

# The diagnostic treasures of synovial fluid

If you know what to look for, synovial fluid will either give you a specific diagnosis of rheumatoid disease or enable you to classify the disorder.

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**D**iagnosis of a rheumatic disease depends on a group of nonspecific signs and symptoms.

Many of the individual criteria for the rheumatic illnesses overlap and may complicate the differential diagnosis. For instance, the American Rheumatism Association guide for rheumatoid arthritis, one of the best understood and most common diseases, has 11 diagnostic criteria. Not one of these (even a rheumatoid factor) is diagnostic in itself.

The site of activity in most rheumatic diseases is the joint, and the most easily obtained specimen is synovial fluid, which minimizes friction between the bones and nourishes cartilage.

Normal synovial fluid is clear and viscous and resembles egg albumin. The few cells in normal fluid are mostly mono-nuclear. Turbidity indicates inflammation.

Evaluation of synovial fluid will either provide you with a specific diagnosis or enable you to classify the disorder into one of the four rheumatic disease categories: noninflammatory, inflammatory, septic, and hemorrhagic (Table 1).

## Indications for arthrocentesis

The first step in differentiating joint pain is a physical examination to determine whether the pain is extra-articular or articular. Extra-articular pain occurs on active motion but not on passive-assisted motion, since muscles, tendons, and ligaments are relaxed on passive motion. Articular pain occurs on both active and passive motion.

The remaining steps (Figure 1) depend on synovial fluid examination.

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The basic indication for arthrocentesis, aspiration of synovial fluid, is the presence of a swollen joint in the absence of previously diagnosed disease.

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Indications for removing synovial fluid are shown in Table 2. Because diagnosis on clinical grounds is often incorrect, always examine the fluid at least once in any arthritic patient, no matter how firm you feel about the patient's illness.

Chronic gout, for instance, frequently mimics rheumatoid arthritis. Even in previously diagnosed joint disease an unexplained flare may indicate some other disorder. Patients with pre-existing joint disease have an increased susceptibility to bacterial arthritis.

The persistence of joint inflammation despite "good medical therapy" may indicate that the initial diagnosis was incorrect or incomplete, and you should take another sample to re-evaluate the diagnosis.

The fluid should be routinely cultured if an effusion is present in patients with unexplained fever or infections of unknown origin, and in patients at high risk of infection, such as drug addicts, diabetics, immunosuppressed patients, and those with neoplastic disease.

## Aspiration technique

Arthrocentesis is a quick, safe office procedure that carries little risk of

infection, and less than one in 7,000 aspirations are so complicated.

Standard rheumatology texts and an excellent guide by Steinbrocker and Neustadt<sup>1</sup> list the common approaches to major joints.

The knee, the most frequently aspirated joint, should be approached medially about one-third of the way down from the superior tip posterior to the structure (Figure 2).

Prior to taking the sample, make sure the patient is not sensitive to local anaesthetics. Prepare the joint surfaces with an application of Beta-dine scrub or iodine, and wipe off the area to be aspirated with an alcohol swab.

You won't need sterile gloves unless the patient has leukopenia or an unusual susceptibility to infection.

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To avoid infection, don't touch the area to be aspirated with your fingers.

If you need to feel for landmarks, do so through the alcohol swab. Be careful not to aspirate through an area of cellulitis, since bacteria may be carried into the joint space.

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Before inserting the needle, anesthetize the area with ethyl chloride or similar spray or one percent lidocaine.

If, after taking the synovial sample, you need to inject medication, remove the syringe from the needle already in the joint with a hemostat and attach a new syringe containing the required medication.

