Signs of a Joint Infection

It is important to distinguish a superficial infection from a true deep infection. That is: an infection in the skin or around the wound, rather than one that is within the joint cavity itself.

Superficial infection usually manifests itself as redness in the skin, which is tender to the touch, and which may become extremely tender over a period of a few days (so-called ‘cellulitis’). When pressed on, the redness goes, only to return as soon as the pressure is removed (blanching). The area involved may be around the wound itself or it may be more distant, most commonly being in the mid-shin area. It should be distinguished from residual redness from the antiseptic solution that is used to prepare the skin. This does not blanch, and often has straight lines delineating it due to the adhesive edges of the dressing which pull off the red tint when removed; thus leaving redness under the central area of the absorbent pad.

If caught early, such a superficial infection may be amenable to oral antibiotics. When more advanced however, and particularly when quite symptomatic, it may best be treated in hospital with intravenous antibiotics. The blood supply to the knee and shin

PROSTHETIC JOINT INFECTION

Dr Keith Holt

Of all the problems that may beset a joint replacement, infection is surely the most concerning, the most difficult to diagnose, and the most difficult to treat. If diagnosed early, simple washout and exchange of the polyethylene component, in combination with appropriate antibiotics, may resolve the issue. In more chronic cases however, removal of all the prosthetic components, and debridement of the joint cavity, is usually necessary. Traditionally, after the infected joint has been removed, antibiotic spacers are inserted and left for 2 to 3 months. This is accompanied by some weeks of intravenous antibiotic therapy which is then followed by a prolonged period of oral antibiotic therapy. When the joint is considered sterile, the antibiotics are ceased: and if no flareup of the infection occurs, and the inflammatory markers measured in the bloodstream remain normal, then a revision replacement can be contemplated. This is known as a two-stage revision, and is successful in 90-95% or so of cases.

In recent times, there has been a drift towards single stage revision whereby the revision replacement is performed at the time of initial removal of the infected prosthesis. The success rate for this, in experienced hands, seems to be around 75-85% of cases. It is to be noted however, that some joints (e.g. the knee) are better suited to this form of revision than others.

Unfortunately, not all prosthetic joint infections can be cured. Some may require lifelong antibiotic suppression, while a few may require either, permanent removal of the joint with or without fusion, or occasionally amputation. These latter procedures, fortunately, are very rarely necessary.

Mild to moderate cellulitis
A superficial infection of the skin, often unrelated to the wound area, and usually ill defined.
area is relatively poor, and the organism involved may be a skin organism that is not overly sensitive to standard antibiotics. Hence, high doses of appropriate antibiotics, some of which only come in intravenous form, may be required.

Importantly, this sort of infection is almost always manageable without surgical intervention and, provided it is attended to early, the underlying joint replacement is not at risk.

**Acute Deep infection** is a more difficult problem. In general, it is not associated by any redness, and the skin may not be tender. Most commonly, it presents with increasing pain, and a decreased ability to bend the knee. If this presents as an acute infection, the most common cause of which is Staph. Aureus (Golden Staph), then this may develop very quickly, often leading to presentation and admission to hospital within 48 hours of commencement. This is an emergency requiring immediate treatment.

While this sort of infection may present within 5 to 7 days of joint implantation, it is in fact more commonly seen later on, perhaps even years later on, where it has developed as a result of spread from an infected, or potentially infected, site elsewhere. Such sites include untreated bladder infections, untreated cuts and abrasions which have become infected, untreated fungal infections of the feet (athlete’s foot) which have become secondarily infected by bacteria, dental work on infected teeth or gums, cellulitis, and so forth.

**Chronic infection** is much more difficult to diagnose. It may take many months to decide that something abnormal is occurring; and frequently, the only symptom may be one of persisting pain beyond what would be considered normal. Even that however, is not always the case, noting that in some instances there is very little pain.

Similarly, there may be very little to find on examination. The knee may not be warm, may not be tender, and the range of motion may be good. Usually however, it will be persistently swollen beyond the normal expected time course, and it will ache.

