Vertebral Osteomyelitis, Discitis, and Spinal Epidural Abscess in Adults

Vertebral Osteomyelitis Guideline Team

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Patient Population: Adult patients with suspected or confirmed vertebral osteomyelitis, discitis, paravertebral abscess, or spinal epidural abscess. (This guideline does not address vertebral osteomyelitis associated with hardware placed at a previous surgery.)

Objectives: To improve the timely diagnosis and initial treatment of vertebral osteomyelitis, discitis or paravertebral abscess with or without spinal epidural abscess in adult patients at Michigan Medicine. This guideline does not address antimicrobial adjustments once microorganisms have been identified, and it does not address indications for surgery.

Key Points

Clinical Presentation

Back pain in a patient who has risk factors (Table 1**)** or clinical features (Table 2) that increase suspicion for vertebral osteomyelitis/ discitis (VO) with or without spinal epidural abscess (SEA).

Diagnosis. Evaluate for VO/SEA as follows:

Perform a complete neurologic examination *[I-C]*

Perform a laboratory evaluation: CBC, ESR, CRP, basic metabolic panel, urinalysis and urine culture, and 2 sets of blood cultures. *[II-C]*

Obtain emergent imaging of the spine if the patient has abnormal neurological findings, or within 6 hours if normal neurological findings (see Figure 1). *[I-C]* Imaging options include:

- MRI with and without contrast of the complete spine is the preferred imaging study. Omit contrast if contrast would delay imaging.
- If MRI is not possible (eg, because of large body habitus, an implanted device, or metallic foreign body), obtain urgent CT myelogram (see Table 3).
- If CT myelogram is not possible, perform CT with IV contrast.

Obtain a biopsy. If imaging suggests VO and blood culture is negative, then obtain urgent/emergent biopsy by radiology using imaging guidance. *[I-C]*

Treatment (see Figure 1)

If the patient has either an abnormal neurological exam or imaging evidence of spinal epidural abscess, then: *[I-C]*

- Immediately initiate antibiotics (Table 4).
- Obtain emergent imaging (Table 3).
- Obtain an urgent neurosurgical consultation.

If imaging shows evidence of VO, then: *[I-C]*

- If the patient is hemodynamically unstable, immediately initiate antibiotics (Table 4).
- If the patient is hemodynamically stable, hold antibiotics until after biopsy, unless blood cultures are positive.
- Consider neurosurgery consultation.
- Perform a neurological check every 4 hours.

If the patient is hemodynamically stable and there are no positive imaging or microbiological findings, then: *[II-D]*

- Consider other diagnoses.
- If pain persists, repeat imaging in 1-3 weeks.

Consult the Infectious Diseases Service to assist with antibiotic management and further evaluation. See Figure 1. *[II-D]*

***Strength of recommendation:**
I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.
Levels of evidence reflect the best available literature in support of an intervention or test:
A = randomized controlled trials; B = controlled trials, no randomization; C = observational trials; D = opinion of expert panel.

Table 1. Risk Factors Increasing Suspicion for VO/SEA

Diabetes (the most common risk factor)
Any risk factor for bacteremia (eg, IV drug use or an indwelling vascular device)
Immunosuppression
Malignancy
Cirrhosis, chronic kidney disease, or alcohol use
HIV or AIDS
Rheumatoid arthritis
History of spinal trauma or fracture
Recent spinal procedure
Other foci of infection

Note: Most patients with VO have at least one risk factor present. If no risk factors are present, consider an alternative diagnosis.

Table 2. Clinical Features Increasing Suspicion for VO/SEA

Back pain, often with insidious onset
- Worsening at night
- Focal
- Associated with other systemic symptoms (eg, anorexia, lethargy, weight loss, vomiting)

Fever is variably present (35-60% of VO patients). Absence of fever does not eliminate the possibility of VO.

Focal neurologic symptoms:
- Limb weakness
- Dysesthesias
- Radicular pain
- Gait disturbance
- Bowel or bladder dysfunction

Symptoms vary with location of VO/SEA (eg, cervical involvement may present with dysphagia; thoracic involvement may manifest with autonomic dysregulation).

