Guideline: Periprosthetic Joint Infection Sampling Guide

Background/ Overview

Microbiological sampling remains a cornerstone for both the diagnosis of periprosthetic joint infection (PJI) and the subsequent antimicrobial management. Where microbiological investigations are performed to a high level, the culture results can assist the surgeon in:

a) Excluding infection and thereby avoid the morbidity of unnecessary surgery and prolonged antibiotic courses

b) Diagnosing infection with a specific pathogen(s) allowing…

   a. Targeted local antimicrobial measures (e.g. antibiotic beads, antibiotic loaded cement spacers, etc).

   b. Targeted systemic antimicrobial therapy (e.g. intravenous and oral therapy including assessment of suitability for rifampicin use).

   c. Consideration of patients suitable for 1-stage exchange surgery.

As with any test, microbiological sampling is neither 100% sensitive nor 100% specific. In order to optimise the quality of information from microbiological sampling all efforts should be made to obtain appropriate specimen types in sufficient numbers from the most appropriate sites.

Contributors

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Purpose

This guideline aims to provide guidance on standard of care microbiological sampling for suspected PJIs.

Scope of Use

This guideline is applicable to orthopaedic RMOs and SMOs who intend on sampling a prosthetic joint with a concern of infection.

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Guideline

A. The timing of empiric treatment antibiotics with respect to microbiological sampling

This section discusses the timing of empiric antibiotics for the treatment of suspected/confirmed PJI. For the timing of administration of usual surgical antibiotic prophylaxis, see the “Intraoperative microbiological sampling” section below.

There are two reasons for the administration of empiric antibiotics to patients with PJI.

1) Stabilisation of the acutely septic patient
2) Maximising the chances of cure (or suppression) of the PJI

Only a minority of patients with PJI require receipt of acute, empiric antibiotic treatment prior to obtaining microbiological samples. In general these patients

present with acute sepsis, haemodynamic instability and/or new end organ dysfunction. Even in these situations, at least two sets of blood cultures should be taken and efforts should be undertaken to obtain microbiological samples as soon as possible after initiating empiric antibiotic treatment (e.g. joint aspirates for easily accessible joints, intraoperative samples from acute operative interventions). For further information including the choice of empiric antibiotics see the "Acute Periprosthetic Joint Infection Guideline".

For the majority of patients with PJI, antibiotics can be safely withheld until after microbiological sampling has been completed. This generally includes 2 sets of blood cultures, joint aspiration (e.g. for knee joints) and intraoperative sampling.

i. Patients undergoing surgery with debridement, antibiotics and implant retention (DAIR)

Patients undergoing DAIR procedures with the intention of cure (as opposed to long-term antibiotic suppression) have been shown to have lower chances of cure the longer operative intervention is delayed.[1] Therefore, there should be a degree of urgency for these select patients to have expedited operative debridement and microbiological sampling. These patients should receive empiric antibiotic treatment immediately after completion of intraoperative microbiological sampling.

Most guidelines would suggest limiting the use of DAIR strategies with a curative intent to patients with acute infections (<3 weeks duration) with stable prostheses and no sinus tract.[2, 3] For further information see the "Surgical Strategies in the Management of Periprosthetic Joint Infections Guideline".

ii. *Patients with chronic PJIs and/or undergoing implant exchange surgery*

Patients with chronic PJIs and/or undergoing implant exchange surgery should have all antibiotics withheld until after completion of all microbiological sampling. Ideally antibiotics should be withheld for a minimum of 14 days prior to sampling. This includes patients who have culture positive, pre-operative joint aspirates.

The rationale for delayed antibiotics in this scenario is as follows:

1) Administration of antibiotics prior to operative debridement (and sampling) is unlikely to have any significant impact on the chances of infective cure for chronic PJIs and/or those undergoing implant exchange surgery
2) Intraoperative cultures remain the most sensitive and specific culture technique. Administration of antibiotics prior to sampling will decrease the culture yield, particularly in chronic PJIs where organism turnover is dramatically reduced.
3) The specificity of preoperative aspirate culture results using intraoperative culture as the gold standard approximates 91%.[4] Intraoperative cultures therefore remain critically important to confirm the validity of aspirate results.
4) Patients with chronic PJIs and/or undergoing elective implant exchange surgeries have a low risk of developing interval sepsis whilst awaiting operation.

B. Preoperative joint aspiration

i. What is the role of preoperative joint aspiration in PJI?

Preoperative joint aspiration can provide invaluable information in cases of suspected PJI.

