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Infection with spinal instrumentation: Review of pathogenesis, diagnosis, prevention, and management

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Abstract

Background: Instrumentation has become an integral component in the management of various spinal pathologies. The rate of infection varies from 2% to 20% of all instrumented spinal procedures. Every occurrence produces patient morbidity, which may adversely affect long-term outcome and increases health care costs.

Methods: A comprehensive review of the literature from 1990 to 2012 was performed utilizing PubMed and several key words: Infection, spine, instrumentation, implant, management, and biofilms. Articles that provided a current review of the pathogenesis, diagnosis, prevention, and management of instrumented spinal infections over the years were reviewed.

Results: There are multiple risk factors for postoperative spinal infections. Infections in the setting of instrumentation are more difficult to diagnose and treat due to biofilm. Infections may be early or delayed. C Reactive Protein (CRP) and Magnetic Resonance Imaging (MRI) are important diagnostic tools. Optimal results are obtained with surgical debridement followed by parenteral antibiotics. Removal or replacement of hardware should be considered in delayed infections.

Conclusions: An improved understanding of the role of biofilm and the development of newer spinal implants has provided insight in the pathogenesis and management of infected spinal implants. This literature review highlights the mechanism, pathogenesis, prevention, and management of infection after spinal instrumentation. It is important to accurately identify and treat postoperative spinal infections. The treatment is often multimodal and prolonged.

Key Words: Biofilm, infection, instrumentation, spinal surgery

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INTRODUCTION

Instrumentation, now an integral component in the treatment of numerous spinal pathologies, is correlated with a 2-20% infection rate. The ability to manage postoperative wound infections has become, therefore, more critical and challenging, as they are positively associated with extended hospitalizations, increased morbidity and healthcare costs, poorer long-term outcomes, and greater dissatisfaction with the initial operative procedure.

Nevertheless, there are no universally accepted protocols for treating deep wound infections utilizing spinal

instrumentation. Traditionally, it was thought that spinal instrumentation can act as a *locus minoris resistentiae* for bacteria and therefore explanation of the hardware was critical. However, more current practices vary in terms of the need for implant removal. This manuscript reviews the mechanism, pathogenesis, prevention, and management of infection following the application of spinal instrumentation, and reports on how biofilms impact these infections.

COMPREHENSIVE LITERATURE REVIEW OF INSTRUMENTED SPINAL INFECTIONS

A comprehensive review of the literature from 1990 to 2012 was performed utilizing PubMed and several key words: Infection, spine, instrumentation, implant, management and biofilms. Current articles that reviewed the pathogenesis, diagnosis, prevention and management of instrumented spinal infections were identified.

Epidemiology and risk factors for spinal infections

The incidence of surgical site infections (SSIs) after adult spine surgery varies from 0.7% to 20% [Table 1].[9,10,13,15,17,22,26-28,41,47,56,70,79,88,89,96,104,120,150,154] Although the type of spinal surgery most significantly correlates with infection rates, there are multiple other preoperative, intraoperative, or postoperative factors that also contribute to the risk of infection following spinal fusions; age, male sex, steroid therapy, diabetes, smoking, American Society of Anesthesiology (ASA) score, obesity, malnutrition, presence of comorbidities, and previous surgery [Table 1].[5,23,38,41,45,70,76,82,84,97,98,122,123,142]

Table 1: Risk factors for surgical site infection

Risk factor type	Patient-specific factors	Surgery-specific factors
Preoperative	Advanced age Male sex Steroid therapy Diabetes mellitus Tobacco/alcohol use High ASA score Obesity Malnutrition Immunocompromised state	Preoperative hospital stay Prior surgery Trauma Tumor/malignancy
Intraoperative		Length of surgery >5 hours Posterior approach Number of levels operated Instrumentation Implant material (i.e., Titanium vs stainless steel) Use of allograft Blood transfusion Use of cell savers Use of microscope/O-arm/C-arm open surgery as opposed to MIS Staged surgery
Postoperative	Urinary/fecal incontinence Poor wound care Postoperative ICU stay	CSF leak

ASA: American Society of Anesthesiology, ICU: Intensive Care Unit

The risk of intraoperative/postoperative infection is increased by utilizing a posterior surgical approach, applying instrumentation, using allograft, requiring a blood transfusion, and longer operations. The utilization of intraoperative equipment (e.g., surgical microscopes, fluoroscopy, intraoperative computed tomography [CT]) also increases the risk of infection through breaches in sterile technique. Additional strict adherence to proper postoperative wound care is also critical in minimizing the risk of postoperative wound infections.[38]

