Synovial Fluid

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Macroscopic Examination

- Macroscopic analysis includes color, clarity, and viscosity.
- Normal synovial fluid is *colorless* or *pale yellow* and *clear*.
- **Print** can be clearly read through a tube containing synovial fluid.
- Pathologic specimens may be colored yellow, white, or red, and the clarity may be translucent, cloudy, or opaque.

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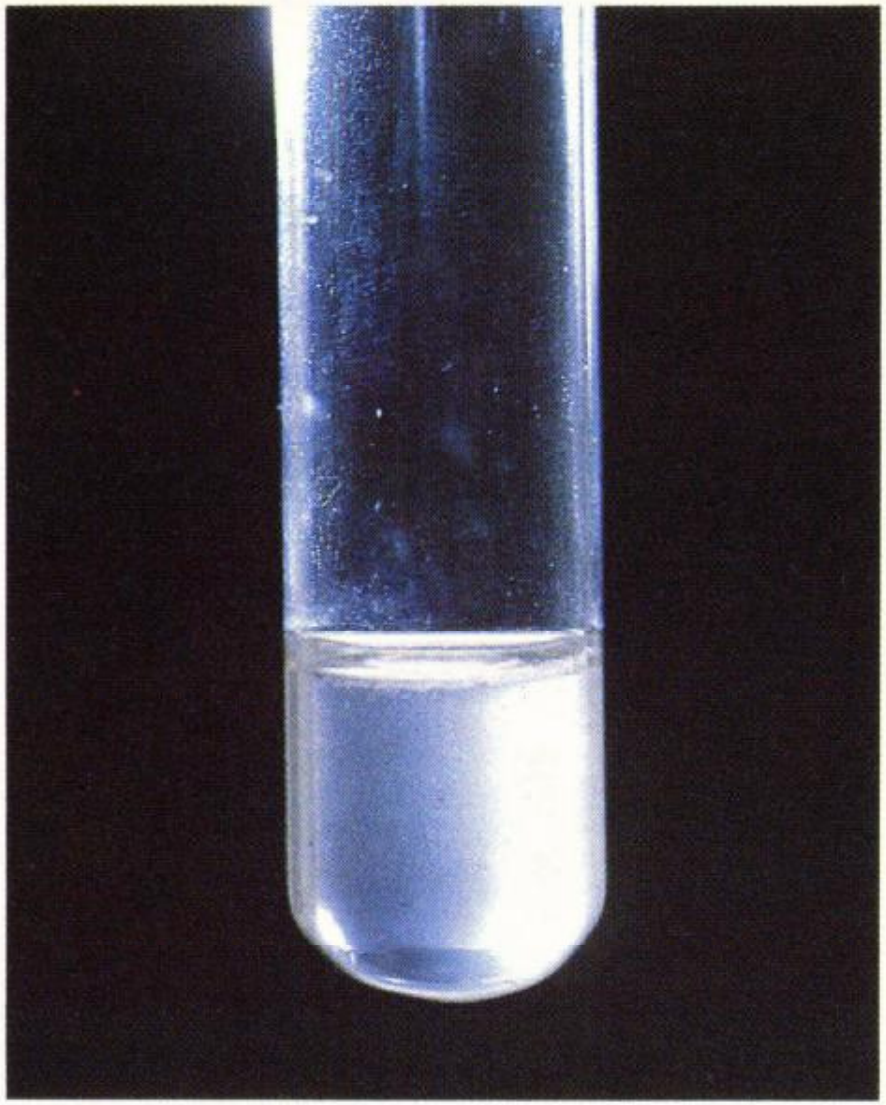

Figure 2–1.
Clear colorless fluid from a patient with asthma who received high-dose corticosteroid therapy. This effusion was obtained from a painful knee swelling that developed during corticosteroid withdrawal.[6] Such colorless fluid is as close to normal joint fluid as is possible in an effusion.

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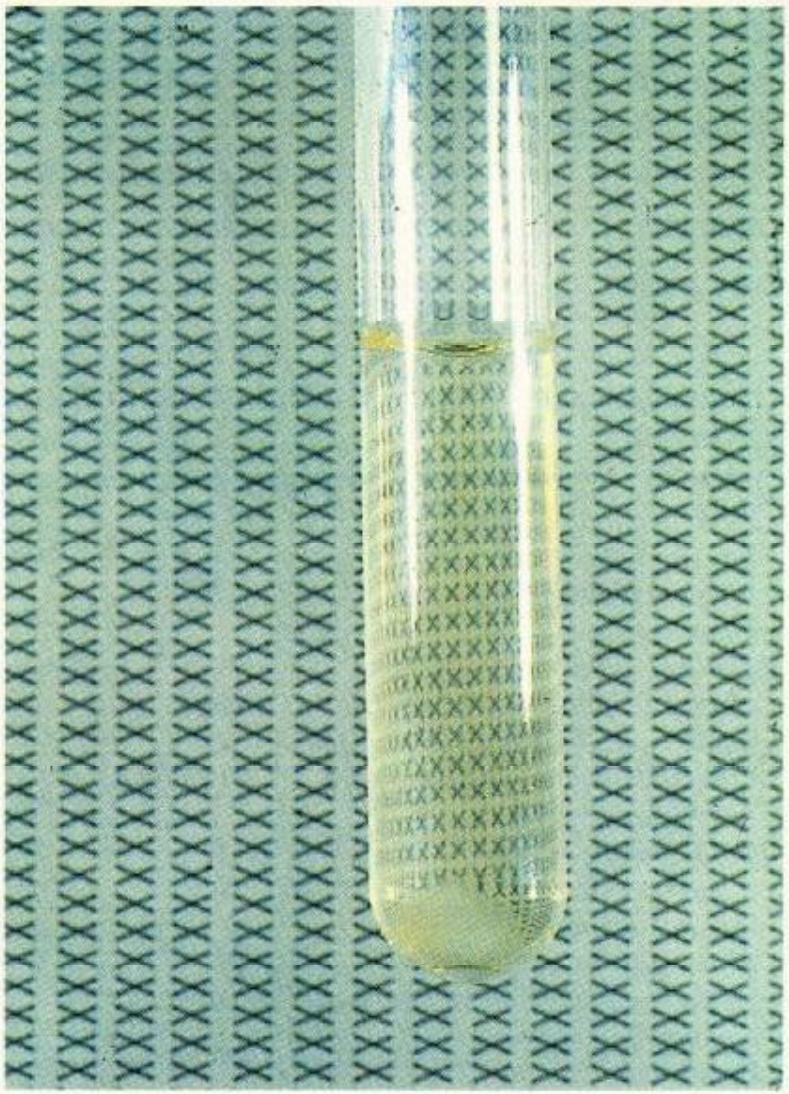

Figure 2–2.
Clear transparent "noninflammatory" fluid from a patient with osteoarthritis. Letters are clearly visible through the fluid. The pale yellow hue is typical of uncomplicated osteoarthritic effusions.

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Macroscopic Examination, cont.

- As with other fluids, breakdown products of heme cause a yellow color, leukocytes make the fluid white, erythrocytes impart a red color, and cells (nucleated cells or erythrocytes) cause a cloudy appearance.
- If *particles* are present, they should be noted. These may be *fragments of cartilage* (wear particles) or particles containing *collagen* or *fibrin* (rice bodies).
- Particles may also be seen in *metallosynovitis* from a prosthetic implant.

