

Staging and Staging Application in Osteomyelitis

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Osteomyelitis is traditionally staged by the Waldvogel classification system. The Waldvogel classification is an etiologic system and does not readily lend itself to guiding surgical or antibiotic therapy. Other classifications have been developed to emphasize different clinical aspects of osteomyelitis. These classifications include those of Ger, Kelly, Weiland, Gordon, May, and Cierny-Mader. The Cierny-Mader classification is based on the anatomy of bone infection and the physiology of the host. The Cierny-Mader classification permits the development of comprehensive treatment guidelines for each stage. The Cierny-Mader classification is used to demonstrate the application of staging for the diagnosis and treatment of osteomyelitis.

Introduction: Staging

Osteomyelitis can be classified by duration, pathogenesis, location, extent, and host status. There is no universally accepted classification system for osteomyelitis, although a number of classifications have been suggested to help guide therapy and to allow for comparison of published results.

The first osteomyelitis staging system was described in 1970 by Waldvogel [1]. He described three categories of osteomyelitis: hematogenous, contiguous focus, and osteomyelitis associated with vascular insufficiency [1]. Hematogenous osteomyelitis is predominantly encountered in the pediatric population, with 85% of cases found in patients younger than 17 years of age. In children, the bone infection usually affects the long bones, while in adults the lesion is usually located in the thoracic or lumbar vertebrae. Hematogenous osteomyelitis is more common in males of any age [2].

Osteomyelitis secondary to a contiguous focus of infection can derive either from a direct infection of bone from a source outside the body (e.g., soft-tissue trauma, open fracture, or surgery) or from the continuous spread of infection from an adjacent focus (e.g., soft-tissue infection, dental abscess, or decubitus ulcer). In terms of age distribution, contiguous-focus osteomyelitis is biphasic. The infection occurs in younger individuals secondary to trauma and related surgery and in older adults secondary to decubitus ulcers and infected total-joint arthroplasties [1].

Osteomyelitis associated with vascular insufficiency is usually seen in individuals with diabetes mellitus. Of the 31 patients in Waldvogel's study with this form of osteomyelitis, 25 were diabetic, 5 had severe atherosclerosis not related to diabetes, and 1 had vasculitis secondary to rheumatoid arthritis [1]. All of the infections affected the toes, metatarsals, tarsals, or hindfoot. The ages of patients in this group mainly ranged between 40 and 70 years.

Of all classification systems, Waldvogel's remains the major osteomyelitis classification system. However, Waldvogel's classification is an etiologic system and does not readily lend itself to guiding surgical or antibiotic therapy. Other classification systems have been developed to emphasize different clinical aspects of osteomyelitis.

Ger's classification system, published in 1982, addressed the physiology of the wound as it relates to osteomyelitis. His categories included simple sinus, chronic superficial ulcer, multiple sinuses, and multiple skin-lined sinuses [3]. If the wound is not appropriately managed, the bone infection cannot be arrested. Early coverage of open tibial fractures with soft tissue will prevent the later development of osteomyelitis, ulceration, and perhaps nonunion.

Kelly's classification system was published in 1984 [4]. Kelly noted osteomyelitis in the adult can be divided into four categories: hematogenous osteomyelitis, osteomyelitis in a united fracture (fracture with union), osteomyelitis in a nonunion fracture (fracture with nonunion), and postoperative osteomyelitis without fracture [4]. Kelly's classification system emphasized the etiology of the infection and its relationship to fracture healing.

In 1984 Weiland [5] defined chronic osteomyelitis as a wound with exposed bone, positive bone cultures, and drainage for >6 months. A similar wound with drainage of <6 months was not considered to be a site of chronic osteomyelitis. He further divided the infection on the basis of soft tissue and the location of bone involved [5].

Type I osteomyelitis was defined as open, exposed bone without evidence of osseous infection but with evidence of soft-

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tissue infection. Type II osteomyelitis showed circumferential, cortical, and endosteal infection. The radiographs demonstrated a diffuse inflammatory response, increased bone density, and spindle-shaped sclerotic thickening of the cortex. Other radiographic findings included areas of bony resorption and often a sequestrum with a surrounding involucrum. Type III osteomyelitis revealed cortical and endosteal infection associated with a segmental bone defect.

