Management of infected TKR


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Infection;
Total knee replacement;
Revision arthroplasty

Summary
Treatment of infected total knee replacement is complex. A thorough clinical and diagnostic assessment is essential followed by careful planning of treatment. The ultimate goal is eradication of infection, and restoration of a pain-free and functional knee. An algorithm based on a literature review is set out.

Introduction
Infection after total knee replacement (TKR) is a potentially devastating complication and is one of the most common reasons for revision TKR. The reported rate of infection following TKR is 1%–2.5%. It results in significant patient morbidity and higher treatment expenses and poses a therapeutic challenge to the surgeon. It has been estimated that surgical treatment of infections following TKR requires 3–4 times the resources of the hospital and surgeon compared with a primary TKR and twice the resources of aseptic revision TKR.

Treatment options are:

- resection arthroplasty, and
- amputation.

We reviewed the literature on the management of infected TKR and discuss various management strategies and the rationale for each and present an algorithm based on current evidence (Fig. 1).

Types of infection
Infection is classified as superficial or deep. The Centre for Disease Control (CDC) criteria for superficial infection are shown in Table 1. Deep infection may be:

- intra-operative positive cultures,
- early infection,
- late or chronic infection, and
- haematogenous infection (Table 2).

The diagnosis of superficial infection is often unreliable; the reliability of the third criteria (Table 1) for superficial infection has been challenged recently because of low inter-observer agreement, arising from the lack of objectivity in judging tenderness, redness, localised swelling and heat.
Thus, the surgeon should have a low threshold for proceeding to debridement of the knee.

**Diagnosis**

A high index of suspicion and careful consideration of several factors is essential in diagnosis.

**Clinical features**

These include knee pain, swelling, reduced knee movements, fever, local erythema, local warmth, wound discharge, and wound breakdown, etc.

Pain is the most common presenting symptom of an infection of a knee arthroplasty. Thus onset of pain different from preoperative pain should raise the suspicion of infection. It typically occurs while the patient is at rest or wakes the patient at night. It is usually not aggravated by weight-bearing, although component loosening giving rise to such pain may be a sequel of infection.

Usually, fever during the first 5 days of the postoperative period is physiological due to the inflammatory process. Thus, pyrexia by itself in the absence of other features of infection does not warrant further investigation during this period.

Even in the absence of infection, the local temperature around a newly replaced knee can remain elevated for up to 6 months postoperatively.

Serous discharge in the first few days following surgery should be addressed with caution. Persistent discharge from the wound beyond 7 days is a serious problem as a superficial discharge may often arise from a deep source of infection.

**Investigations**

Clinical suspicion of infection should be confirmed by investigation, which should initially include a full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and plain radiographs. Wound swabs are discouraged as they complicate the clinical situation by yielding skin contaminants. Empirical use of antibiotics is also condemned by many authors as it leads to multi-drug-resistant infection and it may mask the clinical features of infection long enough to preclude the option of early debridement and prosthetic salvage.

CRP and ESR are non-specific inflammatory markers. Both may be elevated in inflammatory, infectious and neoplastic processes. CRP usually peaks between 5 and 7 days following surgery and then gradually decreases. Any peak after this period should increase the suspicion of infection but it must be noted that it remains elevated for as long as 6 weeks in non-rheumatoid patients following the index.

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**Table 1** Criteria for superficial infection (Centre for Disease Control).

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1</td>
<td>Purulent drainage from the superficial infection</td>
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<tr>
<td>2</td>
<td>The superficial infection yields organisms from the culture of aseptically aspirated fluid or tissue, or from a swab and pus cells are present</td>
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<tr>
<td>3</td>
<td>At least two of the following symptoms and signs of inflammation: pain or tenderness, localised swelling, redness, heat, and (a) the superficial infection is opened by a surgeon to manage the infection, unless the incision is culture-negative or (b) a clinician’s diagnosis of superficial incisional infection</td>
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Thus, the surgeon should have a low threshold for proceeding to debridement of the knee.
surgery. In rheumatoid patients it may take up to 18 weeks to return to preoperative levels. High CRP (> 10 mg/L) levels after these intervals should raise the suspicion of infection. The measurement of ESR and CRP together increases the predictability of periprosthetic infection. Spanghel et al. (1999) have observed that when both the measurements are normal i.e. ESR (< 30 mm/h) and CRP (<10 mg/L), the probability of infection is 0.00; when both tests are positive, the probability of infection rises to 0.83.\(^10,11\)

**Joint aspiration**

When the inflammatory markers are elevated with a clinical suspicion of infection, formal joint aspiration is indicated to establish the diagnosis. Joint aspirate should be sent for Gram staining, and cultured for anaerobic and aerobic bacteria and fungi. Gram staining has a sensitivity of as low as 12%, but a specificity of 98.8.\(^4\) The most common organisms reported are *Staphylococcus(s) aureus*, coagulase-negative *Staphylococcus*, methicillin-resistant *S. aureus*, *S. epidermidis* and *Pseudomonas aeruginosa.*\(^12\)