Surgical factors contributing to spinal infections

Multiple factors increase the rates of infection following spinal surgery.[62,109,110,112,122] These include the staging of surgery (multiple sequential operations), operative time >5 hours, blood transfusions, use of allograft, and a greater number of operated levels Direct intraoperative bacterial contamination of the surgical wound from the local milieu is another important factor that contributes to early postoperative spinal infections. A higher infection rate is also related to the introduction of spinal instrumentation and is variously attributed to; increased wound exposure to air (longer surgical duration), greater soft tissue dissection, and increased muscle/skin retraction. Furthermore, the longer the implants are exposed to air the greater the risk of infection; thus the relevant instrumentation trays should not be opened until it is time to place the implants.

Attributes of closed suction drainage to limit spinal infections

The use of closed suction drainage is thought to lower the risk of SSI as even small postoperative hematomas can provide a medium for bacterial overgrowth. Although routine postoperative drainage of spinal wounds does not uniformly decrease the incidence of early postoperative spinal infections, Ho *et al*. established that the failure to drain wounds correlates with a significantly higher risk of delayed spinal infections.[17,18,62,72,102]

Increased infection risk with posterior spinal instrumentation

A well-recognized risk factor for the development of postoperative spinal wound infections is the utilization of posterior instrumentation. However, this finding is largely based on suboptimal retrospective analyses; only two studies actually document a clear, statistically significant increase in infection rates associated with the use of spinal instrumentation.[23,30,41,45,70,76,84,85,97] While instrumentation itself increases the likelihood of developing a SSI, its correlation with longer surgical times and more extensive posterior exposure independently contribute to higher infection rates.[81,82,97,98] Dissection and retraction of the

posterior musculature also devascularizes the paraspinal muscles, increases the potential for blood loss, and results in larger dead spaces, which also contribute to the risk of infection.

Lesser risk of infection with anterior spinal instrumentation

In contrast, anterior spinal exposures are correlated with a reduced risk of infection as exposures typically traverse relatively avascular tissue planes, and avoid significant muscle dissection.[48,84,97,98,154] It has yet to be determined whether minimally invasive spine surgery (even with instrumentation) is associated with lower infection rates vs. open surgery.[96,98,101,128]

Risk of infection may vary with type of implant and susceptibility to biofilm

The risk of infection may also vary with the type of implant due to an increased susceptibility to the development of biofilm.[6,129,149,152] This topic is discussed in detail later in the manuscript.

Nonsurgical factors increase the rate of postoperative spinal infections

There are multiple nonsurgical issues that appear to increase the rate of postoperative spinal infections. Olsen *et al*. performed a multivariate analysis involving 2316 spinal procedures and found that the following variables significantly increased the likelihood of postoperative infections; diabetes, suboptimal timing of prophylactic antibiotic therapy, elevated pre-or postoperative serum glucose levels, obesity, and two or more residents on a case.[98]

Timing of administration of preoperative antibiotics increases postoperative infection risk

The timing of administration of preoperative antibiotics is strongly correlated with an increased risk of postoperative infection. Ideally, preoperative prophylactic antibiotics should be administered within an hour of surgery (e.g., cephalosporin except in penicillin allergic patients); administration up to 15 minutes prior to the incision may be even more effective.[10,15]

Postoperative incontinence increases postoperative infection rate

Postoperative incontinence following laminectomy and/or fusion has also been reported to be independently associated with increased risk of postoperative infection.[98]

Spinal surgery for tumor resection increases spinal infection risk

Spinal surgery for tumor resection is also independently associated with an increased risk of postoperative infection.[98]

Early postoperative spinal infections

Definition of early spinal infections

Early infections, defined as those occurring within a month of surgery, are attributed to the intraoperative inoculation of the surgical wound with the microorganism. They typically become evident within 2-3 weeks of surgery.

