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Fungal Meningitis Outbreak Larger Than Predicted

October 11, 2012 (**UPDATED October 12, 2012**) — The number of people exposed to potentially contaminated methylprednisolone acetate produced by the New England Compounding Center (NECC) in Framingham, Massachusetts, is closer to 14,000 — not 13,000 — as originally reported on October 8, federal health officials said today.

"These 14,000 patients received the medication as a steroid injection either into the spinal area or into a joint space such as a knee, shoulder or ankle," said J. Todd Weber, MD, incident manager of the multistate meningitis outbreak at the Centers for Disease Control and Prevention (CDC). More than 12,000 of these people have been contacted to date, he said.

As of today, the CDC said a total of 170 cases (including the 14 deaths) have been reported across 11 states: Florida (7 cases, 2 deaths), Idaho (1 case), Indiana (21 cases, 1 death), Maryland (13 cases, 1 death), Michigan (39 cases, 3 deaths), Minnesota (3 cases), New Jersey (2 cases), North Carolina (2 cases), Ohio (3 cases), Tennessee (49 cases, 6 deaths), and Virginia (30 cases, 1 death).

First Case of Joint Infection Reported

Notably, the 170 cases include 1 joint infection case "just reported" to CDC, Dr. Weber said.

"CDC and the Michigan Department of Community Health have confirmed today the first patient with evidence of joint infection following injection with the implicated medication. Laboratory results are not complete at this time, so we cannot be sure if this is a fungal infection," Dr. Weber added.

"We expect through our patient notification efforts we may see additional patients come forward with infections of the joint. They may present with fever, increased pain, redness, warmth, or swelling in the joint where they received the injection," he said.

The first patient with fungal meningitis from Tennessee had documented evidence of Aspergillus infection. Since that time, the laboratory-confirmed cases of fungal meningitis have all had infection caused by the fungus Exserohilum. To date, CDC laboratories have confirmed the presence of Exserohilum in 10 people with meningitis and Aspergillus in only 1 person with meningitis (the first patient), Dr. Weber said. CDC is also aware of 3 additional Exserohilum cases confirmed by other laboratories, he said.

"Historically, fungal meningitis is very rare and Exserohilum has not been seen previously as a cause of fungal meningitis. This is new territory for public health and the clinical community," Dr. Weber said.

He emphasized that Exserohilum can be difficult to detect in samples from patients. Clinicians "should not assume fungal testing that is negative means that there is no infection. In other words, patients who received an injection with 1 of the 3 recalled lots of steroid may be diagnosed with meningitis but their fungal testing may be negative. In these cases, patients should still be treated for fungal meningitis."

Updated Clinical Guidance

The CDC has posted updated clinical guidance for central nervous system and/or parameningeal infections associated with injection of potentially contaminated steroid products.

At this time, CDC is recommending that patients with confirmed fungal meningitis receive 2 antifungal drugs — voriconazole, preferably at a dose of 6 mg/kg every 12 hours (intravenous initially) and to continue receiving this high dose for the duration of treatment, if possible; and liposomal amphotericin B, preferably at a dose of 7.5 mg/kg intravenously daily (higher than standard dose).

"These drugs are very strong and can be very difficult for patients to tolerate over a long period of time. We are working with our clinical experts to determine the best dose and the best length of time to treat patients. As additional information comes, it is possible that these recommendations will change," Dr. Weber said.

At this time, the CDC does not recommend initiation of antifungal prophylaxis in exposed patients who are asymptomatic. These patients should be closely monitored for development of symptoms, with a low threshold for performing lumbar puncture should the patient become symptomatic.

Also at this time, the CDC does not recommend empiric antifungal therapy for symptomatic patients who have normal results on laboratory examination of cerebrospinal fluid. These patients should be closely monitored and re-evaluated for progression of symptoms. Should the patient's symptoms progress, a lumbar puncture should be repeated immediately, the CDC advises.

"Not Out of the Woods Yet"

Dr. Weber acknowledged that "we know we are not out of the woods yet. Patients who develop symptoms of meningitis or joint infection in the coming weeks need to be evaluated promptly."

The onset of symptoms is typically between 1 and 4 weeks; however, there are reports of longer time between injection and onset of symptoms, Dr. Weber said, "so patients and their doctors will need to be vigilant for at least several months following the injection."

Symptoms include fever, new or worsening headache, nausea, and new neurologic deficit consistent with deep brain stroke. Almost all patients have reported headaches and almost half have reported fever, back pain, or nausea. Some of these symptoms were mild, CDC says.

The CDC has also posted formal case definitions for the outbreak.

"Given the severity of fungal meningitis, time is of the essence. We know we can save lives by identifying patients early and getting them on appropriate antifungal therapy," Dr. Weber said.

Instructions for clinical teams regarding diagnostic testing and submitting of specimens have also been posted.

During the briefing, Deborah M. Autor, JD, deputy commissioner for global regulatory operations and policy at the Food and Drug Administration (FDA), said, "It is our goal here at FDA to understand and contain the health risk as quickly as possible. We consider this a top priority and we are dedicating many, many resources to this investigation."

"Once the immediate crisis is contained we want to work to closely with Congress, compounders, states, and all stakeholders to strengthen the system to try to prevent tragedies like this in the future," she said.

Although the investigation is ongoing, Madeleine Biondolillo, MD, director of the Massachusetts Department of Public Health's Division of Health Care Quality in Boston, said it appears that "NECC under Massachusetts board of pharmacy licensing regulations was licensed to deliver compounded products in response to individual patient specific prescriptions. And it looks through the investigation as though they have violated that aspect of the state licensing regulation, despite their assertion that they were operating under the regulations."