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OSTEOMYELITIS

Part of "15 - COMPLICATIONS"

The term *osteomyelitis* usually refers to bone infections caused by bacteria; however, certain fungi such *Blastomyces dermatiditis* and *Coccidioides immitis* can occasionally be responsible (956). Over the past 20 years there has been a significant change in the organisms responsible for chronic osteomyelitis. The incidence of gram-negative and polymicrobial infections has increased significantly. The incidence of pure *S. aureus* infections has fallen dramatically. Osteomyelitis can arise from organisms

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that have reached the bone via the bloodstream (hematogenous osteomyelitis) or organisms that have reached bone via the external environment from trauma (exogenous osteomyelitis). These can further be subdivided into acute, subacute, and chronic osteomyelitis.

Classification

Historically, osteomyelitis was classified as either acute or chronic depending on the duration of symptoms. A classification system based on the etiology of the osteomyelitis was developed: type I (hematogenous), type II (osteomyelitis with fracture union), type III (osteomyelitis without fracture union), and type IV (postoperative or posttraumatic osteomyelitis without fracture). Weiland et al. (968) in 1984 suggested another classification scheme based on the nature of the bony involvement. The categories in this system were the following: type I—open, exposed bone without soft tissue infection; type II—circumferential cortical and endosteal infection; and type III—associated with a segmental defect. May and co-workers (593) in 1989 proposed yet another classification scheme for osteomyelitis, focusing on the tibia. This system was based on the nature of the bone following soft tissue and bony debridement. They proposed the following categories: type I—intact tibia and fibula able to withstand functional loads with no reconstruction needed; type II—intact tibia unable to withstand functional loads requiring bone grafting; type III—<6 cm tibial defect with an intact fibula requiring cancellous bone grant, tibiofibular

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synostosis, or distraction histogenesis; type IV—<6 cm tibial defect and intact fibula requiring distraction histogenesis, tibiofibular synostosis, or a vascularized bone graft; and type V—≥l6 cm tibial defect without an intact fibula requiring a possible early amputation.

Probably the most widely used system of classification for adult osteomyelitis is that of Cierny and Mader (157,158). This system is based on four factors: the degree of osseous involvement, the site of involvement, the degree of impairment caused by the disease, and the general condition of the host (158) (Table 15-37; Fig. 15-9). Type I is medullary

osteomyelitis (examples of which include hematogenous osteomyelitis and infections of intramedullary rods). Type II is superficial osteomyelitis confined to the bone surface. Type III is localized osteomyelitis involving the full thickness of the cortex. Type IV is diffuse osteomyelitis involving the circumference of the cortex. The general condition of the patient is based on those factors that affect the response to infection and treatment. Class A patients have normal systemic defenses, metabolic capabilities, and vascular supply to the limb. Class B patients have a local or systemic deficiency in wound healing (immunosuppressed, on corticosteroids, peripheral vascular disease). Class C patients are those in whom the treatment morbidity is worse than the presenting condition (156). These patients have a poor prognosis for cure.

Anatomic type	
Stage 1	Medullary osteomyelitis
Stage 2	Superficial osteomyelitis
Stage 3	Localized osteomyelitis
Stage 4	Diffuse osteomyelitis
Physiologic class	
A Host	Normal host
B Host	Systemic compromise (Bs)
	Local compromise (Bl)
	Systemic and local compromise (Bls)
C Host	Treatment worse than the disease

SYSTEMIC OR LOCAL FACTORS THAT AFFECT IMMUNE SURVEILLANCE, METABOLISM, AND LOCAL VASCULARITY

Systemic (Bs)	Local (Bl)
Malnutrition	Chronic lymphedema
Renal, hepatic failure	Venous stasis
Diabetes mellitus	Major vessel compromise
Chronic hypoxia	Arteritis
Immune disease	Extensive scarring
Malignancy	Radiation fibrosis
Extremes of age	Small vessel disease
Immunosuppression or immune deficiency	Neuropathy
	Tobacco abuse (≥2 packs of cigarettes per day)

From Cierny G, Mader JT, Pennick H. A clinical staging system of adult osteomyelitis. *Contemp Orthop* 1985;10:17–37, with permission.

TABLE 15-37. CIERNY AND MADER STAGING SYSTEM

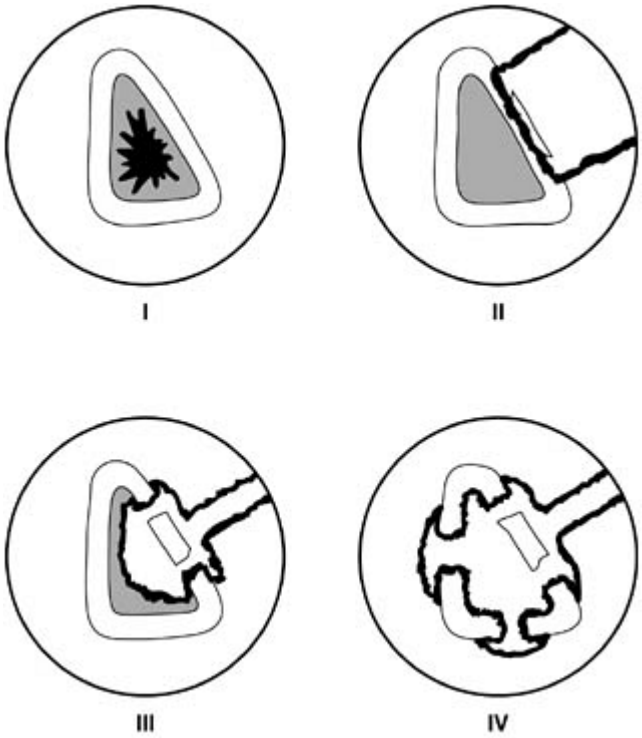

FIGURE 15-9. The four types of chronic osteomyelitis shown diagrammatically. (From Cierny G III, Mader JT. *Orthopaedics* 1984;7:10, with permission.)

Pathogenesis of Musculoskeletal Infection

Microorganisms are primitive representations and precursors of tissue cells. They often exist as microbial aggregates in a biofilm slime layer colonizing surfaces within which they are resistant to antagonists. Nutrients and free energy are concentrated at the surfaces of the three-dimensional architecture of these bacterial colonies. Colonization of surfaces is not always, synonymous with infection. Bacteria such as *Staphylococcus epidermidis*, streptococcol species, and gram-negative groups are naturally found on skin, oral mucosa, and the intestinal tract. However, through evolution, bone and cartilage have not been intended to support bacterial colonization and thus are especially susceptible to infection.

The first step in bacterial colonization is the process of adhesion to permanent tissue or biomaterial attachment (377). Typically, the host's defense mechanisms are usually able to eliminate these bacteria. There are, however, situations in which bacteria remain viable: (a) the inoculum is larger than threshold levels, (b) host defense mechanisms are impaired, (c) the tissue on which the bacteria colonize is traumatized, (d) a foreign body is present, and (e) the surface (or tissue) is acellular or inanimate (e.g., bone, cartilage, and biomaterials).

Surface adhesion of bacteria depends on physical characteristics of the bacterium, the fluid interface, and substratum (199,338,377). Adhesion is based on time-dependent specific

protein adhesion-receptor interactions, as well as carbohydrate polymer synthesis in addition to charge and physical forces (377).

Bacteria randomly arrive near a bone surface or biomaterial surface by direct contamination, contiguous spreading, or hematogenous

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seeding. Any surface, whether a eukaryotic cell or a biomaterial, exposed to a biologic environment spontaneously acquires a glycoproteinacous film (293,366,377,278,379 and 380,388). The surface is anionic and initially repels bacteria (which are also anionic). Juxtaposition of the bacteria with a tissue surface or biomaterial is therefore accomplished by Van der Waals forces. This interaction allows bacteria to develop “irreversible” cross-links with the surface (adhesin receptor interaction) (199,256,377). Following anchorage to the surface, bacteria begin to proliferate within the polysaccharide slime layer and a “biofilm-enclosed” colony of bacteria forms. Biofilm (or slime) is formed by bacterial extracapsular exopolysaccharides that bind to surfaces and participate in cell-to-cell aggregation. In these biofilms, the bacteria are resistant to host defenses and may resist antibiotic action. Thus, infection may develop, spread, and persist in this environment.

Adherence to Bone

Damaged bone acts as a substratum for bacterial colonization. Bone is a relatively acellular composite structure of calcium hydroxyapatite crystals and a collagen matrix. This organic matrix is arranged as helical polypeptides composed of proline, hydroxyproline, glycine, and alanine (579). Proline-rich proteins can act as ligands for bacterial adhesion. Devitalized bone devoid of normal periosteum presents a collagen matrix to which bacteria can bind. Moreover, bone sialoprotein has also been suggested as a ligand for bacterial binding to bone (377).

