Interim Recommendations for Diagnosing and Managing Suspected Fungal Meningitis Associated with Epidural Anesthesia Administered in Matamoros, Mexico

Clinician Outreach and Communication Activity (COCA) Call

Thursday, June 8, 2023
Continuing Education

- Continuing education is not offered for this webinar.
To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.
Today’s Presenters

- **Tom Chiller, MD, MPHTM**  
  Chief, Mycotic Diseases Branch  
  Division of Foodborne, Waterborne, and Environmental Diseases  
  National Center for Emerging and Zoonotic Infectious Diseases  
  Centers for Disease Control and Prevention

- **Dallas Smith, PharmD, MAS**  
  LT, U.S. Public Health Service  
  Epidemiologist, Mycotic Diseases Branch  
  Division of Foodborne, Waterborne, and Environmental Diseases  
  National Center for Emerging and Zoonotic Infectious Diseases  
  Centers for Disease Control and Prevention

- **Luis Ostrosky-Zeichner, MD, FACP, FIDSA**  
  Professor and Chief, Division of Infectious Diseases  
  McGovern Medical School  
  University of Texas Health Science Center, Houston  
  Chief Epidemiology Officer  
  Memorial Hermann Healthcare System
Outbreak of Fungal Meningitis Associated with Epidural Anesthesia Performed in Matamoros, Mexico — 2023

Tom Chiller, MD, MPHTM
Chief
Mycotic Diseases Branch
Division of Foodborne, Waterborne, and Environmental Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
tnc3@cdc.gov

Dallas Smith, PharmD, MAS
Epidemiologist
Mycotic Diseases Branch
Division of Foodborne, Waterborne, and Environmental Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
rhq8@cdc.gov
Recent Previous Outbreak:
Fungal Meningitis, Durango Mexico, November 2022

- 1,480 patients possible exposed to contaminated epidural anesthesia
- 80 patients identified with meningitis
- 39 died

- *Fusarium solani* isolated from several patients
  - *Alternaria* from one patient

- Mexico determined that poor IPC practices may have been the cause
Fungal meningitis linked to epidural injections performed in two clinics in Matamoros, Mexico — January–May 2023

May 8, 2023:
Through Emerging Infections Network (EIN), CDC learned of two unusual meningitis cases in Texas with prior epidural anesthesia.

May 13, 2023:
Mexico closed two clinics implicated in fungal meningitis outbreak.

May 16, 2023:
Level-2 Travel Health Notice was published.

May 17, 2023:
HAN Health Advisory was published.

May 18, 2023:
CDC sent state-specific reports later that day.

May 20, 2023:
CDC received list of exposed patients at the two clinics in Mexico.

May 26, 2023:
CDC and Mycoses Study Group held webinar focusing on diagnostic and treatment recommendations for this fungal meningitis outbreak.

May 28, 2023:
UCSF identified Fusarium solani in a CSF specimen through metagenomics.

May 31, 2023:
CDC's MDB lab and University of Washington identified Fusarium solani in CSF specimens through a pan-fungal PCR test.

June 3, 2023:
CDC received a list of patients from U.S.-based patient coordinator of Clinica K-3.
Public Health Emergency of International Concern (PHEIC) Timeline

May 19, 2023: International component: confirmation that patients from Mexico, US, Canada, and Colombia were affected.

May 20, 2023: Risk assessment completed by CDC through PHEIC assessment team.

May 21, 2023: World Health Organization (WHO) notified of proposed PHEIC.
Case definitions

In patients who received a procedure with epidural anesthesia in Matamoros, Mexico, since January 1, 2023:

• **Person under investigation:**
  • LP results not yet available
  AND
  • No symptoms, or symptomatology unknown.

• **Suspected case:**
  • LP results not yet available
  AND
  • Patient has symptoms suggesting CNS infection (e.g., fever, headache, stiff neck, nausea/vomiting, photophobia, or altered mental status).

