Review article

Recommendations for the treatment of osteomyelitis

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\textbf{Abstract}

With the advances in surgical treatment, antibiotic therapy and the current resources for accurate diagnosis and differentiated approaches to each type of osteomyelitis, better results are being obtained in the treatment of this disease. After a careful literature review carried out by a multiprofessional team, some conclusions were made in order to guide medical approach to different types of osteomyelitis, aiming to obtain better clinical outcomes and reducing the social costs of this disease. Acute and chronic osteomyelitis are discussed, with presentation of the general epidemiological concepts and the commonly used classification systems. The main guidelines for the clinical, laboratory and imaging diagnosis of infections are discussed, as well as the guidelines for surgical and antimicrobial treatments, and the role of hyperbaric oxygen as adjuvant therapy.

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\textbf{Background}

With the advances in surgical treatment, antibiotic therapy, and the current resources for accurate diagnosis and differentiated approaches to each type of osteomyelitis, better results are being obtained in the treatment of this disease. On the other hand, as a result of high-energy trauma with extensive damage to soft tissues requiring more aggressive treatments for open and closed fractures, we have seen a higher number of infections arising from surgical procedures related to these traumatic lesions, which often take the form of post-traumatic osteomyelitis and serious soft-tissue infections. In this scenario, with the progressive increase in traumatic injuries and their associated complications, osteomyelitis – particularly post-traumatic osteomyelitis – is a significant public health problem. The objective of this review article is to indicate some recommendations based on scientific evidence that will guide
the medical approach to different types of osteomyelitis, aiming to obtain better clinical outcomes and at reducing the social costs of this disease. Acute and chronic osteomyelitis are discussed, with presentation of the general epidemiological concepts and the commonly used classification systems. The main guidelines for clinical, laboratory and imaging diagnosis of infections are discussed, as well as the guidelines for surgical and antimicrobial treatments, and the role of hyperbaric oxygen as adjuvant therapy. The conclusions of this multidisciplinary review are summarized below.

I. Which classification should be used?

1. An ideal classification of osteomyelitis should consider the different aspects that influence its pathophysiology, addressing all the possible etiologies and parameters of temporal evolution. It should also be closely correlated with the histological data and should include proposals for the treatment of each classification stage. In general, the Waldvogel classification is recommended for its greater clinical applicability, and the Cierny and Mader classification for its clearly defined surgical treatment proposals (Tables 1 and 2).

II. Which subsidiary tests are important for the diagnosis of osteomyelitis?

2. The diagnosis of osteomyelitis considers a range of clinical signs and symptoms, laboratory tests, imaging studies and histological analyses, as well as the identification of pathogens by means of bone tissue or blood cultures.

3. In terms of laboratory tests, serum leukocyte count and inflammatory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), can assist in the initial diagnosis of osteomyelitis. However, these are non-specific tests and are more useful in the control of treatment.

4. The histology of biological samples should be carried out in all suspect cases, and bone biopsy, soft tissue, and bone sequestrum can confirm the diagnosis of osteomyelitis.

5. A definitive diagnosis of osteomyelitis is obtained with microbiological identification of the pathogen in bone, through a bone biopsy. Samples obtained through swabs of the fistula or secretions for use in cultures will result in false positive results, as they identify microorganisms that colonize the skin. At least three different samples of bone tissue should be obtained, in order to increase the positivity of the test. Antimicrobial therapy should be started after collecting culture samples or at the same time as anesthetic induction. Patients should stop any antibiotics two weeks before collecting culture samples, if possible. In cases of osteomyelitis with osteosynthesis or in infected arthroplasties, sonication of the implants significantly increases the identification of pathogens.