Gordon's classification of osteomyelitis was published in 1988 [6]. Gordon classified infected tibial nonunions and segmental defects on the basis of the osseous defects. Type A included tibial defects and nonunions without significant segmental loss. Type B included tibial defects of >3 cm with an intact fibula. Type C included tibial defects of >3 cm in patients whose fibula was not intact. Gordon's classification correlates with the prognosis for successful free-muscle transportation.

May's system of classification was published in 1989 [7]. It focused on the status of the tibia after soft-tissue and skeletal debridement. The system is useful in determining the length of rehabilitation that will be needed, under ideal conditions, before the patient will be able to ambulate without upper-extremity aids. Type I osteomyelitis was defined as an intact tibia and fibula capable of withstanding functional loads (rehabilitation time, 6–12 weeks). Type II osteomyelitis was an intact tibia with bone graft needed only for structural support (rehabilitation time, 3–6 months). Type III osteomyelitis demonstrated a tibial defect ≤6 cm long with an intact fibula (rehabilitation time, 6–12 months).

Type IV had a tibial defect >6 cm and an intact fibula (rehabilitation time, 12–18 months). Type V osteomyelitis had a tibial defect >6 cm long without a usable intact fibula (rehabilitation time, ≥18 months). May's classification system and the estimated time for rehabilitation assists the decision-making process involved in the treatment of posttraumatic tibial osteomyelitis. However, many factors, including age, metabolic status, the mobility of the patient's foot and ankle, neurovascular integrity, and the patient's motivation, can greatly affect the time necessary for rehabilitation.

The Cierny-Mader classification, published in 1984 [8], is based on the anatomy of the bone infection and the physiology of the host (table 1). Cierny-Mader staging allows stratification of long-bone osteomyelitis and permits the development of comprehensive treatment guidelines for each of the 12 stages.

The classification is determined by the condition of the disease process, regardless of its etiology, regionality, or chronicity. The anatomic types of osteomyelitis are medullary, superficial, localized, and diffuse [8]. Stage 1 or medullary osteomyelitis denotes infection confined to the intramedullary surfaces of the bone. Hematogenous osteomyelitis and infected intramedullary rods are examples of this anatomic type. Stage 2 or superficial osteomyelitis, a true contiguous-focus infection of bone, occurs when an exposed infected necrotic surface of bone lies at the base of a soft-tissue wound. Stage 3 or localized

Table 1. Cierny and Mader osteomyelitis staging system.

Classification	Description
Anatomic type	
Stage 1	Medullary osteomyelitis
Stage 2	Superficial osteomyelitis
Stage 3	Localized osteomyelitis
Stage 4	Diffuse osteomyelitis
Physiological class	
A host	Normal host
B host	Systemic compromise (Bs), local compromise (Bl), or systemic and local compromise (Bls)
C host	Treatment worse than the disease

osteomyelitis is usually characterized by a full-thickness, cortical sequestration that can be removed surgically without compromising bony stability. Stage 4 or diffuse osteomyelitis is a through-and-through process that usually requires an intercalary resection of the bone to arrest the disease process. Diffuse osteomyelitis includes those infections with a loss of bony stability either before or after debridement surgery.

The patient is classified as an A, B, or C host (table 1). An A host is a patient with normal physiological, metabolic, and immunologic capabilities [8]. The B host is systemically compromised, locally compromised, or both. When the morbidity of treatment is worse than that imposed by the disease itself, the patient is given the C host classification. The terms acute and chronic osteomyelitis are not used in this staging system since areas of macronecrosis must be removed regardless of the acuity or chronicity of an uncontrolled infection. The stages are dynamic and interact according to the pathophysiology of the disease. They may be altered by successful therapy, host alteration, or treatment. This classification system aids in the understanding, diagnosis, and treatment of bone infections in children and adults.

