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CDC Health Advisory

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Meningitis and Stroke Associated with Potentially Contaminated Product

Summary

The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) are coordinating a multi-state investigation of fungal meningitis among patients who received an epidural steroid injection. Several of these patients also suffered strokes that are believed to have resulted from their infection. As of October 4, 2012, five deaths have been reported. Fungal meningitis is not transmitted from person to person. These cases are associated with a potentially contaminated medication. Investigation into the exact source is ongoing; however, interim data show that all infected patients received injection with preservative-free methylprednisolone acetate (80mg/ml) prepared by New England Compounding Center, located in Framingham, MA.

Background

On September 21, 2012, CDC was notified by the Tennessee Department of Health of a patient with the onset of meningitis approximately 19 days following epidural steroid injection at a Tennessee ambulatory surgery center (ASC). Initial cultures of cerebrospinal fluid (CSF) and blood were negative; subsequently, *Aspergillus fumigatus* was isolated from CSF by fungal culture. On September 28, investigators identified a case outside of Tennessee, possibly indicating contamination of a widely distributed medication. As of October 4, a total of 35 cases* in the following six states have been identified with a clinical picture consistent with fungal infection: Florida (2 cases), Indiana (1 case), Tennessee (25 cases, including 3 deaths), Maryland (2 cases, including 1 death), North Carolina (1 case), and Virginia (4 cases, including 1 death). Fungus has been identified in specimens obtained from five patients, one of whom also had *Propionobacterium acnes,* of unclear clinical significance, isolated from a post-mortem central nervous system specimen.

Infected patients have presented approximately 1 to 4 weeks following their injection with a variety of symptoms, including fever, new or worsening headache, nausea, and new neurological deficit (consistent with deep brain stroke). Some of these patients' symptoms were very mild in nature. CSF obtained from these patients has typically shown elevated white cell count (with a predominance of neutrophils), low glucose, and elevated protein.

Recommendations

On September 25, 2012, the New England Compounding Center located in Framingham, MA voluntarily recalled the following lots of methylprednisolone acetate (PF) 80mg/ml:

- Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #05212012@68, BUD 11/17/2012
- Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #06292012@26, BUD 12/26/2012
- Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #08102012@51, BUD 2/6/2013

On October 3, 2012, the compounding center ceased all production and initiated recall of all methylprednisolone acetate and other drug products prepared for intrathecal administration.

Physicians should contact patients who have had an injection (e.g., spinal, joint) using any of the three lots of methylprednisolone acetate listed above to determine if they are having any symptoms. Although all cases detected to date occurred after injections with products from these three lots, out of an abundance of caution, CDC and FDA recommend that healthcare professionals cease use of **any** product produced by the New England Compounding Center until further information is available.

For patients who received epidural injection and have symptoms of meningitis or basilar stroke, a diagnostic lumbar puncture (LP) should be performed, if not contraindicated. Because presenting symptoms of some patients with meningitis have been mild and not classic for meningitis (e.g., new or worsening headache without fever or neck stiffness), physicians should have a low threshold for LP. While CDC is aware of infections occurring only in patients who have received epidural steroid injections, patients who received other types of injection with methylprednisolone acetate from those three lots should also be contacted to assess for signs of infection (e.g., swelling, increasing pain, redness, warmth at the injection site) and should be encouraged to seek evaluation (e.g., arthrocentesis) if such symptoms exist.

For guidance on diagnostic testing that should be performed on patient specimens, physicians can go to http://www.cdc.gov/hai/outbreaks/meningitis.html. State health departments should be informed of patients undergoing evaluation. Clinicians should report any suspected adverse events following use of these products to FDA's MedWatch program at 1-800-332-1088 or www.fda.gov/medwatch.

*Case Definition
1: A person with meningitis[1] of sub-acute onset (1-4 weeks) following epidural injection after July 1, 2012.
2: A person, who has not received a lumbar puncture, with basilar stroke 1-4 weeks following epidural injection after July 1, 2012[2].
3. A person with evidence of spinal osteomyelitis or epidural abscess at the site of an epidural injection diagnosed 1-4 weeks after epidural injection after July 1, 2012.
[1]clinically diagnosed meningitis meaning 1 or more of the following symptoms: headache, fever, stiff neck, or photophobia **and** a CSF profile consistent with meningitis (elevated protein/low glucose/pleocytosis)
[2]These people, if possible, should have an LP.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Health Alert	conveys the highest level of importance; warrants immediate action or attention.
Health Advisory	provides important information for a specific incident or situation; may not require immediate action.
Health Update	provides updated information regarding an incident or situation; unlikely to require immediate action.

##This Message was distributed to State and Local Health Officers, Public Information Officers, Epidemiologists and HAN Coordinators as well as Clinician organizations##

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