Symptoms and signs of early postoperative spinal wound infections

The signs and symptoms of early postoperative spinal wound infections may include pain, fever, erythema, swelling, warmth, tenderness, and wound drainage. Pain may herald the development of infection particularly when it is escalating in nature. Fever is an unreliable parameter, and often absent. Wound drainage is common for both superficial or deep SSI, and may be present in up to 90% of patients.[110]

Virulent pathogens responsible for early postoperative spinal infections

Early postoperative spinal infections are most frequently due to relatively virulent pathogens such as *Staphylococcus aureus*, beta-hemolytic streptococci, and aerobic Gram-negative bacilli. *Staphylococcus aureus* is the most common bacteria responsible for early postoperative infection after spinal surgery.[13,19,41,45,70,75,97,120,131,143,153] The majority of the cases are due to methicillin-sensitive *Staphylococcus aureus* (MSSA), however, the incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) is escalating.[75,76] Although the majority of infections are due to a single pathogen, a polymicrobial process may involve 10-50% of cases.[81,118]

There has been an increase in the frequency of infections caused by Gram-negative bacteria, and other organisms such as *Pseudomonas aeruginosa*, *Escherichia coli*, Enterobacter, and Acinetobacter.[41,65,67,98,118]

Delayed infections

Although there is no standardized definition for delayed or chronic postoperative spinal infections, many studies have defined these as occurring between 10 days to more than a year after the index procedure/surgery.[9,78,116] Although some authors define delayed infections as those occurring once the original surgical site has healed, most accept the definition of delayed infections to mean those occurring 3-9 months postoperatively.[25,58,59,62,120,146] Furthermore, patients with delayed infections accompanied by spinal instrumentation typically present several months to years later with chronic pain, implant failure, or lack of adequate spinal fusion.[16,27,114,146,148] Although constitutional symptoms may be the only indication of infection, local findings such as increased pain at the incision site and tenderness to palpation of the soft tissue under the incision are usually present. Wound drainage can also occur in delayed spinal infections.[16,27,114,146,148]

Majority of delayed instrumented spinal infections (0.2-6.9%) Occur in scoliosis patients

The majority of delayed infections following instrumented spinal fusions (range 0.2-6.9%) occur following scoliosis surgery.[16,27,56,114,146,150] Factors

promoting the risk of delayed infections after scoliosis surgery include: Failure to use a drain, the necessity for intraoperative blood transfusion, the use of bone allograft, intraoperative and hematogenous seeding, and metal fretting (leading to a sterile inflammatory response).[9,46,95,129,146] Of interest, the incidence of delayed infections does not appear to directly correlate with the number of levels fused.[61,130]

Delayed infections are often culture negative vs. Early infections
Delayed infections are more often culture negative vs. early infections because as they are frequently caused by less virulent pathogens (e.g., Propionibacterium acnes, coagulase negative *Staphylococcus epidermidis*, bacillus, and micrococcus species).[16,27,56,94,114,115,146,150] For some time Propionibacterium was considered a culture contaminant but now it is clear that this organism is responsible for a significant number of late infections following implantation of spinal instrumentation.[14] It has been suggested that postoperative sterile inflammatory processes may create a favorable environment for the growth of low virulence organisms such as Propionibacterium.[57] It is a facultative anaerobe and a fastidious organism that can be hard to detect unless the cultures are evaluated for a prolonged period of time.[12,16,27,114,146,150] A list of organisms responsible for early and late SSIs are summarized in Table 2.

Table 2: Causative organisms for early and late surgical site infections

Authors [reference #]	Causative organisms (%)	Early infection (<90 days) vs. late infection (>90 days) (%)	Monomicrobial vs. polymicrobial (%)
Weinstein *et al*.[143]	*Staphylococcus aureus* 73.9 *Staphylococcus* epi 10.9 *Enterococcus* faecalis 6.5 *Pseudomonas* species 4.3 *Proteus mirabilis* 2.2	Early 93.5 Late 6.5	Monomicrobial 76.1 Polymicrobial 23.9
Cahill *et al*.[18]	*S. aureus* 47.5 MSSA 24.6 MRSA 16.4 Sensitivity unavailable 6.6 *S. epidermidis* 19.7 *Pseudomonas aeruginosa* 16.4 *Escherichia coli* 14.8	Early 52.5 Late 47.5	Monomicrobial 65.6 Polymicrobial 34.4
Fang *et al*.[40]	*S. aureus* 56.3 *S. epidermidis* 37.5 *Enterococcus* 22.9 *E. coli* 8.3 *P. aeruginosa* 8.3 *Enterobacter* 6.3 *Streptococcus* 4.2 *Candida* 2.1	Early 83.3 Late 16.7	Monomicrobial 52.1 Polymicrobial 47.9
Kim *et al*.[72]	MRSA 35 MSSA 30 No growth 20	Early 70 Late 30	Monomicrobial 100 Polymicrobial 0
Levi *et al*.[78]	*S. aureus* 52.9 *Streptococcus* sp. 5.9 *Proteus mirabilis* 5.9 Mixed organisms 29.4 No growth 5.9	Early 94.1 Late 5.9	Monomicrobial 70.6 Polymicrobial 29.4
Clark *et al*.[26]	Culture x 3 days-No growth 90 Culture x 7 days- *S. epidermidis* 50 *Propionibacterium acnes* 25 *Enterococcus* 16.7	Early 0 Late 100	Monomicrobial 100 Polymicrobial 0
Muschik *et al*.[89]	*S. aureus* 13.3 *S. epidermidis* 4.4 No growth 82.2	Early 0 Late 100	Monomicrobial 100 Polymicrobial 0
Richards *et al*.[107]	*Propionibacterium acnes* 52.2 *S. epidermidis* 17.4 *Micrococcus varians* 4.3 *S. aureus* 4.3 No growth 21.7	Early 0 Late 100	Monomicrobial 100 Polymicrobial 0

