Subject: North Carolina’s Final Report on the Multi-state Outbreak of Fungal Infections Associated with Contaminated Methylprednisolone Injections from New England Compounding Pharmacy

Summary

In September 2012, the North Carolina Division of Public Health was notified by CDC of a suspected case of fungal meningitis in a North Carolina resident. This resident was subsequently determined to be part of an extensive, multi-state outbreak of fungal infections associated with contaminated steroid injections. As of September 6, 2013, 750 cases and 64 deaths had been identified among residents of 20 states with 18 cases and 1 death among residents of North Carolina. A collaborative investigation conducted by the CDC, FDA, and state and local health departments identified contaminated methylprednisolone, an injectable steroid, as the source of the outbreak. The steroid was recalled and an expert panel of fungal specialists was convened to determine best practices for diagnosis and treatment of identified cases. This outbreak represents one of the largest healthcare-associated infection outbreaks in the history of the United States.[1]

Background

On the evening of September 27, 2012, the North Carolina Division of Public Health (NCDPH) was notified by the Centers for Disease Control and Prevention (CDC) of a suspected case of fungal meningitis in a North Carolina resident. CDC had been contacted by the treating physician due to concern that this patient might be linked to an ongoing investigation of similar cases among patients who had received injections at a single clinic in Tennessee. Common exposures among the Tennessee patients and the North Carolina resident included epidural spinal injections with methylprednisolone acetate (MPA), an injectable steroid product. A public health investigation was initiated to determine the source of infection and identify other persons who might have been exposed.
Methods

Initial Public Health Response

On September 28, NCDPH activated incident command and sent a health alert to local health departments, microbiology laboratories, and professional medical societies in North Carolina describing the potential outbreak of fungal meningitis associated with epidural spinal injections. Although the source of the outbreak was unknown, MPA produced by a single compounding pharmacy was a common exposure among all known and suspected cases. CDC provided NCDPH with a list of the three North Carolina medical facilities that had received MPA from the compounding pharmacy. NCDPH contacted all three facilities on September 28 and asked them to sequester the product, identify all patients who had been potentially exposed to the product, and contact all patients immediately to advise them of their potential exposure.

Overview of Multistate Investigation

Prior to North Carolina’s suspect case, all known cases were clustered among patients who received injections at a single medical clinic in Tennessee. CDC and the Tennessee Department of Health (TDH) were conducting a joint investigation to determine the likely exposure. [2, 3] Once the North Carolina case was identified, CDC became concerned that the outbreak may be related to a product with a wider distribution. On September 28, CDC sent a call for cases to all public health officials nationwide through the Epidemic Information Exchange (Epi-X). By October 7, 2012, 91 cases and 7 deaths had been identified among residents of 9 states.

As the lead organization, CDC developed and refined a case definition for probable and confirmed cases. This definition was modified over the course of the investigation as new information became available (see box below). Case counts from each state were reported daily to CDC. A case report form was developed to collect information from each case about exposures, injections, and outcomes. Case report forms were completed by state health department staff through physician interviews and medical chart reviews, and then faxed to CDC upon completion. CDC maintained a de-identified record of all cases and each state maintained a protected record of their own cases.

<table>
<thead>
<tr>
<th>Case Definitions</th>
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</thead>
<tbody>
<tr>
<td><strong>Probable Case</strong></td>
</tr>
<tr>
<td>A person who received a preservative-free methylprednisolone acetate (MPA) injection, with preservative-free MPA that definitely or likely came from one of the following three lots produced by the New England Compounding Center (NECC) [05212012@68, 06292012@26, 08102012@51], and subsequently developed any of the following:</td>
</tr>
<tr>
<td>- Meningitis(^1) of unknown etiology following epidural or paraspinal injection(^2) after May 21, 2012;</td>
</tr>
<tr>
<td>- Posterior circulation stroke without a cardioembolic source and without documentation of a normal cerebrospinal fluid (CSF) profile, following epidural or paraspinal injection(^2) after May 21, 2012;(^3)</td>
</tr>
<tr>
<td>- Osteomyelitis, abscess or other infection (e.g., soft tissue infection) of unknown etiology, in the spinal or paraspinal structures at or near the site of injection following epidural or paraspinal injection(^2) after May 21, 2012; or</td>
</tr>
<tr>
<td>- Osteomyelitis or worsening inflammatory arthritis of a peripheral joint (e.g., knee, shoulder, or ankle) of unknown etiology diagnosed following joint injection after May 21, 2012.</td>
</tr>
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</table>

\(^1\) Clinically diagnosed meningitis with one or more of the following symptoms: headache, fever, stiff neck, or photophobia, in addition to a CSF profile showing pleocytosis (>5 white blood cells, adjusting for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present) regardless of glucose or protein levels.

\(^2\) Paraspinal injections include, but are not limited to, spinal facet joint injection, sacroiliac joint injection, or spinal or paraspinal nerve root/ganglion block.

\(^3\) Patients in this category who do not have any documented CSF results should have a lumbar puncture performed if possible, using a different site than was used for the epidural injection when possible.

| **Confirmed Case** |
| A probable case with evidence (by culture, histopathology, or molecular assay) of a fungal pathogen associated with the clinical syndrome. |

Source: [http://www.cdc.gov/hai/outbreaks/clinicians/casedef_multistate_outbreak.html](http://www.cdc.gov/hai/outbreaks/clinicians/casedef_multistate_outbreak.html) (accessed on October 18, 2013)
Early in the investigation, CDC evaluated methylprednisolone, lidocaine, povidone-iodine, and sterile supplies as possible sources of infection. As additional cases were identified, preservative free MPA from the New England Compounding Center (NECC) in Framingham, Massachusetts, emerged as the only common product. CDC and the US Food and Drug Administration (FDA) led the product investigation. The agencies jointly coordinated testing of the MPA produced by NECC, evaluated NECC’s production practices and provided updates to state and local stakeholders about their progress.

As the scope of the outbreak increased, CDC activated their Emergency Operations Center (EOC) and initiated several Epi-Aid investigations. The EOC provided support and coordination for state investigations and the Epi-Aids sought to describe the affected populations, identify common themes, and evaluate response to therapy. In addition, CDC convened a Fungal Expert Panel to provide ongoing guidance for case identification and management.