Although not conclusive alone, culture negative aspirates with low level synovial cell counts (see suggested synovial cell count cut-offs below) provide additional evidence in the exclusion of PJIs.

Culture positive preoperative aspiration cultures can inform surgical options (e.g. 1-stage exchange surgery) and peri-operative antibiotic plans (targeted local and systemic antibiotic choice). In the patient where operative mortality risks are too high, joint aspiration can sometimes represent the only opportunity to obtain joint samples for culture.

Due to a significant rate of false negative and false positive (contaminated) cultures, preoperative joint aspirations do not replace the need for high quality intraoperative sampling.[4]

ii. *Is there a role for intraoperative Gram stain results in the exclusion of PJI?*

No.

Gram stain is a rapid microscopy technique used for identifying the presence of bacteria. A positive Gram stain result requires a significant burden of infection to be present. When positive it is very specific for infection (97-100%) however it is a poor test for exclusion of PJI due to its low sensitivity (19-44%).[5] Gram staining should therefore never be used to exclude PJI.

iii. What synovial cell counts are indicative of PJI?

In the absence of an inflammatory arthropathy (e.g. rheumatoid arthritis), a synovial white cell count ≥1700 cells/μL or a neutrophil percentage >65% is highly suggestive of a PJI in the non-acute setting.[6] In one study of prosthetic knees, a synovial white cell count ≥1700 cells/μL was associated with a sensitivity of 94% and specificity of 88% for PJI.[7]

In acute infection (within six weeks of operation or haematogenous infection), the cell count and neutrophil percentage cut-offs have not yet been determined. One study suggests a synovial white cell count ≥27,800cells/μL (sensitivity 84%, specificity 99%) or a polymorph percentage ≥89% (sensitivity 84%, specificity 69%) as optimal cut-offs

within the first six weeks of primary total knee arthroplasty, however further studies are required to validate these results.[8]

C. Intraoperative microbiological sampling

Intraoperative microbiological sampling represents the gold standard for investigation of suspected PJI. It is the only available technique for determining antibiotic susceptibility of infecting pathogens. Due to the ability to take multiple samples, this reduces the risk of false positive and false negative results as compared to preoperative joint aspirates (a single sample).

i. *Should usual surgical antibiotic prophylaxis be withheld prior to intraoperative microbiological sampling?*

a) Usual surgical antibiotic prophylaxis should be administered on time, prior to microbiological sampling in the following situations…

1) Where there is a low suspicion of PJI
2) Where a PJI has been confirmed and the microbiology is already known

Where there is a low suspicion of PJI and culture results are likely to be negative, usual surgical antibiotic prophylaxis should be given to minimise the risk of surgical site infection. Where the microbiology of a confirmed PJI is already known the benefit of withholding usual surgical antibiotic prophylaxis is felt to be negligible.

b) Usual surgical antibiotic prophylaxis should be withheld until after microbiological sampling for patients with a moderate to high suspicion of PJI.

Where there is a moderate to high suspicion of PJI (including confirmed infection in the absence of an identified pathogen), accurate microbiology is critical to optimising the patients surgical and antibiotic treatment plan and every attempt should be made to identify the infecting pathogen(s).

These recommendations are in line with existing international PJI guidelines.[5, 9]

ii. What specimen types should be taken?

Intraoperative microbiology samples should only consist of deep peri-prosthetic tissue samples and deep joint aspirates (intra-articular fluid/pus).

The following specimen types should NOT be performed.

a) Sinus tract samples

- Sinus tracts inevitably become colonised with bacteria. Sinus tract cultures do not accurately reflect pathogens causing deep infection.[7]

b) Swabs

- Swabs collect a lower infective burden than tissue samples and are more prone to desiccation. Swab cultures are less accurate than tissue cultures which should be taken in preference.[10]

c) Superficial samples.

- Superficial cultures should not be used to infer the results of deep cultures and have no role in the investigation of deep PJI. If superficial samples are taken (e.g. only superficial infection is suspected) they must be clearly labelled as superficial and ideally should indicate why a superficial sample was taken. The interpretation of microbiological results is often performed by clinicians not present in theatre and for whom the site of sampling is critical.

iii. *How many samples should be taken?*

The minimum microbiological sampling for suspected PJI is five deep tissue samples +/- a joint aspirate.