Biofilm

Certain bacteria can adhere to the surface of implants to form a biofilm, defined as a microbial derived sessile community characterized by cells that are embedded in a matrix of extracellular polymeric substances, which they produce.[51-53] Within biofilm, bacterial cells become irreversibly attached to the substratum and/or each other. Biofilm can, therefore, assert some protection for microbial organisms against antibiotics, phagocytes, and other cellular and humoral immune responses.[29,34] Furthermore, bacteria within biofilm often demonstrate an altered phenotype with regard to growth rate and gene transcription (both of which can impact diagnostic and management strategies).[34-41,43-47,51,53,63]

Common organisms have predilection for forming biofilm

Unfortunately the common organisms implicated in postoperative infections after spinal instrumentation like *S. aureus*, coagulase negative Staphylococcus and Propionibacterium, have a predilection for biofilm formation.[28,34,36,52,53,55,63,69,132] Biofilm-associated organisms grow more slowly than planktonic organisms, and biofilm confers a measurable decrease in antimicrobial susceptibility on the associated organisms.[28,34,36,52,53,63,69] Important prerequisites for the formation of biofilms are the inherent characteristics of the substratum (e.g., surface roughness and the relative hydrophobic tendency of instrumentation), which have a significant effect on the rate/extent of adherence, and susceptibility to the formation of biofilm by microorganisms.[11,34,36,50,55,132,137] Additionally, the presence of a seroma or hematoma can alter the surface properties of an implant thereby impacting the overall susceptibility of bacterial adherence and biofilm formation; this complicates the generalization of *in vitro* study findings to the clinical arena.[43,108]

Implant materials exhibit variable susceptibility to biofilm

Implants vary in their susceptibility to the development of biofilm. Bacterial adherence to the implant, a prerequisite for biofilm formation, was studied *in vitro* by Schildhauer *et al*.[121] These investigators reported that *S. aureus* is less likely to adhere to pure titanium as compared with titanium alloys and polished stainless steel; there was, however, no difference in adhesion based on the roughness of the metal surface.[121] Interestingly, tantalum was the least susceptible to adherence. Arens *et al*. reported a lower infection rate with pure titanium as opposed to stainless steel using an animal model; they concluded that this could be related to adherence.[6] A clinical study by Soultanis *et al*. found that the implant material directly impacted the infection rate; titanium had a lower infection rate than stainless steel.[129] Polyethyletherketone (PEEK), a polymer now widely utilized for spinal surgery, shows a relatively high propensity for biofilm formation and, therefore, infection.[149,150]

Biofilm makes identification of causative infectious organism difficult

Biofilm can increase the difficulty of identifying the causative infectious organism. Analysis of nonspinal prosthetic infections with suspected biofilm show that multiple cultures of peri-implant tissue may not be accurate, and can result in missed diagnoses.[8] Even when an organism is identified, the standard antimicrobial susceptibility testing may not correctly predict the efficacy of an agent against biofilm associated bacteria.[29,34,51,52,63,124] The major problem is that, in general, cultures of biofilm (scraped from the implant) do not grow. Sampredo *et al*. reported a technique of vortexing and sonification followed by culturing, which was more sensitive than peri-implant cultures obtained from removing spine implants.[119] This material may provide important information in the future using newer molecular or immunologic methods.[29]

Age of biofilm influences susceptibility to antibiotics

The age of the biofilm influences the susceptibility of instrumented fusions to antimicrobial therapy.[34] The cells within biofilm are protected from host defenses, and mature biofilm infections are even less susceptible to antimicrobial agents than recent biofilm infections. This can be clinically important as in early infections, as the immature biofilm if often less tenacious, and, therefore, can be adequately removed/debrided, thus facilitating eradication of infection while preserving the spinal instrumentation.