Adherence to Biomaterials

Many implants consist of one or more metal or polymer. Biomaterials and other foreign bodies are usually inert and susceptible to bacterial colonization because they are inanimate. Regardless of how inert a metal is, it may still modulate molecular events at its surfaces, specifically receptor-ligand interactions, covalent bonding, and thermodynamic interactions (293,388). The most important feature a particular metal has is its outer surface atomic layer interaction with glycoproteins and prokaryotic and eukaryotic cells. Stainless steel and cobalt-chromium and titanium alloys are resistant to corrosion through elemental composition, crystalline homogeneity, and the surface oxide passivates. Surface oxides form a reactive interface with bacteria.

Hydrophobicity is often used as a parameter to evaluate the cellular adhesiveness of a biomaterial. Certain strains of bacteria owe their hydrophobicity to their synthesized “biofilm” coating. When this coating is washed away, the bacteria become hydrophilic. In general, hydrophobic bacteria adhere better to hydrophobic surfaces. Polymers tend to be more hydrophobic than metals (377).

Antibiotic Resistance

Following bacterial adherence, the resistance to antibiotics increases (663,673). This resistance property seems to be dependent on the type of surface to which the organisms are attached. Organisms that adhere to hydrocarbon polymers are extremely resistant to antibiotics. These same organisms, when attachedto metals, do not resist antibiotic therapy to the same extent. It has been theorized that bacteria within biofilms have a decreased metabolic rate and undergo phenotypic changes that may influence resistance and virulence (377). It has also been shown that bacteria adherent to surfaces are more resistant to antibiotics than free-floating bacteria.

Pathophysiology of Osteomyelitis

Acute Hematogenous Osteomyelitis

It is believed that the vascular architecture of the metaphysis, where the nutrient capillaries form sharp loops, predisposes to the establishment of infection following bacteremia. Bacteria become lodged in the small end arteries and multiply. Shortly thereafter, blood and white blood cells accumulate, resulting in further compromise of blood flow and pressure necrosis of surrounding bone. The pus moves along the haversian canals and medullary canal, which are paths of least resistance. When the pus reaches the cortical surface, it moves beneath the periosteum.

The most commonly involved organism in all age groups is *S. aureus* (193), which is responsible for between 50% and 70% of all such infections in children between 1 month and 5 years of age (193). The second most common organisms are hemolytic streptococci. Both group A and group B streptococci have been implicated in hematogenous osteomyelitis, the latter particularly in the first 2 months of life. In neonates, *Haemophilus influenzae* is an occasional cause of osteomyelitis, but more commonly of septic arthritis (193).

Damage to the metaphyseal blood supply, caused by the release of bacterial toxins and the stripping of the periosteum, results in portions of the bone becoming necrotic. The inner portion of the cortex is supplied by the injured metaphyseal vessels. These areas of dead bone separated from viable bone by granulation tissue are called sequestra. The body responds to sequestra by laying down new bone, involucrum, which surrounds the area of infected bone.

Generally, there are three possible patterns of vascularity. In the infant, epiphyseal extensions of the nutrient artery may allow infections that originate in the metaphysis to seed into the epiphysis. In children, the nutrient artery terminates in end arteries and capillaries adjacent to the growth plate. An infection of the metaphysis is usually prevented from crossing the growth plate. In adults, however, the metaphysis and epiphysis are in continuity, and hematogenous osteomyelitis may be metaphyseal or epiphyseal. The high incidence of infections in the distal femur and proximal tibia may be associated with the relative contributions these regions have to growth.

Chronic Nonhematogenous Osteomyelitis

Acute osteomyelitis that is inappropriately treated can become chronic osteomyelitis.

General factors that may predispose to this condition include degree of bone necrosis, nutrition, infecting organism, age of the patient, comorbidity, and drug abuse (193). The infecting organism varies, generally, with the cause of chronic osteomyelitis. Chronic osteomyelitis resulting from acute osteomyelitis is often caused by *S. aureus*; however,

chronic osteomyelitis occurring after a fracture can be polymicrobial (although in most cases, it is *S. aureus*). Intravenous drug users are commonly found to have *Pseudomonas* or *S. aureus* infections. Gram-negative organisms are now seen in about 50% of all cases of chronic osteomyelitis (193).

Nonhematogenous osteomyelitis is secondary to a contiguous focus of infection. The bacterial organisms enter the bone directly through interrupted tissue planes as a result of fractures or surgical procedures. Bacteria in bone by themselves are insufficient to produce osteomyelitis. A surgical or traumatic insult sets the stage for the secondary infection (646). Periosteum and muscle are injured, creating regions of cortical bone that no longer are perfused adequately. Devitalized bone presents a collagen protein matrix and acellular crystal regions to which bacteria can bind directly (379). The fundamental problem in chronic osteomyelitis is infection that devascularizes a segment of bone, leaving protected pockets of necrotic material to support bacterial growth in relative seclusion from systemic antibiotic therapy.

Posttraumatic Osteomyelitis

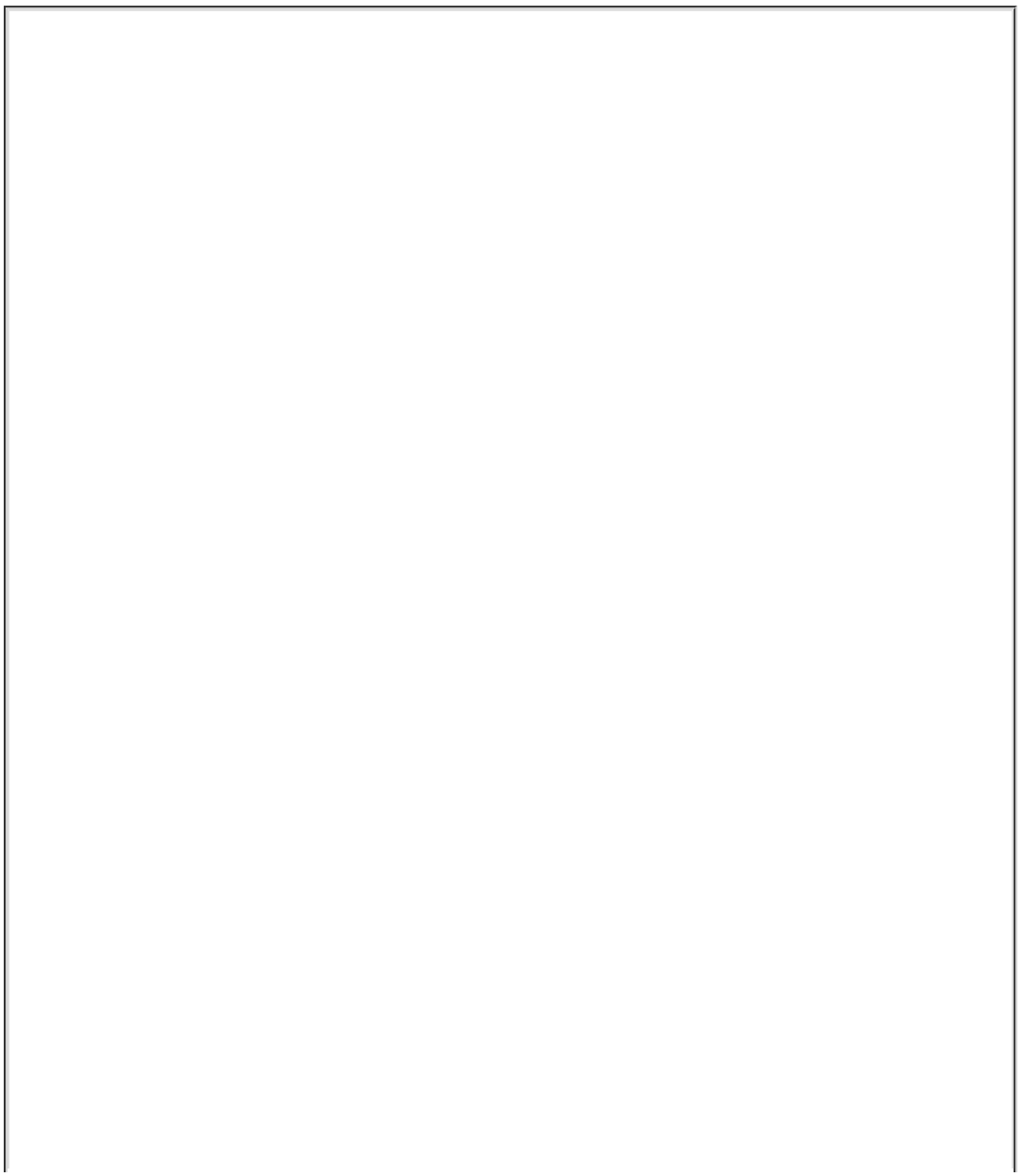
Posttraumatic osteomyelitis is a bone infection resulting from trauma that allows pathogenic organisms to enter bone, proliferate in traumatized tissue, and cause a subsequent infection (611). The environmental conditions that promote infection and tissue damage are present in the face of trauma. Traumatized soft tissue and bone exposes potential binding sites for bacteria such as collagen (924). Traumatized tissue also results in compromised blood supply, leading to tissue and bone necrosis, which promotes infection (924). Moreover, the fixation devices that are required in the management of fractures serve as additional foci for bacterial colonization (924). In the patient with traumatic injuries, additional factors that contribute to the subsequent development of osteomyelitis are the presence of hypotension, inadequate debridement of the fracture site, malnutrition, alcoholism, and smoking (272,434,912).