Host factors are primarily involved with containment of the infection once it is introduced adjacent to or into the bone [8]. A systemically and/or locally compromised host (table 2) does not contain the infection as well as a normal host, and the infection may permeate the bone. The compromised host is more difficult to manage and treat than a normal host. On occasion, host factors may predispose the host to the development of osteomyelitis. These diseases include sickle cell anemia, chronic granulomatous disease, and diabetes mellitus [9]. Host deficiencies that lead to bacteremia favor the development of stage 1 osteomyelitis.

Application of Staging: Cierny-Mader Classification

All of the staging systems described above have obvious merits. Since the Cierny-Mader staging allows stratification of long-bone osteomyelitis and permits the development of

Table 2. Systemic and local factors in class B hosts that affect immune surveillance, metabolism, and local vascularity.

Type of compromise	Factors	
Systemic (Bs)	Malnutrition	
	Renal, hepatic failure	
	Diabetes mellitus	
	Chronic hypoxia	
	Immune disease	
	Malignancy	
	Extremes of age	
	Immunosuppression or immune deficiency	
	Local (B1)	Chronic lymphedema
		Venous stasis
Major-vessel compromise		
Arteritis		
Extensive scarring		
Radiation fibrosis		
Small-vessel disease		
Neuropathy		
	Tobacco abuse (≥ 2 packs/d)	

comprehensive treatment guidelines for each stage, the Cierny-Mader classification will be used as a model for a discussion of the diagnosis and treatment of long-bone osteomyelitis.

Diagnosis

The diagnosis of long-bone osteomyelitis rests on the isolation of the pathogen(s) from the bone lesion, blood, or joint cultures [10]. In stage 1 or hematogenous osteomyelitis, positive blood or joint cultures can often obviate the need for a bone biopsy when there is radiographic or radionuclide scan evidence of osteomyelitis.

Thus, except in Stage 1 osteomyelitis where positive blood or joint fluid cultures may suffice, antibiotic treatment of osteomyelitis should be based on meticulous cultures of bone taken at debridement surgery or of deep-bone biopsy specimens [11, 12]. If possible, culture specimens should be obtained before antibiotic therapy is initiated or after the patient has been off antibiotic therapy for at least 24–48 hours. This time requirement is necessary for two vital reasons. First, since the half-life of many antibiotics is >12 hours, obtaining culture specimens sooner than 24 hours after antibiotic therapy has been stopped may allow the administered antibiotic to interfere with culture growth. Second, since many antibiotics prescribed for osteomyelitis are bacteriostatic, time must be allowed for low numbers of inhibited bacteria to multiply within the host and become detectable by culture techniques.

Sinus tract cultures are not reliable for identifying organisms causing osteomyelitis other than *Staphylococcus aureus* [13]. *S. aureus* and coagulase-negative *Staphylococcus* species are the most common organisms isolated from patients with osteomyelitis. In the immunocompromised patient the physician

must also consider other organisms, including fungi and mycobacteria.

Leukergy, sedimentation rates, C-reactive protein levels, and leukocyte counts are frequently elevated before therapy in the acute disease [14–16]. The WBC count rarely exceeds $15,000/\text{mm}^3$ and the leukocyte count is usually normal in patients with chronic osteomyelitis. The sedimentation rates, C-reactive protein levels, and leukocyte counts may fall with appropriate therapy; however, these values may elevate around each debridement surgery. A sedimentation rate and C-reactive protein level that return to normal during the course of therapy are favorable prognostic signs. However, these laboratory determinations are not reliable in compromised hosts, as these patients are constantly challenged by minor illnesses and peripheral lesions that may elevate these indices.

Radiographic changes in early stage 1 osteomyelitis are often difficult to interpret and lag at least 2 weeks behind the evolution of infection [17]. The earliest radiographic changes are soft-tissue swelling, periosteal thickening or elevation or both, and focal osteopenia. These findings are subtle and may be missed. The more diagnostic lytic changes are delayed and often associated with an indolent infection of several months' duration. Later, when the patient is undergoing appropriate antimicrobial therapy, radiographic improvement may lag behind clinical recovery.

