to unknown 'arthrogenic agent', trigger immune response

PATHOLOGY

- *$CD4^+$ T cells:* react with arthrogenic agent (unknown; thought to be a microbe/self-antigen) → cytokine production → IFN-gamma (T_H1 product) → activate macrophages and synovial cells → synovial, immune cell proliferation → swollen synovial tissue (also known as pannus formation) → IL-17 (T_H17 product) → recruit neutrophils and monocytes → TNF-alpha and IL-1 (macrophage product) → stimulate synovial cells → protease release → hyaline cartilage destruction → ↓ cartilaginous buffer → bone on bone articulation → ↑ bone destruction
- *RANKL (on T cells):* activate osteoclasts' RANK receptor → bone resorption

- *Synovial cells:* directly responsible for protease release, contribution to cytokine milieu
  - Germinal centers within synovium include plasma cells → antibodies against self-antigens, i.e. autoantibodies → specific for citrullinated peptides (CCPs)/arginine residues converted to citrulline
  - Antibodies against fibrinogen, type II collagen, alpha-enolase, vimentin → form antibody-antigen complexes → deposit into joints
  - Antibodies (usually IgM or IgA) against Fc regions of IgG antibodies form RF → deposit into joints
- Chronic inflammation → angiogenesis → increase inflammatory cell response → further joint involvement

Extra-articular involvement

- Pyogens (i.e. IL-1)
  - → Hypothalamus → fever
- Skeletal
  - Protein breakdown
- Skin
  - Macrophage and lymphocytes recruitment → cycle of activation/recruitment → cells around a central necrotic mass → rheumatoid nodules
- Blood vessels
  - ↑ cytokines and ↑ circulating immune cells → altered endothelial cells → ↑ atheromatous plaques formation
- Liver
  - Under chronic inflammation → ↑ hepcidin production → ↓ iron absorption → anemia
- Lung
  - ↑ fibroblasts → lung fibrosis (AKA Caplan syndrome) → ↓ gas exchange (+/- pleural effusion)

COMPLICATIONS

Autoimmune

- AA amyloidosis
- Sjögren syndrome
- Scleritis

Cardiovascular

- ↑ Atheromatous formation → ↑ MI, CVA risk
- Pericarditis → ↑ pericardial effusion risk

Hematologic

- Anemia
- Felty syndrome (RA, splenomegaly, neutropenia)

Musculoskeletal

- Rheumatoid nodules
  - Can form in any body tissue
- Baker (popliteal) cyst formation

Neurological

- Carpal tunnel syndrome
- Mononeuritis multiplex
- C1-C2 instability → ↑ risk of subluxation → spinal cord impingement risk → neurologic involvement
- Serious complication if unknown at time of intubation

Pulmonary

- Pleuritis → ↑ risk of pleural effusion (characteristically ↓ glucose, ↓ complement)
- Interstitial lung disease
- Caplan syndrome

SIGNS & SYMPTOMS

Inflammatory polyarthritis

- Commonly symmetrically affects multiple (> five) joints
- First smaller joints - MCP, PIP, MTP
- Avoids DIP joint
- Chronic disease → ↑ larger joint involvement

Joint characteristics

- Warm, red, and painful joints
- Morning stiffness (lasting > one hour)

Malformation

- Ulnar deviation of MCP joints
- Boutonniere (buttonhole) malformation
- Swan neck

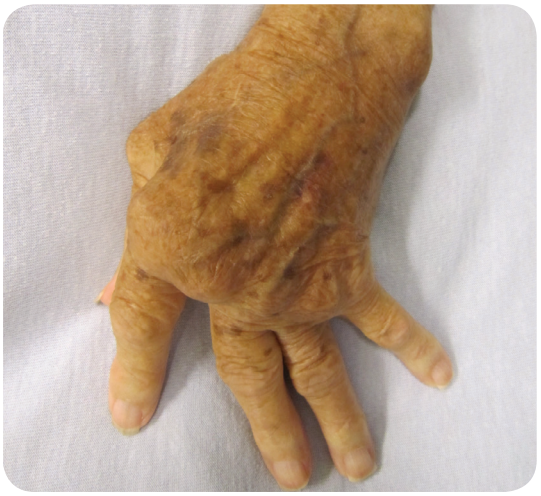

Figure 111.11 Ulnar deviation of the fingers in an individual with rheumatoid arthritis.