Potential future role of antimicrobial coated implants against formation of biofilms

As the role of biofilms has been increasingly recognized in implant-related infections, strategies to prevent bacterial adherence and subsequent biofilm formation are being developed and hold promise. Antimicrobial coated implants represent a potential advance, but many factors need to be addressed before this strategy is applicable to the clinic.[29]

Prevention of spinal implant infection

Perioperative antimicrobial agents utilized to limit infection of spinal implants

Identification of multiple risk factors that contribute to infections following instrumented spinal fusions helps decrease the infection risk. Barker *et al*.'s meta-analysis (utilizing pooled data from six randomized control trials [RCTs]) documented a lower incidence of infection following spinal surgery utilizing antibiotic prophylaxis (Odds ratio, 0.37, 95% CI 0.17-0.78, $P < 0.01$).[10] They recognized the efficacy of a single preoperative dose of a prophylactic antibiotic providing Gram positive coverage. Notably, no other findings proved significant (e.g., the antibiotic utilized, the dosage protocol, the schedule for redosing antibiotics, and the duration of postoperative prophylactic antibiotics).[10,32,33,60,67,71,148]

Other intraoperative adjunctive measures to prevent infection of spinal implants

Little has been published on other adjunctive measures utilized to prevent postoperative SSIs in spinal surgery. The "no shaving" data for spinal and other procedures and the use of sophisticated air filtering systems have been positive.[23,54] Betadine irrigation was deemed superior to saline irrigation in two RCTs.[24,25] Recently, dispersing powdered Vancomycin into the wound just prior to closure has been reported to significantly reduce the risk of postoperative infections; this technique has been rapidly adopted despite the absence of a well designed RCT or case control study.[92,134]

There were no sound data, other than provided by Ho *et al*., to support the benefit of closed suction drainage to prevent acute postoperative surgical-site infection after spine surgery.[17,62,72,102] Finally, data regarding the use of silver-impregnated dressings is sparse, and provides only low evidence to support its widespread efficacy in spinal surgery.[38]

Diagnosis of superficial vs. Deep spinal infection

Infections following instrumented spinal fusions can be superficial or deep. By definition, superficial infections are confined to the dermis and subcutaneous tissue, while deep infections are those occurring below the fascia.[120] Superficial infections generally present within the first 2 weeks after surgery, and are accompanied by fever, increased wound pain, erythema, swelling, warmth, tenderness, and/or drainage. Deep infections may present in a manner identical to superficial infections or may develop long after the surgery (e.g., >6 weeks, to months or years later).

Laboratory evaluation of infected spinal instrumentation

Laboratory studies are an important part of the evaluation of infected spinal implants. Erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and total leukocyte count (TLC) are routinely ordered when there is a suspicion of a postoperative infection.[44,73,74,135,136] ESR and CRP values are, however, considered more useful than TLC in the detection of spinal infection.[90] For each variable, a rising trend in the postoperative period is more suggestive of infection than a single abnormal value as these markers are routinely elevated in the early postoperative period even without infection. Notably, postoperative CRP levels are higher after instrumented spinal surgery vs. simple decompressions. CRP is also an excellent marker for infection as it is relatively stable for each individual, has a narrow normal range, which is minimally impacted by medications and other pathologies (excluding liver failure), and is determined via a quantitative test with predictable kinetics.[44,68,103,136,139] The CRP level generally peaks 2-3 days after surgery and returns to baseline within 2-3 weeks while ESR peaks around day 5, and returns to normal more gradually over 3-6 weeks.[91,139] Despite their utility, these indices can be elevated with/without infections at any site, (e.g., surgical vs. nonsurgical) so a single abnormal value has low specificity for infection and is of little/limited clinical significance. Alternatively, appreciation of the normal kinetics (e.g., a rising trend instead of the expected fall after a postoperative peak) and recognition of abnormal elevations should raise clinical suspicion for postoperative wound infection. Conversely, normal ESR and CRP values may help confirm the absence of infection.

Diagnostic imaging of infected spinal implants

Plain radiography, CT, and magnetic resonance imaging (MRI) are routinely ordered when an infection is suspected. Early implant loosening, rapid loss of adjacent level disc height, and abnormal soft tissue swelling are indirect markers of infection on plain X-rays, but are often not seen until a few weeks after the onset of infection. CT delineates hardware position and bony changes more accurately than plain radiographs, and CT also shows fluid collections, it is not as sensitive to infection as MRI.