• **Probable case:**
  • CSF profile with >5 WBCs/mm³, accounting for the presence of red cells (i.e., subtracting 1 white cell for every 500 RBCs present)
    AND
  • Fungus has not been detected from CSF or tissue by culture, PCR, or mNGS

• **Confirmed case:**
  • Fungus has been detected from CSF or tissue culture, PCR, or mNGS

*Abbreviations:* LP = lumbar puncture; CSF = cerebrospinal fluid; WBC = white blood cell; RBC = red blood cells; PCR = polymerase chain reaction; mNGS = metagenomic next-generation sequencing
As of June 7, 2023:

In patients who received a procedure with epidural anesthesia in Matamoros, Mexico, since January 1, 2023:

- Persons under investigation: **184**
- Suspected case: **13**
- Probable case: **10**
- Confirmed case: **4**
- Deaths: **3** (One probable case and two confirmed cases)
- Not a case: **19**
### Demographic characteristics of exposed U.S. residents

<table>
<thead>
<tr>
<th>Patients, by Clinic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinica K-3</td>
<td>117</td>
</tr>
<tr>
<td>River Side Surgical Center</td>
<td>94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients, by Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>190</td>
</tr>
<tr>
<td>Male</td>
<td>18</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>34 (14–69)</td>
</tr>
</tbody>
</table>
Patients are from 23 U.S. states, D.C., and Puerto Rico
Fungal meningitis has been diagnosed most frequently in Hispanic and Latino patients.

Cases by Ethnicity/Race

- Not Hispanic or Latino - White: 2 cases
- Not Hispanic or Latino - race unknown: 1 case
- Not Hispanic or Latino - Black or African American: 2 cases
- Hispanic or Latino - White: 13 cases
- Hispanic or Latino - Black or African American: 1 case
- Ethnicity and race unknown: 3 cases
Procedure dates for suspected, probable, and confirmed cases ranged from 1/17/23 to 4/28/23
Clinical summary

### Symptom Frequency

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Average</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered mental status</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Body ache (myalgia)</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Light sensitivity</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Migraines</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Stiffness</td>
<td></td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Stiff neck</td>
<td></td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td></td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

### Time frame

<table>
<thead>
<tr>
<th># Days from Procedure to Onset</th>
<th>Average</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19</td>
<td>18</td>
<td>2</td>
<td>32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># Days from Procedure to Hospitalization</th>
<th>Average</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>56</td>
<td>56</td>
<td>14</td>
<td>106</td>
</tr>
</tbody>
</table>
Laboratory summary

- All CSF and blood cultures have been negative, to date
- Six CSF beta-d-glucan (BDG) (>500, >500, >500, >500, 488, 364) and two blood BDG (156, 50) have been positive
- Three pan-fungal PCR tests have identified *Fusarium solani* species complex (CDC MDB and University of Washington)
- UCSF identified *Fusarium solani* species complex through metagenomics
- Mexico had six patients test positive for *Fusarium solani* from CSF by PCR

<table>
<thead>
<tr>
<th>LP Results</th>
<th>Average</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>32</td>
<td>19</td>
<td>57</td>
</tr>
<tr>
<td>WBC (K/µL)</td>
<td>757</td>
<td>24</td>
<td>1761</td>
</tr>
<tr>
<td>Protein (mg/dL)</td>
<td>109</td>
<td>34</td>
<td>254</td>
</tr>
</tbody>
</table>
Compilation of resources

- **Fungal Meningitis Outbreak Webpage**
  - Suspected Fungal Meningitis Outbreak Associated with Procedures Performed under Epidural Anesthesia in Matamoros, Mexico | HAI | CDC

- **Travel Health Notice:**
  - Fungal Infections Following Surgical Procedures in Mexico - Alert - Level 2, Practice Enhanced Precautions - Travel Health Notices | Travelers' Health | CDC

- **HAN #1:**
  - Health Alert Network (HAN) - 00491 | Outbreak of Suspected Fungal Meningitis in U.S. Patients who Underwent Surgical Procedures under Epidural Anesthesia in Matamoros, Mexico (cdc.gov)

- **HAN #2:**
  - Health Alert Network (HAN) - 00492 | Important Updates on Outbreak of Fungal Meningitis in U.S. Patients Who Underwent Surgical Procedures under Epidural Anesthesia in Matamoros, Mexico (cdc.gov)

- **MSGERC clinician-focused webinar**
  - [https://www.youtube.com/watch?v=7hzAxASLcbs](https://www.youtube.com/watch?v=7hzAxASLcbs)

- **Interim Recommendations**
  - Interim Recommendations for Diagnosis and Management of Cases of Fungal Meningitis Associated with Epidural Anesthesia Administered in Matamoros, Mexico
INTERIM RECOMMENDATIONS FOR DIAGNOSIS AND MANAGEMENT OF FUNGAL MENINGITIS ASSOCIATED WITH EPIDURAL ANESTHESIA ADMINISTERED IN MATAMOROS, MEXICO

