



The value of pre-operative aspiration in the diagnosis of an infected prosthetic knee : A retrospective study and review of literature

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The purpose of this study was to compare the results of cultures of preoperative aspiration samples with those of swabs taken intra-operatively. The records of 70 revision arthroplasties of the knee from 69 patients, 49 females and 20 males, were reviewed. The mean age of the patients at time of revision arthroplasty was 67 years (range : 34 to 89). Sixty-eight knees from 67 patients were included. There were 32 true positives, 17 true negatives, 6 false positives and 13 false negatives. This led to a specificity, sensitivity and accuracy of 57%, 84% and 72%, respectively. Based on these findings, pre-operative aspiration has a positive predictive value of 71% and a negative predictive value of 74%.

When the aspiration sample yields a positive culture, the chances are high that the prosthetic knee is infected. When aspiration is negative, infection cannot be ruled out. Our study suggests that, in such cases, a coagulase negative *Staphylococcus* (CNS) infection has to be considered.

Keywords : aspiration ; revision knee arthroplasty ; deep joint infection ; diagnosis.

INTRODUCTION

Latent or low-grade infection should be suspected whenever a knee is painful following arthroplasty. Early acute infection is clinically obvious in most cases : specific local symptoms like redness, swelling, warmth and pain usually go together with fever and a systemic reaction (16, 30). Late chronic

infection with a draining sinus poses no diagnostic problem. On the contrary, subacute or low-grade infection of a total knee arthroplasty (TKA) is frequently a diagnostic problem, and can be misdiagnosed as an aseptic mechanical loosening (11, 16).

There is no single test that can diagnose infection of a prosthetic joint with 100% sensitivity and specificity (42). The diagnosis of infection is based on clinical suspicion, laboratory tests (White Blood-Cell count (WBC), Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP)), aspiration of the joint, plain radiography, arthrography, and radionuclide imaging studies. Investigations should be cost-effective and of minimal inconvenience or risk to the patient, and their number should be limited to those that ensure an accurate diagnosis (42).

The first step in diagnosis is *history taking* : History of fever or illness ? Was the knee red, warm

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or swollen? Recent invasive procedures that could produce bacteraemia, as well as remote sources of infection must be considered (40). Persistent pain typically at rest or at night and progressive stiffness after TKA must raise suspicion of infection (24).

Prolonged postoperative wound drainage, antibiotic (AB) treatment for problems with primary wound healing, and knee stiffness despite extensive rehabilitation efforts may be associated with deep infection (24).

Predisposing factors are rheumatoid arthritis (RA), lupus erythematosus (LE), diabetes mellitus (DM), AIDS, corticosteroids and previous revision surgery (33).

Unfortunately, indiscriminate administration of antibiotics before an appropriate work-up remains a common practice despite clear evidence that this only inhibits subsequent efforts to diagnose deep infection (3).

During *examination*, physical signs such as rubor, dolor, calor, tumour and function deficit may arise attention. The presence of a sinus is very specific for infection of a TKA (4).

Leukocytes counts in peripheral blood are of little benefit in making the diagnosis of an infected TKA. Only 16% of the patients with an infected TKA (21) and 20% of the patients with an infected total hip arthroplasty (THA) (42) had an elevated amount of leucocytes in the peripheral blood.

The *ESR* and the *CRP* level are non-specific markers of acute inflammation. ESR is a measure of erythrocyte rouleaux formation, whereas CRP is an acute-phase reactant produced by the liver. Although the ESR was significantly elevated in nearly all infected prostheses, the diagnostic value of this simple and inexpensive parameter is restricted, because of its very wide variability (26, 41). The specificity of ESR is not very high: 66% of the patients with an elevated ESR had no infection. ESR can be elevated up to one year after uncomplicated hip revision surgery (23). An explanation for the elevated ESR can be an inflammatory synovitis due to the polyethylene or cement particles in the joint (12). Besides, ESR is usually elevated in collagen diseases (10, 20). After THA, ESR was elevated in all cases of periprosthetic infection, but variable in cases of mechanical loosening (41).

Carlsson (9) asserts that an ESR over 40 is an accurate indicator for infection.

Larsson *et al* (23) showed that orthopaedic procedures had a peak CRP response 2 to 3 days after surgery. This was followed by a biphasic rapid decline, and without complications the CRP normalises independently from the ESR.

Monitoring ESR, but especially CRP is useful in the diagnosis of a peri-prosthetic infection (41, 42).

Sequential radiographs may reveal progressive radiolucencies, focal osteopenia or osteolysis of periprosthetic bone, and periosteal new bone formation (30). Radiolucencies are non-specific because these can be seen as well in the presence or in the absence of infection and can be absent during the acute or subacute stages of infection (34, 39). The combination of radiolucency and periosteal reaction is more specific of an infected TKA, than a radiolucency alone on standard radiographs (30).