In stage 2 osteomyelitis, the outer cortex of the bone is involved. There may be periosteal thickening or sclerosis. In stage 3 and stage 4 osteomyelitis, the radiographic changes usually show soft-tissue swelling, osteopenia, lytic changes, and sclerosis. Small and large sequestra may also be present. Because of the degree of the sclerosis and nonspecific radiographic changes, it is often difficult to gauge the extent of infection by studying the radiograph. Gauging the extent of infection may require careful clinical and ultimately surgical evaluation. In stage 4 osteomyelitis it is often difficult to distinguish an infected nonunion from one that is not infected.

Radionuclide scans [18, 19], CT [20, 21], or MRI [22, 23] may be performed when the diagnosis of osteomyelitis is equivocal or to help gauge the extent of bone and soft-tissue infection. Technetium-99m methylidiphosphonate scans demonstrate positive isotope accumulation at areas of reactive bone formation. However, these scans cannot delineate between osteomyelitis and normal fracture healing. Two other radiopharmaceuticals include gallium-67 citrate and indium-111 chloride, which bind to transferrin that leaks from the bloodstream into areas of inflammation. However, since these scans do not show significant bone detail, it is often difficult to distinguish between soft tissue and osteomyelitic infection. It is useful to combine technetium-99m methylidiphosphonate scans with gallium-67 citrate and indium-111 chloride scans in order to make this delineation.

Computerized axial tomography identifies areas of necrotic bone, soft-tissue infection, and altered marrow density due to osteomyelitis. This imaging technique has proved to be ex-

tremely useful in selecting a surgical approach in difficult infections. Last, MRI has been recognized as a useful diagnostic modality because of its superior spatial resolution. However, metallic implants in the region of interest may produce focal artifacts, thereby decreasing the utility of the image. In general, however, it is not usually necessary to perform these scans for long-bone osteomyelitis.

Treatment

Appropriate therapy for osteomyelitis includes adequate drainage, thorough debridement, obliteration of dead space, wound protection, and specific antimicrobial coverage [10, 11]. If the patient is a compromised host, an effort is made to correct or improve the host defect(s) (table 2). In particular, attention should be paid to good nutrition and to a smoking-cessation program, besides dealing with specific abnormalities such as control of diabetes. Thus, an attempt is made to improve the nutritional, medical, and vascular status of the patient and to provide optimal care for any underlying disease.

Antibiotic Management

After cultures are performed, a parenteral antimicrobial regimen is begun to cover the clinically suspected pathogens. Once the organism is identified, specific antibiotic class(es) can be selected by appropriate susceptibility testing methods [24]. Because of the need for prolonged therapy, antibiotics employed in the treatment of bone and joint infection must be nontoxic, convenient to administer, and cost-effective.

Stage 1 or hematogenous osteomyelitis in children usually can be treated with antibiotics alone. Antibiotic therapy alone is possible because the bones of children are very vascular and have an effective immune and metabolic response to infection. Stage 1 osteomyelitis in adults is more refractory to therapy and is usually treated with antibiotics and surgery. The patient is treated for 4 weeks with appropriate parenteral antimicrobial therapy, dated from the initiation of therapy or after the last major debridement surgery. If the initial medical management fails and the patient is clinically compromised by a recurrent infection, medullary and/or soft-tissue debridement will be necessary in conjunction with another 4-week course of antibiotics.

Stage 1 osteomyelitis may be due to an infected intramedullary rod. If the bone is stable, the rod can be removed. The patient is given a 4-week course of antibiotic(s), dated from rod removal. If the bone is unstable, the patient is given suppressive oral antibiotic therapy until bony stability is achieved; then the rod is removed and the patient is given a 4-week course of antibiotics, dated from rod removal.

Oral antibiotic therapy can be utilized for treatment of pediatric stage 1 osteomyelitis. However, it is recommended that the child initially receive 2 weeks of parenteral antibiotic therapy prior to changing to an oral regimen [25, 26]. High doses of the quinolone class of antibiotics have been reported to cause

articular cartilage damage in young animals, generating some concern about the long-term use of these agents in infants and children [27, 28]. Therefore, under most circumstances, pediatric patients should not be given the quinolone class of antibiotics.

In stage 2 osteomyelitis, the patient may be treated with a 2-week course of antibiotics following superficial debridement and soft-tissue coverage. The arrest rate is ~80%.