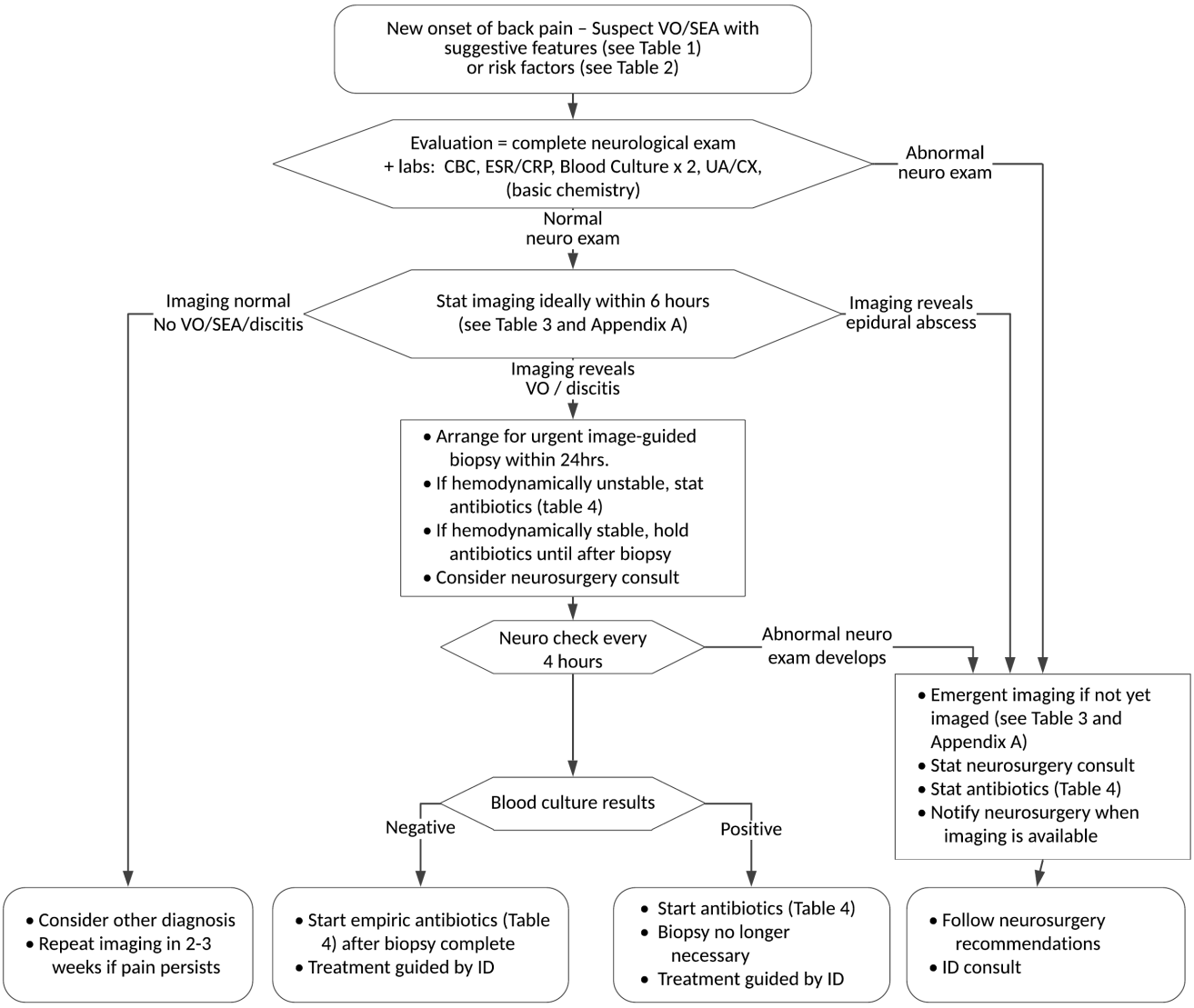
Table 3. Imaging Modality Order of Preference

Select the top ranked modality available and image the entire spine.

1. Obtain an immediate MRI with IV contrast. If this cannot be performed immediately due to contrast allergy, or if using IV contrast would delay the procedure, use next preference.
2. MRI without IV contrast. If MRI cannot be performed (eg, due to large body habitus, an implanted device, or metallic foreign body) use next preference.
3. CT myelogram. If not possible, use next preference.
4. CT with IV contrast. If osseous destruction is present on CT, re-attempt MR or myelogram/CT to evaluate the epidural space.

Note: Scintigraphy (Technetium-99 bone scan, Gallium-67 scan) and metabolic imaging (FDG CT/PET) are not considered primary imaging considerations due to low spatial resolution and specificity.

Figure 1. Evaluation and Initial Treatment of VO/SEA, Excluding Postoperative Infections with Hardware



Note: If abnormal neurological findings are present at any point, shift to right side of algorithm.
CBC: complete blood count; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; ID: Infectious Diseases service; SEA: spinal epidural abscess; UA: urinalysis; UC: urine culture; VO: vertebral osteomyelitis

Table 4. Initial Empiric Antibiotic Treatment of VO/SEA[a]

Preferred: Vancomycin[b] IV per nomogram + ceftriaxone 2 g IV every12 hours

Alternative for suspected or documented pseudomonal infection: Vancomycin[b] IV per nomogram + cefepime[b] 2 g IV every 8 hours

Alternative for penicillin allergy (non-anaphylaxis): Vancomycin IV per nomogram + meropenem[b, c] 2 g IV every 8 hours

Alternative for severe penicillin allergy: Vancomycin[b] IV per nomogram + aztreonam[b] 2 g IV every 6 hours

Alternative for vancomycin allergy or intolerance: Linezolid[c] 600 mg IV every12 hours + other antibiotic as indicated above. (Note: Caution should be advised when using linezolid in patients on medications with serotonergic activity, eg, SSRI and MAOI. Complete information regarding drug interactions with linezolid is available at: https://pharmwebsp.med.umich.edu/AC/_layouts/15/WopiFrame.aspx?sourcedoc=/AC/Antimicrobial%20Use%20Guidelines/Review%20of%20antimicrobial%20agents/Serotonin_Syndrome_Synopsis_3-28-2015.docx&action=default

Consult the infectious diseases service with any questions.
Note: Vancomycin trough target is 15-20 mcg/mL.
[a] Treat vertebral osteomyelitis without spinal epidural abscess with lower doses of antibiotics or cefazolin per Infectious Diseases consultation guidance.
[b] Adjust dose in patients with renal dysfunction.
[c] Use requires prior Infectious Diseases approval.