Five deep tissue samples should be taken regardless of whether the clinical suspicion of PJI is high or low. Some centres have found that a lower number of samples submitted may reflect a lower suspicion of PJI,[11] however…

- Where suspicion is low, repeatedly negative cultures strongly support exclusion of PJI and mitigate the risk of wrongly considering contaminants as evidence of infection.
- Where there is a high suspicion of PJI, multiple samples optimise the chances of identifying the infecting organism(s).

Sensitivity and specificity of five deep tissue samples.

a) Sensitivity

The sensitivity of microbiological culture relies on the laboratory receiving samples with adequate bacterial load for culture. Because of the heterogeneous distribution of bacteria in PJIs, multiple cultures minimise false negatives from sampling bias (e.g. taking a sample from a site of low infective burden). Multiple samples are particularly important for chronic PJIs where the infective burden is lower and biofilm associated bacteria are more difficult to culture due to a reduced metabolic turnover.

When five separate tissue cultures are taken and all are culture negative, histological evidence of infection is present in approximately 3%.[11]

b) Specificity

The organisms which cause PJI include common culture contaminants (e.g. coagulase negative staphylococci). False positive rates with a single positive culture approach 30%. When five separate tissue cultures are

taken, growth of an indistinguishable organism from ≥3 samples has a sensitivity of 66% and a specificity of 99.6%.[11]

iv. *How should samples be taken and from what sites?*

Antiseptic and antibiotic lavage should be withheld until completion of microbiological sampling.

Wherever possible the dedicated periprosthetic joint infection sampling surgical packs ("Debridement biopsy set" – see appendix 1) should be used to ensure availability of the necessary equipment for sampling. Fresh equipment (i.e. new forceps, scalpel etc.) should be used for collection of each successive tissue sample, with forceps handed off by assisting nursing staff to avoid contamination.

All five deep tissue samples should be taken deep to the fascia and accurately labelled on the periprosthetic joint infection sampling forms (appendix 2). Exact sites of biopsy will vary depending on operation type (debridement versus explantation will offer very different sampling sites) however samples should be taken from the most abnormal sites. Appropriate targets include synovial membrane, pseudocapsule and bone at the prosthesis interface. The larger the tissue sample the better the yield, however avoid cement debris in samples and do not send the prosthesis itself (prosthesis sonication is not available at CMDHB). All samples should be sent fresh in sterile containers (see appendix 3).

Where there is synovial fluid/pus, an aspirate should be taken. 4mls should be placed into a purple top tube for cell count and differential and the remainder of the sample placed into a sterile container (see appendix 3). The larger the sample, the higher the culture yield accepting the limitations of the collection container. Subsequent processing (inoculation onto agar and into blood culture bottles) will be performed by the microbiology lab staff.

v. What is an acceptable timeframe for samples to reach the laboratory?

Microbiological samples should follow routine transport times from the operating theatre to the laboratory (i.e. hours rather than minutes). There is no role for urgent microbiological investigations to guide intraoperative management.

vi. How should samples be processed in the Microbiology Laboratory?

Following arrival in the laboratory, specimens should be processed as soon as practicable, ie given similar priority to other sterile site samples. Each specimen should be handled separately. Manipulation of samples should be performed in a class 2 safety cabinet to protect the sample from contamination.

Tissue samples should be homogenised (e.g. using mechanical tissue grinders and sterile equipment). Samples should be inoculated onto non-selective media (e.g. blood and chocolate agar in CO_2 and blood +/- enriched anaerobic agar incubated in anaerobic conditions).

Cultures must be performed on both solid agar and in broth cultures. Broth culture has been shown to be more sensitive than solid media alone, however mixed infections may be less easily detected with broth cultures.

The preferred enrichment broth for tissue samples is not defined, although Robertson's cooked meat or thioglycolate broth are commonly used. Blood culture bottles may also be suitable.

Blood culture bottles are the recommended enrichment for joint aspirates. The bottles inoculated will depend on the volume of sample remaining after cell count, differential and inoculation of solid agar. Suggested division of samples by volume are as follows.

Aspirate volume	Division of sample
8- 20mL	Divide evenly between aerobic and anaerobic adult blood culture bottles.
2-7mL	Divide evenly between paediatric and anaerobic adult blood culture bottles.
1mL	Paediatric blood culture bottle.

vii. *How long should samples be cultured for?*

If no potential pathogen has been isolated after 5 days incubation, plates should be incubated for a total of 10 days. Enrichment broths should be subcultured when visually turbid. Visually negative broths (except monitored blood culture bottles) should be terminally subcultured (e.g subcultured on day 4-5 with subcultured plates held for a further 5-9 days).