MRI scans with/without contrast: Great value in diagnosing infection

MRI scans without and with contrast are of great value in diagnosing discitis, osteomyelitis, and epidural abscesses after spinal surgery. However, it is not often possible to distinguish a sterile seroma from a purulent collection (e.g., differentiation between postoperative changes and infection) utilizing early contrast enhanced CT or MRI studies following the implantation of spinal instrumentation.[8,13,93,106,127]

Radionuclide imaging not primary choice for diagnosing postoperative spinal infections

The use of radionuclide imaging is not a primary imaging modality for diagnosing postoperative spinal infections as recent surgery can result in positive studies even when no infection is present. However, an early negative radionuclide scan may indicate that an infection is not likely present. Alternatively, these scans may prove an effective diagnostic technique for diagnosing delayed infections.

Radionuclide tracer imaging of infected spinal implants

Bone scintigraphy utilizing multiple radionuclide tracers

There are several means by which the skeleton may be imaged using radionuclide tracers. Bone scintigraphy is most commonly performed using technetium-99m (Tc-99m) methylene diphosphate (MDP). Three-phase imaging is the radionuclide procedure of choice for evaluating osteomyelitis in bone not affected by any underlying condition. This tracer binds to the hydroxyapetite crystal; uptake is a function of blood

flow, and the rate of new bone formation. There is a dynamic sequence (e.g., the flow or perfusion phase), followed immediately by the acquisition of static images of the region of interest (e.g., the blood pool or soft tissue phase). The final phase consists of static images of the region of interest obtained 2-4 hours after the initial injection of the tracer. Focal hyperperfusion and hyperemia with increased delayed bony uptake is diagnostic for osteomyelitis. Recent surgery or the presence of hardware may result in a false positive three phase scan.[99] Images can be obtained the next day (referred to as a four phase study) to improve the specificity. Tracer uptake in normal bone usually stops after 2-4 hours but it may continue for several hours longer in the setting of osteomyelitis. Four phase studies are more specific but less sensitive that three phase scintigraphy and have an accuracy of about 85%.[4,66]

Gallium-67 citrate used to localize spinal infections

Gallium-67 citrate (Ga-67) has been used to localize spinal infections for many decades. Within 24 hours, 25% of the radionuclide is excreted by the kidneys; further excretion occurs via the large intestine. Two to three days after the injection, 75% of the tracer is still in the body where it is equally distributed in the liver, soft tissues, and bone.

Utilizing gallium-67 and bone scintigraphy to diagnose osteomyelitis

Gallium accumulates at sites of infection or inflammation via a variety of mechanisms, and osteomyelitis is usually diagnosed by combining Ga-67 with bone scintigraphy.[99] A positive test requires two factors; the two tracers are spatially incongruent, and the relative uptake of the Gallium is greater than that of the bone agent. If the study is negative for osteomyelitis when the gallium images are normal or when the distribution of the two agents is spatially congruent, but there is less uptake of gallium than the bone agent.[99] The overall accuracy of gallium/bone imaging is 65-80%, but the need for two isotopes and multiple imaging sessions make this technique difficult.[87]

Labeled leukocyte imaging of spinal infections

Labeled leukocyte imaging represents a significant advance in the ability to detect spinal infections. The uptake of labeled cells depends on several variables; intact chemotaxis, the number and type of cell labeled, and the cellular response to the infection. A total white blood cell count of 2000/mL is required to obtain satisfactory images. Usually the majority of the labeled cells are neutrophils. However, this technique is less sensitive for processes in which the predominant cellular response is not neutrophilic (e.g., tuberculosis).[42,83,100] There are additional techniques that utilize combined leukocyte/bone marrow imaging and other nuances related to the isotope used.[99]

Fluorine-18 fluorodeoxyglucose-positron emission tomography utilized to diagnose spinal infections

Fluorine-18 (F-18) fluorodeoxyglucose-positron emission tomography (FDG-PET) may also be used to identify spinal infections. However, this technology is expensive and requires sophisticated equipment thus making it not widely available. Similar to radionuclide studies, the utility of FDG-PET is limited in the acute postoperative setting, but is useful for establishing the diagnosis of delayed infections surrounding instrumentation.[133]

Ultrasound detects postoperative fluid collections and helps guide fluid aspiration

Although ultrasonography can detect postoperative fluid collections, it cannot determine whether these represent noninfectious vs. infectious processes (e.g., sonomorphological criteria such as internal echo structures, septation, demarcation from the environment, and reaction of the surrounding tissue). Ultrasound is, however, useful in guiding aspiration of fluid collections resulting in a high diagnostic accuracy.[77]

