

# Synovial fluid tests

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## Abstract

Infection, crystal arthropathies, osteoarthritis, trauma and a variety of systemic diseases can all lead to a painful, swollen peripheral joint, septic arthritis being the most serious cause. Synovial fluid (SF) analysis is widely used to aid the diagnosis and management of both acute and chronic arthritis, and can be diagnostic in patients with bacterial infections or crystal-induced synovitis. Physicians competent in joint aspiration should be encouraged to do this unless they are dealing with a suspected infected prosthetic joint, which should be aspirated in theatre under strict asepsis. SF is usually viscous, clear and essentially acellular, but in diseased states, components of the SF can vary in characteristic ways. Although a positive Gram stain and culture may clinch the diagnosis of septic arthritis, the absence of organisms on Gram staining or a negative subsequent SF culture does not exclude a diagnosis of septic arthritis. A previous systematic review of the literature has shown that although no investigation has sufficient sensitivity and specificity to confirm the diagnosis of septic arthritis in all cases, the single most useful investigation is SF microscopy and culture. All junior doctors should gain experience in joint aspiration to save delays in diagnosis.

**Keywords** Analysis; crystal analysis; gout; hot swollen joint; investigations; pyrophosphate arthropathy; septic arthritis; synovial fluid

## Introduction

Synovial fluid (SF) analysis is widely used to aid the diagnosis and management of both acute and chronic arthritis, and can be diagnostic in patients with bacterial infections or crystal-induced synovitis. This article focuses on the indications for aspiration of a joint, the characteristics and components of the SF, and the current UK recommendations for SF analysis.

## Joint aspiration

Any physician competent to do so can perform aspiration of a native joint. Where sepsis is a possibility, this aspiration should be performed urgently. Doctors in training are often reluctant to aspirate swollen joints, citing concerns such as the iatrogenic introduction of infection to a joint or disturbances of clotting (e.g. anticoagulant therapy). It is vital to appreciate that mortality from septic arthritis is around 11%, whereas the risk of

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## Key points

- Synovial fluid (SF) analysis aids in the diagnosis and management of both acute and chronic arthritis, and can be diagnostic in patients with bacterial infections or crystal-induced synovitis
- Joint aspiration should always be performed before commencing antibiotics, and SF sent for microscopy, culture and crystal search using plane polarized light
- Monosodium urate crystals seen with gout are needle-shaped and strongly negatively birefringent, whereas calcium pyrophosphate dihydrate (CPPD) crystals, seen in pseudogout, are rhomboid-shaped and weakly positively birefringent
- The absence of organisms on Gram stain or a negative subsequent SF culture does not exclude a diagnosis of septic arthritis
- No single investigation is sufficiently sensitive and specific to make the diagnosis of septic arthritis in all cases; the single most useful investigation is SF microscopy and culture

iatrogenic infection is approximately 0.01%, and patients will not die from a haemarthrosis.<sup>1</sup> So if in doubt, always aspirate. The only exception to this is suspected sepsis of a prosthetic joint, which must always be aspirated with full aseptic precautions in an operating theatre.<sup>1–3</sup>

Joint aspiration should always be performed before starting antibiotics, and the fresh fluid sample sent to the laboratory for microscopy and culture.<sup>1–3</sup> Polarized light microscopy should be carried out to establish the diagnosis of a crystal arthritis. As artificial crystals can form on refrigeration, samples should be processed immediately or stored at room temperature before analysis.<sup>1</sup>

Repeat aspiration may be necessary in the treatment of septic arthritis, for which aspiration to dryness is recommended.<sup>1</sup> Repeat SF analysis can also be useful in monitoring the response of septic arthritis to treatment, and for the diagnosis of some cases of gout in which the initial aspirate does not contain detectable crystals.

## Indications for joint aspiration

The presentation of one or more hot swollen joints is a common medical emergency, of which septic arthritis is the most serious. A thorough history and physical examination can provide highly suggestive clues, narrowing the differential diagnosis (Table 1). Routine blood tests can also be useful. SF aspiration is, however, the single most important test in aiding the diagnosis.<sup>2</sup>

## Septic arthritis

In light of the significant morbidity and mortality associated with septic arthritis, prompt differentiation from the other causes of an acute monoarthritis is imperative. SF aspiration, if it yields positive results, can be the key to making the diagnosis, with Gram

stain and culture giving guidance to antibiotic therapy. Any patient, particularly if febrile, presenting with a hot swollen joint should be considered as having septic arthritis until this has been ruled out.