Clinical Problem and Management Issues

Incidence

The annual incidence of VO/SEA is estimated at 2.4 cases per 100,000 persons, but the incidence of infection increases with increasing age. For persons under the age of 20 years, VO/SEA is uncommon (0.3 per 100,000 persons), whereas the incidence is more than twenty-fold higher in older patients (6.5 per 100,000 persons over age 70 years).[2,3]

Diagnosis and Timing Issues

Although VO/SEA is rare, it is relatively easy to treat when recognized. However, failure to recognize, diagnose and treat it in a timely manner can lead to permanent paralysis or spinal deformity. Unfortunately, diagnostic delays occur frequently, with reports of time from symptom onset to diagnosis ranging from 11 to 59 days.[4]

Factors contributing to these delays include:

- The difficulty of the diagnosis. There is no classic history and physical exam findings that easily and reliably identify VO/SEA. The primary symptom of back pain is a common complaint frequently associated with many less immediately serious conditions.
- Inconsistent approaches to diagnosis and treatment. Differing approaches to VO/SEA limit the development of standardized and evidence-based procedures. For example, there are inconsistencies regarding the timing of empiric antibiotics and which antibiotic combination to use.
- Delays in performing needed studies and obtaining consultations. The risk of rapid progression of VO/SEA means that the processes of care such as imaging and consultations must be performed more rapidly than organizational infrastructures may allow. For example, imaging within a few hours is necessary to help confirm the diagnosis and initiate appropriate treatment. However, care systems are often not in place to assure that imaging can occur on evenings or weekends, resulting in delays of a day or longer in performing some urgent ("stat") imaging orders.

Microbial Etiology

The majority of cases of VO in adults arise from hematogenous seeding of bacteria to the subchondral vertebral body endplate region. Inoculation from spinal surgery or spread from contiguous soft tissue infection may also occur. The most common bacterial cause of vertebral osteomyelitis is *Staphylococcus aureus* (32-67%). Occasionally, coagulase-negative staphylococci may cause VO with or without spinal epidural involvement. Gram negative organisms, such as *Escherichia coli* (21%), often from a urinary tract source, are the next most common bacteria identified. *Pseudomonas sp.* are associated with approximately 6% of cases, and should be suspected when the patient has a history of IV drug use or exposure to inadequately chlorinated water (eg, hot tub, water slide, swimming pool).[2,5]

A less common cause of VO in the U.S., tuberculous VO, occurs in patients with previous *Mycobacterium tuberculosis* exposure, usually patients who have emigrated from areas with endemic tuberculosis, or those who are co-infected with HIV, immunosuppressed, or older.[3,6] VO associated with *Brucella sp*. also occurs in older patients, usually related to travel or emigration from a country with endemic Brucellosis.[3] Finally, fungal VO is much less common, but has been well reported.

Infections of the spine result in a spectrum of disease with varying clinical presentations. Vertebral infection usually arises from bacterial seeding of the vertebral endplate. Infection then spreads to contiguous vertebral bodies (vertebral osteomyelitis). Frequently the paravertebral muscles are involved with muscle abscess. In 17% of cases, infection spreads to the epidural space resulting in spinal epidural abscess. Timely identification of spinal epidural abscess is essential, as one fourth of patients with this condition develop motor weakness or paralysis.[2]

Diagnosis

History and Physical Examination

Recommendations:

- Check for factors that increase suspicion for VO/SEA:
  - For risk factors, see Table 1.
  - For clinical features, see Table 2.
- If VO/SEA is suspected, perform a detailed neurological exam.
- If the patient has an abnormal neurological exam or point tenderness, initiate an urgent investigation for possible SEA.
- If VO/SEA is considered in the differential diagnosis, obtain prompt diagnostic testing (laboratory, imaging).

Vertebral osteomyelitis most commonly occurs in the sixth and seventh decades, more often in males (with a male to female predominance ranging from 1.5-3.1:1). Risk factors are listed in Table 1.

Since the most common mode of infectious spread in VO patients is hematogenous, any risk factor for bacteremia should remain the most important screening tool.

A detailed neurologic exam is essential for any patient suspected of having VO/SEA. Objective neurologic findings are the exception rather than the rule; when present they can range from mild (radicular pain corresponding to a nerve root) to moderate (motor weakness, sensory loss, bowel or bladder dysfunction) to severe (paralysis).

In the presence of an abnormal neurologic exam, point tenderness should prompt an urgent investigation for possible SEA, as delay in diagnosis can result in permanent neurologic deficits. Progression of severity suggests infectious spread into the epidural space with nerve root and eventual cord compression. The presence of point tenderness on spinal palpation can help differentiate VO from other causes of back pain.

No pathognomonic signs or symptoms confirm the diagnosis of VO/SEA. A normal exam does not exclude the diagnosis. The classic triad of fever, back pain, and neurologic deficit in SEA are insensitive markers; in one case series, sensitivity was 7.9%, specificity 99%, positive predictive value 83%, and negative predictive value 68%.

The consequences of a missed diagnosis of VO/SEA are potentially devastating. Therefore, when VO/SEA is being considered in the differential diagnosis, further diagnostic testing with laboratory and imaging evaluation is necessary.

