Chapter 11

SYNOVIAL FLUID ANALYSIS

Synovial Fluid

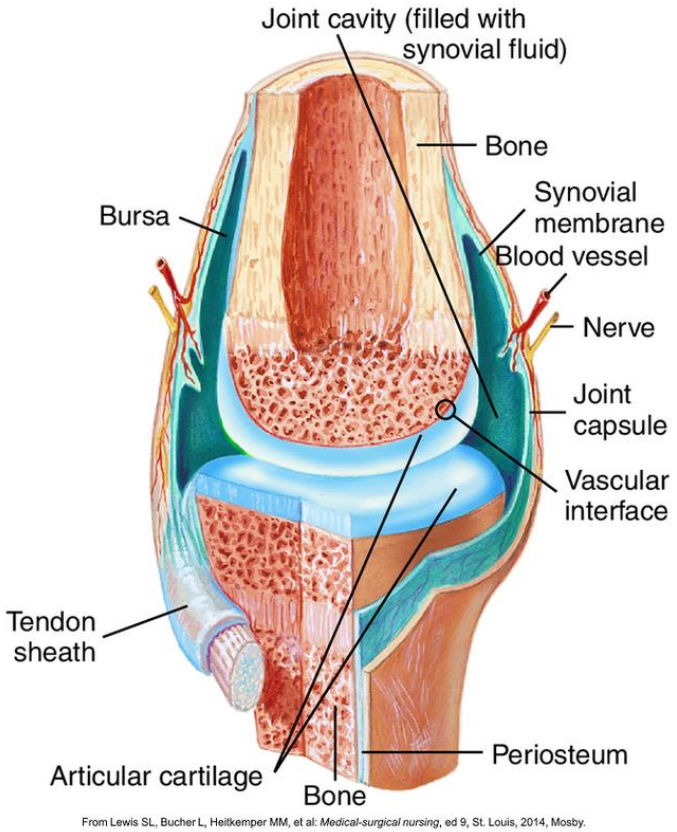
Bathes and lubricates joints

Present in areas where friction can develop, such as joints, bursae, and tendon sheaths

Joint space is lined with synovial membrane composed of two types of synoviocytes:

- More predominant type that is actively phagocytic and synthesizes degradative enzymes such as collagenases
- Other type synthesizes hyaluronate, a mucopolysaccharide

Figure 11-1. A schematic representation of the knee: a diarthrodial joint. From Lewis SL, Bucher L, Heitkemper MM, et al: *Medical-surgical nursing*, ed 9, St. Louis, 2014, Mosby.



Formation

Formed by ultrafiltration of plasma across synovial membrane and from secretions by synoviocytes

Results in viscous fluid to serve as a lubricant for joints and a nutrient source for metabolically active articular cartilage

Composition of fluid:

- Glucose and uric acid same as plasma
- Total protein and immunoglobulins vary from one-fourth to one-half that of plasma

Joint Disorder Classification

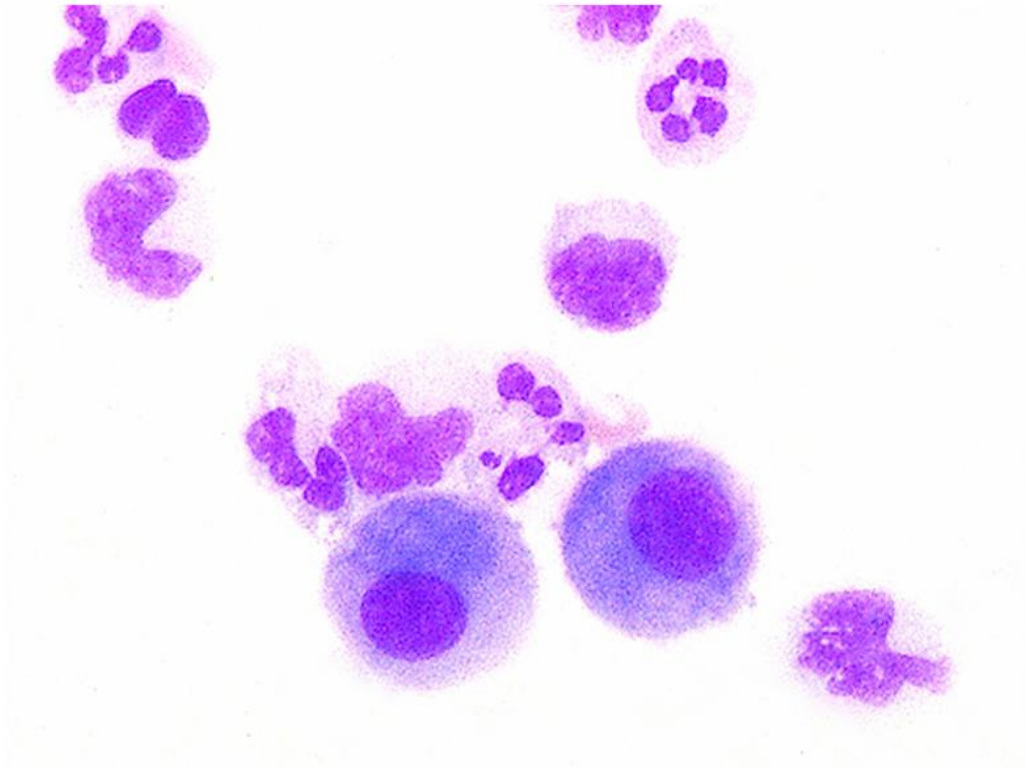
Four principal categories:

- Noninflammatory
- Inflammatory
- Septic
- Hemorrhagic

Categories can overlap, and several can occur at the same time in the same joint

Variations of test results can occur depending on the stage of disease process in the patient

Figure 11-2. Synoviocytes in synovial fluid, ×400. Note their morphologic similarity to mesothelial cells in serous fluids. From Rodak BF, Fritsma GA, Doig K: *Hematology: clinical principles and applications*, ed 3, St. Louis, 2007, Saunders.



From Rodak BF, Fritsma GA, Doig K: *Hematology: clinical principles and applications*, ed 3, St. Louis, 2007, Saunders.

TABLE 11.2 Classification of Synovial Fluid Based on Laboratory Examination

Test	Normal	Group I Noninflammatory	Group II Inflammatory	Group III Septic	Group IV Hemorrhagic
Volume, mL	<3.5	>3.5	>3.5	>3.5	>3.5
Color	Pale yellow	Yellow	Yellow-white	Yellow-green	Red-brown
Viscosity	High	High	Low	Low	Decreased
WBC count, cells/μL	<200	<3000	2000–100,000[12]	10,000–>100,000[12]	>5000[12]
Neutrophils	<25%	<25%	>50%	>75%	>25%
Glucose concentration	Approximately equal to plasma level	Approximately equal to plasma level	Less than plasma level	Less than plasma level	Approximately equal to plasma level
Glucose: P–SF* difference	≤10 mg/dL[12] (≤0.55 mmol/L)	<20 mg/dL (<1.11 mmol/L)	>20 mg/dL (range, 0–80)[6] (>1.11 mmol/L)	>40 mg/dL (range, 20–100)[6] (>2.22 mmol/L)	<20 mg/dL (<1.11 mmol/L)
Culture	Negative	Negative	Negative	Positive	Negative
Associated diseases	—	Osteoarthritis Osteochondritis Osteochondromatosis Traumatic arthritis Neuroarthropathy	Crystal synovitis† (gout, pseudogout) Rheumatoid arthritis‡ Reactive arthritis§ Systemic lupus erythematosus¶	Bacterial infection Fungal infection Mycobacterial infection	Trauma Blood disease (e.g., hemophilia, sickle cell disease) Tumor Joint prosthesis

Arthrocentesis

Percutaneous aspiration from a joint using aseptic technique and disposable sterile equipment

If possible, patient should be fasting a minimum of 4 to 6 hours

Blood sample collected at same time

Normal fluid volume is 0.1 to 3.5 mL, so sample of fluid may be very small

Arthrocentesis of a joint with no fluid buildup can result in a “dry tap”

Collection and Handling

Sample normally collected in three portions:

- Tube #1: no anticoagulant tube for chemical and immunologic studies
- Tube #2: anticoagulant tube for microscopic studies
- Tube #3: sterile anticoagulant tube for microbiological studies

Best anticoagulant is sodium heparin or liquid ethylenediaminetetraacetic acid (EDTA), since they do not form crystals; sodium polyanetholesulfonate (SPS) also acceptable for microbiological studies

Transport and analyze at room temperature; evaluate immediately

Physical Examination—Color

Normal is pale yellow or colorless and clear

Red or brown are associated with trauma during collection procedure or disorders that disrupt synovial membrane allowing blood to enter joint cavity