**North Carolina Case Finding and Response**

Three facilities in North Carolina received MPA from NECC: High Point Surgery Center, Surgical Center of Wilson, and North Carolina Orthopedic Clinic (Duke-affiliated). The High Point and Wilson clinics primarily gave spinal injections and the NC Orthopedic Clinic gave peripheral joint injections.

**Initial Patient Outreach**

NCDPH notified the facilities of the outbreak on September 28th and asked them to sequester any remaining MPA, identify all patients who had been potentially exposed to the product, and contact all patients immediately to advise them of their potential exposure. NCDPH provided support to the facilities over the weekend of September 29–30 to facilitate prompt patient notification. Priority was given to patients who had received spinal injections, as no joint infections had been described in the early phase of the investigation. NCDPH provided a phone script for the facilities to use when contacting each individual to ensure each patient received the same information. Patients were called at least three times by phone. If a patient could not be reached after three attempts, NCDPH coordinated with local communicable disease nurses to conduct home visits. A small number of individuals were still unreachable despite multiple attempts to visit them at home. In these cases, the communicable disease nurse called the patient’s personal physician (found on the clinic visit record from the facility that gave the MPA injection) to identify the emergency contact listed in the patient’s medical chart. Neighbors were approached to determine if an unreachable patient was on a vacation or business trip, and to ask if additional contact information was available. Through this variety of methods, all patients were contacted about their potential exposure and advised to seek medical attention immediately if they developed any signs or symptoms of infection. By October 1, 81% of spinal injection patients had been contacted, and notification was complete on October 5. Notification of all joint injection patients was complete on October 11.

**Additional Patient Outreach & Monitoring**

NCDPH and the three facilities agreed that continued contact with all exposed individuals was a priority. It was anticipated that additional information would be learned during the outbreak investigation that could impact patient care and that patients would need to be monitored closely for signs and symptoms of illness. Each facility designated a single person as the outbreak liaison. Patients were given the name and contact information for this individual and were instructed to call this person with any questions, concerns, or symptoms. The patients were also given the 24/7 on call line for the Epidemiologist On-Call at NCDPH. The facility outbreak liaison maintained direct contact with the patients and reported updates to NCDPH. These updates were provided to NCDPH at least once daily during the early phase of the investigation.

As the outbreak progressed and the number of cases rapidly increased, NCDPH decided to institute a proactive symptom monitoring protocol for all individuals who had received a spinal injection with the implicated product. The following protocol was provided to the two spinal injection facilities on October 9, 2012, along with a Microsoft Excel spreadsheet with a suggested patient tracking format.

1. Asymptomatic patients who were initially contacted greater than or equal to 8 weeks after their most recent epidural steroid injection:
   - No additional contact necessary.
   - If patient calls to report symptoms, please notify NCDPH

2. Asymptomatic patients who were initially contacted less than 8 weeks after their most recent epidural steroid injection:
   - Call and speak with patient once more, preferably on or before October 12, 2012
   - Evaluate patient for symptoms and refer for clinical evaluation if appropriate
- If patient remains asymptomatic, emphasize that symptoms could still develop several weeks after the last injection and that it is important to report any new symptoms immediately and be evaluated by a doctor as soon as possible.
- Ensure patient has appropriate contact information for clinic.

3. Patients who reported symptoms at initial contact and meet one of the following conditions: A) refused clinical evaluation and/or lumbar puncture, B) had clinical evaluation and lumbar puncture was not indicated, C) had clinical evaluation and normal cell count on lumbar puncture:

- Contact the patient at least weekly by phone to assess symptoms (improved, stable or worsening).
- If symptoms are worsening or new symptoms have occurred, refer for clinical evaluation.
- Continue weekly phone calls until patient is 8 weeks* from their last epidural steroid injection.
- During first follow up phone call, explain to patient that they will be receiving weekly phone calls to ensure they are continuing to do well after their exposure.
- Patient should be reminded to call clinic immediately if symptoms develop between phone calls.

In addition to the symptom monitoring protocol, patients were contacted each time CDC issued critical new information.

Exposed individuals who reported symptoms of meningitis or other infection were referred to an infectious disease physician for immediate evaluation. The physician determined the need for lumbar puncture, MRI, or other testing. NCDPH determined if patients met case definition by reviewing all available medical information. Initial testing was performed at the patient’s local hospital laboratory. Clinical specimens were also shipped to CDC via the North Carolina State Laboratory for Public Health (SLPH) for fungal evaluation.

By early December, identification of new meningitis cases was becoming less frequent. However, paraspinal and spinal infections were being identified with increasing frequency. Evidence from other states suggested that subtle findings on MRI could represent clinically significant infections and that a coordinated approach of infectious disease physicians, neurosurgeons, and neuroradiologists was necessary to adequately assess exposed individuals. NCDPH hosted a strategic planning conference call on December 13. Each spinal injection facility was asked to invite infectious disease colleagues from their local referral center, neurosurgeons, radiologists, neuroradiologists, hospital administrators, and outbreak liaisons. NCDPH provided an update on the new information about MRI findings and worked with the facilities to come up with a strategy for appropriately evaluating each patient in need of an MRI. Each hospital then set up a special protocol for the evaluation of these patients.

Communications

In North Carolina, the patients exposed to MPA from NECC were well defined and the outreach described above ensured that NCDPH was aware of any individuals with symptoms who were undergoing evaluation. However, given the widespread distribution of contaminated MPA, NCDPH was concerned that individuals who had been exposed to MPA in another state might seek care in North Carolina. Alternately, North Carolina residents could have received injections with the contaminated MPA in another state before returning home. It was therefore essential to keep all clinical providers in the state aware of the outbreak and updated regarding new developments to ensure that potential cases would be quickly identified and reported to NCDPH and appropriate diagnostic and treatment measures would be initiated.

Towards this end, NCDPH developed a communications plan for providers in North Carolina. Provider memos were distributed to medical society list serves, major medical systems, hospital based public health epidemiologists, local health departments, microbiology laboratories, and to public health leaders in North Carolina’s Health Alert Network (NC HAN). A multidisciplinary stakeholder “Update on the Outbreak” conference call was hosted on October 22 to provide a verbal update on the outbreak and to allow for interactive dialogue. Attendees included clinicians, hospital administrators from major medical centers, medical societies, and partner state agencies.

