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# Interim Treatment Guidance for Central Nervous System and/or Parameningeal Infections Associated with Injection of Potentially Contaminated Steroid Products

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The pathogens involved in this cluster of infections are still under investigation. At present, there is culture and/or histopathologic evidence of fungal infection in at least nine patients; isolates have included *Aspergillus* spp. and *Exserohilum* spp. At least one patient also had *Propionibacterium acnes* of unclear clinical significance isolated from a post-mortem central nervous system (CNS) specimen. When initiating treatment for patients with meningitis (i.e., cerebrospinal fluid [CSF] pleocytosis regardless of glucose and protein levels), epidural abscess, and/or vertebral osteomyelitis of unknown etiology who are linked to the cluster, clinicians should continue to follow routine empiric treatment protocols to cover for potential bacterial pathogens and add empiric broad-spectrum antifungal therapy to the treatment regimen because of the severe adverse outcomes of untreated invasive fungal infection. These recommendations are based upon current evidence that at least two fungal pathogens are involved, and the possibility that additional pathogens may be identified as the investigation continues. CDC has consulted with national experts on treatment options for fungal CNS and/or parameningeal infections in patients associated with this cluster. The following represents interim guidance and may change as new information becomes available.

Consult an infectious disease physician to assist with diagnosis, management, and follow-up which may be complex and prolonged.

After collecting cerebrospinal fluid for culture, initiate empiric combination antifungal therapy using the following regimen in addition to routine empiric treatment protocols to cover for potential bacterial pathogens until the etiology of the patient's CNS and/or parameningeal infection has been identified:

- Voriconazole, preferably at a dose of 6mg/kg every 12 hours (IV initially) and to continue on this high dose for the duration of treatment, if possible. Regular monitoring of serum concentration is advisable.

AND

- Liposomal Amphotericin B (preferred over other lipid formulations), preferably at a dose of 7.5 mg/kg IV daily (higher than standard dose). If nephrotoxicity is a potential concern, particularly in older patients, the dose may be decreased to 5mg/kg IV daily. Administration of 1L normal saline prior to infusion may be considered to minimize risk of nephrotoxicity.

- Avoid routine use of intrathecal amphotericin B, either the deoxycholate or the lipid formulations, due to limited data on its use and associated toxicities.

Adequate duration of treatment is unknown but likely will require prolonged antifungal therapy (e.g., months) tailored by the clinical response to infection.

Individual management decisions, including choice of long-term antifungal regimen, should be made in consultation with infectious disease physicians experienced in the treatment of fungal infections. Clinicians should be vigilant for potential relapse of infection after completion of therapy.

At this time, CDC does not recommend initiation of antifungal prophylaxis in exposed patients who are asymptomatic and/or have normal CSF laboratory examination.

These patients should be closely monitored for development of symptoms, with a low threshold for performing lumbar puncture should the patient become symptomatic.

There is currently no clear evidence for the use of adjuvant steroid therapy. If used, careful monitoring of clinical status is warranted.