White cell count with the differential cell count should also be performed on the aspirate. A sensitivity of 75%, specificity of 96% and accuracy of 90% is noted with knee aspirates in diagnosing infection prior to revision.\(^13\) Indeed Duff et al. (1996) reported 100% sensitivity, 100% specificity and 100% accuracy.\(^14\) That said, a negative first aspirate does not rule out infection. If the suspicion of infection remains following the first aspiration, then any antibiotic therapy should be discontinued for a minimum of 10 days to 2 weeks, and aseptic aspiration should then be repeated on at least two further occasions.\(^13,15\)

**Radionuclide imaging**

Radioisotope scans are not particularly useful in the acute postoperative period.\(^5\) \(^11^1\)In-labelled white blood cells in combination with \(^99\)mTc-sulphur colloid marrow imaging is superior to other scans in the assessment of infection in total joint replacement, with a reported sensitivity, specificity and accuracy of 100%, 91% and 95%, respectively.\(^16,18\) (F) fluorodeoxyglucose F-FDG imaging is less accurate. Thus, a combination scan of \(^11^1\)In-labelled white blood cells and \(^99\)mTc-sulphur colloid marrow is currently the investigation of choice in diagnosing periprosthetic infection.\(^16\)

**Current research in diagnostics**

Serum Interleukin-6 (IL-6) has been evaluated as a marker of periprosthetic infection. Increased levels have been shown to be positively correlated with the presence of periprosthetic infection.\(^17\)

It is important to distinguish between a septic and aseptic failures in revision arthroplasty situations.\(^18\) Neutrophils at the site of a *S. aureus* infection express different genes than neutrophils at a site of an aseptic inflammation such as gout. Based on these principles new simple diagnostic tests could be designed to differentiate between a septic and aseptic inflammatory process. This is probably a more sensible and a promising approach towards the diagnosis of periprosthetic infection and may circumvent current problems associated with blood tests and cultures.\(^19\) Further studies are necessary before this can be used clinically.

**Treatment**

Superficial infection should be debrided and treated with appropriate antibiotics (Fig. 1). Debridement includes excision of infected soft tissue and scar in an elliptical fashion down to the joint capsule. Great care must be taken to ensure that there is no extension of infection into the joint.\(^15\) If discharge is persistent or deep infection is suspected, it should be treated aggressively. If the patient is being treated empirically with antibiotics, these should immediately be discontinued and the patient closely monitored with a reassessment in a week to 10 days.\(^13,15\)

Once deep infection is confirmed, treatment involves either prosthetic retention or prosthetic removal. The clinical presentation is usually helpful in determining whether the prosthesis needs removal.\(^4\) When feasible, most patients prefer to retain their existing prosthesis or insertion of a new prosthesis rather than one of the non-prosthetic treatment alternatives.\(^9\)

Prosthetic retention after debridement is indicated in a selected group of patients (Table 3).\(^4,9\) Debridement should be open as arthroscopic debridement is less efficacious.\(^20\) There are two reasons for this. Firstly, exchange of the polyethylene liner cannot be accomplished arthroscopically and secondly adequate debridement cannot be performed.

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
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<tbody>
<tr>
<td>Timing</td>
<td>Positive intra-operative culture</td>
<td>Early postoperative infection</td>
<td>Acute haematogenous infection</td>
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<tr>
<td>Definition</td>
<td>&gt;2 positive intra-operative cultures</td>
<td>Infection within one month after surgery</td>
<td>Haematogenous seeding of site of previously well functioning prosthesis</td>
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<tr>
<td>Treatment</td>
<td>Appropriate antibiotics</td>
<td>Debridement and salvage of prosthesis</td>
<td>Debridement with salvage or removal of prosthesis</td>
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### Table 2  Classification of deep infections.\(^4\)
For open debridement, an elliptical incision should be made excising the scar.

The deep fascia and capsule should be opened through the previous incision. Then a thorough and careful debridement should be carried out. Sometimes a fibrous membrane may need excision. Multiple tissue samples (at least two) should be collected for microbiology and histological examinations. The glycocalyx membrane around the polyethylene liner should be removed and liner should be excised and the knee thoroughly washed with at least 3 L of antiseptic-saline solution. Specific antibiotics should be started based on the culture and sensitivity report. Post-operatively, inflammatory markers (ESR & CRP) should be checked twice weekly. Repeat debridement may be needed if infection does not settle. Multiple debridements can be successful in early infections in a healthy host but if infection persists two-stage revision will need to be undertaken.

### One-stage revision arthroplasty

One-stage revision has been reported as being successful when performed within 4 months of the index procedure, in patients with less than 4 weeks of symptoms, antibiotic sensitive gram-positive organisms, well-fixed components with no radiological evidence of osteitis, and in young healthy patients. If successful it substantially reduces the treatment cost. However, when treatment by irrigation and debridement is unsuccessful, eradication of the infection seems most likely with a two-stage procedure or an arthrodesis.