NCDPH epidemiologists partnered with the Office of the Chief Medical Examiner (OCME) to ensure open communication about suspicious deaths and autopsy requests for cases. OCME contacted NCDPH epidemiologists about deaths suspicious for fungal infection so that they could investigate and determine if the deceased individual had been exposed to contaminated MPA. NCDPH epidemiologists provided weekly case updates to OCME and coordinated autopsy of patients who succumbed to their illness.

NCDPH issued press releases on October 1 and October 5 to alert the public about the outbreak. NCDPH also responded to public inquiries through the 24/7 Epidemiologist On Call line throughout the course of the outbreak.
NCDPH maintained close contact with CDC and other state health departments through daily conference calls. NCDPH’s early identification and monitoring of the exposed cohort also allowed NCDPH to contribute data to CDC to assist with the development of clinical guidance.

**Product Recalls**

As the FDA investigation into NECC progressed, sequential product recalls were issued. On September 28, NCDPH received a list of 3 facilities that received the 3 suspected lots of contaminated MPA. All facilities were immediately contacted and asked to sequester the product. On October 3, the North Carolina Board of Pharmacy (NCBOP) revoked NECC’s license to distribute products in North Carolina. On October 5, the FDA determined that it could not guarantee the sterility of intrathecal injections compounded by NECC and issued a recall of all NECC intrathecal products. NCDPH received a list of all 22 facilities in North Carolina that had received these products, and contacted all facilities (with the assistance of NCBOP) to ensure they knew about the expanded recall and were sequestering the affected products. This process was complete by close of business on October 5. On October 7, FDA expanded the recall to include all products compounded by NECC. A list of all NECC sales was released to state health departments on October 15, and during October 16–17, NCDPH and NCBOP contacted all 84 facilities in North Carolina that had received any product from NECC.

**Results**

**National Case Count and Source Identification**

As of September 6, 2013, 750 cases had been identified among residents of 20 states, including 64 deaths. (Figures 1–2) Manifestations of illness include meningitis, stroke, paraspinal or spinal infection, and peripheral joint infection. Early in the outbreak, meningitis and stroke were the primary clinical outcomes. Patients with these syndromes had the highest case fatality rate. On October 7, peripheral joint infections were first identified as a clinical outcome. These infections have accounted for 4% of all cases to date. (Figure 2) On November 14, paraspinal or spinal infections were first identified as a clinical outcome. These syndromes were identified with increasing frequency over the ensuing months and account for 63% of all cases to date. Paraspinal or spinal infections include epidural abscess, phlegmon, arachnoiditis, discitis, or vertebral osteomyelitis and are most often diagnosed through magnetic resonance imaging (MRI) studies. As of May, 2013, one hundred and forty-nine cases had experienced more than one clinical syndrome, primarily meningitis and paraspinal/spinal infection. The case fatality rate decreased as the outbreak progressed, possibly as a result of earlier case identification and treatment. On April 11, 2013, CDC notified states of a case of relapsed meningitis in a patient who had been treated with antifungal therapy for 4.5 months. [4]

Fungal organisms have been identified in clinical specimens (cerebrospinal fluid, tissue, joint fluid) from confirmed cases. The predominant fungal organism is *Exserohilum rostratum*, identified in 152 cases. *Exserohilum* is a mold commonly found in soil and plants, but rarely associated with human infection. [5] Other fungal species identified from case specimens have included: *Aspergillus* species (4 cases), *Cladosporium* spp. (6), *Alternaria* sp. (4), *Bipolaris* sp. (1), *Chaetomium* sp. (1), coelomycete fungus (1), *Epicoccum nigrum* (1), *Paecilomyces* (1), *Penicillium* sp. (1), *Scopulariopsis brevicaulis* (1), and *Stachybotrys chartarum* (1). [6]

All case patients received one or more injections of preservative free MPA produced by NECC. The joint investigation by CDC and FDA identified three contaminated lots of MPA associated with cases. (See box for detailed lot information.) *Exserohilum rostratum* was identified as a contaminant in 2 of the 3 contaminated lots. Non-pathogenic fungal organisms were also recovered from all 3 lots. The three contaminated lots were recalled on September 26, 2012 and all NECC products were recalled on October 7. An FDA Form 483 was released on October 26 outlining non-sterile conditions in the compounding center. On October 31, Ameridose, a sister compounding pharmacy owned by the same individuals as NECC, also recalled all products due to an inability to confirm the sterility of their products.
Contaminated Lots of MPA

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


In total, 13,534 individuals from across the United States received one or more spinal (89%) or peripheral joint (12%) injections with the contaminated medications. [7] (Figure 3, Table 1)

North Carolina Case Patients

Three hundred and thirteen individuals were exposed to contaminated MPA at 3 North Carolina facilities. (See box.) Of the 313 individuals, 68% received peripheral joint injections and 32% received spinal injections. (Table 1)

List of North Carolina Facilities that Received Three Recalled Lots of methylprednisolone Acetate (PF) from New England Compounding Center

<table>
<thead>
<tr>
<th>Facility</th>
<th>Contaminated Lots Received</th>
<th># Patients Exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Point Surgery Center</td>
<td>05212012@68, 06292012@26, 08102012@51</td>
<td>74</td>
</tr>
<tr>
<td>North Carolina Orthopedic Clinic</td>
<td>05212012@68, 06292012@26, 08102012@51</td>
<td>26</td>
</tr>
<tr>
<td>Surgery Center of Wilson</td>
<td>05212012@68, 06292012@26, 08102012@51</td>
<td>213</td>
</tr>
</tbody>
</table>

During ongoing patient outreach and symptom monitoring, 74/313 (24%) reported signs or symptoms concerning for infection. (Table 2) The majority of these patients (99%) had received spinal injections. Fifty-seven percent (42/74) were evaluated for meningitis with a lumbar puncture; among these, 74% had a single lumbar puncture, 19% had two lumbar punctures, 5% had three lumbar punctures, and 2% had four lumbar punctures. Repeated lumbar punctures were preformed due to worsening or progressive symptoms. Seventy-eight percent of symptomatic individuals (58/74) underwent at least one MRI to evaluate for possible spinal or paraspinal infection. Thirty-six percent of symptomatic individuals (27/74) were evaluated with both a lumbar puncture and an MRI. Twenty-four percent of symptomatic individuals (18/74) meet case definition as a result of laboratory testing and radiographic imaging. (See Table 2 for data stratified by facility.)