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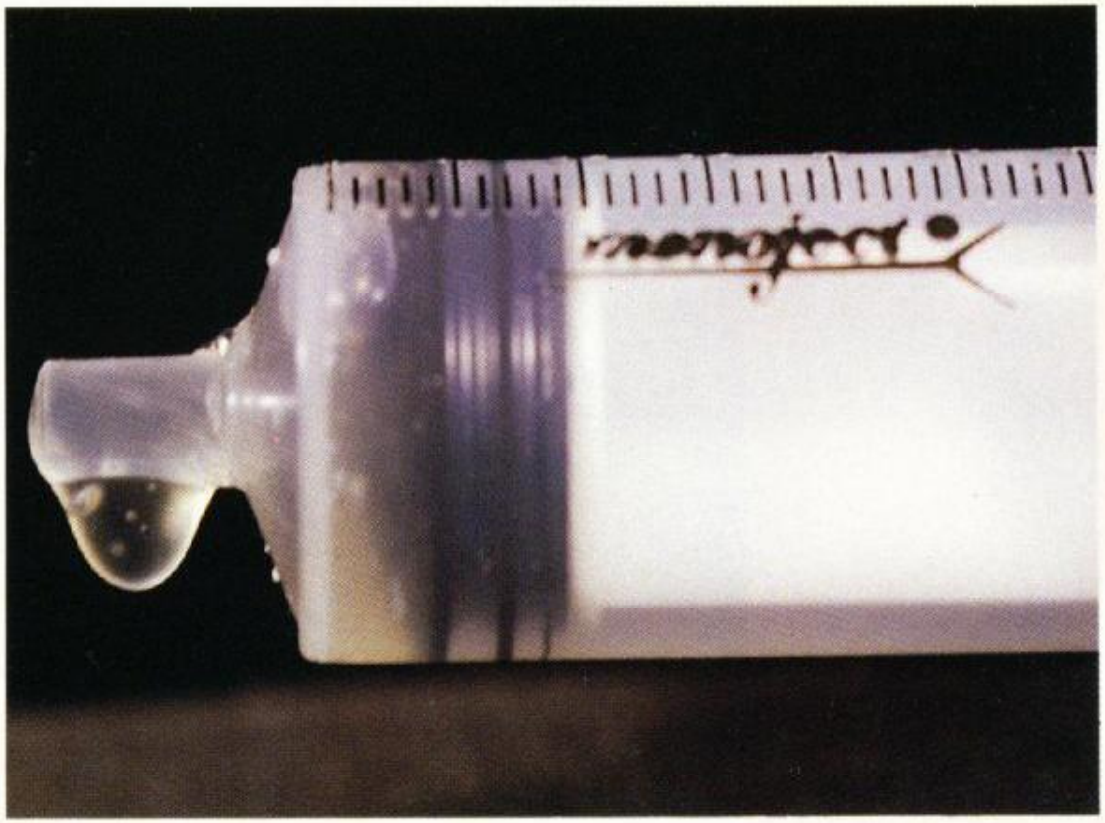

Figure 2–3.
Clear "noninflammatoray" fluid inside a plastic syringe might appear cloudy. An important step is to transfer joint fluid to a glass tube before assessing its opacity.

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Figure 2–4.
Faintly straw-colored light "noninflammatory" fluid from a patient with osteoarthritis.

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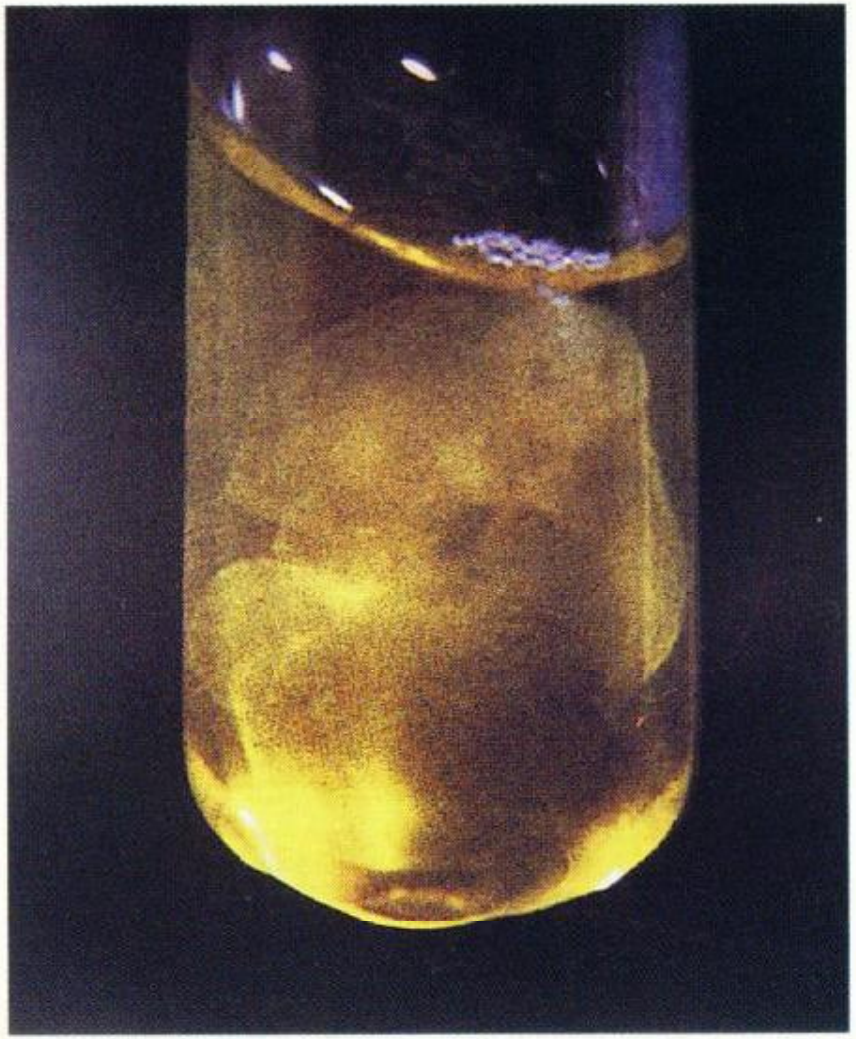

Figure 2–8.
Spontaneous clot formation is noted in mildly inflammatory fluid. Normal or noninflammatory fluid would contain almost no fibrinogen and should not clot.

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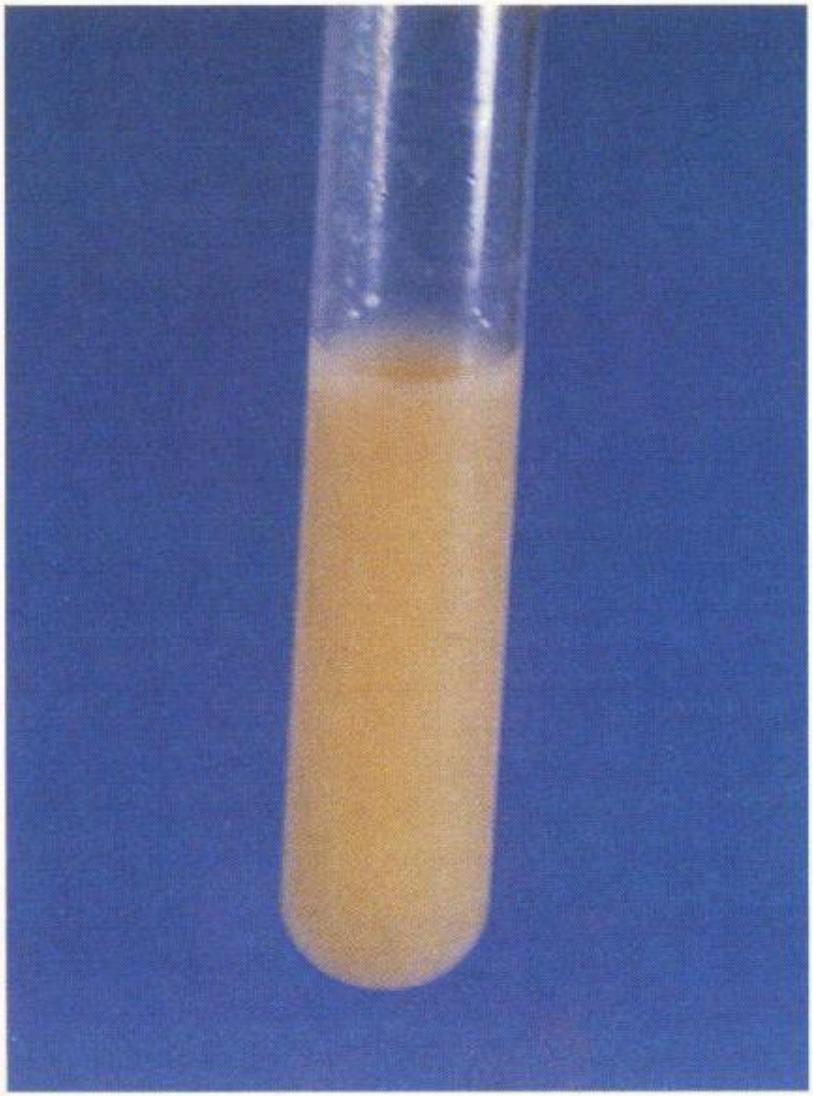