6. The use of complementary imaging methods can be important in the early diagnosis of osteomyelitis. It can also assist in rapid start of treatment and follow-up, enabling ineffective treatments to be modified. In acute osteomyelitis, a plain radiography shows osteomyelitis only after two weeks. Magnetic resonance imaging (MRI) is considered the main type of imaging in the evaluation of bone infections, as it can detect osteomyelitis as early as three to five days of infection. Computed tomography (CT) is of little use in the diagnosis of acute infection, but is important for investigating bone sequestra and planning surgery. Three-phase bone scintigraphy, scintigraphy with Gallium-67 and the positron emission tomography (PET-CT) are examinations that help in the differentiation of doubtful cases.

III. What are the recommendations for the treatment of osteomyelitis?

7. The success of osteomyelitis treatment, particularly in cases related to implants, is closely linked to extensive surgical debridement and adequate antibiotic therapy.
8. Starting empirical antibiotics in anesthetic induction prevents the risks of bacteremia arising from surgical manipulation of infection without adequate antibiotic coverage. Yet, it does not interfere with the positivity of cultures taken during the procedure. Empirical antibiotic can also be started after collecting culture samples in non-septic patients.

9. Empirical coverage of *Staphylococcus aureus* is recommended, given the epidemiological importance of this agent. The local prevalence of methicillin resistance, even in community-acquired cases, is variable and should also be observed.

10. Acute infections can be treated initially with extensive surgical cleaning associated with antibiotic therapy lasting four to six weeks. Chronic infections should be treated with extensive surgical debridement, removal of any implants and antibiotic therapy lasting three to six months.

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**Introduction**

Osteomyelitis, which was named by Nelaton in 1844, is one of the oldest reported diseases known to the scientific community. However, the available epidemiological data are scarce, probably due to the different pathophysiological mechanisms involved in the genesis of the disease, which makes it difficult to estimate the incidence and prevalence in the general population.\(^4\)\(^,\)\(^5\)

Osteomyelitis can be defined as an inflammation of the bone tissue caused by an infectious agent. This infection may be hematogenic, contiguous to an adjacent infectious focus, or even the result of direct bacterial inoculation from a traumatic mechanism. In general, hematogenous osteomyelitis is caused by a single agent, while other types can show polymicrobial infection.\(^6\)\(^,\)\(^7\) Hematogenous osteomyelitis has more consolidated data in the medical literature, and is considered a predominantly pediatric disease, with 85% of patients aged below 17 years.\(^8\) In adult patients, it is estimated that 47–50% of all osteomyelitis are post-traumatic. Vertebral osteomyelitis occurs in 2–7% of patients.\(^9\)\(^,\)\(^10\)

Chronic osteomyelitis represents a major health problem due to its significant morbidity and low mortality rate.\(^3\)\(^,\)\(^5\)\(^,\)\(^8\)\(^,\)\(^10\) This infection occurs in approximately 5–50% of open fractures, in less than 1% of closed fractures with osteosynthesis, and in 5% of acute hematogenous disease.\(^5\) The main problem associated with chronic bone infection is the capacity of the microorganisms to remain in necrotic bone tissue for long periods, especially in tissues that has not undergone adequate surgical debridement.

**Classification systems for osteomyelitis**

Osteomyelitis is a highly heterogeneous disease in its clinical presentation, pathophysiology and treatment. The various clinical syndromes that comprise this entity, although grouped under the same name, should be classified according to their common characteristics, enabling standardization of conducts and comparison of the outcomes of different clinical studies.\(^1\)

Various classification systems have been described in the medical literature, and the adoption of any one should be suitable for the particularities of each treatment center. Recently, new classifications have been described.\(^12\) However, further clinical studies are needed before they can be adopted. In general, the Waldvogel classification\(^2\) is recommended for its greater clinical applicability, and the Cierny and Mader\(^3\) classification for its clearly defined treatment proposals.