Trauma may lead to interference with the host response to infection. Tissue injury or the presence of bacteria triggers activation of the complement cascade that leads to local vasodilation, tissue edema, migration of polymorphonuclear leukocytes (PMNs) to the site of injury, and enhanced ability of phagocytes to ingest bacteria (17). Trauma has been reported to delay the inflammatory response to bacteria, to depress cell-mediated immunity, and to impair function of PMNs, including chemotaxis, superoxide production, and microbial killing (435). The commonly used system of Cierny and Mader has been shown to have greatest correlation with the general condition of the patient rather than the specifics of bone involvement.

Organisms in Trauma

The presence of bacteria in an open wound is not sufficient to cause infection.

Approximately 60% to 70% of open fractures are contaminated by bacteria, but a much smaller percentage go on to develop infection (924). Moreover, the bacteria recovered from clinical infections are most likely to be hospital acquired pathogens such as *S. aureus* or gram-negative bacilli (including *Pseudomonas aeruginosa*) (390,567) (Table 15-38). However, other bacteria should be considered, depending on the environment, specifically, *C. perfringens* and farm injury, *Pseudomonas* Aeromonas hydrophilia following fresh water injury, and *Vibrio* and *Erysipelothrix* in salt water injury. There are some unusual organisms that can cause osteomyelitis (Table 15-39). Bacteria that cause infection are those that can colonize host tissue and cause damage. In humans, the risk of subsequent infection is highly correlated with the degree of soft tissue injury associated with an open fracture (924). Infection rates in type IIIB open fractures, those in which extensive soft tissue stripping does not allow for adequate coverage over the site, are prone to infection in up to 40% of cases (193).



Etiology	Infecting Organisms	Initial Empiric Therapy
Acute hematogenous osteomyelitis	*Staphylococcus aureus*	Nafcillin or oxacillin
Posttraumatic	*S. aureus* Streptococci Gram-negative bacilli	Cefotaxime or ceftizoxime or ampicillin-sulbactam
Postoperative infection	*S. aureus* Gram-negative bacilli	Cefotaxime or ceftizoxime
Prosthetic device infection	*Staphylococcus epidermidis* *S. aureus* Gram-negative bacilli	Vancomycin and gentamicin
Soft tissue infection	*S. aureus* Streptococci Anaerobes Gram-negative bacilli	Cefotaxime or ceftizoxime or ampicillin-sulbactam
Puncture wound of foot	*Pseudomonas aeruginosa* *S. aureus*	Ciprofloxacin or ceftazidime and gentamicin
Dog/cat bites	*Pasteurella multocida* *Capnocytophaga* (DF2) *S. aureus* Streptococci	Ampicillin-sulbactam or imipenem
Diabetic ulcer	*S. aureus* Streptococci Enterococci Gram-negative bacilli Anaerobes	Ceftizoxime or cefotaxime or ampicillin-sulbactam or clindamycin plus gentamicin or clindamycin plus ofloxacin
Infected decubitus ulcer	*S. aureus* *Proteus mirabilis* *Enterobacter* *E. coli* Streptococci Anaerobes	Cefotaxime or ampicillin-sulbactam
Sickle cell disease	*Salmonella* *S. aureus*	Ofloxacin or cefotaxime
Intravenous drug users	*S. aureus* *P. aeruginosa* *Serratia marcescens*	Nafcillin and gentamicin
Human bites/clenched fist injury	*Eikenella corrodens*	Ampicillin-sulbactam or imipenem

From Cunha B, Dee R, Klein N, et al. Bone and joint infections. In: Dee R, Hurst L, Gruber M, et al., eds. *Principles of orthopaedic practice,* 2nd ed. New York: McGraw-Hill,1997:317–344, with permission.

TABLE 15-38. MOST LIKELY PATHOGENS CAUSING CHRONIC OSTEOMYELITIS

Pathogen	Therapy of Choice	Alternative Therapy
Brucella	Doxycycline and gentamicin	Trimethoprim-sulfamethoxazole
Salmonella	Third-generation cephalosporin or quinolone	Trimethoprim-sulfamethoxazole
Bacteroides spp.	Clindamycin or metronidazole	Ampicillin-sulbactam or imipenem
Blastomyces	Amphotericin B	Itraconazole
Cryptococcus	Amphotericin B	Fluconazole
Coccidioides	Amphotericin B	Ketoconazole or itraconazole
Actinomyces	Penicillin G	Minocycline
Actinomadura	Dapsone and streptomycin	Trimethoprim-sulfamethoxazole
Nocardia	Trimethoprim-sulfamethoxazole	Minocycline
Mycobacterium tuberculosis	Isoniazid, rifampin, ethambutol, pyrazinamide	Streptomycin

From Cunha B, Dee R, Klein N, et al. Bone and joint infections. In: Dee R, Hurst L, Gruber M, et al., eds. *Principles of orthopaedic practice,* 2nd ed. New York: McGraw-Hill, 1997:317–344, with permission.

TABLE 15-39. UNUSUAL ORGANISMS CAUSING OSTEOMYELITIS

Clinical Manifestations

Patients often have a history of infection of another site, such as the throat or skin, or have a history of trauma. They usually complain of substantial pain in the affected area. They may have difficulty with weight bearing. Moreover, reduced activity, malaise, and anorexia may be exhibited. General physical findings include fever, tachycardia, and listlessness. Local findings include swelling and warmth, occasional redness, tenderness to palpation, drainage, and restricted range of motion of adjacent joints.

With a history of trauma, clinical risk factors for infection include a history of open fracture, severe soft tissue injury, a history of substance abuse and smoking, inadequate previous treatment, and an immunocompromised state. Clinical factors affecting treatment that need to be assessed include the time of onset of the infection, the status of the soft tissues, the viability of the bone, the status of fracture healing, implant stability, the condition of the host, and the neurovascular exam.

Laboratory Findings

Elevations in the white blood cell count with a left shift, erythrocyte sedimentation rate, and C-reactive proteins are often seen. The erythrocyte sedimentation rate may be normal in the first 48 hours but rises to levels above 100 mm/h, and may remain elevated for weeks (193). Its gradual declination is an indicator of treatment response. Since bacteremia and septicemia are often present, blood cultures should be performed to identify infecting bacteria. Blood cultures are positive in about 50% to 75% of cases (193). Although not a sensitive test for septic arthritis, the detection of antibodies (C-reactive protein) to the teichoic acid cell wall of *S. aureus* has been useful in the detection of acute osteomyelitis.

The sensitivity approaches 82% in the acute situation and declines to 43% in chronic osteomyelitis (193).

Radiographic Imaging

Within the first few days, soft tissues near the metaphyseal region of the bone may appear swollen. Radiographically, detectable demineralization may not be seen for at least 10 days (125). When present, it usually signifies trabecular bone destruction. If the infection spreads to the cortex (usually within 3 to 6 weeks), a periosteal reaction may be evident. Unfortunately, radiologic findings in the initial presentation of acute osteomyelitis are often normal. The most common radiographic sign of early bone infection is rarefaction, representing diffuse demineraliza-tion

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secondary to inflammatory hyperemia. One study reported that in cases of eventually proven osteomyelitis, 5% of radiographs were abnormal initially, 33% were abnormal by 1 week, and 90% were abnormal by 4 weeks (987).

Bone Scans

Technetium-99m is the principal radioisotope employed in most bone scans (37,61,102,123,186,216,260,283,292,342,407,442,623). Technetium is formed as a metastable intermediate during the decay of molybdenum-99. It is relatively inexpensive since it is readily available (201). Technetium decays with a 6-hour half-life. After intravenous injection, there is rapid distribution of this agent throughout the extracellular fluid. Within several hours, more than half the dose will accumulate in bone, while the remainder is excreted in the urine. There is evidence to suggest that the technetium phosphates bind to both the organic and the inorganic matrix. There is preferential incorporation into metabolically active bone.

Bone images are usually acquired 2 to 4 hours following intravenous injection of the radioisotope. A triple phase bone scan is one that is useful for examining inflammation and related

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processes. Following the initial injection, dynamic images are captured over the specified region. These are followed by static images at later time points. The first phase represents the blood flow phase, the second phase immediately postinjection represents the bone pooling phase, and the third phase is a delayed image made at 3 hours when there is decreased soft tissue activity. Classically, osteomyelitis presents as a region of increased blood flow and should appear “hot” on all phases, with focal uptake in the third phase. Other processes such as a healing fracture, a loose prosthesis, and degeneration do not appear hot in the early phase despite a hot appearance in the delayed phase. Reported sensitivities of bone scintigraphy for the detection of osteomyelitis vary considerably from 32% to 100%. Reported specificities have ranged from 0% to 100% (806,954).