Figure 2–9.
Cloudy, purulent fluid from the knee of a patient with acute septic arthritis owing to streptococcus type A.

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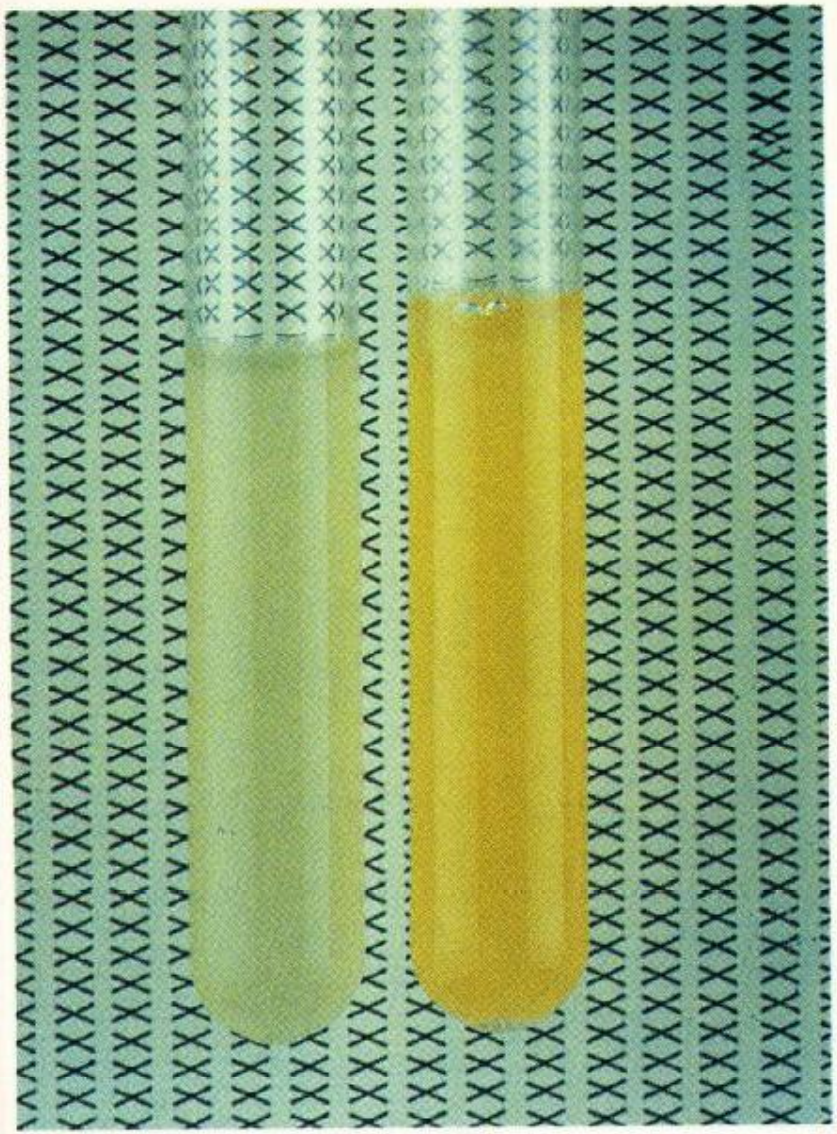

Figure 2–10.
Moderately cloudy fluids from patients with gout (left) and rheumatoid arthritis (right). Fluids are translucent but not transparent.

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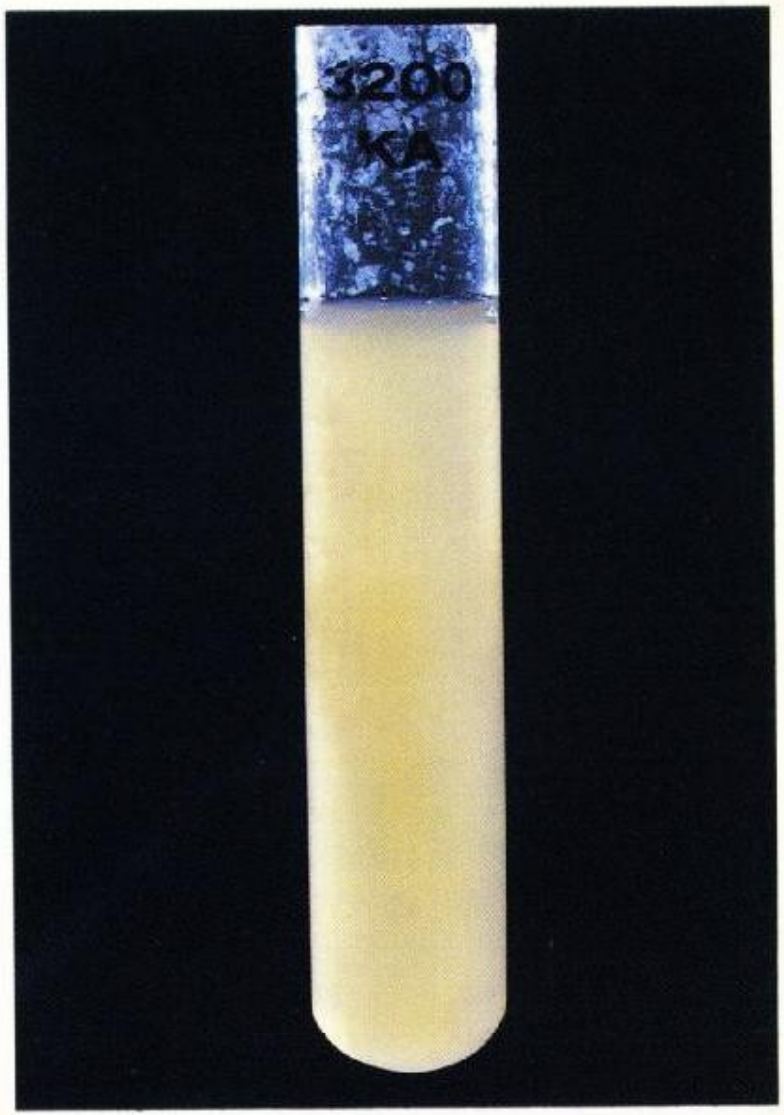

Figure 2–12.
Purulent fluid from a patient with calcium pyrophosphate deposition disease and pseudogout.[4] Note the whitish appearance owing to the crystals, cell clumps, and fibrin threads.