**Waldvogel classification**

This classification was described in 1970 and is still the most important and widely used system in clinical studies. The authors divide osteomyelitis according to its physiopathology and the duration of infection. Based on the physiopathology, infections are classified into three groups: hematogenous osteomyelitis; osteomyelitis secondary to a contiguous focus of infection; and osteomyelitis associated with peripheral vascular insufficiency (Table 1). Based on the length of evolution, the infections are classified as acute osteomyelitis and chronic osteomyelitis (recurrences). The authors do not determine a time of evolution that would distinguish between chronic and acute cases.

**Cierny and Mader classification**

The Cierny and Mader classification was described in 1984, as an attempt to address some aspects that were not covered by previous classifications. In this classification, osteomyelitis is divided according to bone anatomy and physiological factors of the host (Table 2). The authors describe four anatomical stages, according to the bone involvement, and three types of host, depending on the patient’s clinical conditions. It was developed mainly for infections in long bones.

**Diagnosis**

Correct diagnosis of bone infections presents many difficulties, as many tests are not widely standardized. The clinical signs and symptoms, along with the inflammatory markers, are also nonspecific. Imaging examinations may elucidate very little in the acute phase of the disease and may not be very specific in the chronic phase, and obtaining tissue samples for culture does not always help confirming the diagnosis. Diagnosis of osteomyelitis requires a set of clinical signs and symptoms, laboratory tests, imaging studies, histological analysis and, finally, the identification of pathogens by means of bone tissue or blood cultures, particularly in cases of hematogenous osteomyelitis.\(^13\)

Clinical suspicion is critical to start medical investigation, and its manifestations depend on several factors, such as the length of infection (acute or chronic), infection site and type of bone involved.\(^13\)\(^,\)\(^14\)

In acute forms of osteomyelitis and in those of hematogenous origin, local symptoms, such as pain, heat, edema, and hyperemia, and systemic symptoms, such as fever, general malaise, and adynamia, appear up to two weeks after the
initial infection. However, the clinical presentation of the dis-
ease can be quite variable. Diagnosis is easier in patients who
present cutaneous fistula or open wound with bone exposure
following open fractures, but very difficult in patients who
have only progressive pain. In chronic forms of osteomyel-
itis, the clinical presentation is highly variable. The systemic
symptoms are usually absent and the local symptoms, such as
hyperemia, heat, edema and fistulization, often appear inter-
mittently, or even years after the beginning of bone infection.

Laboratory tests

Acute infections are often associated with leukocytosis and
neutrophilia – a change that is rarely found in chronic
osteomyelitis. Inflammatory markers, such as ESR and CRP,
are often elevated in acute hematogenous osteomyelitis in
children. However, these are nonspecific tests and are more
important in the control of treatment. The serum procal-
citoxin levels for the diagnosis or follow-up of hematogenous
osteomyelitis in children or in diabetic patients did not prove
effective in several studies. Serum level of interleukin-6 is
most commonly studied as a diagnostic tool of bone infections
associated with joint prosthesis.

Histological tests

Samples of bone, soft tissue and bone sequestra should be sent
for histological analysis after biopsy or surgical debridement,
as these can confirm the diagnosis of osteomyelitis. In acute
osteomyelitis, polymorphonuclear leukocytes are pre-
dominant, while in chronic forms, lymphocytes, osteoblasts
and osteoclasts are predominant. In suspicious cases of
osteomyelitis, histological examination may lead to diagnostic
confirmation in up to 50% of patients. Frozen samples of
bone tissues obtained during surgery with more than five neu-
trrophils per field present sensitivity ranging from 43% to 84%
and specificity of 93–97% in bone infections associated with
orthopedic implants.

Microbiological tests

At least three bone samples should be obtained, in order to
increase the positivity rate of the test. Antimicrobial therapy
should be started after collecting culture samples or at the
same time as anesthetic induction. Patients should stop any
antibiotics two weeks before collecting culture samples, if
possible. Slow-growing bacteria, such as Propionibacterium
acnes, may be associated with osteomyelitis with osteosyn-
thesis, and in these cases it is important to prolong the incubation
time of the culture plates for up to 14 days. In fact, bone cul-
tures can produce false-negative results in up to 40% of cases,
especially in patients using antibiotics.

