Interim Treatment Options – Outbreak of Unknown Meningitis
As of October 3, 2012

At present, the etiologic agent of this cluster of meningitis has not been clearly identified. However, a mold species has been isolated from CNS specimens from at least two patients linked to the outbreak, one of whom also had *Propionobacterium acnes* of unclear clinical significance isolated from a post-mortem CNS specimen. Two additional patients have preliminary histopathologic evidence of fungal infection. When treating patients with meningitis who meet the outbreak case definition,[1] clinicians should continue to follow routine treatment protocols for meningitis of unclear etiology, including covering for potential bacterial causes of meningitis. In addition, until the etiology is better defined, clinicians are encouraged to add empiric antifungal therapy to the treatment regimen because of the severe adverse outcomes of untreated fungal meningitis. CDC has consulted with national experts on the following guidance; these treatment options for fungal meningitis in patients associated with this cluster are interim, and may change as new information becomes available.

Initiate empiric antifungal therapy using the following regimen:

- At a minimum, all patients should receive voriconazole (if no contraindications), 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. Periodic monitoring of serum concentration is advisable.

- Consider combination therapy with liposomal Amphotericin B (preferred over other lipid formulations), preferably at a higher dose of 7.5 mg/kg IV daily. 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 use of intrathecal amphotericin B, either the deoxycholate or the lipid formulations, due to limited data on its use and associated toxicities.

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

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 meningitis. Clinicians should be vigilant for potential relapse of infection.

[1]A person with meningitis of sub-acute onset (1-4 weeks) following epidural injection after July 1, 2012. Meningitis is defined as having 1 or more of the following symptoms: HA, fever, stiff neck, or photophobia **and** a CSF profile consistent with meningitis (elevated protein, low glucose, and pleocytosis).