Ten questions on prosthetic shoulder infection

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Abstract

Prosthetic shoulder infection can cause significant morbidity secondary to pain and stiffness. Symptoms may be present for years before diagnosis because clinical signs are often absent and inflammatory markers may be normal. An emerging common culprit, *Propionibacterium acnes*, is hard to culture and so prolonged incubation is necessary. A negative culture result does not always exclude infection and new synovial fluid biochemical markers such as α defensin are less sensitive than for lower limb arthroplasty. A structured approach is necessary when assessing patients for prosthetic shoulder joint infection. This includes history, examination, serum inflammatory markers, plain radiology and aspiration and/or biopsy. A classification for the likelihood of prosthetic shoulder infection has been described based on culture, pre-operative and intra-operative findings. Treatment options include antibiotic suppression, debridement with component retention, one-stage revision, two-stage revision and excision arthroplasty. Revision arthroplasty is associated with the best outcomes.

Keywords

chronic infection, clinical assessment, *Propionibacterium acnes*, prosthetic shoulder infection, revision arthroplasty, shoulder arthroplasty infection

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Introduction

Shoulder arthroplasty has become increasingly popular over the last decade. In 2013, the National Joint Registry for England, Wales & Northern Ireland recorded 3880 primary shoulder replacements.¹ As a result of this increase in volume, the incidence of prosthetic shoulder infection is expected to rise.

Compared with its lower limb equivalent, the identification of chronic infection around a prosthetic shoulder joint is more challenging. Clinical signs may be absent, biochemical markers normal and the organism difficult to culture.^{2,3} Nevertheless, a logical stepwise approach is necessary when considering the aetiology of persistent pain, and infection should always be included in the differential diagnosis. We pose ten questions with respect to prosthetic shoulder infection, thus providing a structure for the evaluation and management of the symptomatic patient.

1. How common is prosthetic shoulder infection?

The reported infection rate following anatomic total shoulder replacement is 1% to 3.9%.⁴ For reverse polarity designs, it is higher due to an increase in dead space and haematoma formation.^{5,6} Historically, up to 15.3% were affected, although this has improved over the last decade to 1% to 8%.^{7–13} The National Joint Registry recorded 'infection' as the indication in 12% of revision shoulder operations in 2013.¹⁴ The true rate is likely to be higher because some intra-operative specimens may subsequently grow organisms.

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2. What are the risk factors?

A recent multicentre study identified the following risk factors: young age, male sex and arthroplasty for trauma.¹⁵ In contrast to other studies, there was no correlation with the American Society of Anesthesiologist score.^{4,16,17} A further study of over 200,000 patients identified 'superobesity' as a risk factor.¹⁸

It is accepted that revision surgery increases the risk of infection, the incidence of which is as high as 15%.^{19–22} The actual value may be higher because infection may be unrecognized and misclassified as aseptic failure.²³ Reverse designs are six times more likely to become infected compared to unconstrained total shoulder arthroplasty.¹⁵

3. What is the likely organism?

Prosthetic shoulder infections may be acute or chronic. Chronic infections tend to involve low-grade, low-virulence organisms that do not elicit a pronounced inflammatory response.²⁴ In contrast to lower limb joints, the infecting organism for shoulders is commonly *Propionibacterium acnes* (*P. Acnes*), and is present in 17.6% to 60% of cases.^{24–27} Other common organisms include *Staphylococcus epidermidis* and *Staphylococcus aureus* (Table 1).

4. What are the signs and symptoms of chronic infection?

Diagnosing chronic prosthetic joint infection can be challenging. Pain, stiffness or both may be the only symptoms.²⁸ Patients may complain of ongoing inadequate pain relief following index surgery, or of deterioration after an initial successful result. Symptoms may be longstanding, even for several years, given their often low level nonspecific nature.²² In contrast to acute infections, examination of the joint may be unremarkable. Signs suggestive of an acute infection include pyrexia, sinus, increased warmth, swelling and erythema.

5. How should the patient be assessed in clinic?

A thorough history is mandatory, including details of presenting local and systemic symptoms, risk factors, previous operations and related complications, past medical history and medications. There may be a history of wound infection following previous surgery. Clinical signs of infection should be assessed: increased warmth, erythema, swelling, sinuses, reduced range of movement and pyrexia. Other non-infective causes of the symptoms should be considered, such as component malposition, mechanical failure or referred pain from adjacent areas.