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TABLE 1

**JOINT DISEASES**

**Noninflammatory**

- Osteoarthritis
- Osteochondritis dessicans
- Osteochondromatosis
- Traumatic arthritis
- Neuroarthropathy

**Inflammatory**

- Gout
- Pseudogout
- Reiter's disease
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Psoriatic arthritis

**Septic**

- Bacterial infection
- Fungal infection
- Tuberculous infection

**Hemorrhagic**

- Hemophilia
- Trauma
- Pigmented villonodular synovitis

TABLE 2

**INDICATIONS FOR ARTHROCENTESIS**

- Undiagnosed joint disease
- Unexplained flare-up in previously diagnosed joint disease
- Persistence of joint inflammation despite "good medical therapy"
- Effusion in a patient with fever of unknown origin
- Effusion in a patient at high risk to infection
- Effusion in a patient with infection of unknown origin
- Relief of discomfort
- Instillation of drugs

Always evaluate synovial fluid before injecting drugs into a joint, since injection of steroids into an infected joint could be disastrous.

**Specimen requirements**

When collecting specimens, 3 to 5 ml is the preferred sample size, although even a few drops of liquid can be successfully examined for cell counts, differential cell count, and crystals.

The more fluid you submit for mi-

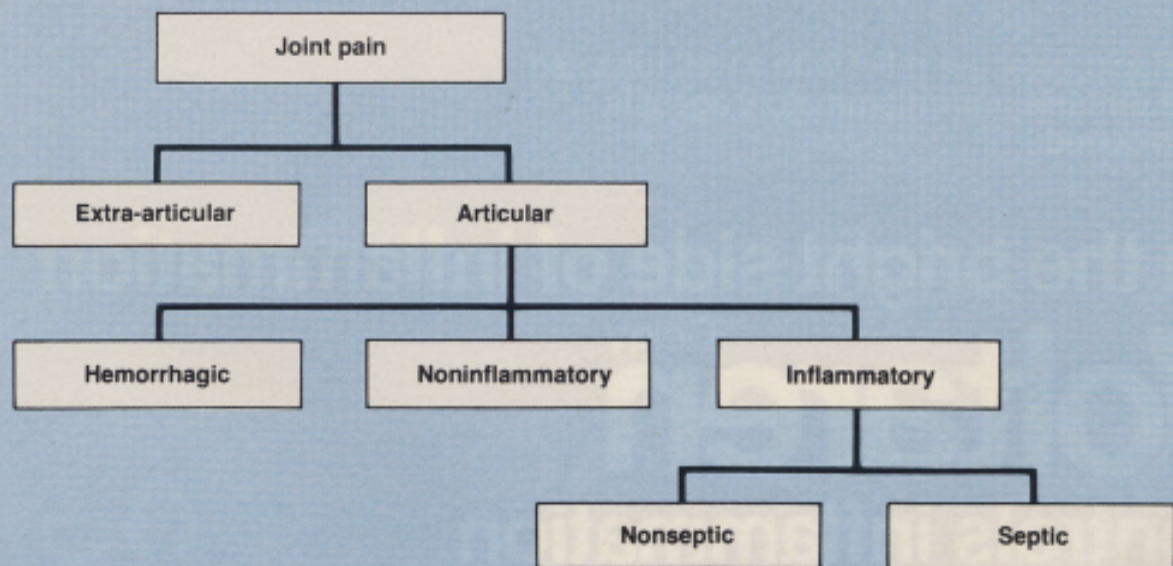
crobiologic culture, the greater the likelihood of a positive culture if bacteria are present.

Collect the culture specimens in a sterile tube. To prevent contamination, change the needle on the syringe when you transfer the specimen to the tube.

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FIGURE 2

**ALGORITHM FOR DIAGNOSING ACUTE JOINT PAIN**



Cell count, differential analysis, and crystal examination of synovial fluid are done on anti-coagulated specimens to avoid clotting of some pathologic specimens that may contain fibrinogen. You should not use oxalate, since it contains crystals that could be confused with pathologic ones.

Some organisms, such as mycobacteria, fungi, and the gonococcus, are notoriously difficult to culture from synovial fluid.

If you suspect the presence of gonococcal organisms, take samples for urethral, cervical, anal, blood, throat and skin vesicle cultures. Such multiple cultures will increase the diagnostic yield about 50 percent in synovial fluid alone to approximately 95 percent.