At operation, intra-operative frozen section is a useful tool in diagnosing infection. At least three samples should be collected from suspected areas such as joint pseudo-capsule and interface membrane. Each sample should be sent for frozen section and cultures. If the polymorphonuclear leucocyte count is more than 10 then active infection is likely, if less than 5 then active infection is unlikely.

### Two-stage revision arthroplasty

Two-stage revision is the most commonly performed operation for the infected TKR. It involves removal of implants and debridement followed by re-implantation at a later date once infection is controlled.

The knee is approached through the previous scar and multiple samples are collected. Intra-operative collection of the samples into Rosenow’s broth has been shown to improve aero-anaerobe recovery. The prosthesis and all the cement should be removed followed by thorough debridement and washout. Many temporary spacers are in use. The antibiotic impregnated cement spacer is favoured as it is associated with a lower incidence of re-infection. Some authors advise use of antibiotic beads in addition to cement spacers. Specific antibiotics should be administered and patient be monitored with twice weekly inflammatory markers. Some authors advocate cultures of the knee aspirate 4 weeks after stopping the antibiotics and before second stage re-implantation. We believe that this is unnecessary as a routine and should be restricted to those patients with a suspicion of persistent infection and in the presence of elevated inflammatory markers. Once infection control is established the second stage re-implantation is performed and multiple tissue samples should be taken at the second stage procedure.

Two-stage re-implantation has been reported as successful in 80.0% of knees with low-virulence organisms (e.g. coagulase-negative Staphylococcus, Streptococcus), 71.4% with polymicrobial organisms, and 66.7% with high-virulence organisms (methicillin-resistant S. aureus).

Re-implantation was successful in 82% of patients with a primary diagnosis of osteoarthritis and in 54% of patients with rheumatoid arthritis (p = 0.024). The success rate was 92% if infection occurred after primary arthroplasty but only 41% if after multiple previous knee operations (arthroscopy, osteotomy, or revision total knee arthroplasty).

### Antibiotic therapy

Empirical antibiotic treatment for suspected periprosthetic infection should be guided by the class of the infection and the findings of Gram-staining. Until final culture results are available, acute haematogenous infections should be treated initially with a combination of cefazolin and gentamicin. All chronic and acute post-operative infections with Gram-positive bacteria and all cases in which a Gram stain fails to identify bacteria should be managed with vancomycin. Infections with Gram-negative bacteria should be managed with a third- or fourth-generation cephalosporin. Infections with mixed Gram-positive and Gram-negative bacteria should be treated with a combination of vancomycin and a third- or fourth-generation cephalosporin. If culture results and other confirmatory tests are not positive by the fourth post-operative day, termination of empirical antibiotic therapy should be considered. Duration of antibiotic treatment during one- or two-stage revision is controversial. Most studies suggest antibiotic treatment for 4–6 weeks. A recent study by Hart et al. (2006) suggested that 14 days of intravenous vancomycin during two-stage revision produced comparable results.

<table>
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<tr>
<th>Table 3 Criteria for debridement and retention of prosthesis.</th>
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<td>Indications</td>
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<tr>
<td>An acute infection within 4 weeks after prosthesis implantation</td>
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<tr>
<td>Late hematogenous infection in an otherwise well-functioning prosthesis</td>
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<tr>
<td>A susceptible microorganism that can be treated by oral antibiotics</td>
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<tr>
<td>A good soft tissue envelope</td>
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<tr>
<td>A well-fixed prosthesis</td>
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They used custom-made antibiotic impregnated cement spacers and antibiotic cement beads based on the culture results of preoperative knee aspirates. They concluded that an extended course of antibiotic does not alter the incidence of recurrent or persistent infection. More multicentric studies are required to confirm the efficacy of these protocols.

Long-term antibiotic suppression alone is an option in selected patients. This should be considered only in extreme situations, as this strategy will not eliminate deep periarticular infection and is generally associated with a very poor prognosis. This treatment should be considered only when all of the following criteria are met:

1. it is not feasible to remove the prosthesis, most often because of a medical condition that precludes an operative procedure,
2. the microorganism is of low virulence,
3. the microorganism is susceptible to an oral antibiotic,
4. the antibiotic can be tolerated without serious toxicity, and
5. the prosthesis is not loose.

The presence of other joint prostheses should be considered a contraindication for this treatment.

Salvage procedures

Arthrodesis and amputation are the last options in patients who have had several attempts at revision. Currently the most common indication for an arthrodesis of the knee is failed infected total knee arthroplasty. Knee arthrodesis can be an effective treatment option for relieving pain and restoring some function after the failure of a total knee arthroplasty as the result of infection.

Permanent resection arthroplasty or amputation usually results in a poor outcome. Amputation is indicated in life-threatening infection, persistent infection, irreparable soft-tissue deficiency, severe bone loss, and the wishes of the patient. Following multiple failed attempts at reconstruction, amputation rates following TKR in general are 0.02–0.18%, but higher rates of up to 6% were also reported. Resection arthroplasty may be best tolerated by patients who are willing to accept loss of ambulation, such as those who are already disabled because of multiple joint involvements.

References