Sonication significantly increases the identification of the
pathogens when osteomyelitis occurs in the presence of
osteosynthesis, including infected arthroplasties. Sonication
consists of subjecting the implants to low-frequency ultra-
sonic, and consequent rupture of protective extracellular
polymeric surface over the bacteria contained in the biofilms.
The bacteria, thus released from the biofilms into the liquid
medium, remain viable and are cultivated in solid and liquid
culture media.

Imaging diagnosis and nuclear medicine

In acute osteomyelitis, initial plain radiography does not show
any changes. After around three to four days there may be an
increase in soft tissues. Bone changes appear after two weeks,
and poorly delineated lytic lesions can also be observed, sim-
ulating an aggressive lesion. A lamellar periostal reaction
is also evident. Plain radiographies have a positivity rate of
only 20% after two weeks, but are necessary to rule out other
orthopedic illnesses (tumors, fractures).

MRI is considered the main type of imaging in the eval-
uation of bone infections, revealing changes as early as the
first few days of the disease. Bone marrow edema is also
evident in MRI (as poorly defined areas of hyposignal in T1-
weighted sequences and hypersignal in T2, with post-contrast
enhancement). As the disease progresses, abscesses appear,
with typical peripheral enhancement in the contrast phase.
In children, the infection characteristically crosses the growth
cartilage, unlike neoplastic changes. The specificity of MRI is
higher than that of bone scintigraphy in the diagnosis of
infection.

CT is of little utility in the diagnosis of acute infection.
Its role is restricted to the study of bone sequestra in case of
subacute and chronic infections, indicating potential infection
activity.

Ultrasond examination may be of use, especially in
younger patients, as it reveals edema of the soft tissues
around the bone, periostal thickening, and subperiostal col-
lections. An area of hyperemia can also be observed in the
color Doppler. This method provides very little data on intra-
ossseous extension, and is of limited use in this regard.

Imaging methods are of little utility in the therapeutic
management of bone infections. Radiographic changes may
still be present, despite adequate treatment. In these cases,
functional methods, especially PET-CT, play a more important
role.

Nuclear medicine uses radiotracers with known biological
properties in order to outline an image of a physiological
process of the organism. Some of the most common
indications of nuclear medicine methods are in cases of sus-
pected osteomyelitis with doubtful clinical or radiographic
signs, when there are image artifacts in the radiological
methods and in the developmental follow-up or response to
treatment.

PET-CT is a technique that uses positron-emitting iso-
topes to form images, the main one being fluorine-18-labeled
fluorodeoxyglucose. It provides improved spatial resolution,
better sensitivity, and better specificity when compared to
conventional scintigraphy (96% and 91%, respectively). It can
be considered one of the best techniques in nuclear medicine,
but it is a high-cost examination and is only available in a few
diagnostic centers, which limits its use.

Bone scintigraphy is an examination that has histori-
ically been used to differentiate osteomyelitis from soft tissue
infections. It uses diphosphonate radiotracers marked with
technetium-99 metastable isotope (99mTc), methylene diphos-
phonate (99mTc-MDP) being one of the most commonly used.
It is performed in the so-called three-phase mode: the first flow phase with dynamic images acquired immediately after intravenous injection of the radiotracer, for 1 min; the second phase, steady-state, with static images of the region of greatest interest, acquired 5 min after injection of the radiotracer; and the third phase, the late phase, with whole-body images, acquired after 2 h of injection of the radiotracer. It presents reasonable sensitivity (70–89%), but low specificity (16–36%).

Gallium scintigraphy uses gallium-67 citrate, an iron analog radiotracer that concentrates in inflamed tissues due to the higher blood flow and increased concentration of transferrin, to which it binds. It should be used in conjunction with bone scintigraphy for the evaluation of cases of osteomyelitis, where it shows a greater uptake of the radiotracer and infers the presence of active infectious process.