### Classification by lab test

Laboratory evaluation of synovial fluid will enable you to determine if the fluid is normal (Table 3) or to which pathologic category the disorder belongs (Table 4). Depending on your own facilities, you may be able to do some of the determinations in the office.

You can perform two important tests — colour/cloudiness and viscosity — when you aspirate the fluid.

Evaluate the degree of cloudiness by trying to read a printed page through a tube of joint fluid.

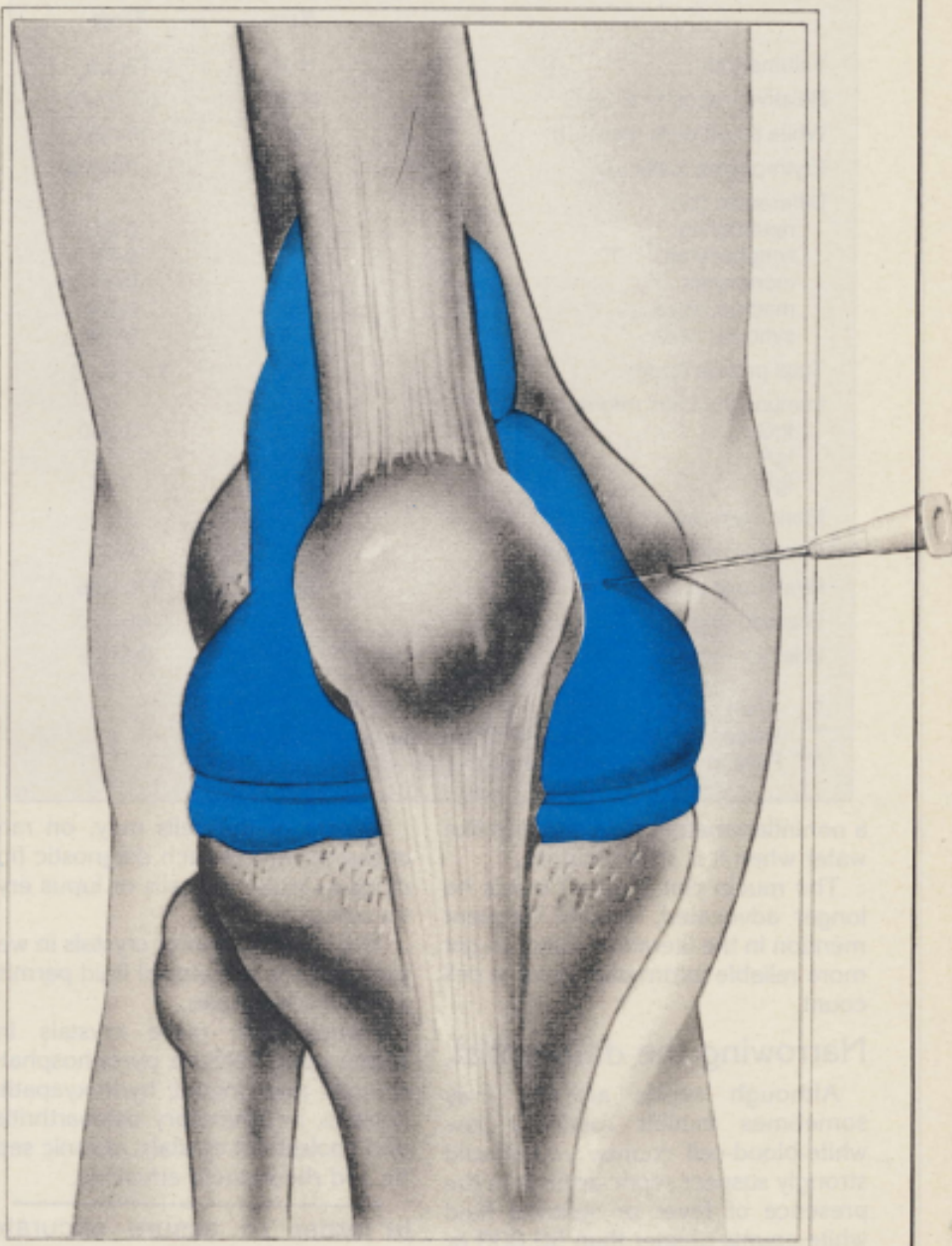
Once the cell count rises above 2,000 per  $\mu\text{l}$ , the turbidity won't permit you to read clearly. The more turbid the fluid, the higher the cell count.