A diagnosis of periprosthetic infection should be considered in any patient with unexplained persistent and intrusive pain. Baseline biochemical tests should be requested, including C-reactive protein (CRP), estimated sedimentation rate (ESR) and white cell count. Although specific, these tests are not sensitive.^{2,29} Thus, an elevated result is strongly suggestive of periprosthetic infection (in the absence of another cause), although normal values do not exclude the diagnosis.

Plain radiographs are recommended. Implants should be inspected for subsidence, alignment and osteolysis.³⁰ Loosening of a recently implanted prosthesis increases the suspicion of infection, although images are often normal.³¹ Computerized tomography allows superior assessment of bone stock, bone perforations, component malposition and component migration.³⁰ Radionucleotide bone scans are generally not considered as sufficiently sensitive to be diagnostic of infection.³²

6. What should I do if the patient has persistent unexplained pain but all investigations are normal?

The patient should be offered synovial fluid aspiration and arthroscopic or open biopsy for culture and histology if it is dry.^{3,28} The presence of synovitis, metallosis, loose bodies, adhesions, rotator cuff integrity and glenoid stability should be noted intra-operatively.³ Some studies have suggested that at least three tissue specimens in direct contact with the implant should be obtained, whereas others recommend at least four.^{3,33} We advocate five separate samples, which are collected in a universal container and transported to the laboratory as soon as practically possible. Each specimen should be obtained with a different scalpel and tissue forceps which are then immediately discarded. The common culprit, *P. acnes* is difficult to culture because it is slow growing therefore incubation times should be a minimum of 14 days.^{28,34–36} An even longer incubation time has been suggested, although this increases the risk of contamination.^{37,38} Laboratory processing of the samples and transfer to broth should ideally occur in high-efficiency particulate laminar airflow followed by 16 days of incubation. Frozen section analysis of samples should also be requested and the number of polymorphonuclear leukocytes (PMN) per high power field ($\times 400$) be counted. Traditional diagnostic criteria are less sensitive for *P. acnes* compared to other organisms (50% and 67%) but may be optimized by increasing the threshold to 10 PMN per five high power fields (72% and 75%).²⁴

A relatively recent development involves synovial fluid analysis for biomarkers such as α defensin and

Table 1. Common infecting organisms in prosthetic shoulder infection.

Study and Year	Organism on tissue culture	Number	%
Singh et al. ²⁶ (2012)	Coagulase negative <i>Staphylococcus aureus</i>	3	21.4
	<i>Propionibacterium acnes</i>	3	21.4
	<i>Staphylococcus aureus</i>	3	21.4
	<i>Clostridium</i>	1	7.1
	<i>Pseudomonas</i> spp.	1	7.1
	<i>Bacillus</i> sp.	1	7.1
	<i>Enterococcus</i>	1	7.1
	Methicillin-resistant <i>Staphylococcus aureus</i>	1	7.1
Sabesan et al. ²⁷ (2011)	Coagulase negative <i>Staphylococcus aureus</i>	4	23.5
	<i>Propionibacterium acnes</i>	3	17.6
	<i>Staphylococcus epidermidis</i> and <i>Propionibacterium acnes</i>	2	11.8
	<i>Enterococcus</i>	2	11.8
	<i>Serratiamarcescens</i>	1	5.9
	<i>Pseudomonas</i> and <i>Staphylococcus epidermidis</i>	1	5.9
	<i>Providencia</i> and <i>Enterococcus faecalis</i>	1	5.9
	Unavailable	3	17.6
Piper et al. ²⁵ (2009)	<i>Propionibacterium acnes</i>	7	38.9
	Coagulase negative <i>Staphylococcus</i> spp.	5	27.8
	<i>Staphylococcus aureus</i>	4	22.2
	<i>Pseudomonas aeruginosa</i>	1	5.6
	<i>Corynebacterium</i> sp.	1	5.6
Grosso et al. ²⁴ (2014)	<i>Propionibacterium acnes</i>	18	60.0
	Non- <i>Propionibacterium acnes</i>	12	40.0

interleukin-6. Several studies have considered the role of α defensin in the evaluation of painful hip and knee replacements with a sensitivity and specificity at (or approaching) 100%.^{39–41} These results have not been replicated for shoulder replacements, with sensitivity dropping to 63%.⁴² Furthermore, inadequate volumes were aspirated in 25%. Interleukin-6 may be a useful alternative, potentially avoiding the morbidity of an open biopsy. Frangiamore et al.⁴³ report a sensitivity of 87% and specificity of 90% for shoulder arthroplasty.