Fluid can appear greenish or purulent in some conditions (infections) and milky in others (tuberculous arthritis, systemic lupus erythematosus)

Clarity

Numerous substances that can affect synovial fluid clarity can be identified by microscopic examination:

- White blood cells (WBCs), red blood cells (RBCs), and synoviocytes
- Crystals, fat droplets
- Fibrin, cellular debris, rice bodies

Rice bodies are white, free-floating substances made up of collagen covered by fibrinous tissue

- Resemble polished, shiny grains of rice of various sizes
- Seen in many arthritic conditions—most commonly in rheumatoid arthritis

Viscosity

High viscosity due to high concentration of mucoprotein hyaluronate

During inflammatory conditions, hyaluronate can be depolymerized by enzyme hyaluronidase present in bacteria and some neutrophils

Other diseases can inhibit production and secretion of hyaluronate by synoviocytes

Assess by expelling fluid from collection syringe and observing for a normal string formation, at least 4 cm long, before breaking

Clot Formation

Normal synovial fluid does not clot

Spontaneous clot formation indicates abnormal presence of fibrinogen

Pathologic processes that damage synovial membrane can cause fibrinogen to be present

Traumatic arthrocentesis with blood contamination can also cause fibrinogen to be present, causing clot formation

Microscopic Examination

Use hemacytometer to count cells

Normal saline used as diluent if necessary, depending on cell count

May need extended time for cells to settle in hemacytometer if sample very viscous

Hyaluronidase buffer may be used as diluent if necessary, to reduce viscosity for more efficient counting

Cell Counts

RBCs normally less than 2000/µL

Increased RBCs from traumatic tap or hemorrhagic effusions

WBCs normally less than 200/µL

Increase typically associated with bacterial arthritis, although other conditions can also cause an increase

WBC counts of limited value in identifying a specific disease process

Differential Cell Count

Cytocentrifugation used to concentrate cells and preserve morphology

Normally about 60% of WBCs are monocytes or macrophages, 30% lymphocytes, and 10% neutrophils

Differential counts of limited value because they can differ not only with disease process but also with stage of disease

More than 80% neutrophils associated with bacterial arthritis and urate gout

Crystal Identification

Important microscopic examination

Maintain sample at room temperature and perform examination immediately

Can use wet preparations or cytospin slides

Polarized microscopy should be used to identify crystals of monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD)

Thorough examination by skilled microscopist is critical

Monosodium Urate Crystals

Present in gouty arthritis

Needle-like crystals with pointed ends that can distend the cytoplasm of WBCs

Polarized microscopy:

- Strongly birefringent; bright against a black background
- With red-compensator plate, appear yellow when longitudinal axes are parallel to it and blue when perpendicular