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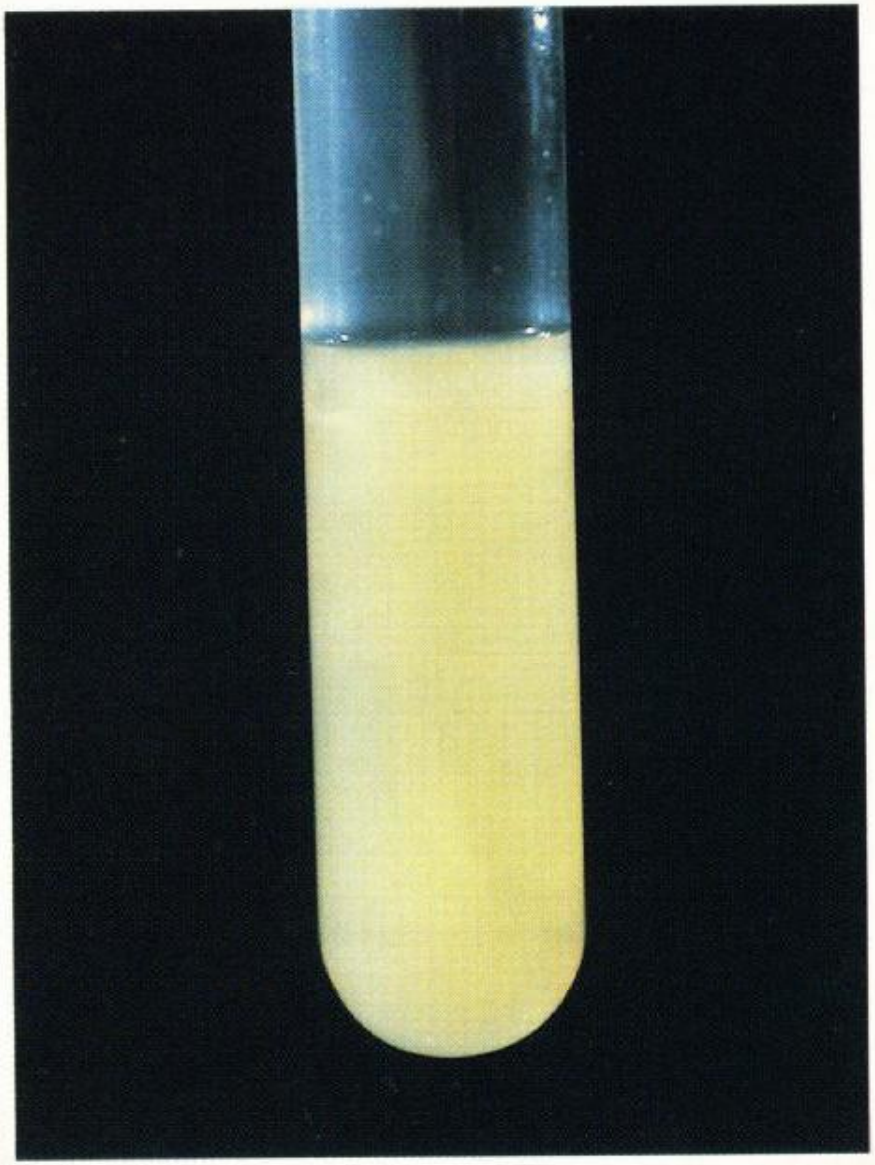

Figure 2–13.
Acute gouty fluid with neutrophils, but the opacity results predominantly from MSU crystals. Such a white color always suggests the crystal deposition diseases.

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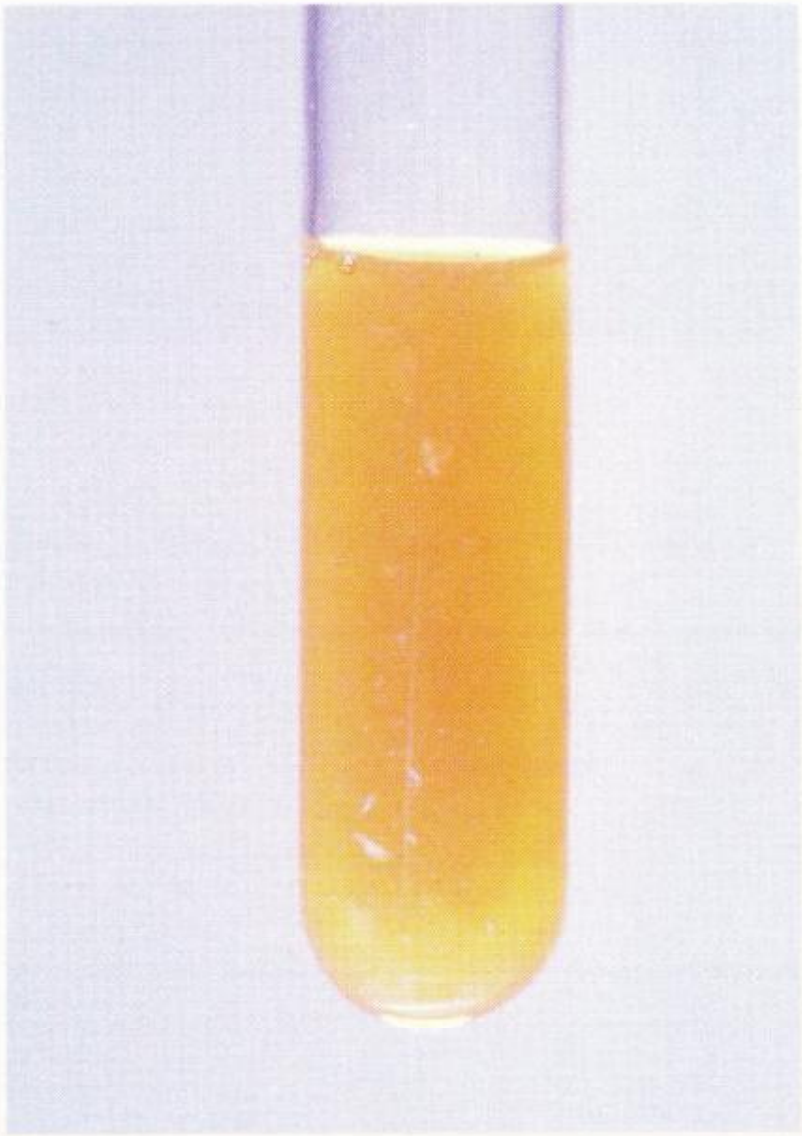

Figure 2–17.
Blood-tinged effusion from a patient with chronic gout. Note the white fragments of microtophi floating in the fluid. Any severely inflamed joint with congested vessels can become bloody from minor trauma.