Common causes of chronic infection are organisms such as Staphylococcus Epidermidis and Propionibacterium Acnes (P. Acnes). Both of these are common organisms which everybody carries on their skin, and both are organisms of low virulence which means that infections may take months to develop, and even longer to diagnose. P. Acnes usually lives around the shoulder area, and hence, this infection is more usually seen in shoulder replacement than in hip or knee replacement. It is very hard to diagnose, and may well be the cause of a number of infections where no organism is ever grown.
How do I know if my joint is infected?

Unfortunately, infection can be very difficult to diagnose. If it is acute, being within a few days of the joint being put in, then an organism may be able to be isolated, either from the joint itself, or from the blood. Similarly, an organism may be able to be isolated from the urine, or anywhere else that may be suspected as the primary source of the infection.

In the chronic situation, it may be very difficult to either isolate an organism, or to decide definitively that that is the cause of the infection. There are lots of reasons for this, but these include the fact that late, slow onset infections are usually caused by weak (often thought of as ‘non-pathological’) organisms. Not only are these hard to culture, but they surround themselves with what is known as ‘biofilm’ which makes them difficult to isolate and culture, and shields them from antibiotics.

A lot of these weak organisms live on all our skins and hence, despite lots of precautions, the culture plates can easily be contaminated by the theatre or laboratory staff. Of these organisms, *P. Acnes* is one of our biggest problems. It is only in recent years that this organism has even been regarded as a pathogen. Because it is carried by everyone, and because it so frequently turns up in culture medium, it is usually regarded as a contaminant; it is difficult to grow, it requires prolonged culture often exceeding a week, and it does not always grow in a standard culture medium. Hence, it has to be suspected and looked for specifically. Fortunately however, there are some better tests that are emerging: better transport medium to bring the organism to the laboratory, and better analytic techniques to look for the organism. Having said all that, it then still has to be decided as to whether or not this is a contaminant or a pathogen. In many instances, this becomes a clinical decision based on the individual case.

In line with the above, investigation of a suspected *P. Acnes* infection requires more than just an aspiration of fluid from the joint. In general, it requires at least one arthroscopy or open biopsy, at which 5 to 10 tissue samples, along with fluid samples, are obtained and sent to the laboratory in an advanced culture medium.

Should I try antibiotics first?

It is important to note that, if there is a suspicion of a joint infection, then no antibiotics should be given prior to aspiration and biopsy: and this may mean a time period of up to 2 months during which time the organisms may grow in sufficient numbers to allow them to be isolated and cultured. Although it may seem sensible to commence antibiotics if an infection is suspected, it turns out that, if this is a deep infection, then oral will antibiotics will, at best, only suppress it, and they definitely will not cure it. In addition, it is important to realise just how critical it is to identify an organism so that specific treatment, including antibiotic therapy, can be commenced. Broad-spectrum antibiotics may control such an infection, but it is much better to focus the treatment on a known organism thereby restricting the antibiotic profile to a narrower range. In general, specific antibiotics will work better than broad spectrum ones.

How can a joint infection be diagnosed?

In the simplest case, which is usually in an acute post-operative infection, one can expect to culture an organism, and thereby proceed to appropriate surgical management, with appropriate antibiotics. Unfortunately, this is the least common scenario, with more chronic, and more late occurring, infections being the majority. For these, diagnosis may be very difficult, and in this situation, an accumulation of circumstantial evidence may be required.

The work-group of the musculoskeletal infection society, in published articles, point out that Peri-Prosthetic Joint Infection (PJI) is one of the most challenging complications to occur after joint arthroplasty. As there is no single accepted set of diagnostic criteria for this entity, this group have proposed a set of diagnostic criteria that may be applied, to try and provide some certainty to this diagnosis.
**Definition of Peri-Prosthetic Joint Infection**

Based on the proposed criteria, as suggested by the work-group, definite PJI exists when:

A. There is a sinus tract communicating with the prosthesis; or

B. A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or

C. Four of the following six criteria exist:

1. Elevated serum Erythrocyte Sedimentation Rate (ESR) and serum C-Reactive Protein (CRP) concentration,
2. Elevated synovial leukocyte count,
3. Elevated synovial neutrophil percentage (PMN%),
4. Presence of purulence in the affected joint,
5. Isolation of a micro-organism in one culture of peri-prosthetic tissue or fluid, or
6. Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of peri-prosthetic tissue at ×400 magnification.