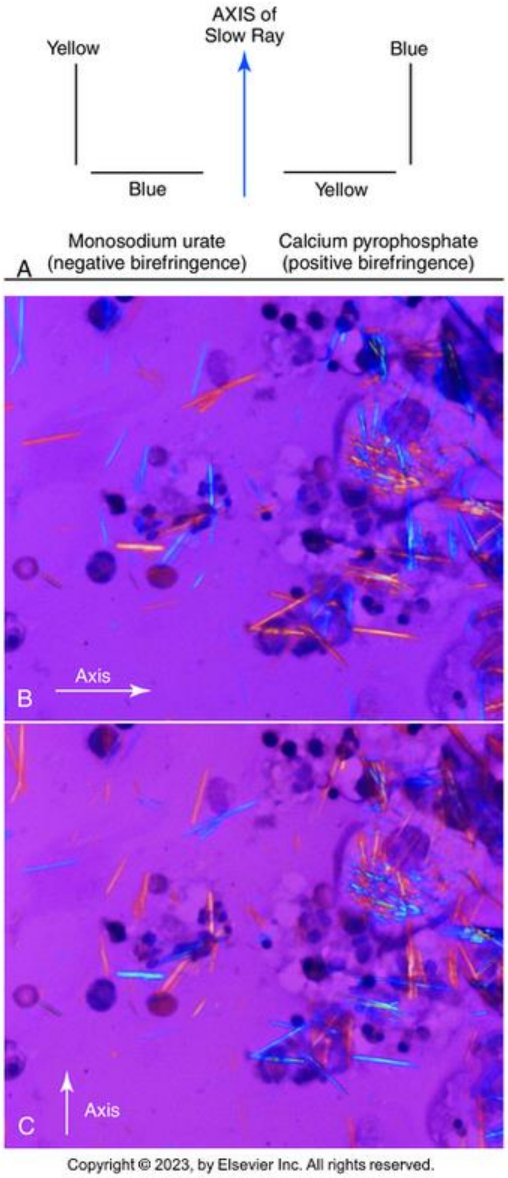


Figure 11-3. **A**, A diagrammatic representation of monosodium urate and calcium pyrophosphate crystals when viewed using polarizing microscopy with a red compensator. The axis indicated is that of the compensator. **B**, Monosodium urate crystals in joint fluid. The crystals with their longitudinal axis parallel to the red compensator plate axis as indicated in the lower left corner are yellow. **C**, With the axis of the red compensator plate perpendicular to the longitudinal axis, the same monosodium urate crystals are blue (polarizing microscopy).

Calcium Pyrophosphate Dihydrate Crystals

Seen in degenerative arthritis and arthritis accompanying metabolic diseases

Smaller and blunter than MSU crystals

Are rodlike or rhomboid; display weak positive birefringence with their colors opposite of that of MSU

With red compensator, appear blue when longitudinal axes are parallel to it and yellow when perpendicular

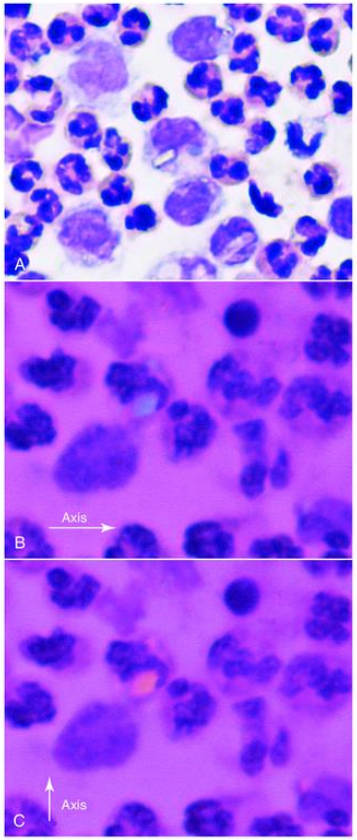


Figure 11-4. **A**, Calcium pyrophosphate dihydrate crystal in joint fluid; brightfield microscopy. **B**, Calcium pyrophosphate dihydrate crystal appears blue; its axis is parallel to that of the red compensator plate (polarizing microscopy). **C**, Calcium pyrophosphate dihydrate crystal appears yellow; its axis is perpendicular to the axis of the red compensator plate (polarizing microscopy).

Crystals

Cholesterol

- Observe on wet preparation or unstained cytospin slide
- Flat, rectangular plates with notched corners
- Seen in chronic inflammation

Hydroxyapatite

- Observe intracellularly but only using electron microscope
- Tiny, needle-like crystals
- Can induce an acute inflammatory reaction similar to that caused by MSU and CPPD crystals

Figure 11-5. Cholesterol crystals in joint fluid; brightfield microscopy.