Gallium-67 citrate binds rapidly to serum proteins, particularly transferrin (18,61,95,123,785,818). There is uptake in the blood, especially by leukocytes. Gallium has been used in conjunction with technetium-99 to increase the specificity of the bone scan (18,61,123,260,407). Several mechanisms have been postulated to explain the increased

activity at sites of inflammation. Enhanced blood flow and increased capillary permeability cause enhanced delivery. Bacteria have high iron requirements and thus avidly take up gallium. Gallium is strongly bound to bacterial siderophores and leukocyte lactoferins. In regions of inflammation, these proteins are available extracellularly and can bind gallium avidly. Chemotaxis also acts to localize gallium-labeled white blood cells at the sites of infection. In a typical study, gallium is injected intravenously and delayed images are acquired (at 48 to 72 hours).

The hallmark of osteomyelitis is focal increased uptake of gallium. Unfortunately, gallium's nonspecific bone uptake can be problematic since any processes causing reactive new bone formation will “light up.” In the case of patients with fractures or a prosthesis, osteomyelitis cannot be diagnosed with gallium alone. Most authors will interpret gallium images along with bone scans. Gallium activity is interpreted as abnormal if it is either incongruous with the bone scan activity or if there is a matching pattern with gallium activity.

Reported sensitivities and specificities for the diagnosis of osteomyelitis range from 22% to 100% and 0% to 100%, respectively (806). Despite its lower than optimal diagnostic value, gallium still has advantages: (a) it is easily administered, (b) it is the agent of choice in chronic soft tissue infections (less effective in bone infections), and (c) it is a useful agent in following the resolution of an inflammatory process by showing a progressive decline in activity.

Indium-111–Labeled Leukocytes

Due to the variable accuracy of both technetium and gallium scans, most laboratories routinely employ indium-111–labeled leukocytes (202,203,260,295,574,598,699,802,805,817,828,940,1004). Indium white blood cell (WBC) preparations require withdrawing approximately 50 mL of autologous whole blood with a leukocyte count of at least 5,000 cells/mm^3. Allowing 1 hour for optimal sedimentation of the whole blood in a heparinized syringe, the leukocyte-rich upper layer is carefully removed by catheter and placed in a centrifugation tube. After centrifugation, the leukocyte-poor plasma supernatant is removed and saved, while the leukocyte-containing pellet is resuspended in normal saline. The leukocytes are labeled with 1 mCi of indium oxine at room temperature for 30 minutes. The unbound indium and oxine are removed by centrifugation. Following intravenous injection, the labeled WBCs redistribute in the intravascular space. Immediate images show activity in the lungs, liver, spleen, and blood pool. The half-life is about 7 hours. After 24 hours, only the liver, spleen, and bone marrow show activity. Normal-healing wounds and fully treated infections show no increase in uptake.

Most results show improved sensitivity (80–100%) and specificity

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(50–100%) for the diagnosis of osteomyelitis (622). Indium-labeled WBC scans are generally superior to bone scans and gallium scans in the detection of infection. McCarthy et al. (598) have reported the diagnostic utility of indium scans in 39 patients with suspected osteomyelitis (confirmed by bone biopsy). Indium scans were 97% sensitive and 82% specific for osteomyelitis. The few false-positive results occurred in patients with

overlying soft tissue infections. An accompanying bone scan can aid in differentiating bone infection from soft tissue infection. In these situations, the indium scan should be performed before the bone scan to avoid false-positive results (from the remaining technetium uptake).

Indium-Labeled Polyclonal Immunoglobulins

This nonspecific polyclonal immunoglobulin (IgG) prepared from human serum gamma globulin and labeled with indium via diethylenetriamine pentaacetic acid (DTPA) chelation is another agent used for the detection of osteomyelitis (700,785). Unlike the indium-labeled WBC scans, this agent is easily prepared by simply adding indium chloride to a sterile kit containing a DTPA-IgG complex. The blood half-life is 24 hours and the primary uptake occurs in the liver. Compared with indium-labeled WBC scans, this technique is easier to perform and has less bone marrow uptake.

Magnetic Resonance Imaging

Magnetic resonance imaging continues to play an important role in the evaluation of musculoskeletal infections (74,88,589,634,757,901,914,930). It has the spatial resolution necessary to evaluate accurately the extent of the infection in preparation for surgical treatment and localizes any abscess cavities. It also has the ability to differentiate between infected bone and involved adjacent soft tissue structures. Images can be acquired in any orientation and there is no radiation exposure. Characteristically, active osteomyelitis displays a decreased signal on T1-weighted images and appears bright on T2-weighted images. The process represents the replacement of marrow fat with water from edema, exudate, hyperemia, and ischemia. The MRI signal characteristics that reflect osteomyelitis are intrinsically nonspecific: tumors and fractures can also increase the marrow water content. In patients without prior complications, MRI has been found to be sensitive (but not specific) for osteomyelitis. When a fracture or prior surgery is evident, MRI is less specific in the diagnosis of infection. In these situations, indium-labeled WBC scans are helpful. Although limited, studies show good results in the evaluation of acute osteomyelitis (sensitivities: 92% to 100%, specificities: 89% to 100%) (806).

Computed Tomography

Computed tomography has assumed a lesser role in the evaluation of osteomyelitis with the widespread use of MRI (205). It remains unsurpassed, however, in the imaging of cortical bone. It is especially useful in delineating the cortical details in chronic osteomyelitis, such as sequestra and foreign bodies (902). It also is useful in evaluating the adequacy of cortical debridement in the staged treatment of chronic osteomyelitis.

Positron Emission Tomography

Positron emission tomography may play an important role in the evaluation of musculoskeletal infections. The technique enables noninvasive detection and demonstration of the extent of chronic osteomyelitis with 97% accuracy (385). Positron emission tomography is especially accurate in the central skeleton within active bone

marrow (385).

Approach to Imaging and Posttraumatic Osteomyelitis

Since bone scan agents and gallium are usually both positive at fracture sites, they have limited value in the detection of infection following a fracture. With no discernible uptake in reactive bone, indium-labeled WBC scans reveal superiority in the detection of infection following a fracture. In a prospective study of 20 patients with suspected osteomyelitis superimposed on a delayed union, Esterhai et al. (261) reported 100% accuracy of indium-WBC scans (261). Seabold et al. (818) have shown that using indium-WBC scans and bone scans (to differentiate between soft tissue infections) can be 97% specific for osteomyelitis.

In chronic or recurrent osteomyelitis, bone scans alone are of little value since they show increased uptake for up to 2 years following successful treatment and resolution of infection (365). Although gallium scans have historically been shown to be the most optimal for following the resolution of chronic osteomyelitis, indium WBC scans appear to be superior. Merkel et al. (622), in a prospective study of 50 patients comparing indium-WBC and gallium scans for the detection of osteomyelitis, found that indium-WBC scans were 26% more accurate than gallium scans (83% vs. 57%).

Aspiration

If the diagnosis of septic arthritis is suspected, it must be ruled out. The most important step in the initial diagnosis of a septic joint is aspiration. The procedure should be performed with aseptic technique. The joint should not be entered through an infected area of overlying skin. The skin should be prepared with an iodine-based solution or alcohol. An 18-gauge (or larger) needle should be introduced into the joint and the fluid aspirated. The fluid should be analyzed for cell count, differential microscopic evaluation, glucose determination, Gram stain, and culture (aerobes, anaerobes, fungi, mycobacteria).

Biopsy

Identification of an organism and determination of antibiotic resistance patterns is crucial to a successful outcome in the management of osteomyelitis. The procedure can usually be done under fluoroscopic guidance. In general, sinus tract cultures should not be used to guide antibiotic treatment (228,332,594,677). In a prospective study, Mousa (652) found that 88.7%

of sinus tract isolates were identical to operative specimens in 55 patients with chronic bone infection. These results were dependent on aspiration of material by syringe from the depths of an active flowing sinus and immediate inoculation on culture media. Bone biopsy remains the preferred diagnostic procedure in chronic osteomyelitis. Histologic and microbiologic evaluation of percutaneous biopsy samples should be combined in cases of suspected osteomyelitis. The sensitivity of culture in the diagnosis of osteomyelitis could be improved from 42% to 84% by the addition of histologic evaluation.

Molecular Diagnostics

These procedures are being developed for diagnosis in osteomyelitis because some infections remain without an identified pathogen, when using standard techniques. This is particularly so in those patients who have been treated with antibiotics shortly before sample collection. These methods target specific macromolecules unique to the infecting pathogens, which are absent in the host cells (250,908). They have the potential to provide rapid results with high accuracy (436). The most commonly used method for the diagnosis of orthopaedic infections is polymerase chain reaction (436). Sequences within bacterial 16S ribosomal RNA have served as targets for amplification and detection (436). Further investigation is required before these techniques can be widely used as they lack sufficient sensitivity and specificity.

Treatment

The management of osteomyelitis relies on a multidisciplinary approach, combining debridement, soft tissue coverage, and antimicrobial therapy to give the patient the best chance of cure (245,299,588,592).