Indium-111 marked leukocyte scintigraphy is considered the best method of nuclear medicine for assessing patients with osteomyelitis, because it is independent of bone remodeling. Because it is a high-cost procedure, and complex to implement, it is available in very few diagnostic centers. It shows good sensitivity (84%) and specificity (80%).

**Antimicrobial treatment**

The rate and extent of antibiotic penetration in bone tissues are seen as determining factors for therapeutic success in osteomyelitis. On the other hand, penetration of an antibiotic into infected bone depends on its pharmacokinetic characteristics, the degree of vascularization, good conditions of soft tissues, and the presence of foreign bodies. Integrating information related to tissue concentration in clinical practice is a stumbling block in the process of antimicrobial selection for the treatment of bone infections.

**Antibiotics with a high bone/serum concentration ratio**

The decision on the clinical usefulness of an antibiotic in osteomyelitis treatment should combine studies on bone concentration with the results of clinical studies in patients with osteomyelitis.

The majority of bone penetration studies are performed in patients undergoing hip replacement surgery, and samples obtained are from uninfected bones. With this in mind, Table 3 shows the bone concentration of the antibiotics presented in clinical studies not involving humans.

**Therapeutic regimens in acute and chronic infections**

The success of osteomyelitis treatment, particularly in cases related to implants, depends on extensive surgical debridement and adequate and effective antibiotic therapy. Starting empirical antibiotics in anesthetic induction prevents the risks of bacteremia arising from surgical manipulation of infection without adequate antibiotic coverage. Yet, it does not interfere with the positivity of cultures taken during the procedure. Empirical antibiotic can also be started after collecting culture samples in non-septic patients.

**Table 3 – Bone penetration of antibiotics.**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Time interval since last dose</th>
<th>Bone/serum concentration ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicilin</td>
<td>2</td>
<td>0.17–0.31</td>
</tr>
<tr>
<td>Amoxicilin + clavulanate</td>
<td>0.5–6</td>
<td>0.01–0.09</td>
</tr>
<tr>
<td>Amoxicilin</td>
<td>0.25–4</td>
<td>0.11–0.71</td>
</tr>
<tr>
<td>Sulbactam</td>
<td>0.25–4</td>
<td>0.11–0.71</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>1</td>
<td>0.18–0.23</td>
</tr>
<tr>
<td>Tazobactam</td>
<td>1</td>
<td>0.22–0.26</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>1</td>
<td>0.11</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>1.6–23.8</td>
<td>0.13–0.19</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0.28</td>
<td>0.07–0.17</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>0.9</td>
<td>0.17</td>
</tr>
<tr>
<td>Cefepime</td>
<td>1–2</td>
<td>0.46–0.76</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>2</td>
<td>0.54</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.25–2</td>
<td>0.18–0.28</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.5–6.5 days</td>
<td>2.5–6.3</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>1–2</td>
<td>0.21–0.45</td>
</tr>
<tr>
<td>Rifampin</td>
<td>2–14</td>
<td>0.08–0.56</td>
</tr>
<tr>
<td>Rifampin (osteomyelitis)</td>
<td>3.5–4.5</td>
<td>0.57</td>
</tr>
<tr>
<td>Ticarcycline</td>
<td>4–24</td>
<td>0.35–1.95</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>0.7–2</td>
<td>0.36–1.0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>0.5–13</td>
<td>0.27–1.2</td>
</tr>
<tr>
<td>Ciprofloxacin (osteomyelitis)</td>
<td>2–4.5</td>
<td>0.42</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.7–6</td>
<td>0.05–0.67</td>
</tr>
<tr>
<td>Vancomycin (osteomyelitis)</td>
<td>1–7</td>
<td>0.27</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.3–1.5</td>
<td>0.4–0.51</td>
</tr>
<tr>
<td>Linezolid (osteomyelitis)</td>
<td>0.9</td>
<td>0.23</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>2</td>
<td>1.08</td>
</tr>
<tr>
<td>Telcooplanin</td>
<td>4–16</td>
<td>0.5–0.64</td>
</tr>
</tbody>
</table>

Adapted from Refs. 40, 42.