Luis Ostrosky-Zeichner, MD, FACP, FIDSA, FSHEA, FECMM
Professor of Medicine and Epidemiology, Memorial Hermann Endowed Chair
Division Director, Infectious Diseases
The University of Texas Health Science Center at Houston
Chief Epidemiology Officer
Memorial Hermann Healthcare System
DISCLOSURES

- Grants from, consulting and/or speaker for:
  - Astellas
  - Merck
  - Pfizer
  - Gilead
  - Scynexis
  - Cidara
  - F2G
  - Pulmocide
  - GSK
# Interim Guidance Process

<table>
<thead>
<tr>
<th>Multidisciplinary group convened on 5/19/23</th>
<th>Groups represented (boots on the ground and experts):</th>
<th>Experience from recent outbreaks, literature, expert opinion</th>
<th>End product hosted in msgerc.org and funguseducationhub.org</th>
<th>Updated as information becomes available</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Epidemiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Local health authority</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pharmacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medical Mycology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neurology</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
DRAWING EXPERIENCE FROM RECENT OUTBREAKS
<table>
<thead>
<tr>
<th>Description</th>
<th>No. of Cases</th>
<th>Persons Potentially Exposed</th>
<th>No. of Cases/100 Persons Potentially Exposed (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>National attack rate, all infections</td>
<td>749</td>
<td>13,534</td>
<td>3.5 (5.1–5.9)</td>
</tr>
<tr>
<td>National attack rate, meningitis and spinal or paraspinal infection</td>
<td>716</td>
<td>12,068</td>
<td>5.9 (5.5–6.4)</td>
</tr>
<tr>
<td>State-specific attack rate, meningitis and spinal or paraspinal infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Florida</td>
<td>25</td>
<td>1,034</td>
<td>2.4 (1.6–3.5)</td>
</tr>
<tr>
<td>Georgia</td>
<td>1</td>
<td>180</td>
<td>0.6 (0.3–2.7)</td>
</tr>
<tr>
<td>Idaho</td>
<td>1</td>
<td>47</td>
<td>2.1 (0.1–10.5)</td>
</tr>
<tr>
<td>Illinois</td>
<td>2</td>
<td>238</td>
<td>0.8 (0.1–2.6)</td>
</tr>
<tr>
<td>Indiana</td>
<td>91</td>
<td>1,362</td>
<td>6.7 (5.4–8.2)</td>
</tr>
<tr>
<td>Maryland</td>
<td>26</td>
<td>1,057</td>
<td>2.5 (1.6–3.5)</td>
</tr>
<tr>
<td>Michigan</td>
<td>239</td>
<td>1,727</td>
<td>13.8 (12.3–15.5)</td>
</tr>
<tr>
<td>Minnesota</td>
<td>12</td>
<td>843</td>
<td>1.4 (0.8–2.4)</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>9</td>
<td>601</td>
<td>1.5 (0.7–2.8)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>50</td>
<td>638</td>
<td>7.8 (5.9–10.1)</td>
</tr>
<tr>
<td>New York</td>
<td>1</td>
<td>405</td>
<td>0.2 (0.01–1.2)</td>
</tr>
<tr>
<td>North Carolina</td>
<td>18</td>
<td>100</td>
<td>18 (11.4–26.5)</td>
</tr>
<tr>
<td>Ohio</td>
<td>20</td>
<td>328</td>
<td>6.1 (3.5–9.1)</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>1</td>
<td>720</td>
<td>0.1 (0.01–0.7)</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>3</td>
<td>266</td>
<td>1.1 (0.3–3.1)</td>
</tr>
<tr>
<td>South Carolina</td>
<td>3</td>
<td>231</td>
<td>1.3 (0.3–3.5)</td>
</tr>
<tr>
<td>Tennessee</td>
<td>151</td>
<td>1,010</td>
<td>14.9 (12.7–17.5)</td>
</tr>
<tr>
<td>Texas</td>
<td>2</td>
<td>58</td>
<td>3.5 (0.6–11.4)</td>
</tr>
<tr>
<td>Virginia</td>
<td>54</td>
<td>645</td>
<td>8.4 (6.4–10.7)</td>
</tr>
<tr>
<td>West Virginia</td>
<td>7</td>
<td>121</td>
<td>3.8 (2.6–11.1)</td>
</tr>
</tbody>
</table>