In stages 3 and 4 osteomyelitis, the patient is traditionally treated with 4–6 weeks of parenteral antimicrobial therapy, dated from the last major debridement surgery [10, 11]. Without adequate debridement most antibiotic regimens fail, no matter what the duration of therapy. Even when all necrotic tissue has been adequately debrided, the remaining bed of tissue must be considered contaminated with the responsible pathogen(s). Therefore, it is important to treat the patient for at least 4 weeks with antibiotics. With good debridement surgery, the arrest rate is ~90%. Outpatient intravenous therapy with long-term intravenous access catheters, such as Hickman or Groshong catheters, decreases hospitalization time [29–31].

Oral therapy with the quinolone class of antibiotics for gram-negative organisms is currently being used for adult patients with osteomyelitis [32, 33]. The currently available quinolones have relatively poor activity against *Streptococcus* species, *Enterococcus* species, and anaerobes [34]. The quinolones have modest activity against *S. aureus* and *Staphylococcus epidermidis*, but resistance is increasing [35]. Coverage of aerobic gram-positive organisms should be obtained with other antibiotics such as clindamycin or amoxicillin/clavulanic acid. Before changing to an oral regimen, it is recommended that the patient initially receive at least 2 weeks of parenteral antibiotic therapy. The patient must be compliant and agree to close outpatient follow-up.

Surgical Management

Surgical management of osteomyelitis can be very challenging. The principles of treating any infection are equally applicable to the treatment of infection in bone. These include adequate drainage, extensive debridement of all necrotic tissue, obliteration of dead spaces, stabilization, adequate soft-tissue coverage, and restoration of an effective blood supply [10]. The goal of debridement is to leave healthy, viable tissue. However, even when all necrotic tissue has been adequately debrided, the remaining bed of tissue must be considered contaminated with the responsible organism. The challenge in treating osteomyelitis, as compared to infection of soft tissue alone, involves bone debridement.

Debridement surgery is the foundation of osteomyelitis treatment. Debridement should be direct, atraumatic, and executed with reconstruction in mind. All dead or ischemic hard and soft tissues are excised unless a noncurative procedure has been chosen. If complete excision will threaten bone stability, external fixation may be necessary prior to or during debride-

ment surgery. At debridement, surgical excision of the bone is carried down to uniform Haversian or cancellous bleeding, termed the paprika sign [8].

Adequate debridement may leave a large bony defect known as dead space. Appropriate management of dead space created by debridement surgery is mandatory in order to arrest the disease and maintain the integrity of the skeletal part. The goal of dead-space management is to replace dead bone and scar tissue with durable vascularized tissue. Complete wound closure should be attained whenever possible. Suction irrigation systems are not recommended because of the high incidence of associated nosocomial infections and the unreliability of these setups [36, 37]. Secondary-intention healing is discouraged since the scar tissue that fills the defect may later become avascular.

Local tissue flaps or free flaps may be used to fill dead space [38–40]. An alternative technique is to place cancellous bone grafts beneath local or transferred tissues where structural augmentation is necessary. Careful preoperative planning is critical to the conservation of the patient's limited cancellous bone reserves. Open cancellous grafts without soft-tissue coverage are useful when a free-tissue transfer is not a treatment option and local tissue flaps are inadequate [41].

Antibiotic-impregnated acrylic beads may be used to sterilize and temporarily maintain dead space [42–45]. The beads are usually removed within 2–4 weeks and replaced with a cancellous bone graft. The most commonly used antibiotics in beads are vancomycin, tobramycin, and gentamicin. While these beads have demonstrated significant efficacy, their removal depends upon secondary surgery and the associated risk factors inherent with this surgery. Therefore, a dead-space management method, such as antibiotic-impregnated degradable beads, may eliminate the risk of an associated secondary surgery. Antibiotics (amikacin, clindamycin) have been delivered locally into dead space with an implantable pump [46].

If movement is present at the site of infection, measures must be taken to achieve permanent stability of the skeletal unit. Stability may be achieved with plates, screws, rods, and/or an external fixator. External fixation is preferred over internal because of the tendency of medullary rods to become secondarily infected and to spread the infection.