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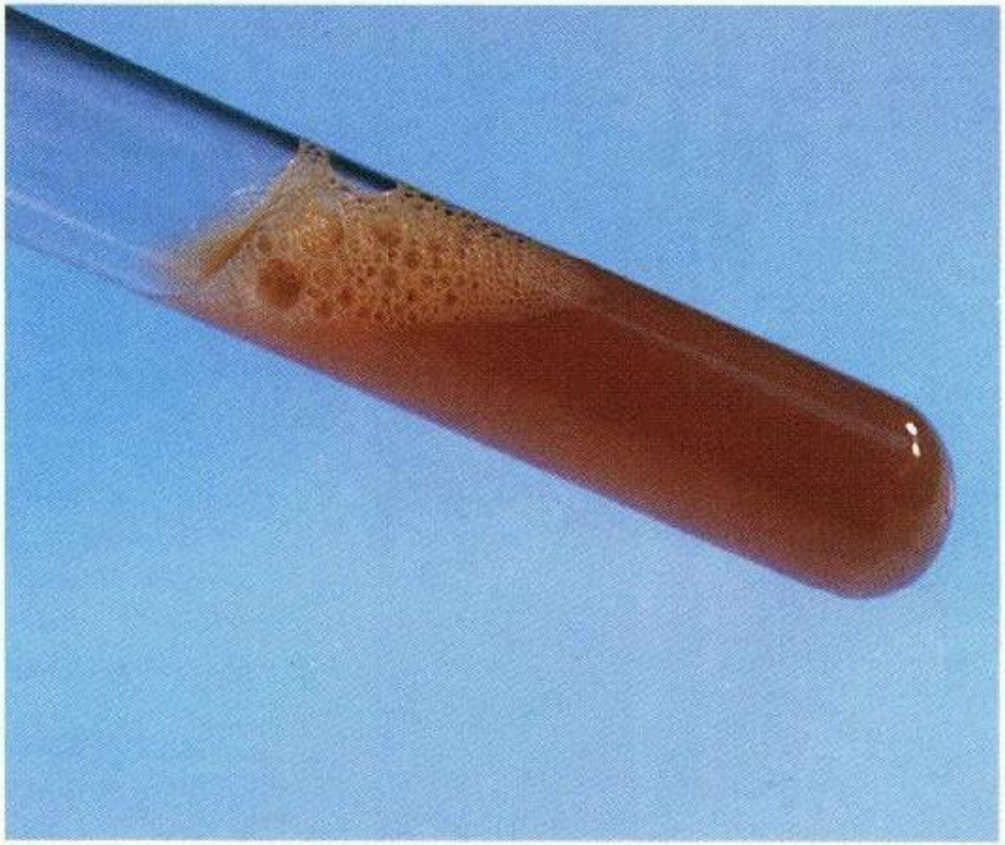

Figure 2–18.
Hemopurulent fluid from a patient with systemic lupus erythematosus and acute septic arthritis. The bubbles were generated when the fluid was re-suspended by agitation.

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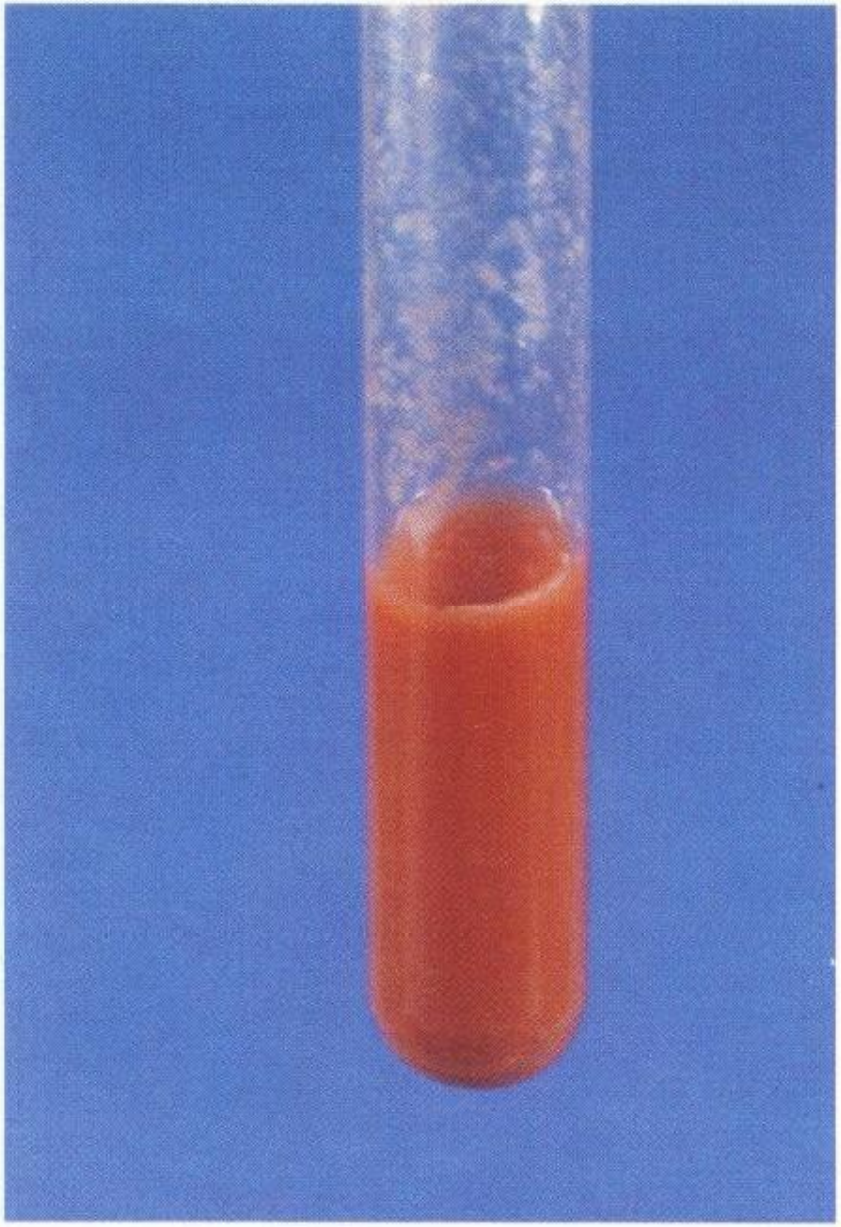

Figure 2–19.
Hemopurulent fluid from a patient with septic arthritis of the shoulder due to streptococcus D.

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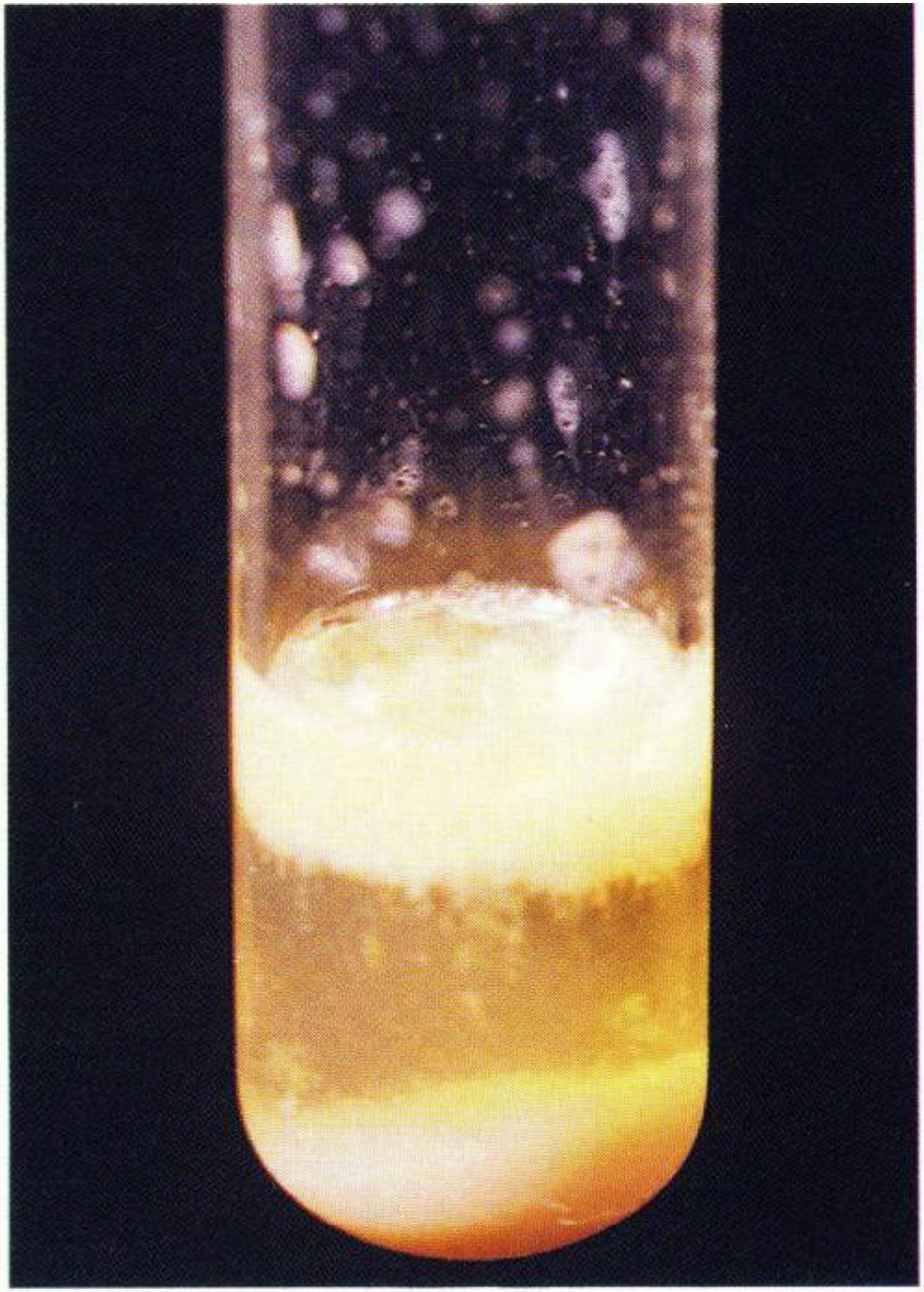
Figure 2–23.
Fat can be prominent in joint effusions in patients with chronic infectious arthritis. This centrifuged purulent fluid from a patient with septic arthritis shows a layer of creamy fat on the surface. The lowest layer consists of neutrophils.