Arthrography can be useful to identify radiolucencies, abscess cavities, bursae and communicating sinuses (39). Bone loss is more accurately demonstrated by arthrography with a radioactive tracer than by standard contrast arthrography (95.5% versus 73.3%) (8). No data are available comparing the usefulness of these investigations in the detection of a periprosthetic infection. Arthrography is an invasive investigation and bears the real risk of contaminating a suspected prosthesis that was clean. An advantage is that contrast solution can be aspirated for culture, but one should reckon with the bactericidal effect of the contrast-solution.

Some authors believe that a *single-phase technetium-99m phosphate bone scan* is useful in making the differential diagnosis between infectious and aseptic bone loss and loosening of the prosthesis (43, 48). Others report a low specificity (1, 17, 37) and low accuracy (29).

Some studies find that a pre-operative *three-phase bone scan* has a limited possibility to differentiate between septic and aseptic loosening (26, 32). They found mainly an unacceptable sensitivity and positive predictive value of respectively 33% and 30%. This limits the possibilities of the three-phase bone scan and considering the price of the investigation, it is not recommendable as the sole

investigation after the standard radiographs. Again there are studies that question this assertion (21, 22) and claim an accuracy of 100% (21). The controversy thus remains.

The use of *sequential technetium-99m and gallium-67 scans* can increase the possibilities to differentiate (1). Scintigraphy with *indium-111 labelled leucocytes* is very sensitive and specific (28, 34). Other authors cast doubt on this because they found the same or even lower value using this technique in comparison with technetium-99m and gallium-67 scintigraphy (1, 29). The combination of a *sequential technetium-99m and an indium-111 labelled leucocytes scan* improves the accuracy for detecting infection to 95% (31).

The objective of our study is to report our experience with pre-operative aspiration before two-stage revision knee arthroplasty, and to compare our data with the recent literature. We determined the specificity, the sensitivity, the negative predictive value, the positive predictive value and the accuracy of pre-operative aspiration, compared with intra-operative cultures. Additional intra-operative investigations are generally used (analysis of synovial fluid, Gram-staining of specimens of the most inflamed-appearing tissue, histological evaluation of frozen sections of the most inflamed-appearing tissue, and intra-operative cultures of periprosthetic tissue) but are not discussed in this review.

Culture of joint fluid obtained by aspiration is the most important diagnostic modality in detecting infected TKA. A leucocyte count of the aspirated fluid may be useful: a leukocyte count of $> 1.7 \times 10^9/L$ in the synovial fluid or a predominance of polymorphonuclear leucocytes of $> 65\%$ is both sensitive (94% to 97%) and specific (88% to 98%) for the diagnosis of periprosthetic knee infection (44). Molecular genetic techniques can help to identify the pathogens (25, 27).

LITERATURE REVIEW

Different databases were searched for original studies dealing with infected prosthetic knees: Medline (period 1966 to July 2005), Cochrane Database of Systematic Reviews (1988 to July

2005), Cochrane Clinical Trial Register (1988 to July 2005) Database of Abstracts on Reviews and Effectiveness, Current Controlled Trials, National Research Register and Embase (January 1988 to July 2005).

Search terms used were: aspiration, total knee arthroplasty, deep joint infection, and diagnosis. Adequate reporting of at least sensitivity or specificity was the minimal criterion for inclusion in this review. The lists of references of included publications were also manually checked to add studies meeting the inclusion criteria and missed by electronic searches. Abstracts from scientific meetings and review articles were excluded.

The number of reports on aspiration of the knee joint is relatively small, as compared to those that concern the hip, and the dimension of the knee studies is smaller. We only found nine studies, the first one dating back to 1983 (19, 35). Most studies were performed in the USA (table I). The risk of introducing an infection by aspiration in a non-infected knee is estimated at 0.01% (51). Puncture through an area of cellulitis is to be avoided (51).

The sensitivity of a pre-operative aspiration fluid culture varies in the literature from 45% (30) to 100% (12). Because of this wide divergence, the value in clinical practice remains unclear. Only a few authors discuss aspirated knees which appear not to be infected. Most studies do not mention the exact indications of aspiration before a revision arthroplasty. Few, if any, previously reported series clearly state that aspirations were performed in all cases. All but two (3, 15) available studies do not mention the use of antibiotics before aspiration, although everyone agrees that the result of synovial fluid culture dramatically changes while taking antibiotics.