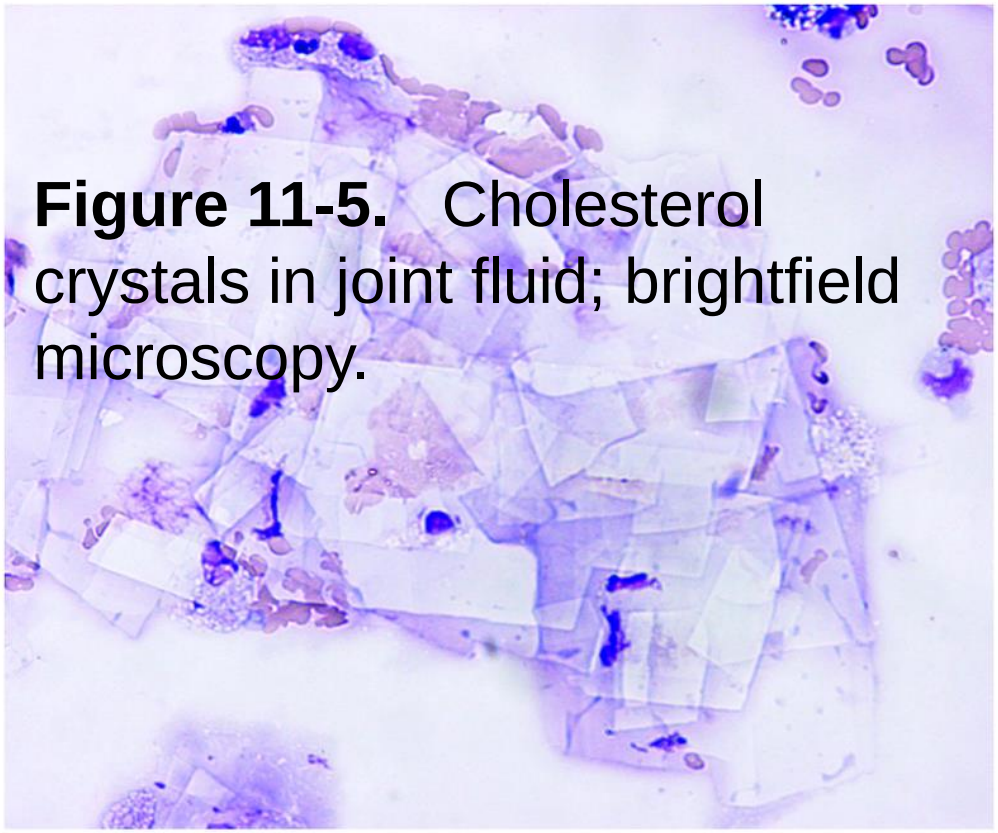
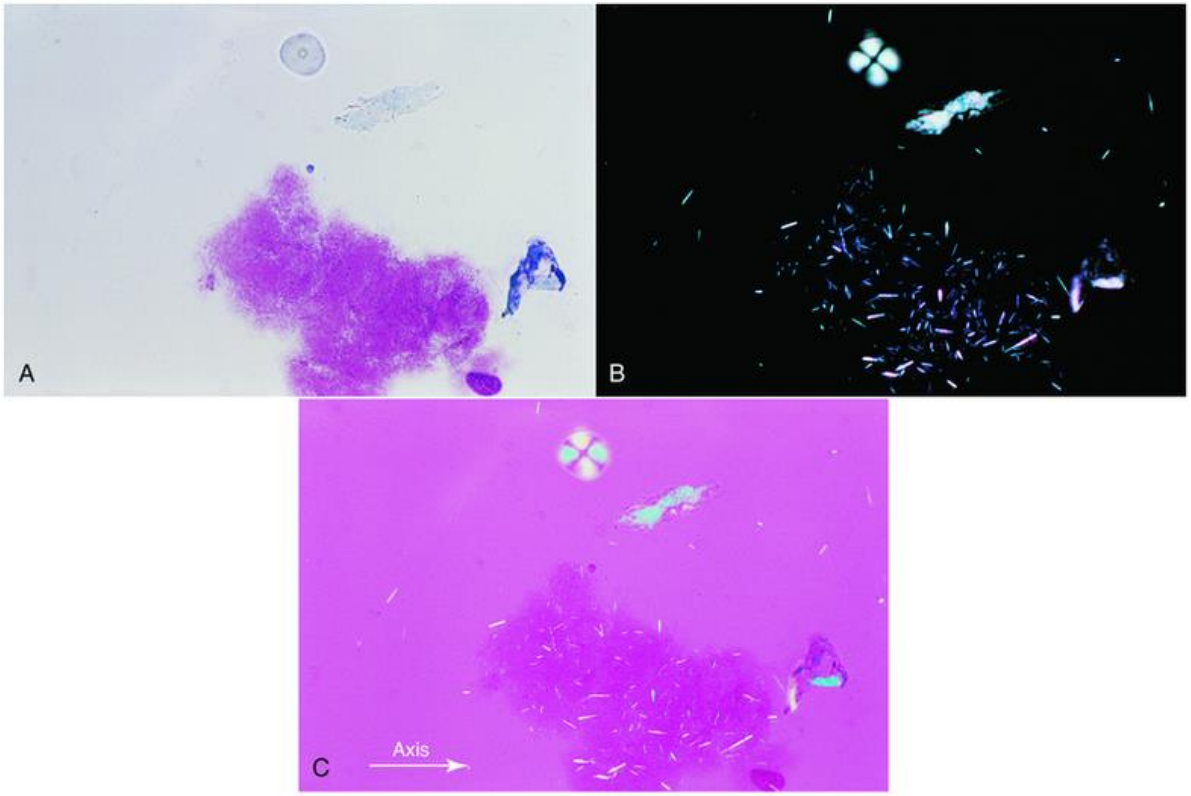