Laboratory Testing

Recommendations:

- Obtain CBC, ESR, CRP, and basic metabolic panel on all patients in whom VO or SEA is considered.
  - Lack of leukocytosis does not exclude the diagnosis.
- Obtain blood cultures from two separate peripheral venipuncture sites. Use blood cultures to confirm the causative organism and to help tailor antibiotic treatment when cultures of biopsy tissue are negative.
- Order a urine culture on all patients.
- If patient has risk factors for active tuberculosis, order a tuberculosis blood test (TB-quantiferon) or place a tuberculosis skin test (PPD).

Blood tests. Common blood tests used in the diagnostic evaluation of patients with suspected VO/SEA include:

- Complete blood count (CBC) with differential
- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP)

These tests can be obtained rapidly, with results usually available within 1-2 hours. Blood cultures are also drawn on initial evaluation, but results will not be immediately available. Blood tests are not completely reliable indicators of disease presence, but can be used in conjunction with:

- Clinical suspicion
- History and physical exam findings
- Diagnostic imaging to confirm the diagnosis

Leukocytosis. The presence of leukocytosis is widely variable (38-80%). Moderate WBC elevation (11.0-17.0) is most common. However, wide ranges have been noted, and the degree of elevation does not predict the severity of disease. The WBC count is highly nonspecific; a lack of leukocytosis should not be used to exclude the diagnosis of VO/SEA.

ESR. ESR is significantly more sensitive than leukocytosis for the early detection of the disease process and should be obtained on all patients in whom VO/SEA is considered. Sensitivity ranges from 68-100%; however, in the case series with 68% sensitivity, only an ESR > 50 mm/hour was considered positive (normal range 0-20 mm/hour). When any value > 20 mm/hour is considered abnormal, sensitivity increases to 84-100%. In a meta-analysis of 915 patients with confirmed spinal epidural abscess, the sensitivity of doing ESR at the initial evaluation was noted to be 94%.

CRP. CRP has a similar sensitivity of 84-100% in cases of confirmed SEA, but it may be a more effective marker of early disease because its serum concentrations rise faster than ESR or WBC, and it is less influenced by other plasma factors. Concentrations of CRP also decrease rapidly with disease resolution and may be used to guide time to treatment completion.

Basic metabolic panel is used to assess for uncontrolled hyperglycemia and uremia, since patients with these conditions have a significantly higher incidence of VO/SEA.

Blood cultures. Obtain cultures from two separate peripheral venipuncture sites whenever possible.

Blood culture sensitivity varies from 31-68%. Positive cultures are more likely to be present when the patient has a more severe, disseminated infection, and less likely when the patient has a localized infection (discitis). *Staphylococcus aureus* is the most common pathogen isolated, although there is an increasing prevalence of gram-negative organisms seen in IV drug users.

Results of blood cultures will not be available for 24-48 hours, so they therefore rarely can be used to guide initial diagnostic or treatment decisions. However, blood culture results are used in conjunction with direct tissue culture to confirm the causative organism, as well as to help tailor antibiotic treatment when cultures of biopsy tissue are negative.

Urinalysis. Urinary tract infection is a frequently missed source of bacteremia. Order a urine culture on all patients suspected of VO/SEA.

Tuberculosis testing. For any patient with suspected VO/SEA and risk factors for having active tuberculosis, order a tuberculosis blood test (TB-quantiferon) or place a tuberculosis skin test (PPD) at the time of initial evaluation. Tuberculous epidural abscess is less prevalent in the United States compared with many Asian countries; however, it must be considered as a potential etiology in the appropriate at-risk patient.

Imaging Modalities and Approach

Recommendations:

When an infectious process involving the spine is of clinical concern:

- Obtain an urgent MRI with and without contrast of the whole spine to assess for occult lesions.
  - If contrast allergy or using IV contrast would delay the MRI, perform MRI without IV contrast.
  - If the initial MRI is negative and suspicion for VO/SEA continues, repeat MRI in 1-3 weeks, as scans can become positive.
- If MRI cannot be performed (eg, large body habitus, implanted or indwelling device, or metallic foreign body), obtain CT myelogram followed by CT scan to assess for spinal canal involvement with compression of neural structures.
- If neither MRI nor a CT myelogram can be performed, obtain a spine CT with IV contrast.

A guide for selecting an imaging modality is presented in Table 3. The characteristics of modalities and sequenced preference among them are reviewed below.

MRI with or without contrast.[7,8] When an infectious process involving the spine is of clinical concern, perform an urgent contrast-enhanced MRI of the whole spine. MRI is the examination of choice due to its superior contrast and spatial resolution, multiplanar capabilities and lack of ionizing radiation. Other imaging modalities are reserved for "problem-solving" (ie, can be useful for further characterization of abnormalities incompletely delineated on MRI), or when MRI is unavailable or contraindicated.

Early MRI (within the first 2 weeks of onset of symptoms) may not demonstrate any abnormalities, or may show only subtle abnormalities that could be attributed to chronic degenerative change.[9] Therefore, if clinical suspicion for a spinal infectious process persists in the setting of a negative or near-negative initial MRI, consider repeating a contrast-enhanced MRI. Scans can become positive as soon as 1-3 weeks after an initial negative study.[10-13] Alternatively, metabolic imaging or scintigraphy could be considered (see Nuclear Medicine section below).