7. How do I interpret these results: is it infected?

Isolating the same organism in several tissue samples is strongly suggestive of infection. The difficulty arises when only one specimen is positive as it may represent sample contamination. Conversely, infection may still be present even when cultures are negative.

These diagnostic challenges led to the development of the Musculoskeletal Infection Society (MSIS) Criteria for knee and hip prosthetic joint infections (Table 2).⁴⁴ When applying this classification, a

Table 2. Musculoskeletal Infection Society (MSIS) criteria for hip and knee prosthetic joint infections.⁴⁴

1. A sinus tract communicating with the prosthesis; OR
2. A pathogen isolated by culture from two separate tissue or fluid samples obtained from the affected prosthetic joint; OR
3. Four of the following six criteria exist:
a. Elevated serum erythrocyte sedimentation rate or serum C-reactive protein concentration
b. Elevated synovial white blood cell count
c. Elevated synovial neutrophil percentage (polymorphonuclear leukocyte %)
d. Presence of purulence in the affected joint
e. Isolation of a microorganism in one culture of periprosthetic tissue or fluid
f. Greater than five neutrophils per high-power field in five high-power fields observed from histological analysis of periprosthetic tissue at 400 times magnification

Table 3. Periprosthetic shoulder infection criteria described by Frangiamore et al.⁴³

Category	Criteria*
Definite infection	At least one positive pre-operative or intra-operative finding of infection and multiple positive intra-operative cultures with the same organism OR One positive pre-operative (aspirate) culture and one positive intra-operative culture with the same organism
Probable infection	At least one positive pre-operative or intra-operative finding of infection and one positive intra-operative culture OR No pre-operative or intra-operative findings of infection and multiple positive intra-operative cultures with the same organism
Probable contaminant	No pre-operative or intra-operative findings of infection and one positive intra-operative culture
No evidence for infection	No pre-operative or intra-operative findings of infection and no positive intra-operative cultures

*Pre-operative or intra-operative findings of infection: pre-operative clinical signs (swelling, sinus tract, redness, drainage), positive erythrocyte sedimentation rate or C-reactive protein value, intra-operative gross findings (purulent drainage, necrosis), positive intra-operative frozen section.

diagnosis of infection is still possible, despite negative culture results, as long as there is a combination of other clinical, biochemical and histological positive results. More recently, a shoulder specific classification was described dividing patients into the following groups: definite infection, probable infection, probable contaminant, no evidence for infection (Table 3).^{24,43} Although 'definite infection' still requires at least two positive microbial culture results of the same organism, the identification of an organism in only one sample still allows a diagnosis of 'probable infection' as long as there is at least one positive pre-operative or intra-operative finding of infection. These positive findings are: swelling, sinus tract, redness, drainage, positive ESR or CRP, intra-operative gross findings (purulent

drainage, necrosis) and positive intra-operative frozen section. Thus, a shoulder with no clinical signs of infection, normal inflammatory markers and normal radiographic appearances can be 'probably infected' as long as there is one intra-operative positive culture and a positive intra-operative frozen section result.