A new type of external fixator allows bone reconstruction of segmental defects and difficult infected nonunions [47]. The Ilizarov external fixation method utilizes the theory of distraction histogenesis whereby bone is fractured in the metaphyseal region and slowly lengthened. The growth of new bone in the metaphyseal region pushes a segment of healthy bone into the defect left by surgery. The Ilizarov technique is used for difficult cases of osteomyelitis when stabilization and bone lengthening are necessary [48]. The method may also be used to compress nonunions and correct malunions. The technique is labor-intensive and requires an extended period of treatment, averaging 9 months, in the device. The Ilizarov pins usually become infected and the device is painful. The Ilizarov is com-

monly used in a small group of patients for reconstruction of difficult deformities that result from osteomyelitis. The Ilizarov external-fixation method is utilized by most tertiary care hospitals.

Infected pseudarthrosis with segmental osseous defects may also be treated by debridement and microvascular bone transfers [49]. Vascularized bone transfer is a useful procedure for the treatment of infected segmental osseous defects of long bones of >3 cm in length. Vascularized bone transfers can be placed after 1 month of inactive sepsis.

Adequate soft-tissue coverage of the bone is necessary to arrest osteomyelitis. Small soft-tissue defects may be covered with a split-thickness skin graft. In the presence of a large soft-tissue defect or with an inadequate soft-tissue envelope, local muscle flaps and free vascularized muscle flaps may be placed in a one- or two-stage procedure [50]. Local and free muscle flaps, when combined with antibiotic therapy and surgical debridement of all nonviable osseous and soft tissue for chronic osteomyelitis, have a success rate ranging from 66% to 100% [51]. Local muscle flaps and free vascularized muscle transfers improve the local biological environment by bringing in a blood supply important in host defense mechanisms, antibiotic delivery, and osseous and soft-tissue healing.

The Cierny-Mader classification of osteomyelitis not only stratifies the disease and host condition but also provides guidelines for the surgical management of the disease. In stage 1 osteomyelitis or medullary osteomyelitis, the nidus of infection is entirely within the medullary canal of the bone. It usually is caused by blood-borne bacteria or the introduction of surgical hardware such as an intramedullary nail. Because of the location, surgical treatment is usually more straightforward than in other types of bone involvement. In pediatric patients without hardware, surgical therapy is usually not necessary. In adults with primary or secondary stage 1 osteomyelitis, a thorough intramedullary reaming and unroofing is usually done, with or without bone grafting. Soft tissues are reapproximated and the limb is protected by external means (brace or cast) until structural integrity of the bone is reestablished by normal remodeling.

In stage 2 or superficial osteomyelitis, the surface of the bone is exposed because of an overlying soft-tissue defect. The superficial cortex becomes involved with the infection and eventually becomes sequestered (stage 3 progression) if treatment is delayed. The most important aspect of treatment is soft-tissue coverage after adequate debridement to bleeding cortex. This may be a simple problem involving local tissue, or it may require free-tissue transfer.

Stage 3 or localized osteomyelitis combines the problems of both stages 1 and 2. The treatment involves the modalities employed for both of these categories of disease. Bone is sequestered, medullary extension of the infection is common, and major soft-tissue defects may be present as well. These patients may require external fixation for structural support while the bone graft incorporates. Complex reconstruction of both the bone and soft tissue is frequently necessary.

Stage 4 or diffuse osteomyelitis combines problems of stages 1, 2, and 3. Instability is a problem before or after surgery. Therefore, treatment often must be directed toward establishing structural stability and obliterating debridement gaps by means of cancellous bone grafts or the Ilizarov technique. Free flaps and vascularized bone grafts are other possible treatment modalities. All of the modalities previously discussed may have a place in the treatment of diffuse osteomyelitis.

Hyperbaric Oxygen Therapy

When osteomyelitis is associated with reduced local blood flow (such as in diabetes), hyperbaric oxygen therapy may be used as adjunctive treatment. We have previously demonstrated that the reduced oxygen tensions in osteomyelitic bone interfere with normal polymorphonuclear leukocyte activity. Hyperbaric oxygen therapy has been shown to increase the oxygen tensions within infected bone, thereby augmenting the polymorphonuclear leukocyte and localized host immune response.

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