A noncontrast MRI is still an excellent test to identify VO/SEA. In patients with a contrast allergy, evaluation for a suspected vertebral inflammatory process with a noncontrast MRI avoids the 13-hour delay needed to complete a typical corticosteroid premedication protocol. A noncontrast spine MRI can essentially rule in or out an inflammatory process of the spine, discs, and spinal canal. However, contrast-enhanced imaging may ultimately be necessary to better delineate the true extent of an abnormality (eg, to identify subtle vertebral endplate abnormalities or subtle epidural extension of an inflammatory process).[14]

Mid-thoracic and lower thoracic spinal infectious processes can present with lower back pain. If a patient with findings suspicious for VO/SEA has only been evaluated with a lumbosacral spine MRI study, then consider additional imaging to include at least the thoracic spine. Ideally, perform complete spinal imaging to assess for occult lesions.

CT myelography. MRI may be contraindicated in a patient with large body habitus, an implanted device, or metallic foreign body. If so, perform a myelogram followed by CT scanning. This will assess for spinal canal involvement by an inflammatory process with compression of neural structures, which is the most serious potential complication of a spinal infection.[15] The CT myelogram will also evaluate for osseous destruction.

CT myelography is as good as MRI for delineating spinal cord or cauda equina compression, although it is a more invasive procedure and utilizes ionizing radiation. However, disc or spinal canal involvement by an inflammatory process that has not yet encroached on the thecal sac is poorly evaluated with CT myelography. It can demonstrate some of the osseous changes of osteomyelitis and even some paraspinal phlegmons or abscesses, but still not as well as MRI.

True allergic reactions to current-generation myelographic contrast media are extremely rare. Because the morbidity associated with potentially delaying making a diagnosis of an acute spinal cord compression can be devastating, consider the risks and benefits before delaying CT myelography in order to complete a 13-hour corticosteroid premedication protocol.

CT with IV contrast. If neither MRI nor CT myelography can be performed, obtain a spine CT with IV contrast. Contrast CT is better than a noncontrast CT because intravascular contrast material may enhance the epidural venous plexus or the periphery of an inflammatory process within the spinal canal, spine, disc, or in the paraspinal region. However, CT with IV contrast is inferior to both CT myelography and MRI because it can potentially miss spinal canal extension (with or without spinal cord compression) by an inflammatory process.

Spinal pathology that is incidentally found on an imaging study and which could potentially explain symptoms should be assessed with urgent dedicated imaging, preferably MRI, of that portion of the spine (see Figure 1 and Table 3). For example, use MRI to assess a destructive vertebral process or a paraspinal lesion that was noted on a chest CT done to rule out pulmonary embolus.

Noncontrast CT (ie, without intrathecal or intravascular contrast) can demonstrate destructive osseous changes of osteomyelitis and even some paraspinal phlegmons or abscesses about as well as CT myelography, but not as well as MRI.[16] Discs and the spinal canal are poorly evaluated with noncontrast CT. One cannot use noncontrast CT alone to assess for spinal canal involvement.

When an interventional MR suite is not available, CT is the imaging modality of choice to guide biopsy of a disc, vertebral body, or paravertebral area.[12] In some cases, as per radiologist preference, fluoroscopically-guided biopsy is an accepted alternative.[17]

Nuclear medicine**.** Possible nuclear medicine studies include FDG CT/PET imaging, gallium-67 citrate scintigraphy, and bone scan. However, each one has limitations that restrict its use to special circumstances.

FDG (^{18}F-fluorodeoxyglucose) CT/PET imaging: While FDG CT/PET might be a viable imaging alternative when MRI is negative or equivocal, it is not considered a diagnostic option for the urgent assessment of VO. There are also logistical issues with obtaining after-hours FDG CT/PET imaging. Some studies suggest that metabolic imaging such as FDG CT/PET is as sensitive as MRI for the detection of VO and potentially more sensitive in the acute phase of VO when MRI may be negative or equivocal with respect to differentiation between degenerative changes and inflammatory changes.[18] However, the limited resolution of FDG CT/PET inhibits the ability to discriminate among vertebral, discal and epidural inflammation, and makes it difficult to assess for involvement of the spinal canal and for spinal cord or cauda equina compression.[7,17]

Gallium (^{67}Ga) citrate scintigraphy: This may be a viable alternative for detecting an acute spinal inflammatory process and differentiating it from degenerative change. However, similar to FDG CT/PET, the resolution remains inferior to MRI. Also spinal canal involvement by an inflammatory process, an important component of the evaluation of these patients, cannot be reliably assessed on gallium citrate scintigraphy.

Bone Scan: 3-phase technetium-99 (^{99m}Tc) bone scanning performed in the absence of other imaging findings has been reported as relatively specific and sensitive for spinal infection.[19] However, these scans also suffer from the same issues described above for FDG CT/PET and gallium scanning: inferior spatial resolution limits evaluation for spinal canal involvement.[7,17] Even when using single-photon emission computed tomography (SPECT) technique, bone scans remains inferior to MRI. A further limitation of bone scanning is its worsening specificity in older patients with multiple co-morbidities (eg, extensive degenerative changes).

Plain radiographs of the spine. Plain radiographs of the spine do not show soft tissues (eg, discs, inflammatory soft tissue, phlegmons, abscesses) and do not demonstrate even minimal osseous changes for at least several weeks after the onset of infection. They have no role in the urgent evaluation of patients with suspected spinal infection,[7,11] with the possible exception of assessing for spinal stability (eg, lateral flexion and extension imaging). Perform such imaging with caution, particularly in a patient with a suspected pseudoarthrosis. When MRI demonstrates findings suggestive of inflammatory involvement of a disc or vertebral body, fluoroscopy (ie, real-time plain radiography), as opposed to CT, may be used to guide biopsy of a vertebral body or disc.