PJI may be present if fewer than four of these criteria are met. The panel also acknowledged that, in certain low-grade infections (e.g., P. Acnes), several of these criteria may not be routinely met despite the suspected presence of a Peri-Prosthetic Joint Infection.

**What other tests are available?**

In addition to standard culture techniques, more advanced techniques looking for micro-organism DNA, RNA or DNA/RNA fragments, are becoming increasingly common.

**PCR (polymerase chain reaction)** is a technique that is used to amplify trace amounts of DNA (and in some instances, RNA) located in any liquid or surface where DNA strands may be deposited. PCR is a method used to amplify (make many more identical copies) of these unique sequences so that they can then be used to determine, with a very high degree of probability, the identity of the source: which in this case will hopefully be the causative organism.

This test is available, and can be performed by most microbiological laboratories (though usually requiring the authorisation of a Clinical Microbiologist).

**Plex ID** is a machine made by Abbott Laboratories which goes one step further in terms of its ability to analyse, identify, and characterise DNA and RNA fragments. In the process of identification it makes use of the PCR technique to amplify the segments of DNA or RNA to be examined. It then subjects these to mass spectrometry in order to get a result. The advantage of such a machine is that it does not rely on culturing organisms, something may take days to weeks, but rather, it can produce results within hours. In addition, it cannot only identify DNA strands that will help determine what organisms are present, it can also identify strands that relate to microbial resistance. This means that, where those strands have been previously identified and are in the data-bank, an aspiration or biopsy can be done early in the day and, within 6 to 8 hours, not only can an organism specific diagnosis be made, but some idea of antibiotic resistance may also be available.

Clearly, this sort of machine is an enormous advance. It allows us to make the diagnosis earlier, more
accurately, and with more information going forwards, Not only does this save time, but it means that the intervention is earlier and more specific, and hence, must improve the chances of definitively treating an infection.

As one can imagine, such machines are expensive to buy, and have significant ongoing running costs. Plus, they require access to a database which is also expensive. Despite its potential advantages therefore, it is currently not available in this state, and perhaps not in this country. There is no doubt however, that this technology will be the way of the future. Certainly, when the price of the machinery and the price of the tests both come down, and the accuracy and specificity of the tests get better, I think we will see these machines in all big laboratories.

Managing an acute infection

An acute infection is one of sudden onset, coming on within days of surgery, or within days of the spread of infection from elsewhere. It presents with acute, and rapidly increasing, pain accompanied by a progressive loss of the ability to flex the knee. Indeed, any attempt to bend the knee, or straighten it, will usually cause pain of significant degree. This is then a cardinal sign of an acute infection, and it discriminates it from other causes of swelling within the joint, be that a bleed or an alternative inflammatory process.

This represents a surgical emergency, not only because of the extreme pain that may be developing, but also because of the toxicity that is created by having a joint full of pus and infected material. Indeed, as the situation worsens, the bacteria and the suppuration (a white cell response) that occurs to try and deal with them, causes increasing pressure within the joint. Ultimately, the barrier of the joint membrane will fail, and the inflamed blood vessels in the wall of the joint will be entered by the bacteria. This then causes a bacteraemia whereby there are organisms in the bloodstream causing systemic toxicity with fevers, falling blood pressure and a progressive unwellness.

If the above continues, the bacteria eventually use the bloodstream as culture medium, thus causing a far more widespread infection known as septicaemia. If allowed to continue, this will cause progressive shut-down of the body’s organs, and may not be reversible.

In this acute situation, the organism is going to be one of the more aggressive, more easily cultured variety. Hence, it is not so important to try and get an organism identified first. Of course, if we were able to identify the organism within 6 to 8 hours, it would be ideal: and we could then be very specific in our choice of antibiotics. It would also not delay surgery more than a few hours, that being something that cannot be delayed too long.