Fluids with white cell counts above 75,000 may resemble pus.

Measure viscosity at the time of aspiration by putting a finger at the tip of the syringe and stringing out the fluid. Non-inflammatory fluids will "string out" longer than 4 cm and will resemble egg albumin in consistency.

You may also drip fluid off the needle and syringe; it will string out if it is

*Continued overleaf*



**Figure 3.** Aspirate the knee joint with a 20-gauge needle inserted at a point 1 to 2 cm medial to the inner border of the patella. Angle the needle slightly posterior and penetrate 2 to 3 cm. When done properly, arthrocentesis carries little risk of infection even without rigid surgical sepsis. Prepare the joint surfaces with an application of Betadine scrub or iodine, and wipe off the area to be aspirated with an alcohol swab. To avoid infection, don't touch this area with your fingers. If you need to feel for landmarks, do so through the swab. Before you insert the needle, anesthetize the area with ethyl chloride spray or one percent lidocaine, making sure that the patient is not sensitive to local anesthetics. Also make sure not to aspirate through an area of cellulitis, since bacteria may be carried into the joint space and cause infection.

TABLE 3

### CHARACTERISTICS OF NORMAL SYNOVIAL FLUID

	Mean	Range
Volume (ml)*	1.1	0.13-3.5
Relative viscosity at 38 C	235	5.7-1160
White blood cells (cells/ $\mu$ l)	63	13-180
Erythrocytes (cells/ $\mu$ l)	160	0-2000
Differential (%)		
neutrophils	6	0-25
lymphocytes	25	0-78
monocytes	48	0-71
macrophages	10	0-26
synovial cells	4	0-12
Total protein (g/dl)	1.72	1.07-2.13
Immunoglobulins (mg/dl)		
IgG	453	33-850
IgA	74	27-177
IgM	37	0-84
Fibrinogen (mg/dl)	0	0
Complement CH <sub>50</sub> (unit/ml)	20**	16-25
Hyaluronic acid (mg/dl)	360	170-405
Glucose (mg/dl)	***	65-120
Uric acid (mg/dl)	***	2.5-7.2

\* Knee

\*\* Values are approximately 10% of plasma values

\*\*\* Fasting values are similar to plasma values

a noninflammatory fluid and drip like water when it is inflammatory.

The mucin clot (Ropes') test is no longer advocated, despite frequent mention in the literature. You can get more reliable information from a cell count.

### Narrowing the differential

Although septic arthritis may sometimes exhibit relatively low white-blood-cell counts, you should strongly suspect septic arthritis in the presence of fever or synovial fluid white counts greater than 50,000 or both.

Occasionally crystalline synovitis and rarely rheumatoid arthritis may cause such an elevation.

Fluids with counts between 2,000 and 50,000 characterize a wide variety of inflammatory arthritides, including septic arthritis.

**Suspected septic arthritis with an increase in mononuclear cells points to a diagnosis of tuberculous infection.**

Review of the cells may, on rare occasion, reveal such diagnostic findings as leukemic cells or lupus erythematosus.

The identification of crystals in wet preparations of synovial fluid permits a specific diagnosis.

Monosodium urate crystals indicate gout; calcium pyrophosphate crystals, pseudogout; hydroxyapatite crystals, inflammatory osteoarthritis; and cholesterol crystals, chronic septic and rheumatoid effusions.

In order to assure accurate identification of crystals, be sure to inform the laboratory of any corticosteroid injections. Besides confusing the diagnosis, steroid crystals may induce a transient inflammatory response.

The laboratory may also detect corticosteroid crystals in some joint-fluid specimens after intra-articular injections.

Their shape depends on the particular preparation the patient has

been taking. Sometimes they mimic sodium urate or calcium pyrophosphate crystals.