Management of infections following spinal surgery with instrumentation

The management of infection after spinal instrumentation is controversial, and requires careful consideration of the two most critical variables: The duration of antimicrobial therapy and whether or not the implants should to be removed. Treatment paradigms have evolved greatly over the past 10-15 years, and the present recommendation is to preserve rather than remove the spinal instrumentation in the majority of cases. However, the timing of infection after surgery (e.g., early vs. delayed) can be an important guiding factor determining the management choice.[9,39,77]

Surgical treatment of early deep postoperative infection following instrumented spinal fusion

The surgical treatment of early deep postoperative infection following spinal instrumentation is variable. There is a lack of consensus as to whether to utilize; irrigation/debridement alone, wound vacuums, continuous irrigation systems, antimicrobial beads, whether to revise instrumentation (e.g., instrumentation failure), whether to prophylactically remove instrumentation, and which antibiotic protocol to utilize.[7,49,78,86,118,140]

Presence of biofilm leads to recommendation to remove infected spinal instrumentation

Given the pathogenic role of prostheses-based biofilm, most infectious disease physicians now recommend removal of the underlying spinal instrumentation.[1,2,115] Removal of the instrumentation offers the advantage of eliminating hardware that may harbor biofilm-related microorganisms thus increasing the chance of eradicating the infection. Nevertheless, this potential advantage must

be weighed against the risks of prematurely removing internal fixators essential for maintaining normal spinal alignment and preserving spinal stability.

A key factor in deciding whether or not to remove spinal instrumentation relates to biofilm. *In vitro* laboratory investigations document that biofilms may develop within 5-6 hours after bacterial inoculation, and the age of the biofilm has major clinical implications related to its tenaciousness and antimicrobial susceptibility.[35] Early surgical intervention of acute infections with wound irrigation/debridement are more readily able to disrupt biofilm formation and facilitate penetration of systemic antimicrobials to allow for resolution of the infection while preserving the instrumentation/stability. This concept is supported by the clinical experience, which demonstrates that expedient treatment of early postoperative infections results in higher rates of infection resolution, preservation of instrumentation, and better clinical outcomes.[2,39,49,90,113,125]

Delayed wound infections often require instrumentation removal / replacement

Although acute infections may be adequately treated by surgical debridement and antimicrobial therapy, the development of a delayed wound infection often requires removal or replacement of the instrumentation.[9,20,78,114,117,141,151] Late-onset infections are caused primarily by organisms known to produce biofilm (e.g., coagulase-negative Staphylococci and Propionibacter acnes). Similar to the management of other bone and joint infections involving prostheses, this makes the eradication of infection difficult without foreign body removal.[58]

More morbidity with retention of spinal instrumentation after delayed infection

Retention of spinal instrumentation after delayed infection is fraught with more morbidity and less success. Ho *et al*. reported the strong propensity for recurrence of infection (up to 50%) in the absence of implant removal. They found that treating infected retained spinal implants with irrigation and debridement was associated with multiple procedures irrespective of the type of organism and graft.[61]

Advocacy of prophylactic removal of infected spinal instrumentation

Prophylactic removal of spinal instrumentation is advocated by some authors to minimize the risk of developing infection relapses or if fastidious organisms like Propionibacter are identified.[28,94] Implant removal in this population subset allows for more thorough debridement, and thus reduces the risk of infection relapse.[27,58,78,94] Concern for destabilizing the spine in delayed infections is less of an issue than in the acute postoperative infections since the fusion has often matured, or there is, at least, a stiff fibrous union. It is possible, however, that even if there appears to be radiographic evidence of fusion, removal of hardware can be associated with pseudoarthosis or loss of correction; thus these patients must be followed carefully.[31,58,94,107] One stage revision of infected instrumentation may be an option as opposed to instrumentation removal for these patients.[94]

General operative treatment

Surgical debridement and irrigation of infected spinal instrumentation

Surgical debridement and irrigation (frequently with a wound drain) have been an important means of treating early postoperative infections following the implantation of spinal instrumentation.[2,39,105] Multiple debridements may be required for successful eradication of infection. Poorly vascularized surgical sites or significant wound defects may mandate the use of complex flaps for reconstruction.[37,147] In addition to surgical debridement and postoperative antimicrobial therapy, the use of suction and/or irrigation systems, antimicrobial beads, or the vacuum-assisted closure (VAC) devices may also improve the outcomes of early infection after the placement of spinal instrumentation in selected patients. Closed suction drainage usually negates the need for secondary wound closures; excellent results have been reported for these irrigation systems.[49,65,81,118,138,143,153]