The surgery to wash out the joint should be done urgently so as to decrease the bacterial load in the joint, and so as to also reduce the number of bacteria going into the bloodstream: and hence reduce general systemic toxicity. Unfortunately, this cannot usually be done with the use of an arthroscope because the organisms can hide underneath the polyethylene tray, this being a place where the antibiotics may not reach, and one that can’t be washed out thoroughly. The way forward therefore, is to do an open washout through the original wound, including a removal of the polyethylene tray, a thorough wash of the underlying metal plate, and insertion of a new polyethylene tibial tray. It should be noted that the old tibial tray cannot be used because the organisms can hide on its surface and cover themselves with biofilm, thus surviving both a washout and a cleansing.

If the above is done early, then the chances of success are very good; and probably of the order of about 90%. The surgery is followed by intravenous antibiotics which are used to kill any residual bacteria that haven’t been removed by excision of the damaged tissues and joint washout. When the surgery precedes a microbiological diagnosis, a regime of best guess antibiotic therapy is instituted, usually with the help of a Clinical Microbiologist. When a definitive culture has been obtained, the antibiotic therapy is refined.

Prolonged intravenous antibiotic therapy, usually of some weeks duration, is then undertaken. In order to do this without damaging peripheral veins, a PICC (Peripherally Inserted Central Catheter) line is usually inserted, this being a long intravenous cannula that delivers the antibiotics into the large veins near the heart, or indeed into the heart itself. By doing this, it avoids the damaging effects that intravenous antibiotics can cause to the smaller veins of the arm. Such a cannula can usually be kept in for up to six weeks providing that the insertion site gets adequate care. These cannulae are not generally hard to insert, and that is a process that is usually performed by a radiologist using ultrasound control.

Managing a chronic infection

The situation here is clearly different to managing an acute infection. Firstly, there may be great difficulty in ever obtaining a microbiological diagnosis. If the patient is not particularly unwell, as is often the case, time can be spent trying to identify the organism causing the problem. This may well mean an aspiration to begin with but, most likely, an arthroscopy to obtain fluid and tissue samples for culture and analysis.

Definitive surgery is usually delayed until such time as a firm diagnosis can be obtained. Sometimes of course, the clinical picture deteriorates thereby necessitating earlier intervention, in which case, a broader spectrum antibiotic regime is started in the hope that an organism will subsequently be identified.

As the infection is chronic, meaning that it has been
going on for weeks or months, the likelihood of removing this by washout and polyethylene exchange alone is small. Occasionally, if it appears that this approach may work, then this approach will be taken. More usually however, this situation requires not only the removal of the polyethylene tibial tray, but also removal of all the metal components and the cement. The reason for this is so that all the places that the organisms can hide, including under the metal components or under the cement, have been exposed, thus allowing antibiotics to reach the remaining tissues.

**Two-stage replacement**

This is the standard, well proven, method of dealing with a chronic deep infection.

**Stage 1** involves removal of the original prosthesis in entirety, followed by the insertion of spacers that contain antibiotic. This is accompanied by high dose intravenous antibiotics, usually for several weeks. In some circumstances, depending on the exact organism that becomes isolated, a conversion to oral antibiotics may then be undertaken. During this period of time, inflammatory markers (the ESR and CRP) are measured. Once these are in the normal range, and have remained in the normal range for a week or so, the antibiotics are then ceased.

Over the next few weeks the inflammatory markers are monitored and, if they show no evidence of recurring infection, then the second stage is proceeded with.

Spacers are made of cement (methyl methacrylate). Although people can walk on these, they make for a high friction joint: hence, they will not tolerate prolonged walking without starting to break up. This means that they all need to be removed within a certain time-frame, even if they are functioning well and causing minimal symptoms.

**Stage 2** involves removing the cement spacers, and inserting a definitive prosthesis again. The spacers themselves are glued in with the same methyl methacrylate cement that they themselves are made from. Generally, they are cemented in loosely such that the cement is not pushed into the interstices of the bone too far. This therefore means that removal is not too difficult, albeit that the cement spacers have to be chipped away bit by bit. This process creates multiple loose pieces which can then be easily removed from the bone.