Eighteen case-patients were reported to CDC from North Carolina; 4 confirmed and 14 probable. One case-patient was classified as meningitis only; 3 as meningitis and paraspinal/spinal infections; 14 as paraspinal/spinal infection; and none as peripheral joint infection. Due to the insidious onset of symptoms, exact illness onset dates were difficult to determine. Using month of report to CDC as a proxy, onsets ranged from September, 2012–May, 2013. (Figure 4) Fifty percent were female. Ages ranged from 44–92 years (median, 62 years). Eighty-nine percent of patients initiated or completed antifungal therapy. The remaining individuals declined therapy or had a contraindication. Nine NC case-patients (50%) were hospitalized at some point in their illness; 5 (28%) underwent surgical intervention; and 1 (6%) had a stroke and subsequently died. (Table 3)

Of the 18 case-patients, 67% had received a single injection of contaminated MPA, 28% had 2 injections, and 6% had 3 injections. None of the facilities in North Carolina documented lot numbers on patient medical records. However, based on a review of distribution data and average usage rates, it is likely that 24% of case-patients in North Carolina were exposed to MPA Lot 05212012@68, 68% to MPA Lot 06292012@26, and none to MPA Lot 08102012@51. Eight percent of injections could not be attributed to a single lot. (Table 4)

All case-patients underwent some form of laboratory and/or radiologic evaluation. Thirteen patients were evaluated with lumbar puncture. Four (31%) had a cerebrospinal fluid (CSF) white blood cell count greater than 5 per high powered field, suggestive of meningitis. Fungal cultures and fungal PCR conducted on the CSF samples from these four patients were negative at both the local hospital laboratory and at CDC. Eighteen case-patients were evaluated with an MRI. Seventeen (94%) had radiologic evidence of paraspinal or spinal infection. Five of 17 underwent surgical intervention and tissue samples were obtained for testing. Three tissue samples were positive for fungal infection at both the local hospital laboratory and at CDC. The North Carolina case-patient who died subsequently underwent autopsy by OCME.
Histopathologic evidence of fungal infection was identified by the medical examiner and by the CDC laboratory. Of note, this case-patient had undergone multiple lumbar punctures that were negative for fungus, highlighting the limitations of this test for confirming fungal infection in the context of this outbreak. (Table 5) Of the four confirmed case-patients with fungal identification from tissue or histopathology, two were identified as *Exserohilum rostratum* and two were cross reactive with a polyfungal PCR that includes *Exserohilum rostratum* and other fungal species.

**Conclusions**

An outbreak of fungal infections associated with contaminated methylprednisolone acetate was identified in September, 2012. The national and state response is ongoing as of October, 2013. Nationally, 750 cases and 64 deaths have been identified. In North Carolina, 18 cases and 1 death have been identified. Early in the outbreak, meningitis and stroke were the more common clinical syndromes; paraspinal and spinal infections were more commonly identified later in the outbreak. Through a collaborative multistate and federal investigation, the source of the outbreak was identified as contaminated preservative free methylprednisolone acetate produced at the New England Compounding Center in Framingham, Massachusetts.

NCDPH and other state and local health departments conducted a time- and effort-intensive patient outreach campaign to rapidly identify all 13,534 individuals who were potentially exposed to the contaminated medication, and ensure appropriate follow up. NCDPH implemented a proactive symptom monitoring protocol and developed a strategic plan for patient evaluation in the context of a multidisciplinary team. Communication and collaboration between the three North Carolina facilities and NCDPH is ongoing to ensure continued care of all exposed patients.
References

Figure 1. National Case Count Map

CDC’s Multistate Fungal Meningitis Outbreak website, accessed on October 18, 2013
http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html

Figure 2. National Case Count

CDC’s Multistate Fungal Meningitis Outbreak website, accessed on October 18, 2013
http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html
Figure 3. Map States with Healthcare Facilities that Received Methylprednisolone Acetate (PF) from Three Recalled Lots

CDC’s Multistate Fungal Meningitis Outbreak website, accessed on May 15, 2013
http://www.cdc.gov/hai/outbreaks/meningitis-facilities-map-large.html

Table 1. Individuals Exposed to Contaminated MPA in the United States and North Carolina, Stratified by Injection Type and Facility.

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>Injection Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>13,534</td>
<td>89% Spinal Injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12% Peripheral Joint Injection</td>
</tr>
<tr>
<td>North Carolina</td>
<td>313</td>
<td>32% Spinal Injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>68% Peripheral Joint Injection</td>
</tr>
<tr>
<td>By NC Facility</td>
<td>313</td>
<td>24% High Point Surgical Center</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8% Surgery Center of Wilson</td>
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<tr>
<td></td>
<td></td>
<td>68% NC Orthopedic Clinic</td>
</tr>
</tbody>
</table>
Table 2. Location of Injection and Clinical Diagnostic Measures taken for Symptomatic Individuals Exposed to Contaminated MPA in North Carolina, Stratified by Facility.

<table>
<thead>
<tr>
<th></th>
<th>Total No. (%)</th>
<th>High Point No. (%)</th>
<th>Wilson No. (%)</th>
<th>NC Orthopedic No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic Individuals</td>
<td>74</td>
<td>55</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Spinal Injection</td>
<td>73 (99)</td>
<td>55 (100)</td>
<td>18 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Peripheral Joint Injection</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Evaluated with Lumbar Puncture</td>
<td>42 (57)</td>
<td>39 (71)</td>
<td>3 (17)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>1 Lumbar Puncture only</td>
<td>31 (74)</td>
<td>29 (74)</td>
<td>2 (67)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>2 Lumbar Punctures only</td>
<td>8 (19)</td>
<td>7 (18)</td>
<td>1 (33)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>3 Lumbar Punctures only</td>
<td>2 (5)</td>
<td>2 (5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>4 Lumbar Punctures only</td>
<td>1 (2)</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Evaluated with MRI</td>
<td>58 (78)</td>
<td>41 (75)</td>
<td>16 (89)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Evaluated with both Lumbar Puncture &amp; MRI</td>
<td>27 (36)</td>
<td>26 (47)</td>
<td>1 (6)</td>
<td>0 (0)</td>
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<tr>
<td>Meet case definition</td>
<td>18 (24)</td>
<td>18 (33)</td>
<td>0 (0)</td>
<td>0 (0)</td>
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</table>
Figure 4. Laboratory Confirmed and Probable Cases of Fungal Infection Associated with Contaminated MPA by Month of Report to CDC --- North Carolina, 2012–2013 (n=18)

Figure updated May 30, 2013.