MRI or CT myelography. Even when a diagnosis of VO is made or suggested by other imaging (eg, chest CT, noncontrast spine CT, scintigraphy), further imaging with MRI or CT myelography is still indicated to evaluate for spinal canal (ie, epidural region) involvement.

Biopsy

Recommendation:

If an inflammatory process is suspected in or around the spine, perform urgent biopsy for timely identification of the etiologic agent.

If an inflammatory process is suspected in or around the spine, urgent biopsy may be indicated for timely identification of the etiologic agent before (and even sometimes after) initiation of appropriate antibiotic coverage. Obtaining an urgent image-guided (eg, CT, fluoroscopy) biopsy by neuroradiology, musculoskeletal radiology, or interventional radiology within 24 hours is a reasonable goal. This should be requested by the primary clinical service in consultation with infectious diseases and neurosurgery. Specific tests to be obtained from a biopsy specimen should be guided by the infectious diseases service, based on the patient's risk factors.

If an initial image-guided biopsy is nondiagnostic, obtain consultations with the infectious diseases and neurosurgical services to determine if repeat image-guided biopsy or even an open biopsy is indicated.

Treatment

Empiric Antibiotic Therapy

Recommendations:

- Initiate antibiotic therapy:
  - In a patient who is hemodynamically unstable, has a positive blood culture or abnormal neurological exam, or has imaging evidence of SEA, immediately initiate antibiotic treatment, before biopsy.
  - In a patient who has vertebral osteomyelitis with epidural thickening but no frank abscess, and does not have hemodynamic instability, positive blood cultures, abnormal neurological exam or imaging evidence of SEA, hold antibiotics until biopsy can be performed.
- Select an initial empiric antibiotic: Unless information is available from prior blood cultures or other cultures, combination therapy with vancomycin and ceftriaxone is recommended (see Table 4).

Initiating antibiotic therapy. Whether to initiate empiric treatment or hold antibiotics until biopsy can be performed depends on the stability of the patient and the associated balance of risk and benefit.

Delaying empiric treatment may result in rapid progression of the infection. However, the early empiric administration of antibiotics might alter the results of subsequent biopsy performed to identify the etiologic agent. Evidence is limited regarding the effects of antibiotics on the sensitivity of cultures of biopsy tissue; however, most literature and experts recommend withholding antibiotics in stable patients until a biopsy can be performed.[2,3,6]

At least one study addresses the yield of biopsy in the setting of antibiotics. In 150 patients with hematogenous-derived vertebral osteomyelitis, 92 (61%) underwent biopsy at a median of 3 days after admission (range 0-69 days). Sixty-five patients had antibiotics started prior to biopsy. There was no association of culture results with previous administration of antibiotics. The authors concluded that vertebral biopsy should be performed in patients with VO despite previous treatment with antimicrobial therapy.[20]

Initial empiric antibiotic drugs. Table 4 presents specific recommendations and dosing for drug combinations. Empiric treatments should be broad enough to treat the most likely bacterial etiologies and have good penetration into the central nervous system. Broad initial treatment reduces the potential for adverse outcomes due to delays in appropriate therapy.

Staphylococcus aureus is the most common microorganism associated with VO/SEA. Therefore, antimicrobial therapy directed at staphylococci is essential. At the time of this guideline, the rate of methicillin-resistance in *S. aureus* at Michigan Medicine is approximately 50%; therefore, vancomycin is the treatment of choice. Provide treatment doses that achieve a vancomycin trough level of 15-20 mcg/mL.

To treat *E. coli* and other gram negative bacilli:

- Ceftriaxone at meningitis treatment doses, 2 grams every 12 hours, is recommended in addition to vancomycin.
- If *Pseudomonas* is suspected due to a history of IV drug use or exposure to inadequately chlorinated water (eg, hot tub, water slide, swimming pool), then administer cefepime with vancomycin.

Alternative treatments for patients with vancomycin or cephalosporin allergies are listed in Table 4.

Empiric treatment for *Mycobacterium tuberculosis* or *Brucella sp.* is generally not indicated at our institution, but may be recommended by the Infectious Diseases consult service, based on patient risk factors.

Management of Identified Microorganism

Recommendation:

- When cultures specify a microbial etiology for vertebral osteomyelitis, use antimicrobial therapy directed at the known organism.
- If no epidural involvement is identified, then lower doses of antibiotics or cefazolin may be indicated per Infectious Diseases consult.

Directed antimicrobial therapy is guided by the infectious diseases consult service. Generally, these infections are treated for 6-8 weeks, but longer durations of treatment may be recommended for patients felt to be high risk for relapse.[6,21]

Management of Abnormal Neurological Findings or Epidural Abscess

Recommendations:

- Either neurological deficit or progressive spinal deformity, with or without neurologic symptoms, is an indication for urgent surgery.[22]
- Immediately start antibiotic therapy. (See previous section "Empiric antibiotic therapy")
- In patients without neurological symptoms, if imaging reveals a possible mass or abscess, obtain urgent neurosurgical consultation.
- In select cases (eg, neurologically stable with known diagnosis and facilities to manage, extended pre-existing paralysis, or significant medical comorbidities), patients may be managed medically with biopsy and antibiotics.