8. What are the treatment options?

Treatment depends on the chronicity of infection, isolation of an organism, organism virulence, component stability and patient fitness for surgery. By definition, early infections occur within 3 months of surgery, sub-acute within 3 months to 12 months and late infections after 12 months.²²

If a patient has co-morbidities preventing surgery, antibiotic suppression is the only option. Surgical alternatives include debridement and retention of the prosthesis, one-stage revision, two-stage revision and excision arthroplasty. The former may be considered for early infections with a known low-virulence organism, although there is a high risk of persistent infection,^{22,45} especially if performed arthroscopically.²¹ Weber et al.¹⁶ achieved eradication of infection with the use of vacuum irrigation therapy, although multiple visits to theatre were required. Open or arthroscopic washout for late infections is associated with poor results.²¹ Revision to another shoulder prosthesis, either via one or two stages, is preferable because functional outcomes are superior.^{21,22}

Several studies report good outcomes following one-stage revision surgery.^{46–48} Ideally the organism should be known pre-operatively and be of low virulence. Successful outcomes may still be achieved without an isolate because the organism was unknown in almost 20% of patients in a study by Ince et al.⁴⁷ They state that infection was eradicated in all 12 of their patients at a mean of 5.8 years follow-up. Three required revision surgery for non-infective complications. A success rate of 94% was reported by Klatte et al.⁴⁸ at a mean follow up of 4.7 years. The advantages of this method include immediate reconstruction with reduced morbidity, minimization of adhesions and lower cost.³⁷

An alternative is two-stage revision surgery. Ghijselings et al.⁴⁹ report one fairly satisfactory and two satisfactory results in their case series. Another study reports eradication of infection in all three of their patients, whereas Coste et al.²¹ and Sperling et al.²² achieved this in six out of 10. There was a 20-point improvement in Constant score, although this was less marked than the improvement in the one-stage group. The advantages of this method are that microbiology and histology results are known prior to reimplantation and the explant can undergo sonification (if available) prior to culture.²⁵ Furthermore, the second stage can be scheduled once serum inflammatory markers are normal, which is particularly useful for higher virulence organisms with a more pronounced inflammatory response. The disadvantage is the higher physiological strain for patients, soft tissue contractures and loss of bone stock.^{17,21,50}

The superiority of one- or two-stage revision is difficult to establish because the evidence is mostly limited to case series. A study by Cuff et al.¹⁰ did compare these methods retrospectively. An eradication rate of 100% was reported in both groups and no statistically significant difference in outcome measures were found. A potential criticism, however, is the inclusion of five infected cuff repairs in addition to 17 hemiarthroplasties, which may bias the results.

Excision arthroplasty is the alternative and may be appropriate in patients who are fit for surgery but too frail for prosthesis reimplantation or where there is unreconstructable massive bone loss. Although the procedure provides pain relief, movement is inferior compared to revision arthroplasty, and infection may persist in up to a third of patients.^{16,21}

9. Which antibiotics are recommended?

Decisions regarding antibiotic type, delivery and duration should be made by a multi-disciplinary team on a case by case basis. The involvement of an experienced bacteriologist is mandatory. Isolation of the infecting organism and identification of sensitivities is critical. If unknown, empirical treatment should cover *P. acnes* and Gram-positive organisms (e.g. vancomycin in combination with a β -lactam).⁵¹ *Propionibacterium acnes* is sensitive to fluoroquinolones, β -lactams and rifampicin,⁵² although treatment efficacy may be increased using combination therapy with rifampicin and daptomycin.⁵³ If the organism is resistant to rifampicin or ciprofloxacin, linezolid may be considered.⁵⁴

There are two schools of thought regarding the mode of delivery and length of treatment. We treat these infections aggressively with long-term antibiotics delivered via a percutaneous intravenous catheter (i.e. a PIC line). Inflammatory markers are monitored and, when normalized in conjunction with absent clinical signs of infection, antibiotics are converted to an appropriate oral regime. The alternative approach is based on the view that this is a soft tissue infection because all metalwork and cement has been removed during first-stage revision. Short-term intravenous and oral antibiotics are consequently considered sufficient.

10. How much clinical improvement is likely following either one- or two-stage revision arthroplasty?

Functional scores, pain and range of movement are likely to improve in the mid-term. The aforementioned study by Cuff et al.¹⁰ reported that 90% of patients experience an improvement in shoulder abduction (mean improvement for the whole population from 36.1° to 75.7°) and forward flexion improves for 86% (mean 43.1° to 79.5°).¹⁰ Mean visual analogue score decreased from 6.3 to 3.5. In another study, the Constant score improved by 31.5 following one-stage procedures and by 20 for two-stage procedures.²¹

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