Figure updated May 30, 2013.
### Table 3. Characteristics of North Carolina Case-Patients (N=18)

<table>
<thead>
<tr>
<th>Case Classification</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>Confirmed</td>
<td>4 (22)</td>
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<tr>
<td>Probable</td>
<td>14 (78)</td>
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<table>
<thead>
<tr>
<th>Infection Category</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis Only</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Meningitis &amp; Paraspinal/Spinal Infection</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Paraspinal/Spinal Infection Only</td>
<td>14 (78)</td>
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<tr>
<td>Peripheral Joint</td>
<td>0 (0)</td>
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<table>
<thead>
<tr>
<th>Gender</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9 (50)</td>
</tr>
<tr>
<td>Female</td>
<td>9 (50)</td>
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<table>
<thead>
<tr>
<th>Age</th>
<th>Years</th>
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<tbody>
<tr>
<td>Median</td>
<td>62</td>
</tr>
<tr>
<td>Range</td>
<td>44 to 92</td>
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<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antifungal Therapy</td>
<td>16 (89)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized</td>
<td>9 (50%)</td>
</tr>
<tr>
<td>Surgical Intervention</td>
<td>5 (28)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Died</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

### Table 4. Exposures Among North Carolina Cases (N=18)

<table>
<thead>
<tr>
<th>Facility</th>
<th>No. Cases</th>
<th>No. Exposed</th>
<th>% Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Point Surgical Center</td>
<td>18</td>
<td>74</td>
<td>24</td>
</tr>
<tr>
<td>Surgery Center of Wilson</td>
<td>0</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td>NC Orthopedic Clinic</td>
<td>0</td>
<td>213</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of Injections</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 injection only</td>
<td>12 (67)</td>
</tr>
<tr>
<td>2 injections only</td>
<td>5 (28)</td>
</tr>
<tr>
<td>3 injections only</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suspected Lot</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA Lot 05212012@68</td>
<td>6 (24)</td>
</tr>
<tr>
<td>MPA Lot 06292012@26</td>
<td>17 (68)</td>
</tr>
<tr>
<td>MPA Lot 08102012@51</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Unable to determine</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

| Total # of Injections | 25      |
Table 5. Laboratory Evaluation among North Carolina Case-Patients (N=18)

<table>
<thead>
<tr>
<th>Evaluated with Lumbar Puncture</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory Evidence of Infection*</td>
<td>4</td>
<td>31</td>
</tr>
<tr>
<td>Fungus Identified - Local</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fungus Identified - CDC</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total with Lab Confirmed Meningitis</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Evaluated with MRI</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiologic Evidence of Infection**</td>
<td>17</td>
<td>94</td>
</tr>
<tr>
<td>Underwent Surgical Intervention</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>Fungus Identified - Local</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>Fungus Identified - CDC</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>Total with Lab Confirmed Infection</td>
<td>3</td>
<td>17</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Evaluated on Autopsy</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histopathologic Evidence of Infection***</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Fungus Identified - Local</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Fungus Identified - CDC</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Total with Lab Confirmed Infection</td>
<td>1</td>
<td>100</td>
</tr>
</tbody>
</table>

*Laboratory Evidence of Infection: White blood cell count >5 per hpf in CSF specimen
**Radiologic Evidence of Infection: Abscess, phlegmon, abnormal or worsening enhancement
***Histopathological Evidence of Infection: As determined by medical examiner
Appendices

A. List of Abbreviations
B. Timeline of Key Events
C. Significant Events Related to Drug Recalls and Contamination
D. North Carolina Health Alerts, Provider Memos, and Press Releases
E. CDC Health Alerts and Advisories
F. Timeline of Situation Reports
G. List of Publications and National Presentations with North Carolina Co-authors
H. Other Publications Related to the Outbreak
I. CDC Epi-Aid Investigations Related to the Outbreak
A. List of Abbreviations