The duration of antibiotic therapy varies from four weeks to six months, and the treatment should be adjusted based on the results of the cultures collected, where necessary. Acute infections can be treated initially with extensive surgical cleaning associated with antibiotic therapy lasting four to six weeks.

Chronic infections should be treated with extensive surgical debridement and removal of any synthesis materials, which can be replaced during the same surgical procedure if there is orthopedic indication. Due to biofilm formation, the total administration time of antibiotics in these infections is three to six months. See Table 4.

**Special antimicrobial – rifampin**

There is no antimicrobial regimen that is perfect for every situation. The ability of rifampin in erradicating slow-growing bacteria in biofilms is well known. Thus, the suggestion to add rifampin to another drug with activity against S. aureus is recurrent in the literature, but this drug should never be used as monotherapy.

**Surgical treatment**

**Hematogenous osteomyelitis**

In order to optimize the surgical treatment of osteomyelitis, it is essential to stage the disease correctly. This includes...
investigating inflammatory activity and culture tests, and conducting imaging examinations.49–52 Sometimes infection in the pediatric age group can be confused with other oncological diseases that occur in this age group.53

Surgical treatment is mandatory when abscess is present. Surgical drainage associated with debridement is performed after confirmation of the diagnosis by bone biopsy in the operating room, with all the resources of asepsis and antisepsis.54

The surgical approach may be open surgery, arthroscopy or puncture/aspiration and flushing. The use of flushing under excessive pressure should be avoided, because in addition to causing injury to the soft parts and bone, the pressure can inoculate microorganisms deeply into the tissues.

Adequate debridement is the best predictor of success in the treatment of osteomyelitis. The surgical approach should be of the “oncology” type, i.e. with broad resection. Nowadays, a wide variety of surgical techniques are available for the reconstruction of both bone and soft tissues.59,52,54

**Acute post-traumatic osteomyelitis**

The treatment of acute osteomyelitis is surgical, particularly in the presence of an implant, because early bacterial identification and effective debridement are the only ways to save this implant. The surgeon should heed the clinical signs of a possible infection. During the postoperative period, when there are pain, local hyperemia, inflammation, serous exudate and suspicion of a hematoma at the surgical site, the surgeon must act quickly, taking the patient back to the operating room for debridement and cultures.55

The most important factor for a successful treatment of patients with bone infection is the quality of debridement. The debridement must achieve a clean and viable wound through a non-traumatic exposure. In acute infection, surgical drainage and copious flushing of the cavity significantly reduce bacterial load at the site. Flushing should be performed with saline solution, with a total volume of 3–9 L, and there is a direct relationship between the amount of saline solution used and the reduction of bacterial load.56–58

In situations in which there is a dead space after the removal of devitalized tissues, the use of polymethylmethacrylate cement impregnated with an antibiotic for local release is a good option. The high local concentration of antibiotics obtained using this technique is far above the MIC for the majority of microorganisms, and it would be impossible to achieve this concentration with the use of systemic antibiotics, due to associated toxicity. The antibiotics used in bone cement must not be thermolabile, due to the exothermic reaction of polymerization of polymethylmethacrylate, which inactivates these agents.59,60

**Chronic osteomyelitis**

In the approach to a patient with chronic osteomyelitis, the choice between palliative treatment and a curative approach should be considered. Surgery is currently the only form of cure in almost all cases; however, it is not always the best option. Therefore, a multidisciplinary approach is important in the assessment of each case, in order to decide on the best treatment.