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Macroscopic Examination, Viscosity

- Viscosity can be measured at the bedside by the physician placing a finger at the tip of the syringe and **stringing out** the fluid or determining *the length of the string after expressing it from the syringe.*
- Normal fluids will form a string greater than **4cm**.
- Clinically, there is no need for a sophisticated measurement of viscosity.

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Macroscopic Examination

Mucin Clot Test

- Like the gross observation of viscosity, the mucin clot test may reflect the *degree of hyaluronate polymerization*.
- *Hyaluronidase* derived from neutrophils most likely has a pathogenetic role in decreasing viscosity.
- The test is **qualitative** and involves the addition of *2% acetic acid* to synovial fluid.
- **Mucin clots are graded as good, fair, or poor.**

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Microscopic, Enumeration

- Cell counts may be done manually or by automated methods. Manual methods require a hemacytometer.
- *Clear fluids usually require no dilution*. *Isotonic saline* is an adequate diluent.
- With most fluids, the nucleated cell and erythrocyte counts can be done in the same chamber.
- If desired, RBC can be lysed using *0.3% saline* as a diluent.
- Solutions containing acetic acid should not be used, since they **coagulate hyaluronate**.

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Microscopic, Enumeration

- Noninflammatory fluids are viscous and create problems in loading the chamber.
- This can be resolved using hyaluronidase, if desired.
- Approximately 400 units of hyaluronidase are added to 1 mL of synovial fluid and incubated for **10** minutes at 37 °C.
- However, since viscous fluids are either normal or noninflammatory, approximate cell counts are clinically acceptable, and excessive personnel time is not justified.

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Automated cell counts

- Automated cell counts have been validated for total nucleated cells and erythrocytes on **impedance-based** and **laser-based optical systems**.
- Acceptable lower limits of detection were set as >0.150 or 0.200 x 109/L for nucleated cells and 0.01 or 0.03 x 1012/L for erythrocytes.
- Samples flagged for cellular interference should be enumerated manually.
- If automated instruments are used, pretreatment of samples with hyaluronidase was considered necessary adding an additional 20 minutes of processing time.

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Morphology

- Differential cell counts are done using **manual** or **automated** methods.
- The former has many advantages that include identification of **unusual cell types**, **crystals**, or **microorganisms**.
- Normal cellular constituents of synovial fluid include neutrophils, lymphocytes, monocytes, histiocytes, and synovial lining cells.

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Morphology, cont.

- **Neutrophils** normally constitute **less than 25%** of all nucleated cells.
- In addition to intact neutrophils, it is not unusual to see necrobiotic changes, many characteristic of apoptotic cells with single or multiple dense, hyperchromatic, homogenous nuclear masses.

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Morphology, cont.

- In pathologic specimens, **neutrophils** may have **dark cytoplasmic inclusions** of **immune complexes** in wet preparations with light microscopy.
- Such cells are called *ragocytes* or *R.A. cells*, the latter name because of the association with **rheumatoid arthritis**.
- In collagen vascular diseases, **typical L.E. cells** may be seen on Romanowsky-stained smears.
- L.E. cells are neutrophils that have engulfed large, round, purple hyaline homogeneous nuclear masses.

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Morphology, cont.

- In **normal fluids**, cells in the *monocyte/macrophage* category normally constitute the majority of cells with a mean value of **48%**.
- On stained smears, monocyte/macrophages with *basophilic cytoplasmic inclusions* have been designated *Reiter cells*.
- Lymphocytes range from few to many in normal fluids, with a mean value of approximately **25%.**
- They have similar morphologic features to blood lymphocytes or may show reactive changes in pathologic fluids.

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Morphology, cont.

- Normally, *synovial lining cells* on average constitute **only 4%** of nucleated cells.
- Many other cell types have been described in pathologic fluids. These include eosinophils, basophils, mast cells, plasma cells, bone marrow cells, chondrocytes, Gaucher cells, platelets, and sickle cells.
- Unlike the other body fluids discussed, malignant cells are *so rarely seen* that it does not impact the routine clinical laboratory.

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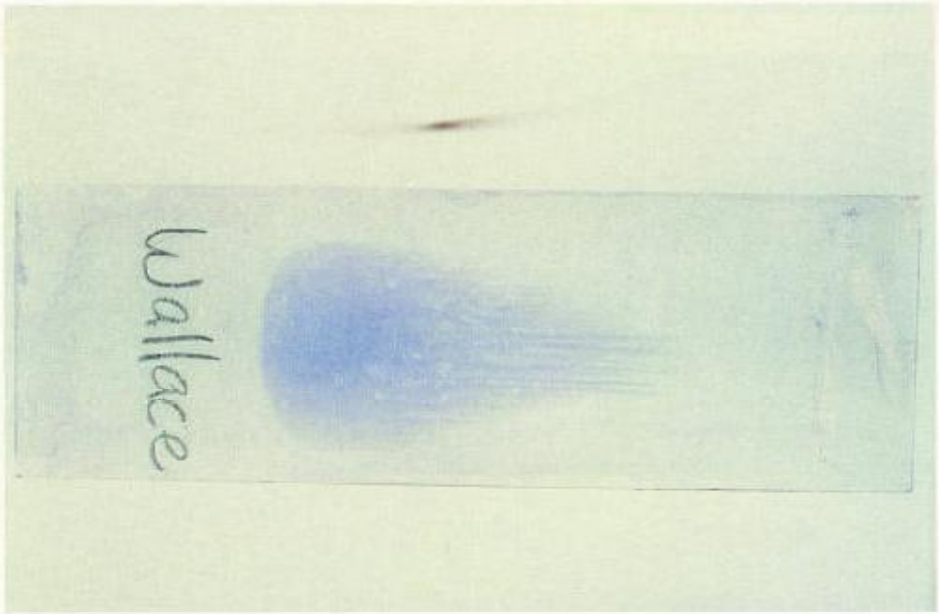
Figure 5–1.
A, Synovial fluid, Wright stain. Satisfactory dry synovial fluid smear. Distribution of stained fluid is even. **B**, Cells commonly seen in synovial fluid include polymorphonuclear cells, lymphocytes, and large mononuclear cells. Wright stain, × 600.