PATIENTS AND METHODS

During a 12-year period from 1992 to 2003, we retrospectively studied all patients who had a revision arthroplasty for an infected TKA. Seventy operations were performed by 6 surgeons in our institution on 69 patients, 49 females and 20 males. One female was operated twice. The mean age of the patients at the time of the revision arthroplasty was 67 years (range: 34 to 89).

Table I. — Studies concerning the value of pre-operative aspiration in the diagnosis of an infected prosthetic knee joint

Study	Year	Location	Knee/Hip	Sensitivity	Specificity	Accuracy
Barrack (3)	1997	U.S.	K	55%	96%	84%
Bekerom, van den	2006	Belgium	K	84%	57%	72%
Duff (12)	1996	U.S.	K	100%	100%	100%
Fuerst (14)	2005	Germany	K	68.8%	96.6%	
Glithero (15)	1993	U.K.	K/H	89%	97%	95%
Insall (19)	1983	U.S.	K	88%		
Levitsky (26)	1991	U.S.	K/H	67%	96%	
Morrey (30)	1989	U.S.	K	45%		
Rand (35)	1983	U.S.	K	82%		
Virolainen (45)	2002	Finland	K/H	75%	100%	
Wilde (46)	1993	U.S.	K	78%		

Patients with an infected but non revised prosthetic knee were not included in the study. For those knees we did not have intra-operative cultures as the reference “gold standard”.

Two patients underwent revision operation after a diagnostic work-up elsewhere ; because aspiration and culture were not performed under the same standardised circumstances, these patients were not considered in our study.

When a patient was currently treated with antibiotics, these were discontinued and aspiration was postponed by 3 weeks. Aspirations were done in the outpatient clinic or in the operating room. In some cases local anaesthesia was used, with Marcaine (Bupivacaine). Fluoroscopic control was never necessary.

Although aspiration is routine in a suspected knee, it was not performed in one haemophiliac patient because of the risk of bleeding and in one patient, who had two fistulas and an obvious diagnosis of infection. These two were excluded from the study.

The patients had a two-stage revision arthroplasty of all components. After removal of the implant, six swabs were obtained at different places and at different times during the operation. Cultures were compared with the cultures from pre-operative aspiration. In some cases, tissue was obtained for histological analysis.

A Gram stain was performed on the pre-operative and intra-operative samples. Molecular genetic techniques were not used routinely to identify the pathogens. Cultures were set on a blood agar medium, chocolate agar medium and a thioglycolate substrate or in some cases haemoculture bottles were used. Growth was identified and tested for antibiotic resistance and sensibility.

A prosthesis was defined as infected when one of the four Bengtsson criteria was present (4).

1. Presence of a sinus at physical examination.
2. Three or more positive tissue cultures intra-operatively.
3. Sepsis with the same pathogen in the blood as in the aspiration fluid.
4. The same pathogen in three or more pre-operative knee aspirations.

Statistics

Software (MS Excel®) was used to collect the data. Sensitivity, specificity and accuracy of a pre-operative aspiration in the diagnosis of an infected prosthetic knee were determined and the positive and negative predictive value of the per-operative aspiration was calculated (table II).

RESULTS

The cultures of aspiration fluid from 68 infected knees in 67 patients were studied : we had 32 true positives, 17 true negatives, 6 false positives and 13 false negatives. This led to a specificity, sensitivity and accuracy of 57%, 84% and 72%, respectively (table III). According to our data the pre-operative aspiration has a positive predictive value of 71% and a negative predictive value of 74%.

In three cases, the micro-organisms identified in the pre-operative aspiration fluid were different from those found in the intra-operative samples.

The pathogens grown from the pre-operative samples were *Saphylococcus aureus* in 12 cases, Coagulase Negative *Staphylococcus* (CNS) in 10 cases, Methicilline Resistant *Staphylococcus*

Table II. — Definitions

Sensitivity	Parameter to indicate the true positives ; the number of patients with a positive aspiration and an infected TKA as a part of the total positive aspirations
Specificity	Parameter to indicate the true negatives ; the number of patients with a negative aspiration and without an infected TKA as a part of the total negative aspirations
Accuracy	Variable to reflect the similarity between the pre-operative aspiration and the intra-operative cultures
Positive predicting value	Rate of infected prosthetic knees as part of the knees with positive pre-operative aspiration
Negative predicting value	Rate of non-infected prosthetic knees as part of the knees with negative pre-operative aspiration

Table III. — Results

Aspiration \ Prosthesis	Infected	Non-infected	Total
Positive	32	6	38
Negative	13	17	30
Total	45	23	68

aureus (MRSA) in 6 cases (in two of these *St. aureus* was found in intra-operative cultures), *Streptococcus pneumoniae* in one case (CNS in per-operative cultures), *Streptococcus agalactiae* in one case, *Streptococcus mitis* in one case and finally *Escherichia coli* in one case (table IV).