Extra-articular manifestations

- Common, systemic signs
  - Fever, fatigue, weight loss
- Rheumatoid nodules
  - Commonly arise on extensor surfaces
- More varied sequelae in severe and/or chronic disease

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Soft tissue swelling
- Bony erosions
- ↓ Bone density
- Narrowed joint space (late finding)

LAB RESULTS

- RF titers
  - High titers associated with more severe disease
  - Eventually present in 80% of affected individuals
- Anti-citrullinated peptide/protein antibodies (anti-CCP)
  - Sensitivity 50–75%; specificity > 90%
- ↑ ESR, ↑ CRP
- Normocytic anemia (anemia of chronic disease)

OTHER DIAGNOSTICS

History

- Symptoms for > six weeks

Physical examination

- Inflammatory (warm, stiff, painful) arthritis of > three joints
- Characteristic malformations
  - Ulnar deviation, boutonniere ("buttonhole") malformation, swan neck malformation

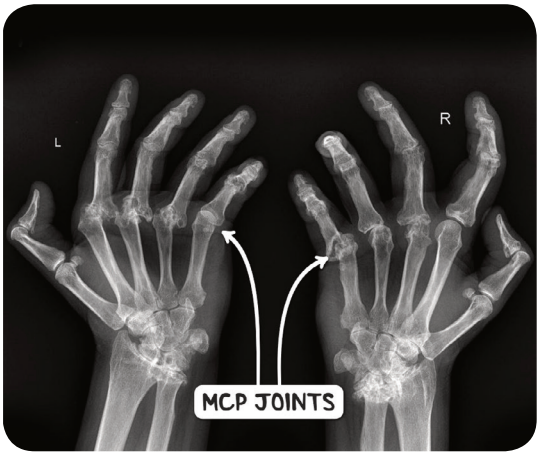

Figure 111.12 An X-ray image of the hands of an individual with rheumatoid arthritis. There is destruction of the metacarpophalangeal joints, the carpometacarpal joints and the wrist.

TREATMENT

MEDICATIONS

- NSAIDs
- Short-term, low-dose glucocorticoid
- DMARD
  - Hallmark of RA treatment
  - Methotrexate (give with folic acid to ↓ side effects)
  - Others: leflunomide, hydroxychloroquine, sulfasalazine
- Biologic DMARDs
  - Adalimumab, etanercept (intercept), infliximab particularly effective (block TNF-alpha, which is thought to underlie most joint damage)

- Abatacept (suppresses T cells)
- Rituximab (suppresses B cells)
- Anakinra (blocks IL-1)
- Tocilizumab (blocks IL-6)

SURGERY

- Only if medication fails
- Severe joint malformation
  - Synovectomy
- Severe malformation, disability
  - Joint replacement

OTHER INTERVENTIONS

- Exercise to maintain range of motion and muscle strength

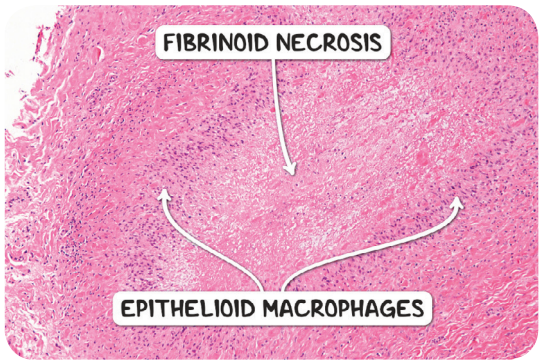

Figure 111.13 A histological section of a rheumatoid nodule. There is granaulomatous inflammation composed of central fibrinoid necrosis and palisading histiocytes.