BOP – Board of Pharmacy

CDC – Centers for Disease Control and Prevention

CD Nurse – Communicable Disease Nurse

CSF – Cerebrospinal Fluid

Epi-X – Epidemic Information Exchange

FDA – Food and Drug Administration

HAN – Health Alert Network

High Point – High Point Surgical Center in North Carolina

LHD – Local Health Department

MA BOP – Massachusetts Board of Pharmacy

MPA – Methylprednisolone Acetate

NC BOP – North Carolina Board of Pharmacy

NCDHHS – North Carolina Department of Health and Human Services

NCDPH – North Carolina Division of Public Health

NECC – New England Compounding Center

OCME – Office of the Chief Medical Examiner

Sit Rep – Situation Report

SLPH – North Carolina State Laboratory for Public Health

TDH – Tennessee Department of Health

Wilson – Surgery Center of Wilson in North Carolina
### B. Timeline of Key Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Agency</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/21/12</td>
<td>NECC</td>
<td>First lot of contaminated steroid injections produced.</td>
</tr>
<tr>
<td>9/18/12</td>
<td>TDH</td>
<td>Received initial report of fungal meningitis after a steroid injection.</td>
</tr>
<tr>
<td>9/20/12</td>
<td>TDH</td>
<td>Identified 2 additional cases through active surveillance. Notified CDC of investigation.</td>
</tr>
<tr>
<td>9/24/12</td>
<td>TDH</td>
<td>Notified Massachusetts Department of Health that NECC is suspected exposure.</td>
</tr>
<tr>
<td>9/25/12</td>
<td>TDH</td>
<td>Notified FDA of investigation.</td>
</tr>
<tr>
<td>9/26/12</td>
<td>NECC</td>
<td>Issued voluntary recall of 3 lots of steroid associated with TN cases.</td>
</tr>
<tr>
<td></td>
<td>TDH</td>
<td>Released Epi-X call for cases.</td>
</tr>
<tr>
<td>9/27/12</td>
<td>NCDPH</td>
<td>Learned of suspected fungal meningitis case in NC resident who received steroid.</td>
</tr>
<tr>
<td></td>
<td>CDC</td>
<td>Shared concern that this may mean outbreak is broader than TN clinic.</td>
</tr>
<tr>
<td>9/28/12</td>
<td>CDC</td>
<td>Shared list of facilities that received compounded steroid product with states.</td>
</tr>
<tr>
<td></td>
<td>TDH/NCDPH</td>
<td>Released updated Epi-X call for cases, noting new suspected case in NC.</td>
</tr>
<tr>
<td></td>
<td>NCDPH</td>
<td>Activated Incident Command</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sent NC Health Alert to medical and public health stakeholders.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Received list of NC facilities who received compounded steroid product.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contacted all NC facilities by phone, sequestered steroid products</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Initiated patient phone calls.</td>
</tr>
<tr>
<td>9/29/12</td>
<td>NCDPH</td>
<td>Maintained contact with NC facilities.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assisted with patient phone calls.</td>
</tr>
<tr>
<td>9/30/12</td>
<td>NCDPH</td>
<td>Assisted with patient phone calls.</td>
</tr>
<tr>
<td></td>
<td>NECC</td>
<td>Voluntarily recalled steroid product.</td>
</tr>
<tr>
<td></td>
<td>CDC</td>
<td>Shared talking points. Did not name NECC in press statements.</td>
</tr>
<tr>
<td></td>
<td>FDA</td>
<td>Began evaluating steroid and other products produced by NECC.</td>
</tr>
<tr>
<td>10/1/12</td>
<td>NCDPH</td>
<td>Reached majority of patients via phone call.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Organized home visits for patients not reachable by phone.</td>
</tr>
</tbody>
</table>

**Outbreak Identified**

- **Exposure:** Unknown
- **Pathogen:** Unknown
- **Clinical syndrome:** Meningitis
Issued press release and developed communication plan.

CDC
Identified Aspergillus species in a patient specimen.

10/2/12
CDC
Hosted first 50-state call. Discussed cases in TN, NC and other states. Initiated multistate investigation.

NCDPH
Assisted NC facilities with their own press releases. Continued home visits for patient notification.

10/3/12
NCBOP
Revoked NECC license in North Carolina

CDC
Identified a second mold in a patient specimen, species in process.

10/4/12
CDC/FDA
Held press conference and named NECC as suspected source.

FDA
Released name and lot numbers of suspected steroid. Disclosed that foreign material visualized in vials of steroid. Briefly posted names and locations of facilities that received steroid. Identified unspeciated fungus in injectable steroid product.

CDC
Identified second mold in patient specimen as Exserohilum rostratum. Activated CDC Emergency Operations Center

NECC
Ceased all production.

NCDPH
Issued second press release. Distributed outbreak update to medical and public health stakeholders.

10/5/12
FDA
Expanded recall to include all intrathecal products from NECC.

CDC/FDA
Posted names and locations of facilities that received steroid.

NCDPH
Completed patient notification through phone calls and home visits. Received list of NC facilities that received intrathecal products from NECC. Called all NC facilities to sequester products. Issued updated second press release, naming NC facilities.

10/6/12
CDC
Hosted 50-state call

10/7/12
CDC
Identified joint infections as clinical outcome. Expanded dates of exposure to steroid product.

FDA
Recalled all NECC products.
10/8/12 CDC   Issued Health Alert with new dates of exposure.
NCDPH   Issued updated alert to clinicians.
Created long-term follow up plan for patients.
10/15/12 FDA   Sent list of all NECC sales to states.
10/16/12 NCDPH/NCBOP Initiated contact with all NC facilities that received any NECC product.
10/17/12 NCDPH/NCBOP Completed contact with all NC facilities that received any NECC product.
FDA   Asked states to refrain from posting list of facilities that received NECC products.
10/18/12 FDA   Identified *Exserohilum rostratum* in “sterile” steroid product from NECC.
10/19/12 CDC   Reported that states had notified >99% of all patients exposed nationwide.
10/22/12 FDA   Posted list of facilities that received any NECC products.
NCDPH   Hosted multidisciplinary stakeholder call – “Update on the Outbreak”
(Major medical centers, state agencies, medical societies)
11/14/12 CDC   Shared concern regarding paraspinal/spinal infections.
NCDPH   Notified NC facilities of concerns regarding paraspinal/spinal infections.
11/20/12 CDC   Asked providers to consider MRI to evaluate patients with worsening pain.
NCDPH   Notified NC facilities of MRI recommendation.
Prepared NC facilities for patient notification.
11/26/12 CDC   Shared preliminary data about MRI identification of paraspinal/spinal infections.
Refrained from recommending active patient notification regarding paraspinal/spinal infections.
NCDPH   Asked NC facilities to begin patient notification regarding paraspinal/spinal infections.
Prepared patient notification script and clinician memo.
12/13/12 NCDPH   Hosted multidisciplinary conference call – “Strategic Planning”
(Facilities, Infectious Disease, Neurosurgery, Radiology)
12/14/12 High Point Completed re-notification of all patients regarding paraspinal/spinal infections.
12/17/12 CDC   Shared final data about MRI identification of paraspinal/spinal infections.
Asked clinicians to have a low threshold for MRI evaluation.
<table>
<thead>
<tr>
<th>Date</th>
<th>Agency</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/20/12</td>
<td>CDC</td>
<td>Sent health alert with final data about MRI identification.</td>
</tr>
<tr>
<td></td>
<td>NCDPH</td>
<td>Shared health alert with NC facilities.</td>
</tr>
<tr>
<td>12/30/12</td>
<td>Wilson</td>
<td>Completed re-notification of all patients regarding paraspinal/spinal infections.</td>
</tr>
<tr>
<td>1/31/13</td>
<td>CDC</td>
<td>Hosted affected states call to assess clinician response to MRI data. NCDPH reported that all patients had been re-notified and assessed.</td>
</tr>
<tr>
<td>2/6/13</td>
<td>CDC</td>
<td>Shared toolkit designed to help states struggling with patient outreach.</td>
</tr>
<tr>
<td>2/7/12</td>
<td>NCDPH</td>
<td>Hosted internal planning meeting to determine next steps in response. NCDPH</td>
</tr>
<tr>
<td>4/11/13</td>
<td>CDC</td>
<td>Secondary meningitis case reported</td>
</tr>
<tr>
<td>Present</td>
<td>NCDPH</td>
<td>Outbreak response ongoing.</td>
</tr>
</tbody>
</table>
### C. Significant Events Related to Drug Recalls and Contamination