To assist with identifying mixed cultures, selective agar is suggested (e.g. CNA, MacConkey and selective anaerobic plates for broth subcultures when the direct cultures have already grown staphylococci or gram-negative bacilli).

viii. Identification and susceptibility testing

All organisms growing from prosthetic joint samples should be identified to species level.

When the same species is present in 2 or more samples, susceptibility testing should be performed.

References

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Definitions/Description

Terms and abbreviations used in this document are described below:

Term/Abbreviation	Description
PJI	Periprosthetic joint infection
RMO	Registered medical officer
SMO	Senior medical officer
DAIR	Debridement, antibiotics and implant retention

Associated Documents

Other documents relevant to this guideline are listed below:

NZ Legislation & Standards	None

CM Health Documents	Acute periprosthetic joint infection guideline Elective arthroplasty urinary screening procedure Periprosthetic joint infection sampling guideline Surgical strategies in the management of periprosthetic joint infections
Other related documents	none

Appendices

Appendix 1: Debridement and Biopsy Set

All routine equipment for microbiological sampling of suspected periprosthetic joint infections can be accessed as a dedicated surgical pack labelled “Debridement + Biopsy Set”.

The pack is available in theatres at Middlemore hospital and Manukau Surgical Centre.

Debridement and Biopsy Set Equipment list

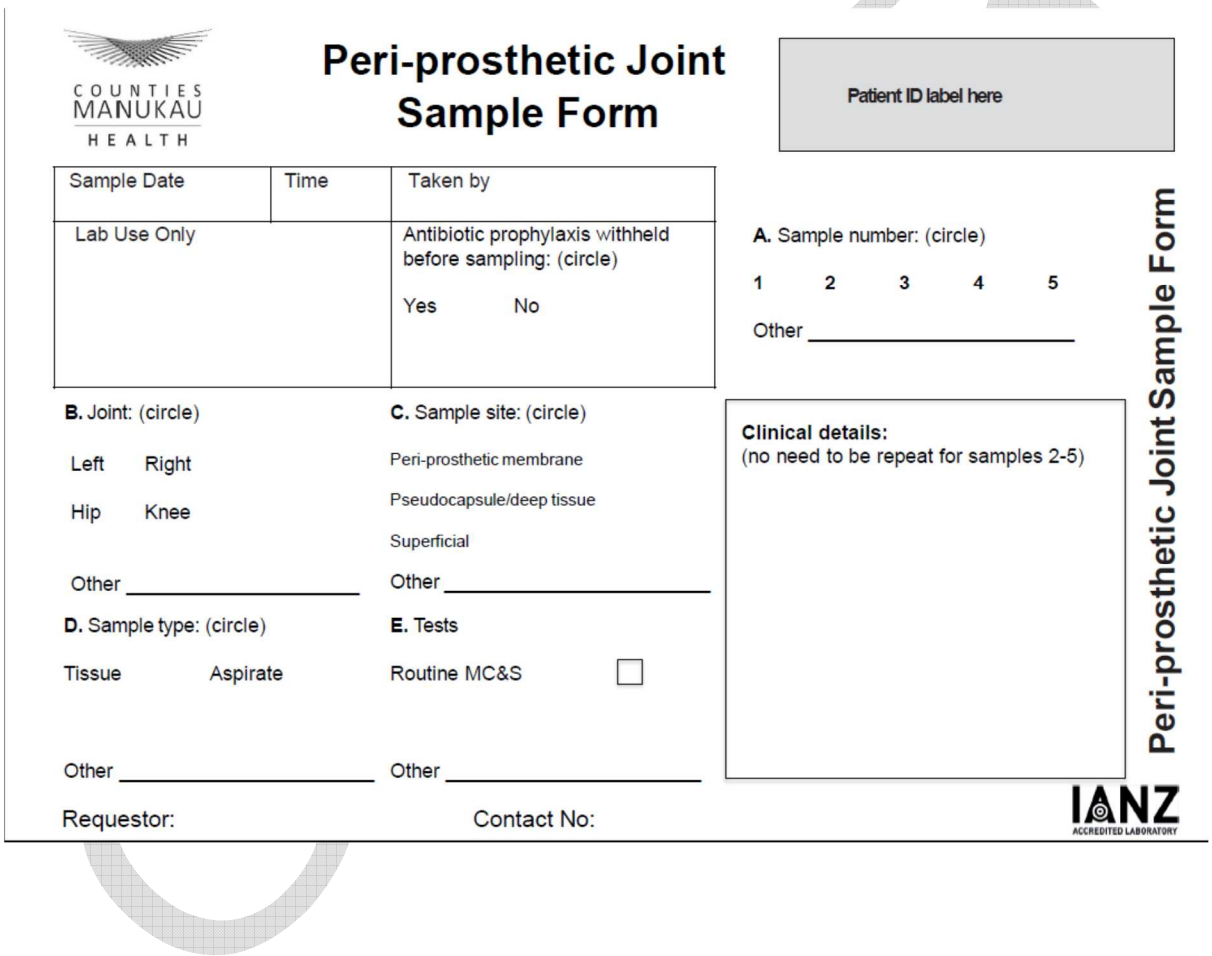
INSTRUMENT	QUANTITY
Russian Mayo Forceps	5
BP Handle NO: 4L	3
Mayfield Bone Rongeur	1
Rushkin Bone Rongeur	1
Hatt Spoon Curette, large 20mm	1
Hatt Spoon Curette, Small 10mm	1