**Peripheral-Joint Infection (N=13)**

**Spinal or Paraspinal Infection (N=424)**

**Stroke without Documented Meningitis (N=7)**

**Meningitis (N=376)**
November 2022
- 1801 exposures, 80 cases, 39 deaths, 31 cases with + Fusarium PCR

INTERIM GUIDANCE
TWO IMPORTANT PRINCIPLES

Infectious diseases and neurology consultation

Consultation with local health department
DIAGNOSTIC APPROACH

- Symptomatic and asymptomatic patients
  - Lumbar puncture
    - Opening pressure
    - Other routine CSF testing (e.g., color, cell counts [WBC with differential, RBC], protein, lactate, glucose)
  - Bacterial, mycobacterial, and fungal stains and cultures
  - Beta-d-glucan (Fungitell®)
  - Aspergillus galactomannan (until etiology of outbreak has been determined)
  - Molecular testing by multiplex PCR
  - Pan fungal PCR or metagenomic testing
  - Reserve/store CSF for future or additional testing
    - Serum Beta-d-glucan and Aspergillus galactomannan

- Brain MRI (with and without contrast) suggested in patients with symptoms and **recommended in patients with abnormal LP**
- Spine MRI suggested in patients with back pain or paresthesia
Empiric antifungal therapy is not recommended for asymptomatic patients with normal CSF profiles.

All patients, especially those with symptoms, should be closely monitored and re-evaluated for new or persistent symptoms.

Clinicians may consider a second diagnostic lumbar puncture two weeks after the original to reevaluate the CSF.

Should the patient have new or persistent symptoms, a lumbar puncture should be repeated.
### THERAPY FOR PATIENTS WITH ABNORMAL LP

**Liposomal amphotericin B**
- 5mg/kg daily, may escalate to 7.5-10mg/kg daily
- Aggressive hydration, monitor for renal toxicity and electrolytes
- Avoid intra-thecal amphotericin B

**Voriconazole**
- 6mg/kg q12h induction, then 4mg/kg q12h
- Weekly levels with a target trough of 4-5mcg/ml
- IV preferred but may transition to PO
- Monitor liver function and neurotoxicity
- Drug interaction
- Alternatives to voriconazole: Posaconazole or isavuconazole

**Suggested minimum duration** 3-6 months, but may be longer

<table>
<thead>
<tr>
<th>Liposomal amphotericin B</th>
<th>AND</th>
<th>Voriconazole</th>
<th>Suggested minimum duration 3-6 months, but may be longer</th>
</tr>
</thead>
<tbody>
<tr>
<td>5mg/kg daily, may escalate to 7.5-10mg/kg daily</td>
<td></td>
<td>6mg/kg q12h induction, then 4mg/kg q12h</td>
<td></td>
</tr>
<tr>
<td>Aggressive hydration, monitor for renal toxicity and electrolytes</td>
<td></td>
<td>Weekly levels with a target trough of 4-5mcg/ml</td>
<td></td>
</tr>
<tr>
<td>Avoid intra-thecal amphotericin B</td>
<td></td>
<td>IV preferred but may transition to PO</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monitor liver function and neurotoxicity</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drug interaction</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alternatives to voriconazole: Posaconazole or isavuconazole</td>
<td></td>
</tr>
</tbody>
</table>
# OTHER CONSIDERATIONS

## Monitoring after cessation of therapy

- Close monitoring, prompt evaluation if recurrent symptoms
- Low threshold for lumbar puncture
- Radiologic abnormalities may persist for month and do not necessarily signal failure

## Complications

- Increased intracranial pressure
- Serial LPs and/or mannitol
- Vasculitis and/or brain edema
  - Steroids controversial but favorable outcomes reported in Durango. Slow taper if used.
- Strokes and intracranial hemorrhage have occurred and signal bad prognosis
THANK YOU!

@DrLuisO
Luis.Ostrosky-Zeichner@uth.tmc.edu
To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.
Today’s COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*

- **What:** Video recording

- **Where:** On the COCA Call webpage
  

*A transcript and closed-captioned video will be available shortly after the original video recording posts at the above link.*
Upcoming COCA Calls & Additional Resources

- Join us for our next COCA Call, Thursday, June 15 at 2 PM ET.
  Topic: [Evaluating and Supporting Patients with Long COVID in Returning to Work](#)

- Continue to visit [https://emergency.cdc.gov/coca/](https://emergency.cdc.gov/coca/) to get more details about upcoming COCA Calls.

- Subscribe to receive notifications about upcoming COCA calls and other COCA products and services at [emergency.cdc.gov/coca/subscribe.asp](https://emergency.cdc.gov/coca/subscribe.asp).
Thank you for joining us today!

[Image of CDC building]

emergency.cdc.gov/coca