Once the spacers have been removed, along with any loose cement, a definitive revision prosthesis can be inserted. Sometimes it is possible to re-implant a primary type prosthesis again, but often, during the processes of debridement, insertion of spacers and subsequent removal, there is significant loss of bone and soft tissue. For this reason, it is more likely that the best option is not to use a primary prosthesis, but rather, to use a revision prosthesis: and the outcome studies would suggest that, in most situations, this is the best option.

A revision prosthesis usually involves the use of stems which go into the marrow cavities of each bone to provide extra stability. In addition, the prosthesis selected may, in itself, be more ‘constrained’ - to increase the stability of the joint itself. There is a whole range of prostheses made allowing progressive increases in stability right up to, and including, a rotating hinge prosthesis. In the latter, the femoral and tibial components are linked together with a hinge mechanism which provides ultimate stability. The hinge takes the place of both cruciate ligaments and both collateral ligaments. It is called a rotating hinge because, despite the stability provided by the connecting mechanism, the tibial component is allowed to rotate, both internally and externally, on the femoral component, thus providing more normal knee function.

Insertion of a definitive revision prosthesis can be
quite difficult because of reduced exposure to the joint. Once the knee has been opened and closed two or three times, the tissues become thickened and stiff, thus making it very difficult to retract these to provide adequate exposure. If the exposure has to be increased to allow the prosthesis can be inserted, then the commonest way of doing this is to take off the tibial tubercle with the patella tendon attached. This means that the entire extensor mechanism (quadriceps tendon, patella, patella tendon and tubercle) can be moved out of the way.

The upside of creating adequate exposure is that it allows the surgery to proceed in an optimal manner. The downside of moving the tibial tubercle is that it has to be replaced at the end of procedure. Generally however, this is not too difficult, the tubercle being able to be screwed back to the residual tibia. This has to be done by angling the screws so that they miss the tibial stem which has been inserted. Frequently, the screws leave some residual symptoms, so they are often removed a few months down the line when the bone has fully healed.

As one would expect, the second stage revision surgery is followed by a period of antibiotic therapy; initially being intravenous but then being followed by a period on oral antibiotics. This regime may take some weeks to complete, and will depend on clinical improvement as well as improvement in the inflammatory markers such as the CRP and ESR.

The success rate of a two-stage revision replacement is in the order of 90% to 95%, but it is not 100%. Nevertheless, it remains the gold standard in terms of removing the infection. The problem of this technique however, is that it requires two major surgical procedures; and the resulting functional outcome is certainly not as good as a primary knee replacement. The tissues are thickened, scarred and stiff, so the knee does not bend as well as it did following the initial replacement. In addition, those thickened tissues may well be symptomatic in their own right causing some aches and pains with use, particularly when using a bent knee for activities such as stair climbing, cycling, and so forth.

Single stage revision

This technique is not new but, in recent times, it has been gaining in popularity. In essence, it misses out the first step described above where spaces are inserted. The advantage of this is that only one surgical procedure is involved and, as a consequence, the soft tissues are much more pliable, allowing better access for surgery, and leading to better function afterwards.

This procedure involves a removal of the infected prosthesis, a thorough debridement of the infected joint (including any draining sinus that may have worked its way through to the skin), followed by insertion of a definitive prosthesis. In order to achieve this, it is very important that the organism concerned has been identified pre-operatively and, usually, this is done by arthroscopic harvesting of knee joint fluid and tissue to be sent off for analysis.

At the time of surgery, fresh tissue and fluid samples are sent for further analysis and culture. Antibiotics specific to the organism that is believed to be the major causative agent are then commenced. Once the knee has been adequately debrided, and the infected prosthesis and cement removed, the resulting cavity can be filled with surgical packs which have been soaked in antibiotic solution. These are then left in situ for around 30 minutes to allow the antibiotic to soak up into the ends of the bone and into the soft tissues surrounding the joint.