<table>
<thead>
<tr>
<th>Date</th>
<th>Company</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/21/12</td>
<td>NECC</td>
<td>Produces first lot of contaminated MPA</td>
</tr>
<tr>
<td>9/26/12</td>
<td>NECC</td>
<td>Issues voluntary recall of 3 suspected lots of MPA associated with TN cases</td>
</tr>
<tr>
<td>9/30/12</td>
<td>NECC</td>
<td>Issues voluntary recall of all lots of MPA</td>
</tr>
<tr>
<td>10/3/12</td>
<td>MA BOP</td>
<td>Negotiates voluntary surrender of NECC’s Massachusetts license</td>
</tr>
<tr>
<td>10/3/12</td>
<td>NC BOP</td>
<td>Suspends NECC’s North Carolina license</td>
</tr>
<tr>
<td>10/4/12</td>
<td>NECC</td>
<td>Ceases production of all products</td>
</tr>
<tr>
<td>10/5/12</td>
<td>FDA</td>
<td>Issues recall for all intrathecal products produced by NECC</td>
</tr>
<tr>
<td>10/6/12</td>
<td>NECC</td>
<td>Issues voluntary recall of all NECC products</td>
</tr>
<tr>
<td>10/7/12</td>
<td>FDA</td>
<td>Issues recall for all NECC products</td>
</tr>
<tr>
<td>10/26/12</td>
<td>FDA</td>
<td>Releases Form 483 describing results of NECC site investigations</td>
</tr>
<tr>
<td>10/31/12</td>
<td>Ameridose</td>
<td>Voluntarily recalled all Ameridose products</td>
</tr>
<tr>
<td>11/1/12</td>
<td>CDC</td>
<td>Identified contamination in NECC products</td>
</tr>
<tr>
<td>12/3/12</td>
<td>CDC</td>
<td>Additional contamination identified in NECC products</td>
</tr>
</tbody>
</table>

### D. North Carolina Health Alerts, Provider Memos, and Press Releases

<table>
<thead>
<tr>
<th>Date</th>
<th>Title</th>
<th>Received By</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/28/12</td>
<td>North Carolina Health Alert Network</td>
<td>LHD, CD Nurses, Micronet, Medical societies</td>
</tr>
<tr>
<td>9/28/12</td>
<td>Communicable Disease Health Alert</td>
<td>LHD, CD Nurses</td>
</tr>
<tr>
<td>10/1/12</td>
<td>NC DHHS Press Release</td>
<td>Entire state</td>
</tr>
<tr>
<td>10/2/12</td>
<td>Communicable Disease Health Alert</td>
<td>LHD, CD Nurses</td>
</tr>
<tr>
<td>10/9/12</td>
<td>Provider Memo #1</td>
<td>Clinicians</td>
</tr>
<tr>
<td>10/5/12</td>
<td>NC DHHS Press Release</td>
<td>Entire state</td>
</tr>
<tr>
<td>10/9/12</td>
<td>Facility Guidance Memo #1</td>
<td>NC Facilities who received NECC Products</td>
</tr>
<tr>
<td>10/15/12</td>
<td>Provider Memo #2</td>
<td>Clinicians</td>
</tr>
<tr>
<td>10/22/12</td>
<td>Provider Memo #3</td>
<td>Clinicians</td>
</tr>
<tr>
<td>10/29/12</td>
<td>Facility Guidance Memo #2</td>
<td>NC Facilities who received NECC Products</td>
</tr>
<tr>
<td>10/31/12</td>
<td>Provider Memo #4</td>
<td>Clinicians</td>
</tr>
<tr>
<td>11/27/12</td>
<td>Provider Memo #5</td>
<td>Clinicians</td>
</tr>
<tr>
<td>12/7/12</td>
<td>Provider Memo #6</td>
<td>Clinicians</td>
</tr>
<tr>
<td>3/5/13</td>
<td>Provider Memo #7</td>
<td>Clinicians</td>
</tr>
<tr>
<td>Date</td>
<td>HAN</td>
<td>Title</td>
</tr>
<tr>
<td>----------</td>
<td>---------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>10/4/12</td>
<td>CDC HAN 327</td>
<td>Meningitis and Stroke Associated with Possibly Contaminated Product</td>
</tr>
<tr>
<td>10/8/12</td>
<td>CDC HAN 328</td>
<td>Update: Multistate Outbreak of Meningitis and Stroke Associated with Potentially Contaminated Steroid Medication</td>
</tr>
<tr>
<td>10/17/12</td>
<td>CDC HAN 329</td>
<td>Update: Multistate Outbreak of Fungal Meningitis and Joint Infections Associated with Contaminated Steroid Medications</td>
</tr>
<tr>
<td>10/23/12</td>
<td>CDC HAN 330</td>
<td>Issuance of Guidance on Management of Asymptomatic Patients Who Received Epidural or Paraspinal Injections with Contaminated Steroid Products</td>
</tr>
<tr>
<td>11/1/12</td>
<td>CDC HAN 332</td>
<td>Voluntary Recall of All Ameridose Medical Products</td>
</tr>
<tr>
<td>11/20/12</td>
<td>CDC HAN 333</td>
<td>Contaminated Identified in Additional Medical Products from NECC</td>
</tr>
<tr>
<td>11/20/12</td>
<td>CDC HAN 335</td>
<td>Update: Multistate Outbreak of Fungal Meningitis and Other Infections Associated with Contaminated Steroid Medication</td>
</tr>
<tr>
<td>12/3/12</td>
<td>CDC HAN 337</td>
<td>Update: Additional Contamination Identified in Medical Products from New England Compounding Center</td>
</tr>
<tr>
<td>12/20/12</td>
<td>CDC HAN 338</td>
<td>Update: Multistate Outbreak of Fungal Infections among Persons Who Received Injections with Contaminated Medication</td>
</tr>
<tr>
<td>3/4/13</td>
<td>CDC HAN 342</td>
<td>Notice to Clinicians: Continued Vigilance Urged for Fungal Infections among Patients Who Received Contaminated Steroid Injections</td>
</tr>
</tbody>
</table>
F. Timeline of NCDPH Situation Reports