Abnormal neurological findings or an epidural abscess can rapidly progress, requiring urgent assessment and treatment. Therefore, timely management is necessary to avoid permanent disability. Neurological deficit or progressive spinal deformity, with or without neurologic symptoms, is an indication for urgent surgery. Asymptomatic spinal epidural abscesses may also be treated surgically or drained percutaneously with interventional radiology guidance to prevent the development of neurologic deficits.[23] Drainage of paravertebral abscesses is indicated if abscesses are accessible; however, this intervention is not urgent.

In any patient who has suspected VO/SEA with neurological symptoms suggestive of possible spinal cord or cauda equina compression**,** obtain urgent imaging, immediately initiate antibiotics (see Table 4), and obtain an urgent neurosurgical consultation, as indicated on the right side of Figure 1.

In patients without neurological symptoms, if imaging reveals a possible mass or abscess, obtain urgent neurosurgical consultation. The neurosurgical consultant will ultimately determine the need for and timing of surgery.

In select cases SEA can be managed medically, in a similar manner as for VO (see below), with biopsy and antibiotics.[24] Reported criteria for non-operative management include:

- Known pathogenic organism, neurologically stable, availability of MRI or CT for rapid follow-up, and close, serial neurosurgical or nursing monitoring.[25,26]
- Patients with pre-existing paralysis for an extended duration (> 36-48 hours) may not need surgical intervention.
- Significant medical comorbidities may preclude urgent surgical intervention.

Management of these patients should be guided by the infectious diseases consult service.

Management of Neurologically Stable Patients with VO

Recommendations:

- When VO is suspected from imaging, arrange for image-guided biopsy within 24 hours.
- Obtain neurosurgery consultation.
- If the patient is hemodynamically unstable, has abnormal neurological findings, or has a positive blood culture, immediately initiate antibiotic treatment.
- Obtain an infectious diseases consultation to help with long-term management.
- If image-guided biopsy is negative, obtain a neurosurgery consultation for consideration of an open biopsy.

Neurologically stable patients must be managed in a timely manner, including proceeding with a diagnostic evaluation, while monitoring their neurological status. When VO is suspected from imaging, arrange for urgent image-guided biopsy within 24 hours. Consider obtaining a neurosurgery consultation.

As described earlier, immediately initiate antibiotics for a patient who is hemodynamically unstable, has abnormal neurological findings, or a positive blood culture (Table 4). In a patient without these findings, hold antibiotics until image-guided biopsy can be performed.[27] If blood cultures are positive, biopsy of the spine is not necessary, as the bloodstream organism is usually the organism in the VO/SEA.

Continue neurological checks every 4 hours until biopsy is performed, antibiotic treatment has started, and symptoms are improving. Development of abnormal neurological findings would then trigger a change in management, as described above for patients with abnormal neurological findings.

Once image-guided biopsy has been performed, limit empiric antibiotics. Obtain an infectious diseases consultation to help with long-term management. If image-guided biopsy is negative, consider consultation with neurosurgery for an open biopsy.

Imaging Normal, No Evidence of VO/SEA

Recommendations:

- When no evidence of VO/SEA is present on imaging or other tests (left side of Figure 1), consider other diagnoses.
- If clinical concern for VO persists, consider:
  - FDG CT/PET or scintigraphy (gallium or bone scan) to assess for early changes of VO.
  - Repeating MRI in 1-3 weeks to see if results have become positive.

Infectious Diseases Consultation for Long-term Management

Recommendation:

Consult the infectious diseases service to assist with antibiotic selection and timing of administration for suspected cases of VO.

Several studies have shown that infectious diseases consultation on patients with *Staphylococcus aureus* bacteremia is associated with improved adherence to evidence-based therapies and up to a 56% decrease in mortality.[28,29] Infectious Diseases consultation is recommended for all patients with *S. aureus* bacteremia, with or without vertebral osteomyelitis, because of the high risk for infection at secondary sites, including VO and endocarditis.

Related National Guidelines

The literature search revealed no established national guidelines specifically addressing VO/SEA.

Related National Performance Measures

At this time no major national programs have clinical performance measures related to VO/SEA. These programs include: Centers for Medicare & Medicaid Services (Physician Quality Reporting Measures for Group Practice Reporting option, Clinical Quality Measures for financial incentive for Meaningful Use of certified Electronic Health Record technology), National Committee for Quality Assurance: Healthcare Effectiveness Data and Information Set, and programs in our region (Blue Cross Blue Shield of Michigan: Physician Group Incentive Program clinical performance measures, Blue Care Network: clinical performance measures).

Guideline Development Methodology

Funding

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Guideline Development Team and Disclosures

The multidisciplinary guideline development team consisted of:

- Primary care physicians: Megan R. Mack, MD
- Specialists: Benjamin S. Bassin, MD, Emergency Medicine; Carol E. Chenoweth, MD, Infectious Diseases; Mark E. Oppenlander, MD, Neurosurgery; Rakesh D. Patel, MD, Orthopaedic Surgery; Douglas J. Quint, MD, Radiology.
- A guideline development methodologist: F. Jacob Seagull, PhD, Learning Health Sciences.
- Literature search services were provided by informationists at the Taubman Health Sciences Library, University of Michigan Medical School.