The steps in the treatment of chronic osteomyelitis consist of correct microbiological diagnosis; improvement of the host’s defenses; stabilization of underlying diseases; correct anatomical localization of bone involvement; adequate antimicrobial therapy; surgical debridement of all devitalized tissue; repair of soft tissues; and bone reconstruction and rehabilitation.6

All devitalized tissues need to be removed, and the surgical technique used will depend on the extent of the bone lesion.57,61–67 Wound closure by any means is imperative when vital structures (e.g., vessels, nerves, tendons, bone) are exposed, which may often require local flaps, or more complex flaps located further away (microsurgical). Only complete resection of all the devitalized tissues, with the establishment of adequate blood flow, will lead to effective systemic antimicrobial therapy and resolution of the infection. A resection margin of 5 mm68 should be respected.

The use of antibiotic-coated cement may be an option in cases where there is dead space to be filled after the

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**Table 4 – Suggested empirical initial antimicrobial regimens for osteomyelitis.**

<table>
<thead>
<tr>
<th>Clinical situation</th>
<th>Initial antimicrobial</th>
<th>Possible oral regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community associated</td>
<td>Acute (child&lt;4 months or NB)</td>
<td>Oxacillin, cefazolin or clindamycin + ceftazidime or cefepime</td>
</tr>
<tr>
<td>Healthcare associated</td>
<td>Child and adults (for example, infection after fracture fixation)</td>
<td>Glycopeptide + ceftazidime, cefepime, imipenem/tazobactam or carbapenem agents</td>
</tr>
<tr>
<td>Hemoglobinopathy</td>
<td>Salmonella spp. and other GNBs should be considered</td>
<td>Ceftriaxone or fluoroquinolone</td>
</tr>
</tbody>
</table>

* Considering local prevalence of CA-MRSA.
* Considering local patterns of bacterial susceptibility.
debridement and before the site is definitively closed. Commercially available antibiotic-impregnated cement spacers may be used for this purpose, but manual mixing of the antibiotic cement at the time of use is possible. The most commonly used antibiotic is vancomycin at a dosage of 2–4 grams per 40 g of cement. Other antibiotics may also be used, provided they are not thermolabile, due to the exothermic reaction of the polymethylmethacrylate.  

Another measure is the use of vacuum-assisted closure, which has shown excellent results. Its correct use can significantly improve the condition of the soft tissue wound in terms of its granulation, characteristics of vascularization, and reducing its size.  

**Adjuvant treatment – HBO**

Hyperbaric oxygen therapy (HBO) is a form of adjuvant therapy that has been used worldwide for more than sixty years.  

It is used in patients with infectious, inflammatory, immunological, and ischemic tissue changes. The treatment involves respiration of 100% oxygen under hyperbaric conditions, i.e. under pressures artificially elevated above the atmospheric pressure at sea level, with the patient being placed inside a pressure-resistant hyperbaric chamber. In this setting, large quantities of oxygen under pressure penetrate the blood, are dissolved in the plasma, and reach the tissues. Tissue hyperoxegenation causes specific therapeutic effects, including stimulation of bacterial lysis by leukocytes, increase in proliferation of fibroblasts and collagen, and neovascularization of ischemic or irradiated tissues. The effects of HBO, such as immunomodulation, reduction in pro-inflammatory mediators, and reduction in effects of ischemia-reperfusion in ischemic tissues, are extremely useful for the treatment of infections. The use of hyperbaric oxygen (O₂HB) is associated with all the other therapeutic measures, making them more effective. Wound healing time is accelerated, the esthetic results are better, and the final cost of treatment is also reduced.

**Conflicts of interest**

The authors declare that the meeting for the elaboration of these guidelines was possible due to educational grants received from MSD, Bayer Schering-Pharma and Sanofi-Aventis. Any author received any fee.

**Appendix A. The members of the Diretrizes Panamericanas para el Tratamiento de las Osteomielitis e Infecciones de Tejidos Blandos Group**

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