<table>
<thead>
<tr>
<th>Date</th>
<th>Situation Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/28/12</td>
<td>Initial Sit Rep</td>
</tr>
<tr>
<td>10/1/12</td>
<td>Sit Rep #2</td>
</tr>
<tr>
<td>10/2/12</td>
<td>Sit Rep #3</td>
</tr>
<tr>
<td>10/3/12</td>
<td>Sit Rep #4</td>
</tr>
<tr>
<td>10/4/12</td>
<td>Sit Rep #5</td>
</tr>
<tr>
<td>10/5/12</td>
<td>Sit Rep #6</td>
</tr>
<tr>
<td>10/7/12</td>
<td>Sit Rep #7</td>
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<td>10/8/12</td>
<td>Sit Rep #8</td>
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<td>10/9/12</td>
<td>Sit Rep #9</td>
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<tr>
<td>10/10/12</td>
<td>Sit Rep #10</td>
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<tr>
<td>10/11/12</td>
<td>Sit Rep #11</td>
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<td>10/12/12</td>
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<td>10/13/12</td>
<td>Sit Rep #13</td>
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<td>10/14/12</td>
<td>Sit Rep #14</td>
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<td>10/15/12</td>
<td>Sit Rep #15</td>
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<tr>
<td>10/16/12</td>
<td>Sit Rep #16</td>
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<td>10/16/12</td>
<td>Sit Rep #16B</td>
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<td>10/17/12</td>
<td>Sit Rep #17</td>
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<tr>
<td>10/18/12</td>
<td>Sit Rep #18</td>
</tr>
<tr>
<td>10/19/12</td>
<td>Sit Rep #19</td>
</tr>
<tr>
<td>10/22/12</td>
<td>Sit Rep #20</td>
</tr>
<tr>
<td>10/23/12</td>
<td>Sit Rep #21</td>
</tr>
<tr>
<td>10/24/12</td>
<td>Sit Rep #22</td>
</tr>
<tr>
<td>10/25/12</td>
<td>Sit Rep #23</td>
</tr>
<tr>
<td>10/26/12</td>
<td>Sit Rep #24</td>
</tr>
<tr>
<td>10/29/12</td>
<td>Sit Rep #25</td>
</tr>
<tr>
<td>10/30/12</td>
<td>Sit Rep #26</td>
</tr>
<tr>
<td>10/31/12</td>
<td>Sit Rep #27</td>
</tr>
<tr>
<td>11/1/12</td>
<td>Sit Rep #28</td>
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<td>11/2/12</td>
<td>Sit Rep #29</td>
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<tr>
<td>11/5/12</td>
<td>Sit Rep #30</td>
</tr>
<tr>
<td>11/7/12</td>
<td>Sit Rep #31</td>
</tr>
<tr>
<td>11/9/12</td>
<td>Sit Rep #32</td>
</tr>
<tr>
<td>11/14/12</td>
<td>Sit Rep #33</td>
</tr>
<tr>
<td>11/19/12</td>
<td>Sit Rep #34</td>
</tr>
<tr>
<td>11/21/12</td>
<td>Sit Rep #35</td>
</tr>
<tr>
<td>11/26/12</td>
<td>Sit Rep #36</td>
</tr>
<tr>
<td>12/3/12</td>
<td>Sit Rep #37</td>
</tr>
<tr>
<td>12/5/12</td>
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<td>3/6/13</td>
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G. List of Outbreak-Related Publications and National Presentations with North Carolina Co-authors

RM Smith, MK Schaefer, A Purfield, AA Cleveland, MA Kainer, J Finks, J Duwve, E Fontaine, A Chu, B Carothers, A Reilly, J Fiedler, AD Wiese, C Feaster, L Gibson, S Griese, T Chiller, K Benedict, JR Harris, ME Brandt, BJ Park.


H. Other Publications Related to the Outbreak (Incomplete List)


MMWR: Multistate Fungal Meningitis Outbreak — Interim Guidance for Treatment (October 19, 2012)


I. CDC Epi-Aid Investigations Related to the Outbreak

Epi-Aid 2013_001
Cluster of meningitis in patients following epidural injection_TN/MultiState

On October 1, 2012, EIS Officer Dr. Duc Nguyen and Dana Pepe (epi elective student) departed for Tennessee to assist the Tennessee Department of Health with the cluster investigation of meningitis patients following epidural injection. Dr. Rachel Smith will lead multi-state case finding from Atlanta.

Epi-Aid 2013_005
Clinical Characterization of Case-Patients Identified as Part of an Outbreak of Fungal Infections_IN,VA

On October 16, 2012, EIS Officers, Dr. Francisca Abanyie and Dr. Andrew Geller, will depart for Indianapolis, Indiana to assist the Indiana Department of Health with the investigation. They will be joined by epidemiology elective student Carmen Robinson. On October 17, 2012, EIS Officer Dr. Satish Pillai will depart for Roanoke, Virginia to assist the Virginia Department of Health with the investigation. Virginia EIS Officer Dr. Jennifer Espiritu will join the Epi-Aid investigation on or about October 18, 2012.

Epi-Aid 2013_007
Outbreak of Fungal Infections Associated with Medications Produced by New England Compounding Center, Framingham, MA_FL

On October 24, 2012, EIS Officers, Drs. Eyal Lesham and Stephen Ko, and CDC Medical Officer, Dr. Ryan Fagan, will depart for Tallahassee, Florida to assist the Florida Department of Health with the investigation.

Epi-Aid 2013_015
Outbreak of Fungal Infections Associated with Medications Produced by New England Compounding Center_MA

On November 12, 2012, EISOs, Drs. Raymund Dantes, Melissa Briggs, Kainne Dokubo, and Kenneth Quinto will depart to respective states to assist with the clinical characterization of disease progression in case-patients identified as part of an outbreak of fungal infections associated with medications produced by New England Compounding Center, Framingham, MA. Dr. Dantes will assist the Michigan Department of Community Health; Drs. Melissa Briggs and Kainne Dokubo will assist the Tennessee Department of Health; and Dr. Kenneth Quinto will assist the New Jersey Department of Health.