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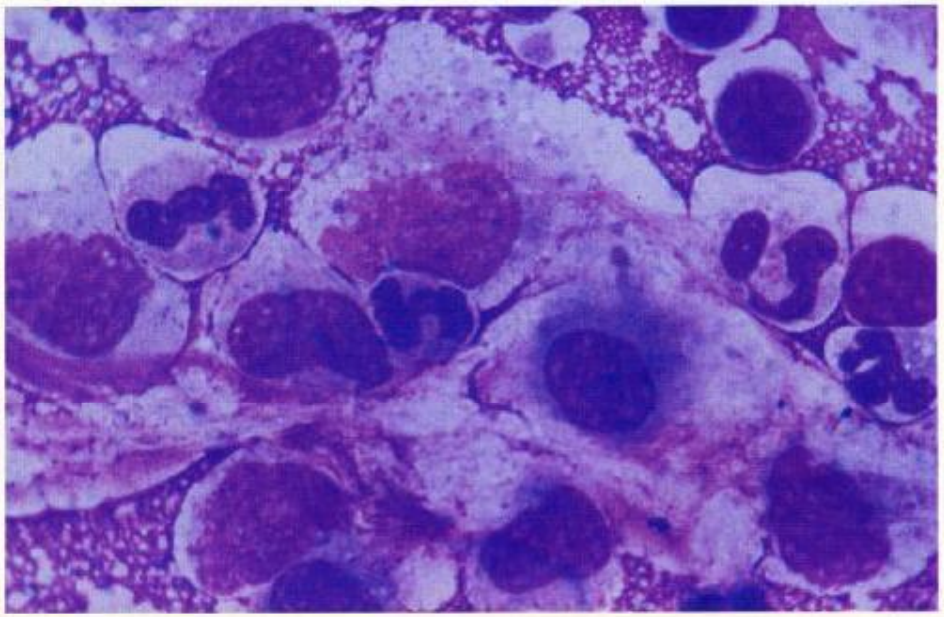

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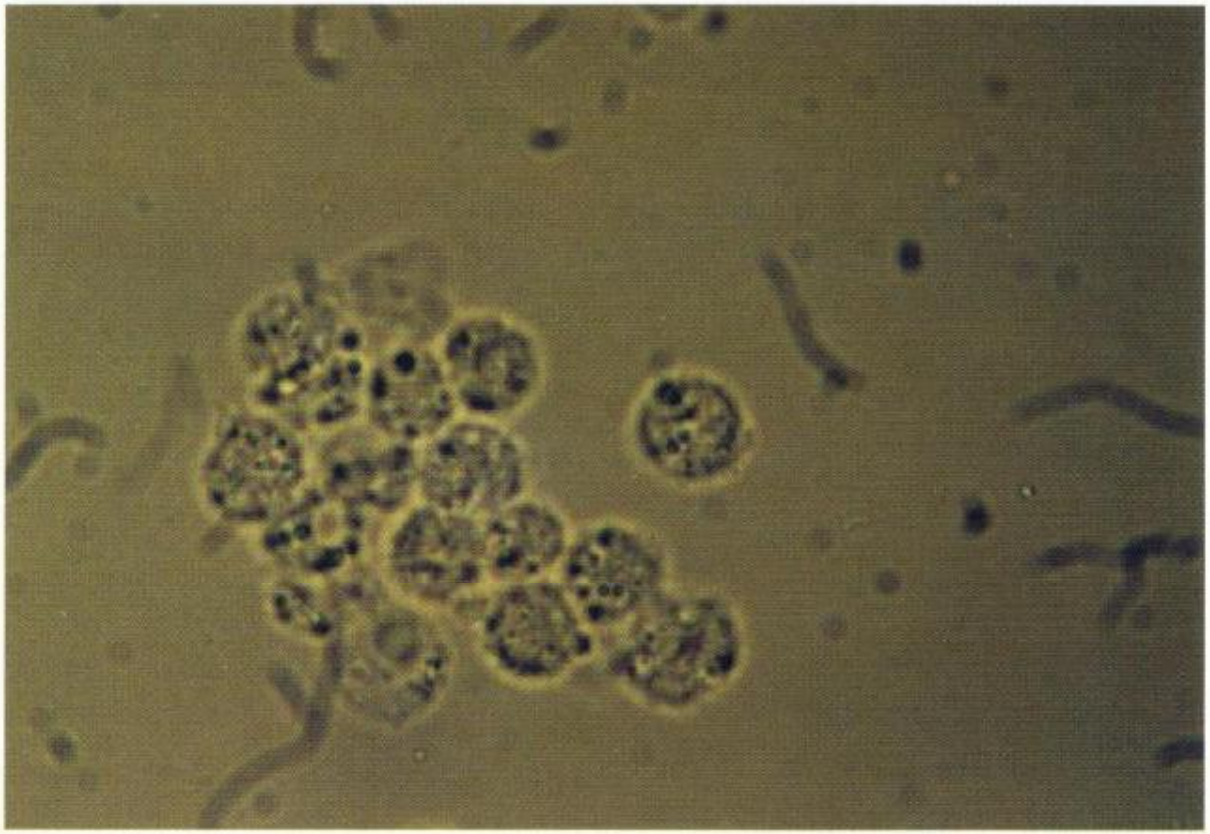
ragocytes or *R.A. cells*

Figure 4–1.
Wet drop preparation of synovial fluid from a patient with rheumatoid arthritis. Note abundant intracytoplasmic inclusions, probably due to immune aggregates in vacuoles.[1,7] These inclusions must be differentiated from apatite clumps, small pyrophosphate crystals, fat droplets, bacteria, and cell detritus. Ordinary light microscopy, × 400.



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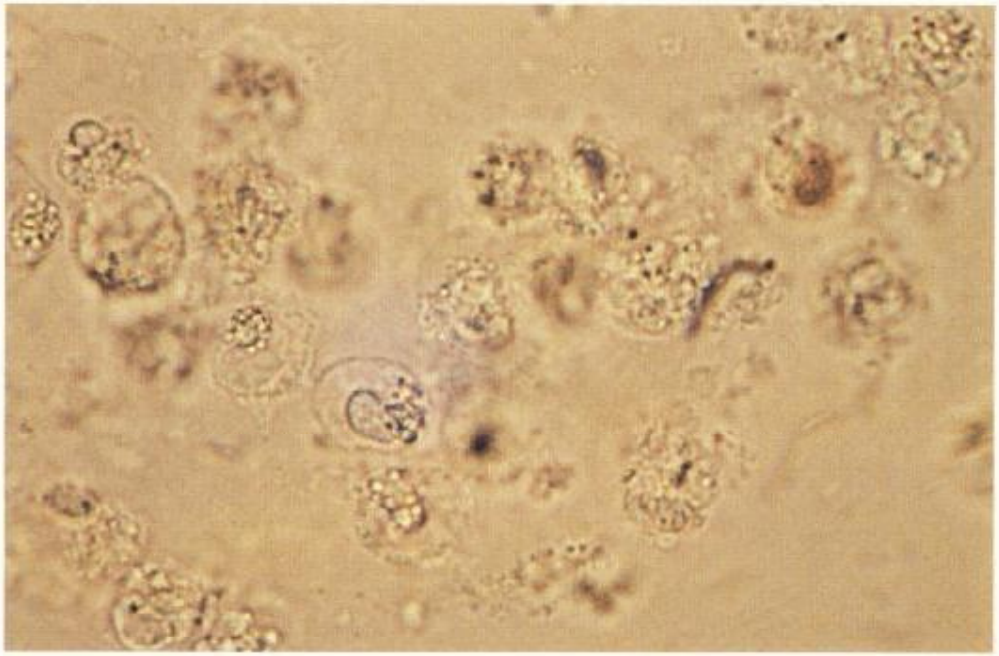