General Approach

After a clinical diagnosis of acute osteomyelitis has been made, aspiration of the bone should be performed to identify the pathogen. All material obtained from aspiration should be sent for a Gram stain, culture and sensitivity (aerobic/anaerobic), and fungal and mycobacterial cultures. Blood cultures should also be obtained. Even though aspiration in the early stage of disease may fail to obtain any fluid or pus, it is very useful in obtaining the infecting organism. However, there is danger that the pus may be so thick that it may yield a negative aspiration.

In early acute hematogenous osteomyelitis, antibiotic therapy without surgical intervention may result in cure, provided the blood supply has not yet been compromised and adequate antibiotic levels in bone can be obtained. The mainstay of treatment remains rapid identification of the responsible pathogen and the initiation of appropriate antibiotic therapy. *S. aureus* is the most common cause of acute hematogenous osteomyelitis in both children over the age of 1 year and adults (377).

Historically, acute *S. aureus* osteomyelitis required 4 to 8 weeks of intravenous therapy (750). Subsequent studies have shown that early conversion to oral therapy can be equally effective (752,906). The decision to convert to oral therapy is based on clinical factors. Typically, fever, pain, swelling, and local inflammation begin to resolve after 4 to 10 days of appropriate intravenous therapy. If an appropriate oral agent is available and the patient is compliant, the remainder of therapy can be completed on an outpatient basis. The duration of treatment depends on the pathogen. *S. aureus* or enteric gram-negative organisms require a minimum of 4 weeks of treatment. Infections caused by *H. influenzae, Neisseria meningitidis*, or streptococci may require only 14 days of treatment. The decision to discontinue treatment should be based on both the clinical response of the patient and a falling erythrocyte sedimentation rate (197). Regardless of the method of antibiotic administration, it appears that maintaining a peak serum bactericidal titer of greater than 1:8 (751) or a trough level of greater than 1:2 (973) is predictive of successful therapy.

Indications for surgical drainage or debridement must be individualized, and include the presence of a subperiosteal abscess, a coexistent septic arthritis, and failure to respond to appropriate antibiotic therapy after 36 to 48 hours (161,197).

Antibiotic Therapy

Factors involved in choosing the appropriate antibiotics include infection type, infecting organism, sensitivity results, host factors, and antibiotic characteristics (572). Antibiotic classes used in the treatment of osteomyelitis include penicillins, β-lactamase inhibitors, cephalosporins, other β-lactams (aztreonam and imipenam), vancomycin, clindamycin, rifampin, aminoglycosides, fluoroquinolones, trimethoprim-sulfamethoxazole, metronidazole, and new agents including teicoplanin, quinupristin/dalfopristin, and oxazolidinones (572) (Table 15-40, Table 15-41, and Table 15-42).

Organism	First-Choice Antibiotics	Alternative Antibiotics
Methicillin sensitive		
Staphylococcus aureus or coagulase negative	Nafcillin 2 g every 6 hours or clindamycin 900 mg every 8 hours	Cefazolin Vancomycin
Staphylococcus species	Nafcillin 2 g every 6 hours or clindamycin 900 mg every 8 hours	Cefazolin Vancomycin
Methicillin resistant		
Staphylococcus aureus or coagulase negative	Vancomycin 1 g every 12 hours	SXT or minocycline ± rifampin
Staphylococcus species	Vancomycin 1 g every 12 hours or clindamycin 900 every 8 hours[a]	SXT or minocycline ± rifampin
Group A streptococcus *Streptococcus pyogenes*	Penicillin G 2 mU every 4 hours	Clindamycin, cefazolin, vancomycin
Group B streptococcus *Streptococcus agalactiae*	Penicillin G 2 mU every 4 hours	Clindamycin, cefazolin, vancomycin
Penicillin sensitive		
Streptococcus pneumoniae	Penicillin G 2 mU every 4 hours	Erythromycin, clindamycin
Intermediate penicillin resistance		
Streptococcus pneumoniae	Cefotaxime 1 g every 6 hours	Erythromycin, clindamycin
Penicillin resistant		
Streptococcus pneumoniae	Vancomycin 1 g every 12 hours L-ofloxacin 500 mg daily	Sparfloxacin
Enterococcus species	Ampicillin 1 g every 6 hours[b] Vancomycin 1 g every 12 hours	Ampicillin-sulbactam

[a] Dose every 8 hours if sensitive to clindamycin.
[b] In a serious *Enterococcus* species infection ampicillin ± sulbactam plus an aminoglycoside is used.
SXT, sulfamethoxazole-trimethoprim.
From Mader J, Shirtliff ME, Bergquist SC. Antimicrobial treatment of OM. *Clin Orthop* 1999;360:47–65, with permission.

TABLE 15-40. GRAM-POSITIVE ORGANISMS: INITIAL CHOICE OF ANTIBIOTICS FOR THERAPY (ADULT DOSES)

Organism	Antibiotics of First Choice	Alternative Antibiotics
Acinetobacter species	Ceftazidime 1 g every 8 hours	Gentamicin, imipenem
Enterobacter species	Cefotaxime 1 g every 8 hours; mezlocillin; ceftazidime	L-ofloxacin, gentamicin
Escherichia coli	Ampicillin 1 g every 6 hours; gentamicin; SXT	Cefazolin, L-ofloxacin
Haemophilus influenzae	Cefotaxime 1 g every 8 hours; ampicillin-sulbactam; SXT	Ampicillin,[a] L-ofloxacin
Klebsiella species	Cefazolin 2 g every 8 hours; cefotaxime	L-ofloxacin, gentamicin
Proteus mirabilis	Ampicillin 1 g every 6 hours; gentamicin	L-ofloxacin, cefazolin
Proteus vulgaris *Proteus rettgeri* or *Morganella morganii*	Cefotaxime 2 g every 8 hours	Mezlocillin, L-ofloxacin, or gentamicin
Neisseria gonorrhoea	Ceftriaxone 125 mg	Doxycycline, L-ofloxacin, ampicillin[b]
Providencia species	Cefotaxime 2 g intravenously every 8 hours	SXT tobramycin
	Gentamicin 1.67 mg/kg every 8 hours	Ticarcillin clavulanic acid
Pseudomonas aeruginosa	Ceftazidime[c] 2 g every 8 hours or ciprofloxacin[c] 400 mg every 12 hours; piperacillin[c] 3 g every 6 hours	Ticarcillin clavulanic acid Tobramycin, imipenem
Serratia marcescens	Cefotaxime 2 g every 8 hours	Ofloxacin, gentamicin

[a] Non–β-lactamase–producing strain of *Haemophilus influenzae*.
[b] Nonpenicillinase-producing strain of *Neisseria gonorrhoea*.
[c] In a serious infection should be used with an aminoglycoside—gentamicin or tobramycin 5 mg/kg per day every 8 hours.
SXT, sulfamethoxazole-trimethoprim.
From Mader J, Shirtliff ME, Bergquist SC. Antimicrobial treatment of OM. *Clin Orthop* 1999;360:47–65, with permission.

TABLE 15-41. GRAM-NEGATIVE ORGANISMS: INITIAL CHOICE OF ANTIBIOTICS FOR THERAPY (ADULT DOSES)

Organism	Antibiotic of First Choice	Alternative Antibiotics
Bacteroides fragilis group	Clindamycin 900 mg every 8 hours	Ampicillin-sulbactam
	Metronidazole 500 mg every 8 hours	Ticarcillin-clavulanic acid
Prevotella species	Clindamycin 900 mg every 8 hours	Ampicillin-sulbactam, cefotetan
	Metronidazole 500 mg every 8 hours	Ticarcillin-clavulanic acid
Peptostreptococcus species	Penicillin G 2 mU every 4 hours	Clindamycin, metronidazole, cefotetan
Clostridium species	Clindamycin 900 mg every 8 hours	Metronidazole, penicillin

From Mader J, Shirtliff ME, Bergquist SC. Antimicrobial treatment of OM. *Clin Orthop* 1999;360:47–65, with permission.

TABLE 15-42. ANAEROBIC ORGANISMS: INITIAL CHOICE OF ANTIBIOTICS FOR THERAPY (ADULT DOSES)

Several excellent reviews have been published regarding antibiotic therapy in osteomyelitis (332,333,570,571,883). One of the most important developments in antimicrobial therapy has been the introduction of the oral quinolones. Oral ciprofloxacin has a broad spectrum of activity against both gram-positive and gram-negative organisms. It has a long half-life, low toxicity, and excellent penetration into bone (334,372,568). In randomized trials, ciprofloxacin was as safe and effective as parenteral therapy against a wide variety of organisms, particularly *P. aeruginosa*, with a 2-year success rate of 77% (332). Its efficacy

against *S. aureus* is controversial, and some authors suggest the use of combination therapy for the treatment of gram-positive infections (332,955). The problem of emerging antibiotic resistance also is under investigation (221). This agent is not approved for use in skeletally immature patients (570).