Appendix 2: Periprosthetic Joint Infection Sampling Form

Middlemore hospital utilises a specific laboratory form for microbiological samples of suspected periprosthetic joint infections. A separate form should be used for each sample submitted to the laboratory.

Specific details on the site of sampling are required for each form however clinical details do not need to be repeated as long as adequate detail is provided on sample 1.

The form can be printed, cut out and used from the appendix below if no forms are available in theatres.



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Peri-prosthetic Joint Sample Form

Patient ID label here

Sample Date	Time	Taken by
Lab Use Only		Antibiotic prophylaxis withheld before sampling: (circle) Yes No

A. Sample number: (circle)

1 2 3 4 5

Other _____

B. Joint: (circle)

Left Right

Hip Knee

Other _____

C. Sample site: (circle)

Peri-prosthetic membrane

Pseudocapsule/deep tissue

Superficial

Other _____

D. Sample type: (circle)

Tissue Aspirate

Other _____

E. Tests

Routine MC&S ☐

Other _____

Clinical details:
(no need to be repeat for samples 2-5)

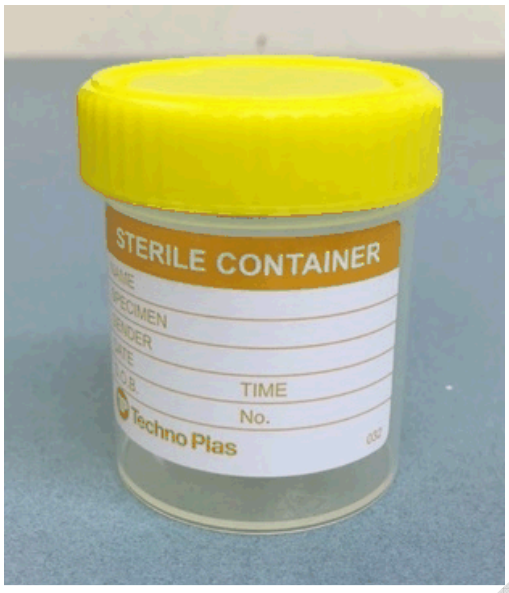
Requestor: Contact No:

IANZ ACCREDITED LABORATORY

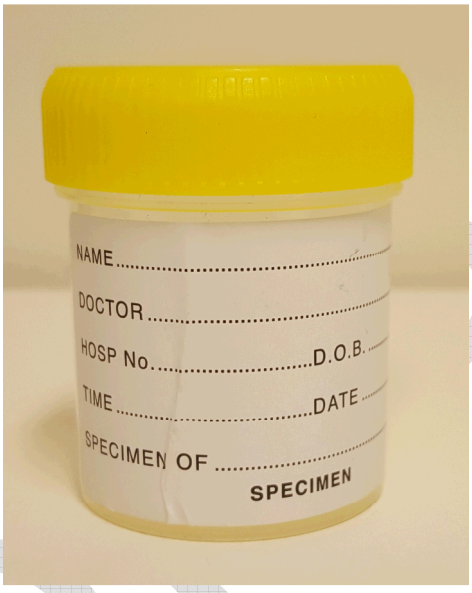
Peri-prosthetic Joint Sample Form

Appendix 3: Sterile containers for microbiology samples

Microbiology samples should all be submitted fresh in sterile containers. A sterile container is shown below. Note the difference between these containers and non-sterile urine collection containers.



Sterile sample container



Non-sterile urine collection container