You can also use a polaroid microscope to diagnose crystal arthritis rapidly. All you need is two pieces of polaroid (one in the ocular and one in the condenser) and an inexpensive or homemade first-order red compensator.

With a little practice you can instantly diagnose gout or pseudogout.

Interpretation of synovial-fluid glucose level requires knowledge of the patient's simultaneous serum glucose.

Ideally, glucose measurement should be done in the fasting state. After an eight hour fast the normal serum synovial-fluid difference is less than 10 mg/dl; levels 25 mg or more below the serum level suggest inflammation, and differences greater than 40 mg suggest sepsis.

In the usual clinical situation — the nonfasting state — synovial glucose levels less than half of those of concomitant serum specimens indicate a septic process. Rarely, they indicate rheumatoid arthritis effusions.

Although many doctors order protein values, you can get better and less expensive information about inflammation from a white-cell count. Normally, synovial-fluid complement levels are lower than serum levels; in most inflammatory conditions, complement behaves like an acute-phase reactant and becomes elevated. Remarkably high levels are seen, for example, in Reiter's Syndrome.

Complement levels are especially useful in differentiating immune-mediated rheumatic conditions. In rheumatoid arthritis, serum sickness, SBE, and in viral immune-complex arthritis (rubella and hepatitis), complement levels are usually less than one-third of those of simultaneous serum specimens.

In lupus, both serum and complement levels are low, whether C3, T4 or CH<sub>50</sub> levels are measured. (We prefer the first two tests in our laboratory, since they are more stable and easier to perform). The tests are indicated, however, only when there is confusion on clinical grounds and you need further evidence.

The differential diagnosis of an inflamed joint usually includes bacterial

TABLE 4

## PATHOLOGIC CLASSIFICATION OF SYNOVIAL FLUIDS

Test	Normal	Noninflammatory	Inflammatory	Septic	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
Leukocyte count (cells/ $\mu$ l)	<180	200-2,000	2,000-100,000	10,000 to >100,000	>5,000
Neutrophil percentage	<25	<25	>50	>75	>25
Glucose (mg/dl)	blood	~ blood	>25 mg/dl lower than blood	>25 mg/dl lower than blood	~ blood
Culture	negative	negative	negative	often positive	negative

arthritis and necessitates cultures and Gram stains to rule in or rule out the disorder.

Bacterial infections may be superimposed on pre-existing noninfectious joint disease.

**Suspect bacterial arthritis in the presence of corticosteroid administration, diabetes, drug abuse, trauma, needle injections through cellulitis, and extra-articular infection.**

The bacteria most often involved in synovial infections are *Staphylococcus aureus*, *Hemophilus influenzae*, *Neisseria*, B-hemolytic streptococci. Anaerobic bacteria may rarely cause suppurative arthritis.

In certain parts of the country, fungal infections may be a common source of a synovial abnormality.

Cultures are positive in 90 percent of all bacterial arthritis cases but in only 50 percent of gonococcal, tuberculous, and fungal arthritis cases. □

#### Suggested Reading

Steinbrocker, O, and Neustadt, D: *Aspiration and Injection Therapy in Arthritis and Musculoskeletal Disorders*, Harper and Row, New York, 1972.

## Antique electro-magnetic machine presented to Adler Museum

A hundred years or so ago the medical profession had great faith in the curative power of a mild electric shock for a variety of nervous diseases.

Simple electro-magnetic devices were produced for this purpose. The patient held an electrode in either hand, the handle was cranked and a current flowed.

Mr Horst Burckhardt, Managing Director of Uniplan (Pty) Ltd, picked up just such a century-old machine

one day while strolling around the Portobello Road, London.

Feeling that it properly belonged in a museum he asked Sue Ormrod, former Advertisement Manager of 'The Electrical Engineer', to present it to the Adler Museum of the History of Medicine, University of the Witwatersrand, Johannesburg.

Pictured at the presentation are, from the left, Dr Cyril Adler, founder of the museum, Sue Ormrod, holding the machine, and Tony Fry, editor of 'The Electrical Engineer'.