Figure 11-6. Synovial fluid with mass of hyaluronate, small monosodium urate (MSU) crystals, starch granule, and fibers. Cytocentrifuged preparation, Wright's stain, ×400. **A**, Brightfield microscopy; starch granule and fiber. Note that no crystals are evident in the pink mass. **B**, Polarizing microscopy; presence of MSU crystals is evident, fibers have strong birefringence, and the starch granule shows a typical Maltese cross pattern. **C**, Compensated polarizing microscopy; needle-shaped crystals with their long axis parallel to the red compensator plate are yellow, which indicates that the crystals have negative birefringence and are MSU. Note that the starch granule has positive birefringence (i.e., quadrants parallel to axis of compensator are blue). The fibers show both negative and positive birefringence. From Ringsrud KM, Linne JJ: *Urinalysis and body fluids: a color text and atlas*, St. Louis, 1995, Mosby.



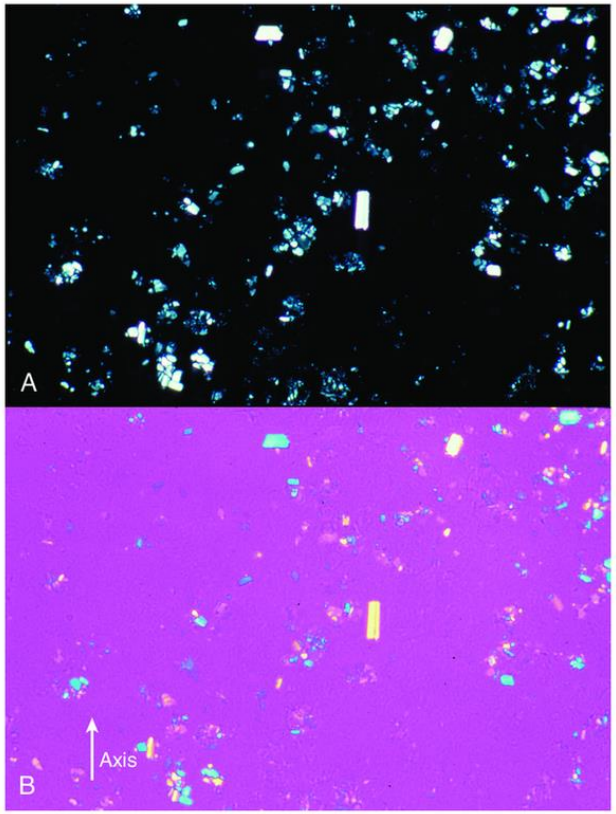
From Ringsrud KM, Linne JJ: *Urinalysis and body fluids: a color text and atlas*, St. Louis, 1995, Mosby.

Crystals (Cont.)