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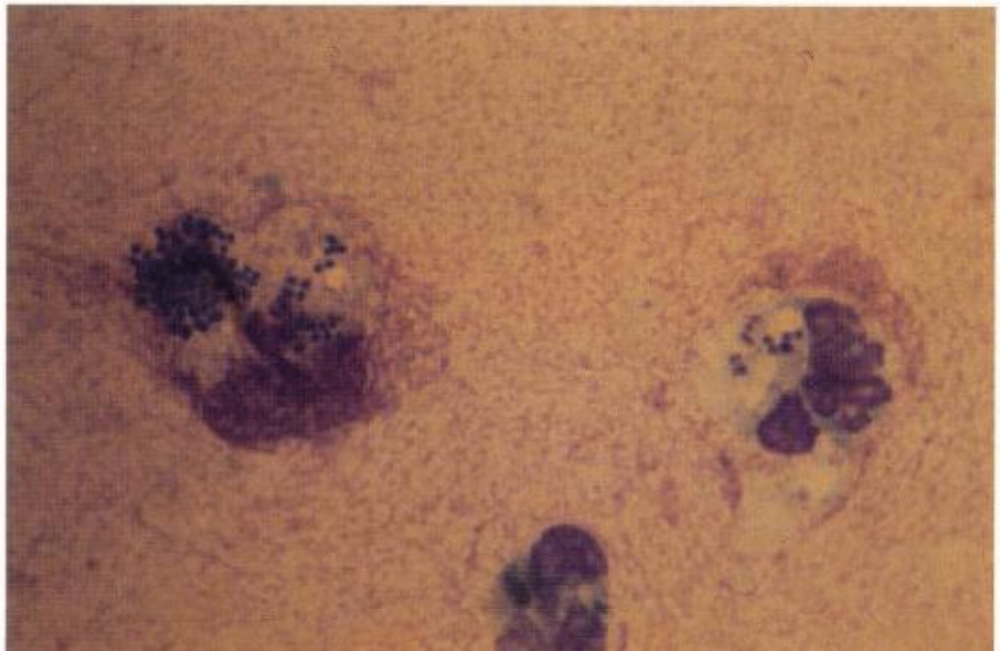

B

Figure 4–4.
A, Cells containing abundant intracytoplasmic inclusions due in large part to numerous phagocytized bacteria in a patient with staphylococcal arthritis. Some part of the inclusions may be debris from degenerated cells. Ordinary light, × 400. B, Abundant intracellular cocci seen with Wright stain. This occasional finding is usually associated with a large number of bacteria in the synovial fluid. Wright stain, ordinary light, × 600.

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Crystals

- Polarization Microscopy
- Polarization microscopy is one of the cornerstones in the laboratory analysis of synovial fluids, and is essential for the diagnosis of crystalline joint disease.
- Because the crystal has two different indices of refraction, the material is said to be birefringent, a property detected by polarization microscopy.

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Crystals, cont.

- A polarizing microscope is a light microscope that has two additional filters, designated a polarizer and analyzer.
- The substage light source emits light vibrating in all planes. The light is then screened by the polarizer, a grid that filters out all rays of light except the ray vibrating parallel to the direction of the lines of the grid.
- The polarized light then passes through the condenser and the specimen slide to the analyzer, similar to the grid of the polarizer, and then through the eyepiece lens to the eye.

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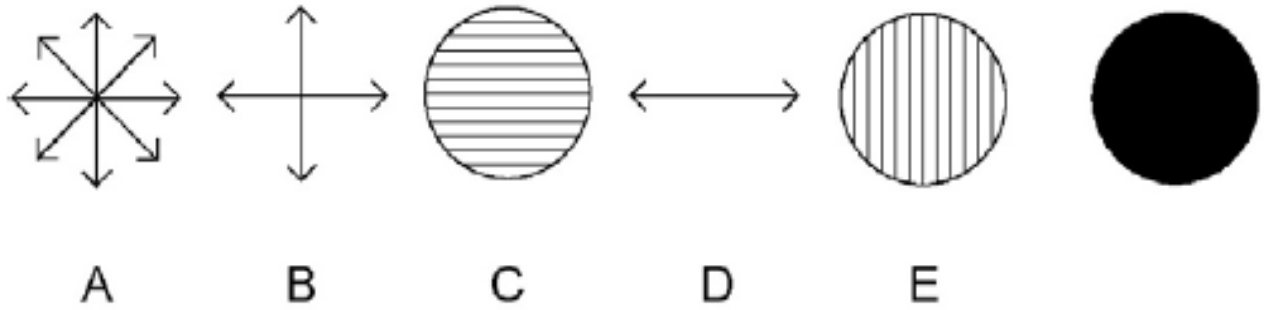

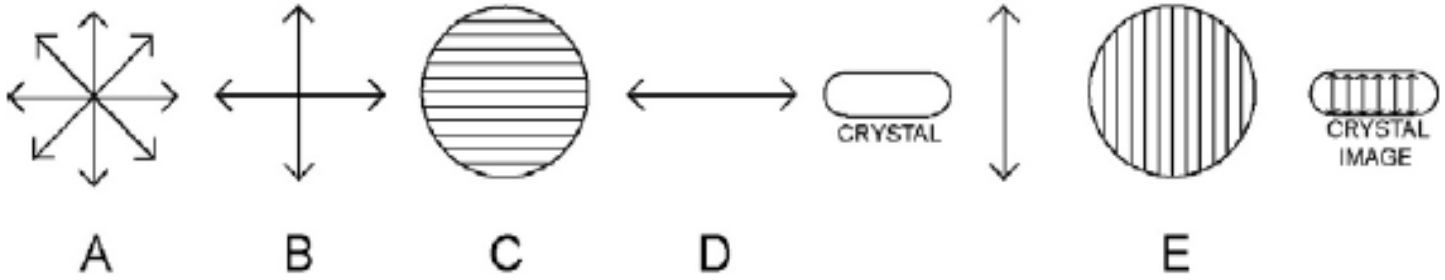

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Crystals, cont.

- Some suggestions regarding technique for crystal identification include the following:

1. *Both wet and stained* cytocentrifuge preparations should be examined.
2. Crystals may be missed with light microscopy by bright light. *Lowering the condenser improves contrast.*
3. No examination for crystals is complete without polarization microscopy.
4. Dust, scratches, and debris must be distinguished from pathologic crystals.

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Crystal Identification

- Although several types of crystals have been noted in synovial fluid, *monosodium urate* and *calcium pyrophosphate dehydrate* are the most frequent.

- Other crystals of pathologic significance include
  1. *basic calcium phosphate*,
  2. *steroid crystals*, and
  3. *cholesterol*.

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Monosodium urate (**MSU**)

- Monosodium urate (**MSU**) crystals are associated with **gout**.
- They may be difficult to visualize with bright light.
- With polarization microscopy, they are 2 to 10 µ thin, needle-shaped, bright crystals with negative birefringence.
- Numerous **MSU** intra-leukocyte crystals are seen in acute gout.
- If gout is suspected clinically but crystals are not detected, some studies suggest that repeat examination after 24 hours of storage at 4 °C improves the diagnostic yield.

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