All our 13 false negative aspirations appeared to be infected with coagulase negative staphylococci.

DISCUSSION

Every painful prosthetic knee should be considered infected until proven otherwise (7, 27, 45). Infection after TKA can present a diagnostic challenge. When the causative micro-organism can be identified prior to revision, the patients as well as the surgeon are better prepared. The surgeon can start a more specific antibiotic therapy immediately after the intra-operative samples have been collected. Re-implantation of a prosthesis into an unrecognised infected host bed, without appropriate debridement, is likely to result in persistent infection (14).

Today most surgeons prefer revision of an infected TKA in two stages under cover of a specific intravenous AB treatment continued for a minimum of 2 weeks to 6 months (6, 19, 30, 35, 36, 47, 49). Many surgeons use an AB impregnated polymethylmethacrylate spacer block after the infected prosthesis is removed (5, 47). When the micro-organism is identified and an appropriate antibi-

Table IV. — Number of knees classified per micro-organism

Micro-organism	true positive pre-operative aspirations	true positive intra-operative cultures
<i>St. aureus</i>	12	14
CNS	10	11
MRSA	6	4
<i>Str. pneumoniae</i>	1	0
<i>Str. agalactiae</i>	1	1
<i>Str. mitis</i>	1	1
<i>E. coli</i>	1	1

ogram is known pre-operatively, a specific AB can be added to the cement spacer.

Aspiration is an essential part of the work-up for subacute or chronic infection (3, 12). Aspiration is a reliable diagnostic modality. As all other diagnostic tools used in the investigation of a possible infection, pre-operative aspiration does not provide 100% sensitivity and specificity. When a pre-operative aspiration is positive, there is a high chance of an infected prosthetic knee. When the aspiration is negative a CNS infection should be considered. Aspiration is easy to perform in an outpatient clinical setting and the associated costs are low.

In this study of knee aspiration, we observed false positives as well as false negatives. False positives are less frequent. Compared to other studies, the number of false negatives and the specificity (57%) in our study are higher. The percentage of false positives in knee aspirations is much lower than in hip aspirations (2). Barrack *et al* (3) blame, without scientific evidence, the abundant bacterial flora in the inguinal region compared to the knee region. Moreover, in knee aspiration less soft tissue has to be traversed before the needle reaches the joint space and one attempt is usually sufficient to place the needle in the knee joint, in contrast to the

hip joint. Arthrography and fluoroscopy are more often necessary in hip aspiration and are a potential source of contamination.

False negative aspirations can be due to a localisation of the infection on bone, or the bone-cement interface without repercussion on the synovial fluid. Bacterial concentration can reach a higher level on a foreign material than in the synovial fluid due to the presence of a glycocalyx mantle (11, 13, 16). Moreover, a local anaesthetic (marcaine) and saline-solutions used during aspiration could have a bacteriostatic effect and explain some of the false negatives (38).

To limit false negative aspirations, it is recommended to stop antibiotics not three weeks, but one month before aspiration (18, 24) and to repeat the aspiration weekly when infection is highly suspected (18). When the AB therapy is interrupted the patient has to be closely followed to recognise early phases of sepsis. The patient's work-up must include a thorough enquiry about AB use (name of product, duration and end of treatment).

All 13 false negative aspirations in our study were in cases infected with coagulase negative *staphylococci*, possibly because some patients did not stop AB therapy early enough before aspiration as advised and very slow growing CNS remain undetected. The bacteria are no longer present in the synovial fluid but are still at the interface of the TKA.

Following Bengtson's criteria (4) we do not consider one or two positive intra-operative cultures as an indication of a prosthetic infection. When intra-operative cultures are contaminated, we expect a micro-organism of the normal healthy skin flora (such as CNS, especially *St. epidermidis*).

CONCLUSION

When infection is suspected in a prosthetic knee, aspiration should be considered, before further treatment is planned, thus before arthroscopic debridement or revision arthroplasty.

When the result of aspiration is positive, infection of the prosthetic knee is very likely. When the aspiration is negative, infection is not ruled out. According to our study, one has to consider a CNS infection in these cases.

The most important arguments in favour of routine aspiration are its reliability, the low cost, and the ease of execution in an outpatient clinic setting.

When taking the patient's history, it is very important to enquire about the use of antibiotics. Of course it is important, like for every diagnostic tool, to integrate its result in the clinical context, taking account of the results of other technical investigations.

In 4 of the 32 true positive aspirations, the prosthetic knee appeared to be infected with a MRSA. This is an alarming finding.

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