Most coagulase-negative staphylococci are methicillin resistant, and are recognized as virulent pathogens (332). Teicoplanin is a new glycopeptide antibiotic with activity similar to vancomycin. It has a sufficiently long half-life to allow once-daily dosing. It can also be administered by intramuscular injection or rapid intravenous infusion. In several trials, teicoplanin was as effective as vancomycin against all gram-positive organisms and had a low rate of adverse events. The prospect of once-daily intramuscular dosing and low toxicity may make this agent

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attractive for the outpatient treatment of methicillin-resistant gram-positive infections (832).

Oral Versus Parenteral Antibiotics

Four to 6 weeks of parenteral antibiotic therapy following the last debridement has become the standard length of antibiotic therapy (395,956,957). With increasing health care costs and strategies to contain these expenses, patients can be treated on an outpatient basis with a variety of indwelling catheters such as peripheral inserted catheter lines, heparin locks, and implantable catheters. The cost of intravenous antibiotics at home for 6 weeks can range from $3,500 to $10,000 (340). The rate of serious complications from the use of intravenous catheters ranges from 10% to 30% (181,570).

In adults, combined intravenous and oral therapy or oral therapy alone has not been well reported; however, preliminary comparative studies suggest equivalent efficacy between oral and parenteral ciprofloxacin for susceptible organisms as well as between oral ciprofloxacin and standard parenteral antibiotic therapy (568). In a study comparing the clinical outcome of treatment of a series of patients with osteomyelitis by single-stage, aggressive surgical debridement and appropriate soft tissue coverage followed by intravenous antibiotics for 5 to 7 days and oral therapy for 6 weeks, with that of a historical series treated with the same surgical protocol and intravenous antibiotics for 6 weeks, Swiontkowski and colleagues (895) found that short-term antibiotic therapy was successful in 91% of patients, and outcome was no different between series. These results suggest that treatment failures are caused by inadequate debridement rather than the duration of intravenous antimicrobial treatment.

Local Antibiotics

The local deposition of antibiotics has received increased attention (84,85,129,271,627,745,837). These techniques use a space-filling carrier agent that elutes high concentrations of antibiotic into the local tissue. Advantages include local levels of antibiotics that surpass the minimal inhibitory concentration for most pathogens, with minimal systemic levels or complications and the ability to perform primary wound closure. The carrier agent can be either biologic, as in the case of bone graft, demineralized bone matrix, or calcium hydroxyapatite (186), or biologically inert, such as

polymethylmethacrylate (PMMA) or plaster of Paris (198,1000). Carrier agents such as bioabsorbable polymers (DL-lactide:glycolide polymer) (130,326,675), porous apatite-wollastonite glass ceramic, bioerodable polyanhydrides, fibrin clot (923), and polylactide/polyglycolide implant (326) have been described. Work is also being done to incorporate antibiotics into fracture fixation implants. In a rabbit study, Darouiche and colleagues (200) found that an antibiotic-coated intramedullary fixation device reduced the rate of device-related osteomyelitis following infected fracture fixation from 62% to 9%.

If staged management is not necessary, then a biologic agent may be more appropriate. It is important to remember that the elution characteristics of each antibiotic/carrier agent combination are unique and should be understood before it is used. The antibiotic should be water soluble, nontoxic to tissue, bactericidal, available in powder form, and heat stable if used in PMMA (745). Miclau and associates (627) performed a direct comparison of the elution rate of tobramycin from bone graft, demineralized bone matrix, plaster of Paris, and PMMA. Cancellous bone graft released 70% of its antibiotic load in the first 24 hours. Demineralized bone matrix showed a similar elution, with 45% total release in the first 24 hours. Neither agent was detectable at 14 days. Thus, it is important to adjust the dose of antibiotic mixed with bone graft and demineralized bone matrix to prevent a potentially toxic serum level secondary to rapid absorption. Plaster of Paris released 17% of its antibiotic load over the first 24 hours, with measurable elution at 21 days. PMMA eluted only 7% during the first 24 hours, with trace amounts detectable at 14 days.

While staged management may be more time-consuming, it is generally thought to be safer and more effective. In a cohort study, Chan and colleagues (144) found that a two-stage protocol

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using antibiotic-impregnated PMMA beads followed by antibiotic-impregnated autogenous cancellous bone graft resulted in an infection arrest rate of 94.4% and had no adverse effects on bone graft incorporation.

Combinations of antibiotics and PMMA have been used extensively in the treatment of infected total joint replacements, and the elution characteristics of many antibiotics from this material have been studied thoroughly (666). Several authors have published recommendations for the appropriate mixing ratio for various antibiotic and PMMA combinations (156,745). Tobramycin/gentamicin has remained the antibiotic of choice when using antibiotic-impregnated PMMA beads, although there have been reports of the use of other antibiotics including vancomycin and ciprofloxacin. In a study evaluating *in vitro* elution of tobramycin and vancomycin PMMA beads and spacers from Simplex and Palacos cement, Greene and colleagues (369) found that the Palacos beads and spacers showed elution at higher levels and remained above the minimum inhibitory concentration longer than did the Simplex beads, and that tobramycin had superior elution compared to vancomycin (369). Ciprofloxacin-impregnated PMMA cement beads allowed for an elution concentration that was equivalent to the minimum inhibitory concentration for at least 7 days postimplantation (230).

The use of antibiotic-impregnated PMMA beads in the treatment of chronic osteomyelitis has been reported in several series. Blaha and colleagues (84) conducted an eight-center trial comparing the use of PMMA/gentamicin beads and short duration antibiotic therapy (5

days) with conventional 4- to 6-week intravenous antibiotic therapy in a matched set. The authors noted no statistical difference in treatment success between the two groups, but the conventionally treated group had a higher rate of adverse reactions (54%) than did the PMMA/gentamicin bead group (30%), largely because of the systemic effects of the intravenous antibiotics (elevated renal and liver function test results). The PMMA/gentamicin bead group averaged 20% fewer days in the hospital, with a significant cost savings. In a rabbit model, Evans and Nelson (271) found a trend toward higher cure rates when PMMA/gentamicin beads were implanted and conventional antibiotic therapy was used compared with either modality alone (271). Ostermann and colleagues (697) compared 240 open fractures treated using systemic antibiotic prophylaxis with 845 open fractures treated using local application of antibiotic beads in addition to prophylaxis. Local application of antibiotic beads reduced the incidence of infection from 12% to 3.7%.

While clinical results have been good with the use of PMMA/antibiotic-impregnated beads, there are problems with their use. These include a required second surgery for their removal, local immune compromise, a short period of local bactericidal levels of antibiotics, and the presence of a substrate for bacterial colonization (572). These concerns have led to the increased use of biodegradable antibiotic-impregnated calcium hydroxyapatite implants.

The use of calcium hydroxyapatite ceramic as a biocompatible carrier for antibiotics has been investigated (837). Calcium hydroxyapatite ceramic previously has been shown to have excellent biocompatibility (248) and mechanical properties. Removal is not necessary because the material is slowly resorbed and provides a calcium source necessary for new bone formation in the repair process after infection (572). This material showed elution characteristics significantly more prolonged than those of either PMMA or plaster of Paris. In one study, gentamicin concentrations reached a peak 8 days after implantation but still showed bactericidal concentrations after 90 days, with 30% of the drug remaining. In a rat model, Solberg and colleagues (859) showed that hydroxyapatite cement as a carrier of gentamicin was an effective adjuvant in treating chronic osteomyelitis and was as effective as gentamicin-impregnated PMMA beads. A cohort study had no recurrences of infection using calcium hydroxapatite as a drug delivery system in the treatment of chronic osteomyelitis. Further research is necessary, but this class of materials may have significant utility in the adjuvant treatment and dead-space management of chronic osteomyelitis.

Surgical Treatment

Failure to respond to treatment of acute osteomyelitis after 36 hours means that pus is probably present in the metaphysis and possibly in the subperiosteal region. The bone should be exposed at the site of maximal tenderness and swelling. The periosteum is incised longitudinally and pus is evacuated. Specimens are sent for Gram stain, culture, and sensitivity. All devitalized soft tissue is excised and the entire area is irrigated with several liters of normal saline (21). The skin may be loosely closed, but provision should be made for free drainage via drains. The utility of closed suction remains unclear.

Appropriate therapy of chronic or posttraumatic osteomyelitis includes adequate drainage, thorough debridement, obliteration of dead space, stabilization when necessary, wound

protection, and specific antimicrobial therapy. The outcome of osteomyelitis depends on those factors that constitute Klemm's triad: (a) the vitality and stability of bone, (b) the virulence and antibiotic sensitivity of the organisms, and (c) the condition of the soft tissue envelope. Selection of an antibiotic to which the infecting organism is sensitive is ineffective if the antibiotic never reaches the site of infection. This problem is typical of infected tibial fractures since dead bone is not perfused.

In an obviously infected posttraumatic osteomyelitis, the priority, initially, is soft tissue care and antibiotic therapy. Following appropriate culture and biopsy, a thorough debridement of all infected soft tissues and bone is required. All nonvital tissue (including bone) should be excised and the wound left open. The extent of bone debridement is critical and requires experience. Remove all dry, white, dead cortex, leaving only bleeding bone. Following debridement, the infected area is thoroughly irrigated. If extensive bone loss or instability persists, a procedure should be performed to achieve stability. A subsequent debridement can be done and the wound closed over antibiotic beads. Complex soft tissue reconstruction will depend on the stability of the bone (1014).