Antibiotic impregnated beads and suction/irrigation devices utilized to treat infected spinal instrumentation

Glassman *et al.* described the successful treatment of infection following the implantation of spinal instrumentation by placing antibiotic impregnated beads and utilizing close suction irrigation techniques.[49] The efficacy of suction irrigation using antibiotics to treat acute and delayed spinal instrumented infections has also been reported.[65,81,118,143] The duration of treatment with this latter technique ranges from 5 days to 2 weeks. Some surgeons stop the irrigation when the CRP and ESR are normalized; others wait until the outflow drainage is clear.

Vacuum-assisted closure facilitates wound healing and eradicates spinal infections

VAC is a useful adjunct that facilitates wound healing and eradication of complex postoperative bacterial spinal infections.[20,21,64,67,80,86,141,144,145,155,156] VAC is a relatively new technique that utilizes controlled negative pressure to evacuate wound edema fluid, thereby increasing regional blood flow, decreasing the bacterial load, and promoting the formation of granulation tissue.[7,144] The efficacy of the VAC that utilizes a porous polyurethane foam sponge, which is cut to fit into or over the wound, has been validated in animal studies.[93] The foam is covered by a sealant film that extends several centimeters beyond the margins of the wound to create an air-tight barrier. Continuous or intermittent negative pressure is applied to the sponge via a tube, which leads to a collection container.[144,155] The VAC is applied only after the

wound is thoroughly debrided. The sponge is changed or removed 2-7 days after application (e.g., until the wound is clean and can be closed over drains). One of the earliest reports was by Yuan-Innes *et al.*, who successfully treated two patients with infected and exposed spinal hardware; others have had similar positive experiences.[20,86,155] Conversely, there have been reports of less than optimal outcomes (multiple debridements, need for instrumentation removal or replacement) using the VAC particularly when dealing with MRSA or multibacterial infections.[80,106] Additionally severe complications (e.g., uncontrolled sepsis and severe blood loss) have been reported to be associated with utilizing the VAC; patients undergoing this therapy, therefore, should be carefully monitored.[67]

Antimicrobial therapy

Duration of antimicrobial therapy

Another unresolved aspect of postoperative infections after spinal instrumentation relates to the duration of pharmacological treatment. It is optimal to base antimicrobial choice on the culture results, and antibiotic sensitivity of the organisms. Although there is general agreement on the need for 6-8 weeks of parental therapy, data addressing the need for and duration of long-term oral suppressive antibiotic therapy are lacking.[111,126] The mean duration of antibiotic therapy may be much longer as reported in the study by Kowalski *et al.*, who found that with early postoperative infections, treatment with longer-term suppressive antibiotic therapy was associated with higher chances (80% vs. 33%) of eradicating infections and retaining implants vs. those who did not receive suppressive therapy.[78] Additionally, hyperbaric oxygen therapy was reported to be a useful adjunctive therapy for treating instrumented spinal fusions, especially in patients who have failed primary antimicrobial therapy.[3]

CONCLUSION

It is important to recognize the clinical symptoms and signs of postoperative spinal infections, and confirm the diagnosis with appropriate laboratory and imaging studies. Prompt, aggressive debridement coupled with utilizing the correct antibiotic therapy (typically 6-8 weeks of intravenous antibiotics) and, in some cases, chronic suppressive antibiotic treatment (e.g., for up to 1 year), have yielded the most successful results. Instrumentation can usually be preserved in patients with early infections (e.g., <6 weeks), but instrumentation removal should be considered for infections presenting in a delayed fashion (e.g., >6 weeks to even years). Patients should be adequately followed for one postoperative year, to ensure that the infection has been fully eradicated. Emerging techniques are increasingly preventing the formation of biofilm on instrumentation, facilitate the removal of biofilm, and increase the culture yield of biofilms on implant surfaces. For example, implant sonication provides cultures for direct identification of active and/or persistent biofilm, while the introduction of enzymes that dissolve the biofilm matrix (e.g., DNase and alginate lyase) and quorum-sensing inhibitors that increase biofilm susceptibility to antibiotics may further help manage postoperative infection. These and other techniques may further enhance the potential for successfully salvaging instrumentation, while eradicating spinal infections. Additionally, changes in antibiotic prophylaxis to prevent postoperative infections following spinal instrumentation remain active areas for further investigation.

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