### Crystal arthropathies

SF analysis is critical in the diagnosis of the crystal arthropathies gout and pseudogout (pyrophosphate arthropathy). Aspiration of the most affected joint usually yields the diagnosis, but aspiration of suspected tophi can also confirm the diagnosis of gout during the interval between attacks.<sup>1</sup>

### Unexplained joint swelling

When a diagnosis of septic arthritis or a crystal arthropathy is unlikely, the main value of SF analysis is to permit classification into an inflammatory or non-inflammatory category.

### Classification of joint effusions

Table 2 illustrates the classification and some of the possible differential diagnoses of joint effusions.

### Characteristics and components of synovial fluid

SF normally functions as a biological lubricant providing low-friction and low-wear properties to articulating cartilage. A small amount of SF is normally found in all joints. SF is usually viscous, clear and essentially acellular, but in diseased states components of the SF can vary in characteristic ways. An overview of this variation is shown in Table 3.

### Differential diagnosis of septic arthritis and historical clues

Disease	Historical clues
Gout	Acute presentation, previous history of gout in the great toe, family history, trigger drugs such as thiazides
Pseudogout	Presentation similar to but often milder than that of gout, commonly affects the knees or wrists in elderly patients
Inflammatory arthritis	History of psoriasis, inflammatory bowel disease or iritis suggests a seronegative arthropathy
Reactive arthritis	History of gastroenterological or genitourinary symptoms
Haemarthrosis	Develops rapidly after an episode of trauma, history of coagulopathy
Trauma	Recent trauma
Cellulitis/bursitis	Recent trauma or bite
Lyme disease	History of rash, systemic features (e.g. malaise, myalgia and headache, possible exposure to deer tick)

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Table 1

### Types of joint effusions and common causes

Effusion	Diseases
Infective	Bacteria, fungi, mycobacteria
Crystal	Gout, pseudogout
Inflammatory	Rheumatoid arthritis, systemic lupus erythematosus, Reiter's syndrome, ankylosing spondylitis, ulcerative colitis, psoriatic arthritis
Non-inflammatory	Osteoarthritis, trauma, osteochondritis, sickle cell disease
Haemorrhagic	Trauma, haemophilia, haemangioma, anticoagulant therapy, tumours

Table 2

### Colour and clarity

As increasing amounts of plasma and nucleated cells enter the SF, this can give rise to a yellow appearance to the fluid, as is often the case in infective, inflammatory and crystal arthropathies. A rusty-brown to red colour change is indicative of old or fresh blood within the SF. The clarity of the SF can also change, SF becoming more opaque with increased numbers of nucleated or red blood cells or crystals.

### Viscosity

Within an inflamed joint, it is thought that the release of proteolytic enzymes into the SF leads to the decreased viscosity that is generally seen in inflammatory effusions. However, in some cases of septic arthritis, particularly when the fluid is frankly purulent, the SF can be more viscous than normal.

### Gram stain and bacterial culture

Although a positive Gram stain and culture can clinch the diagnosis of septic arthritis, a systematic review by Mathews et al. found that the absence of organisms on Gram stain, or a negative subsequent synovial fluid culture, does not exclude a diagnosis of septic arthritis.<sup>2,4</sup> As such, if clinical suspicion is high, it is imperative to treat as septic arthritis, even in the absence of laboratory confirmation.<sup>1,3</sup> The authors suggest that the gold standard for the diagnosis of septic arthritis is the clinical opinion of a physician experienced in the management of patients with musculoskeletal disease, integrating the clinical and laboratory variables.<sup>1,3</sup>

### Synovial fluid white cell count (WCC)

There has been much controversy over the value of synovial total and differential WCC. A systematic review by Margaretten et al. in 2007 argued that WCC of the SF can provide a simple way of distinguishing between infected and non-infected joints while awaiting the results of the Gram staining and culture. They showed that a WCC  $>100,000 \times 10^9/\text{litre}$  had a sensitivity of 29% and a specificity of 99%, and a WCC  $>50,000 \times 10^9/\text{litre}$  had a sensitivity of 62% and a specificity of 92%, whereas a WCC  $>25,000 \times 10^9/\text{litre}$  had a sensitivity of 77% and a specificity of 73%.<sup>5</sup> The systematic review by Mathews et al. came to the conclusion that the sensitivities of these tests were too low to be clinically useful.

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