During the treatment process, patients require adequate nutrition, exercise, and encouragement to stop smoking. Antibiotic selection should be based on the organisms cultured. The duration of antibiotic therapy should be approximately 6 weeks.

Irrigating Solutions

Several studies have examined the relative merits of various irrigating solutions in the debridement of infected soft tissue and

bone (26,232,246,319,651,781). Irrigation with saline alone has been shown in animal studies to reduce colony counts by half in contaminated wounds (63); however, conflicting studies have shown no beneficial effect of saline (141,169). The effect of irrigation with various irrigating solutions in removing adherent staphylococci from bone and soft tissues has been reported (26,79). Studies have shown *in vitro* that while solutions such as betadine and hydrogen peroxide are effective in eliminating bacteria, they are toxic to osteoblasts. Detergents (soaps) have been shown to be the only irrigating solutions that remove additional bacteria above the effect of mechanical irrigation alone (26,79). Moreover, soap solutions have been found to have minimal effects on bone formation and osteoblast numbers *in vitro* (79). The proposed mechanism of their effect is based on the formation of micelles that overcome the strength of the interaction between the organisms and bone.

Debridement Techniques

The cornerstone of the successful treatment of chronic osteomyelitis is the complete removal of all involved bone and soft tissue. The goal is to convert a necrotic, hypoxic, infected wound to a contaminated live wound that can be sterilized by appropriate antibiotic therapy. The precise debridement necessary depends on the anatomic type of osteomyelitis. An atraumatic approach with removal of all nonviable tissue is always necessary. Sinus tracts present for more than 1 year should be excised and sent for pathologic examination to rule out an occult carcinoma (298). Soft tissue retraction should

be minimal, and flaps should not be created.

Meticulous debridement is one of the most important initial steps in the treatment of infected bone and soft tissue. Bone should be exposed in an extensile manner. Efforts should be made to limit any periosteal stripping that may further devitalize the bone. Reactive new bone surrounding an area of chronic infection is living and usually does not require debridement. The sequestrum needs to be identified and removed, whereas the involucrum may be preserved. Rapid debridement may be achieved with a high-speed bur used with continuous irrigation to limit thermal necrosis. The presence of uniform, punctate bleeding, referred to as the paprika sign, is characteristic of living bone.

Laser Doppler flowmetry (LDF) may facilitate an accurate assessment of the microvascular status of bone, thereby identifying it for removal (244,893,894). LDF is the only *in vivo* method of blood flow determination that provides instantaneous determinations of perfusion and is nondestructive. Duwelius and Schmidt (244) found that patients who had recurrence of infection following surgical debridement of osteomyelitis had LDF values significantly lower than those patients without recurrence.

Intramedullary reaming has also been suggested as a method by which to debride medullary infection. If reaming is chosen as a technique for debridement, one should overream the medullary canal by 2 mm. Lavage can be performed from the entry portal with egress through a vent or previous locking screw holes. Dull reamers and the generation of heat should be avoided to prevent further cortical necrosis.

Intramedullary reaming of the canal as a debridement technique has shown favorable results in the treatment of osteomyelitis. In one series, 25 patients with posttraumatic osteomyelitis (of whom 22 were treated with intramedullary reaming) were followed for at least 6 months (693a). At a mean postoperative evaluation of 26 months, 21 of the 22 patients were free of any recurrent infection. In a more recent study, 40 patients suffering from chronic osteomyelitis were treated with intramedullary reaming. Only four patients suffered a recurrent infection following intramedullary reaming (694).

Reaming is contraindicated if endosteal scalloping exists, or if the medullary infection is too proximal (or distal) for a tight reamer fit. In these situations, a trough must be created to debride the canal directly. An oval shape of the trough is biomechanically the most desirable in comparison to other geometries and results in little diminution of the bone's torsional strength.

Stabilization

Indications for stabilization are simply those in which the stability of the bone is compromised postdebridement or there is mechanical instability of a preexisting implant. Greater than 30% loss of circumferential cortical contact or any segmental resection requires stabilization. Options for fixation include external fixators, plates, and intramedullary nails.

External Fixation

External fixators can be large pin, unilateral frames or small wire circular frames. Hybrid

frames consisting of both small wire and large pins are also available. External fixation is the preferred method of stabilizing bone when infection exists. Following a thorough debridement of soft tissue and bone, a unilateral frame can be applied across the bony defect. This method also preserves any remaining blood supply to the debrided bone. Occasionally, it may be necessary to go above the knee or across the ankle to achieve stability. Resection of bone and shortening may be a useful technique to restore stability and improve soft tissue coverage.

When a debridement has necessitated a segmental resection of bone, the application of a circular external fixator can stabilize the bone ends and facilitate distraction osteogenesis (128). While there are significant advantages for the surgeon in using the technique, external fixation has its drawbacks. The length of time in the frame is a major problem for patients, often waiting several months before removal. On average, about 2 months are required for every centimeter of lengthening. Moreover, healing at the docking site is not reliable and often requires bone grafting. Additionally, pin-site infections, pin loosening, and premature consolidation of bone are common in those patients treated with circular external fixators (702).

Green (368) compared the use of circular external fixators alone with open cancellous bone grafting for intercalary defects in long bones. He found docking-site healing problems in the external fixator group and donor-site morbidity in the bone graft group. Cierny and Zorn (158a) in a similar study of patients with segmental tibial defects found that patients treated with the “Ilizarov” external fixator experienced shorter operating room times, shorter hospital stays, and similar complication rates to those treated with bone grafting and soft tissue coverage procedures.

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Ueng and colleagues (928) followed 15 patients with femoral diaphyseal infected nonunions managed with a two-stage protocol including antibiotic-impregnated beads, definitive external skeletal fixation, and staged bone grafting, and found no recurrence of osteomyelitis (928). Similarly, Marsh and colleagues (587) found that segmental excision, distraction osteogenesis, and gradual correction of deformity was 100% effective in eliminating infection in a series of patients with osteomyelitis. The promising outcomes with external fixation support its use in the treatment of bone defects in osteomyelitis.

When using external fixation, patient selection is paramount for success. Recently, an “external fixation risk index (EFRI)” has been proposed for identifying those patients who are at an increased risk of a major complication (failure of implant, failure of union) following the application of external fixation (854). Alcohol use, low socioeconomic status, and smoking history were all independent predictors of poor outcomes with external fixation. Moreover, the odds of having an adverse outcome increased nine times when all three were present.

Plate Fixation

While plates have been used successfully in noninfected bone, they have disadvantages for use in infected bone. The extensive soft tissue dissection necessary with conventional plating techniques may further compromise the blood supply to the debrided bone. Plate fixation should therefore be avoided as a stabilization technique in osteomyelitis. If a plate

currently in place is stable, it may be retained. Bach and Hansen (42), in a randomized trial of 56 patients with open tibial shaft fractures, compared plate fixation with external fixation. Of the 26 patients managed with plates, 13 (50%) needed reoperation; of the 30 patients managed with external fixation, 2 (6.7%) needed reoperation. Thus, despite the limited sample size of 56 patients, the decrease in reoperation with external fixation reached conventional levels of statistical significance (relative risk, 0.13; 95% CI, 0.03–0.54; p <.01). The large risk difference of 43% implies that only two to three patients with open tibial fractures would have to be treated with external fixation compared to a plate to prevent one reoperation.

Intramedullary Fixation

Previous randomized trials have suggested that the overall risk of infection following intramedullary nailing of open tibial shaft fractures is 16.1% (95% CI, 10.6–23.5%) (78). Currently, there is insufficient evidence from randomized trials to suggest that reamed intramedullary nailing of open fractures results in an increased risk of infection. A recent meta-analysis of nine randomized trials comparing reamed and nonreamed intramedullary nails (n = 646 patients) found no increased risk of infection with reaming (relative risk: 0.98; 95% CI, 0.21–4.76) (76).

While intramedullary nails offer advantages over plates in the limitation of soft tissue dissection, their load-sharing capacity, and increased ability to promote bone consolidation, their role in the stabilization of infected bone is unclear. Perry et al. (725) reported a series of actively infected tibial nonunions treated with reamed intramedullary nailing and local and systemic antibiotics. Thirteen of the infections become latent, whereas two remained active and eventually necessitated amputation. In a cohort study of 32 patients who had had an average of 3.2 surgical operations for osteomyelitis, Pape and colleagues (707) found that reaming of the medullary canal was successful such that 84% of patients were able to return to their previous profession and 97% were pain free.