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

No relevant personal financial relationships with commercial entities: Benjamin S. Bassin, MD; Carol E. Chenoweth, MD; Megan R. Mack, MD; Mark E. Oppenlander, MD; Rakesh D. Patel, MD; Douglas J. Quint, MD.

Relevant personal financial relationships with commercial entities: None.

Strategy for Literature Search

Within the Medline (Ovid**)** database, the following terms were used:

1. *osteomyelitis/
2. exp spine/ or spinal diseases/ or spinal cord diseases/
3. 1 and 2
4. *Epidural Abscess/ or *Discitis/
5. (epidural abscess* or discitis or vertebral osteomyelitis).ti.
6. 3 or 4 or 5

Results were limited to: Humans, Adults, English, and 2002 to current. Comments, editorials, and letters were excluded from the search results. This main search retrieved 1,274 references. When the search hedges for Guidelines, Clinical Trials, and Cohort Studies were added, the base results are as follows:
Vertebral Osteomyelitis-Guidelines, total results were 8
Vertebral Osteomyelitis-Clinical Trials, total results were 33
Vertebral Osteomyelitis-Cohort Studies, total results were 337

Within the Cochrane Database of Systematic Reviews, no reviews were found using a title, abstract, or keyword search, specifically ("vertebral osteomyelitis" or "epidural abscess*" or discitis).ti,ab,kw.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

Level of evidence supporting a diagnostic method or an intervention:

A = systematic reviews of randomized controlled trials
B = randomized controlled trials
C = systematic review of non-randomized controlled trials or observational studies, nonrandomized controlled trials, group observation studies (eg, cohort, cross-sectional, case control)
D = individual observation studies (case or case series)
E = opinion of expert panel.

Search details and evidence tables available at http://www.uofmhealth.org/provider/clinical-care-guidelines.

Recommendations

Guideline recommendations were based on prospective randomized controlled trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size. The “strength of recommendation” for key aspects of care was determined by expert opinion.

The strength of recommendations regarding care were categorized as:

I = Generally should be performed
II = May be reasonable to perform
III = Generally should not be performed

Review and Endorsement

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Departments of Infectious Diseases, Emergency Medicine, Internal Medicine, Neurosurgery, Orthopaedic Surgery, and Radiology. The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

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Appendix A. Obtaining Urgent Imaging and Related Sedation or Anesthesia at Michigan Medicine

Obtaining Urgent MRI or CT Myelography

Urgent ("Stat") MRI:

Call the Lead MRI Tech at 734-936-8876. Be prepared to discuss special needs such as sedation/anesthesia (see more below), metal implants or foreign bodies, or large body habitus.

If the Lead MRI Tech cannot facilitate the study within the recommended time frame:

During regular hours (8:00 am to 6:00 pm), ask to speak to the Neuroradiology attending **for MRI**.

After hours (Weekdays 6:00 pm to 8:00 am, and all day on weekends and holidays), call the Radiology Superchief (ext. 734-763-1800 or pager 1800). If this person cannot facilitate the study within the recommended time frame, ask to speak to the **Diagnostic** Neuroradiology Attending on call*.

Urgent ("Stat") CT myelography:

During regular hours (7:00 am to 5:00 pm), call the Lead Neuroradiology Procedure Nurse at 734-615-3774.

After hours (Weekdays 5:00 pm to 7:00 am, and all day on weekends and holidays), call the Radiology Superchief (ext. 734-763-1800 or pager 1800). If this person cannot facilitate the study within the recommended time frame, ask to speak to the **Procedure** Neuroradiology Attending on call*.

Arranging Sedation or General Anesthesia for MRI

Nurse-monitored sedation (eg, for patients with claustrophobia, pain, or inability to remain still):

Discuss need for sedation with the Lead MRI Tech (734-936-8876). The Lead MRI Tech may be able to facilitate the procedure with sedation provided by the radiology nurses. Of note, radiology RN's do not sedate ED or ICU patients.

If the Lead MRI Tech is unable to facilitate the procedure with sedation in a timely manner (eg, lack of radiology nurse capacity, or after hours), the two options for provision of sedation are:

SWAT (Michigan Medicine's in-house critical care team, pager 8000). The SWAT nurse can provide moderate sedation for MRIs 24/7, but this will require that a physician who is credentialed in conscious sedation be present in the MRI area during the scan. During regular hours, a radiologist is present who can perform this role. After hours a physician from the primary service will be required to be present to perform this role. If appropriate, the lead tech will contact SWAT to schedule the test.

Anesthesiology. The anesthesiologists can provide moderate sedation in some situations (eg, the primary hospital physician is not credentialed for moderate sedation), but their availability is limited. If this option is selected, the primary team will be asked to contact the Anesthesia UH OR Clinical Director (pager 8003) to see if they can accommodate the request.

General anesthesia (eg, patient required general anesthesia for MRI in the past or failed imaging using lighter sedation):

Discuss the need for general anesthesia with the Lead MRI Tech (734-936-8876), as above.

If general anesthesia is required, the Lead MRI Tech will direct the primary team to page Anesthesia UH OR Clinical Director (pager 8003) to discuss the case. Anesthesia will then contact lead tech to schedule the test.

* The phone numbers for radiology on-call from 5:00 pm to 8:00 am, as well as holidays and weekends are available at http://www.med.umich.edu/radiology/oncall/ClinSrvcContact-OnCall.pdf