Once the above stage has been given enough time to work, the packs are removed, the joint is re-debrided, and the definitive prosthesis inserted. This is then followed by a period of intravenous antibiotic therapy which, in some parts of the world, is now for a period as short as 1 to 2 weeks. Whether or not this is followed by a period of oral antibiotic therapy is controversial, and it may be that these do not make any difference to the eventual outcome. These treatment algorithms however, are not set in concrete. They are based on small series of patients, with varying types of infection, and with varying degrees of severity. This means that the surgery, and the post-surgical antibiotic therapy, is still designed on a case-by-case basis by the Surgeon and the supervising Clinical Microbiologist.
The likelihood of success of a single stage revision seems to be between 75% and 85%, depending on the nature of the infection, the ability of the surgeon to adequately debride it at the time of revision, and the susceptibility to antibiotic therapy of the organism concerned. Whilst not providing as higher likelihood of success as a two-stage procedure however, its benefits remain significant. It is anticipated that, as this procedure becomes more widespread, protocols will become better, and outcomes will improve. It is likely therefore, that for most people, this will represent the method of choice for the primary management of a chronic infection involving a prosthetic joint.

**The cost of treating prosthetic joint infection**

It is estimated that it costs between $150,000 and $250,000, depending on which health system is involved, to manage each and every prosthetic joint infection.

Clearly, given the rising numbers of joint replacements that are performed, it behoves us to try and prevent infection by every means possible. Nobody believes that every infection can be avoided, and particularly not in diabetics, those with poor blood supply to the limb, those with bad skin disorders which may carry a heavy burden of skin organisms, haemophiliacs, those with other bleeding disorders, and so forth. Despite this, there is a strong push from health funds in the Western World to not fund such revision surgery. Rather, there is a move to pass all of the blame for this complication to the Surgeon and the Hospital. In essence, whilst there may be some rationale for this, and whilst this may force both Surgeons and Hospitals to maximise their efforts to reduce infection, it is likely that the number of infections will never be zero.

Current infection figures suggest an incidence of 1% or less. In good hands, in a good hospital, this should be 0.1% or less (i.e. - less than 1 in 1000 cases).

**Preventing prosthetic joint infection**

There are a number of important factors:

**Patient factors**

1. Controlling blood glucose (diabetics)
2. Controlling any bleeding tendencies, including interference with blood clotting caused by medications, fish oils etc.
3. Maintaining clean healthy skin, which includes preoperative treatment of skin disorders such as psoriasis
4. Dealing with any required dental work prior to surgery
5. Dealing with any background or chronic infections (such as a urinary tract infection) prior to surgery
6. Skin preparation prior to admission using an appropriate anti bacterial wash

**Operating room factors**

1. Creating a clean room by the use of laminar flow air-conditioning and high-pressure air curtains. This provides uniform, directional, non-turbulent airflow at consistent velocity which should not mix with the general room air
2. Using a HEPA (High Efficiency Particulate Air) filter through which the air can be distributed to the operating room. These should have a minimum filtration efficiency of 99.97% and be designed to remove particles greater than 0.3 µm
3. Use of ultraviolet sterilisation of the air, both within the operating room, and entering into the operating room
4. Restricting the opening and closing of doors into the operating room which can introduce particles and turbulent air that may reach the surgical field. This has been shown to have a direct correlation to the number of post-operative infections
5. The use of spacesuits for all those working in the operative field (within the laminar flow zone). These keep all skin particles derived from the surgical scrub team away from the zone above the operating table
6. Regular assessment of particle density and CFU (colony-forming units) within the operating room, something that is recommended every year or so

**Surgical factors**

1. Double skin preparation, prior to commencement, with a suitable antimicrobial solution – usually containing both alcohol and chlorhexidine
2. Use of waterproof drapes which do not become permeable when wet, and do not allow passage of small particles and microbes across them. Nowadays, these are made of treated paper and are disposable. They also have elastic seals where the limb passes through them, and sticky edges where necessary, so as to isolate the surgical field
3. Minimal handling of the skin with instruments
4. The use of antibiotics: peri-operatively, topically in the wound, and in the cement
5. Quick and efficient surgery, something that requires a team that is used to working together. It is known that the longer the instruments are exposed, the higher the risk of contamination
6. The use of mono-filament (rather than braided) sutures in the layer between the joint and the superficial tissues
7. The use of a mono-filament sub-cuticular suture for skin closure, avoiding the use of staples and other devices that pierce the skin
8. No drains