Evidence for the treatment of an infected intramedullary nail has been derived largely from observational data. Pommer and colleagues (738) found that reaming of an infected intramedullary canal resulted in eradication of infection in all patients with initially infected intramedullary nails compared to 62% of those with multiple operations prior to nailing. A series of 20 patients with infection after intramedullary nailing of the tibia was reported by Zych and Hutson (1030). The most common pathogen isolated in their series was *S. aureus*, which was found in 14 patients (64%). Eleven nails were originally inserted without reaming, and nine were reamed. Treatment protocols were based on the time of onset of infection (acute, subacute, and chronic) and the status of bone healing. Six fractures and two nonunions in eight patients were healed at diagnosis of infection and were treated by debridement, nail removal, and antibiotics. Eight fractures and four nonunions in 12 patients were not healed. Four were treated with debridement, nail removal, and external fixation, and four with debridement and nail retention. The overall success rate for eradicating infection was 90%.

Court-Brown et al. (183) reviewed a series of 459 patients with tibial fractures treated by primary reamed nailing. The incidence of infection was 1.8% in closed and Gustilo type I open fractures, 3.8% in type II, and 9.5% in type III fractures (5.5% in type IIIa, 12.5% in

type IIIb). These authors suggested that since bone stability is paramount, the nail is always retained (or exchanged for another). If there is no collection of pus and no discharge, intravenous antibiotics and bed rest are indicated until symptoms resolve. If a collection of pus is identified, it should be incised and drained. The patient should be placed on intravenous antibiotic therapy. If the drainage persists despite these measures, the authors recommend exchange nailing with intramedullary reaming. If drainage of pus is present at the time of diagnosis of the infection, bone resection is often needed. Any avascular bone should be resected and the nail should be exchanged with intramedullary reaming. Soft tissue coverage of the bone should be achieved with delayed bone grafting.

Authors' Approach to Skeletal Stabilization

It must be remembered that skeletal stability is one small part of treatment. If debridement and soft tissue coverage are inadequate, treatment will usually fail. A careful evaluation of preexisting implants should be performed. If the implant is stable, it can be retained. All unstable implants should be removed and plans made to achieve skeletal stability. If there is an unstable implant, good bone quality, a low virulence organism, a good host, and a fracture amenable to intramedullary nailing, then intramedullary fixation is chosen. If there is an unstable implant, poor bone quality, less optimal microbiology (gram-negative or polymicrobial infection), a poor host, and/or a fracture not amenable

to intramedullary nailing, then external fixation is chosen. Plate fixation is generally avoided.

Wound Dressing

In choosing a wound dressing, several characteristics should be considered (262): (a) optimization of wound healing, (b) prevention of infection, (c) ability to absorb exudate, (d) biocompatibility, (e) hypoallergenicity, and (f) occlusivity. Generally, there are four types of wound dressings: semiimpermeable films, hydrogels, occlusive hydrocolloids, and synthetic skin substitutes. Several semiimpermeable membranes are available (OpSite, Tegaderm, Bio-Occlusive). The permeability of these dressings to water and oxygen are 2,500 g/m^2/24 hours and 7,000 mL/m^2/24 hours, respectively (262). The occlusive hydrocolloids (Duoderm) have a permeability to water vapor and oxygen of 30 g/m^2/24 hours and 150 mL/m^2/24 hours, respectively (262). Application of a synthetic dressing is strengthened by a healthy soft tissue border around the wound. Alvarez has reported that reepithelialization beneath a hydrocolloid dressing was greatest, followed by a polyurethane film, air exposure, and wet to dry dressings. However, collagen synthesis was shown to be greater in the wounds exposed to air, followed by the hydrocolloid, polyurethane, and wet to dry dressings. In wounds with exposed bone, dressings should be aimed at preventing wound and bone desiccation and secondary contamination.

Soft Tissue Coverage

Soft tissue reconstruction in osteomyelitis is limited to the use of muscle flaps. The timing of flap coverage in infected bone remains controversial. Although satisfactory results in chronic osteomyelitis have been reported with a single-stage procedure, most authors

advocate a two-stage technique. The first step consists of thorough debridement and culture, and the initiation of empiric antibiotic coverage. Definitive soft tissue reconstruction generally is performed in 5 to 7 days. This interval allows time for the final culture results from the initial debridement to be obtained and specific antibiotic therapy directed against all cultured pathogens to be initiated.

Macroscopically, muscle flaps are pliable enough to completely fill dead space within the debridement cavity with vascularized tissue. They also serve as a vascular bed for immediate skin grafting. Because of the markedly increased blood supply of muscle compared with skin, local oxygen tension, delivery of leukocytes, and antibiotic levels all have been shown to increase in the presence of a muscle flap (31). Anthony and Mathes (31) followed 34 consecutive patients with chronic osteomyelitis of the distal lower extremity treated with debridement, a 10- to 14-day course of culture specific antibiotics, and immediate muscle flap coverage, and found a 96% success rate at a minimum 5-year follow-up. Other authors have reported success rates of 80% to 100% in the use of muscle flaps to cover osteomyelitic wounds (32,591,712,969).

Bone Grafting Techniques

Once all nonviable tissue has been removed and the defect is stable mechanically and biologically, consideration must be given to bone grafting. Standard techniques include open cancellous bone grafting, posterolateral bone grafting, or soft tissue transfer before cancellous bone grafting. Esterhai and colleagues (263) found that treatment of chronic osteomyelitis complicating nonunion and segmental defects of the tibia was less successful with open cancellous bone grafting.

If structural augmentation is required (greater than 30% to 50% volume loss) or nonunion is present, autogenous cancellous bone grafts usually are indicated. In a noncompromised (A-host) patient with a clean wound, these grafts can be placed directly beneath local or transferred muscle at the time of wound closure. Cierny (156) reported a success rate of 93% using this approach and recommended the addition of powdered, pathogen-specific antibiotic to the cancellous grafts at the time of insertion. Some authors recommend staged bone grafting in systemically and/or locally compromised (B-hosts) patients, in the presence of internal fixation, or when massive grafting is required (greater than 50 mL) (156,608). In the interim, the osseous dead space can be maintained with antibiotic-impregnated PMMA beads. Using this technique, the patient is brought back at a later date (2 to 6 weeks) for removal of beads and definitive grafting when the infection is arrested and the host factors are optimized (608).

Segmental defects can be reconstructed using massive cancellous grafting in a staged reconstruction, free bone transfer, or the bone transport techniques of Ilizarov (156,368,1008). The method of Ilizarov offers unique, comprehensive solutions to the problems associated with treating a large infected bone segment. Using the established techniques of stable external fixation, atraumatic corticotomy, and appropriate delay before distraction, large skeletal defects can be spanned. This reconstructive ability permits radical segmental debridement of infected regions. Instead of using necrotic cancellous bone, the dead space is slowly replaced with highly vascular regenerate bone, which has been shown to increase global blood flow to the entire extremity (464). Some authors

suggest that muscle flaps appropriate for the soft tissue defect be used before initiating transport (288). Ilizarov has shown that this may not be necessary because the skin and soft tissue will move with the transporting segment and close the soft tissue defect as the bone gap closes (368,464). Functional use of the limb during treatment is encouraged.

Problems with this technique are numerous. External frames must be in place for extended periods. The patient must be compliant and motivated. Many outpatient visits and adjustments are required, and pin-tract infections are common. Alternative methods have therefore been used. Ueng and colleagues (929) followed 15 patients with large infected tibial defects managed with a two-stage protocol including antibiotic beads, local therapy, and a staged fibular osteoseptocutaneous free transfer, and found no recurrence of osteomyelitis (929).

Authors' Approach to the Treatment of Osteomyelitis

The treatment of osteomyelitis requires a comprehensive and multidisciplinary approach. The classification system of chronic osteomyelitis described by Cierny and Mader is extremely useful. Treatment decisions stem directly from the clinical stage of the

disease. The anatomic extent of the disease and the physiologic status of the host and the local tissues must be understood completely before surgical planning and patient counseling can begin. Previous treatment history should be documented thoroughly, including adverse reactions to antibiotics. Physical examination should include the location of sinus tracts, previous scars, and a thorough neurovascular evaluation. Laboratory testing should include a sedimentation rate and an assessment of nutritional status if this is questionable. Imaging adequate to define the extent of the lesion and the goals of debridement should be performed. Plastic surgery consultation should be considered if soft tissue coverage is a concern. Host factors should be optimized.

Following appropriate culture and biopsy, a thorough debridement of all infected soft tissues and bone is required. All nonvital tissue (including bone) should be excised. The extent of bone debridement is critical and requires experience. Remove all dry, white, dead cortex, leaving only bleeding bone. Intramedullary reaming should be used to debride medullary infection. Following debridement, the infected area is thoroughly irrigated. If extensive bone loss or instability persists, a procedure should be performed to achieve stability. The wound should be closed over antibiotic beads to manage dead space. Empiric antibiotic therapy is begun at this time. Definitive soft tissue reconstruction generally is performed in 5 to 7 days. This interval allows time for final culture results from the initial debridement to be obtained and specific antibiotic therapy directed against all cultured pathogens to be initiated. At the time of definitive wound closure, dead space management is continued with antibiotic-impregnated calcium hydroxyapatite pellets. Once any bony defect is stable mechanically and biologically (at approximately 6 weeks), consideration may be given to bone grafting.