Corticosteroids

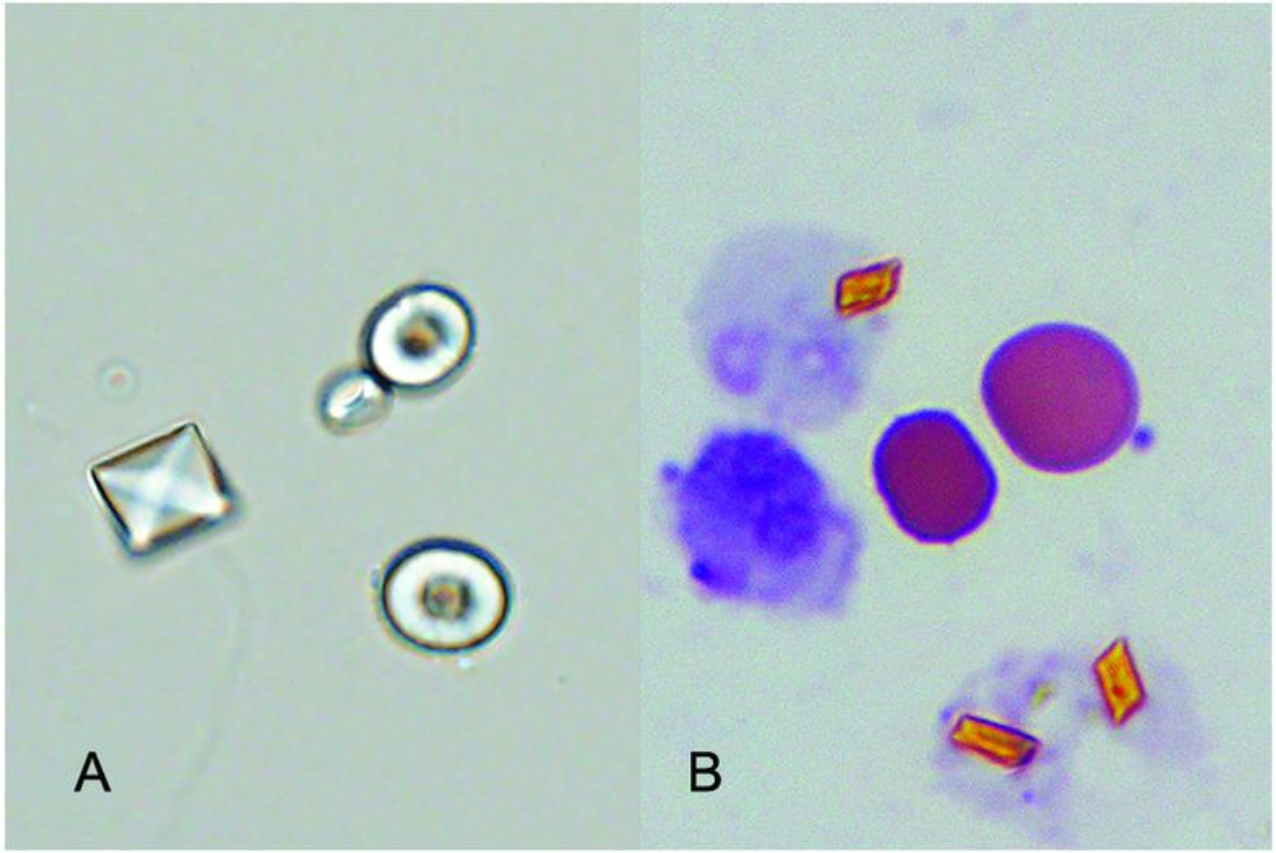
- Seen for months after steroid injections
- Of no clinical significance
- Look like MSU or CPPD but yield conflicting results based on their birefringence

Figure 11-7. Synovial fluid with corticosteroid drug (triamcinolone diacetate [Aristocort]) crystals present. Note their conflicting morphology (suggests calcium pyrophosphate dihydrate [CPPD]) and strong negative birefringence (suggests monosodium urate [MSU]). Wet preparation, unstained; polarizing microscopy, ×400. **A**, Many strongly birefringent drug crystals that morphologically resemble CPPD using polarizing microscopy. **B**, Drug crystals with their long axes parallel to the axis of the red compensator plate are yellow, suggesting MSU crystals. From Ringsrud KM, Linne JJ: *Urinalysis and body fluids: a color text and atlas*, St. Louis, 1995, Mosby.



From Ringsrud KM, Linne JJ: *Urinalysis and body fluids: a color text and atlas*, St. Louis, 1995, Mosby.

Figure 11-8. **A**, A single calcium oxalate dihydrate (*Wheddellite*) crystal and several calcium oxalate monohydrate (*Whewellite*) crystals; brightfield microscopy. **B**, Three hematin crystals. Note their distinctive golden yellow-brown color; also present are RBCs and WBCs. Brightfield microscopy.



Chemical Examination

Glucose
- Some diseases cause decreased glucose in fluid, ½ that present in the patient's plasma

Total protein
- Increased protein as a result of variety of joint diseases
- Only indicates inflammatory process

Uric acid
- Same levels as plasma
- Increased levels in fluid may cause MSU crystals

Lactate
- Increased from anaerobic glycolysis in the synovium
- Clinical value not yet established

Gram Stain and Culture

Offer immediately useful diagnostic information when positive

Most infectious agents are bacterial and come from blood

Other agents include fungi, viruses, and mycobacteria

Sensitivity of the Gram stain depends on organism

- 75% of patients with staphylococcal infections identified as positive by Gram stain
- 50% of gram-negative organisms
- 40% of gonococcal infections

All synovial fluid samples should be cultured