



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.

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- 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**
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Outbreak of Fungal Meningitis Associated with Epidural Anesthesia Performed in Matamoros, Mexico — 2023

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

May 20, 2023:
CDC received list of exposed patients at the two clinics in Mexico. CDC sent state-specific reports later that day

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

June 3, 2023:
CDC received a list of patients from U.S.-based patient coordinator of Clinica K-3

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

May 17, 2023:
HAN Health Advisory was published

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

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

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 21, 2023: World Health Organization (WHO) notified of proposed PHEIC

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



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**

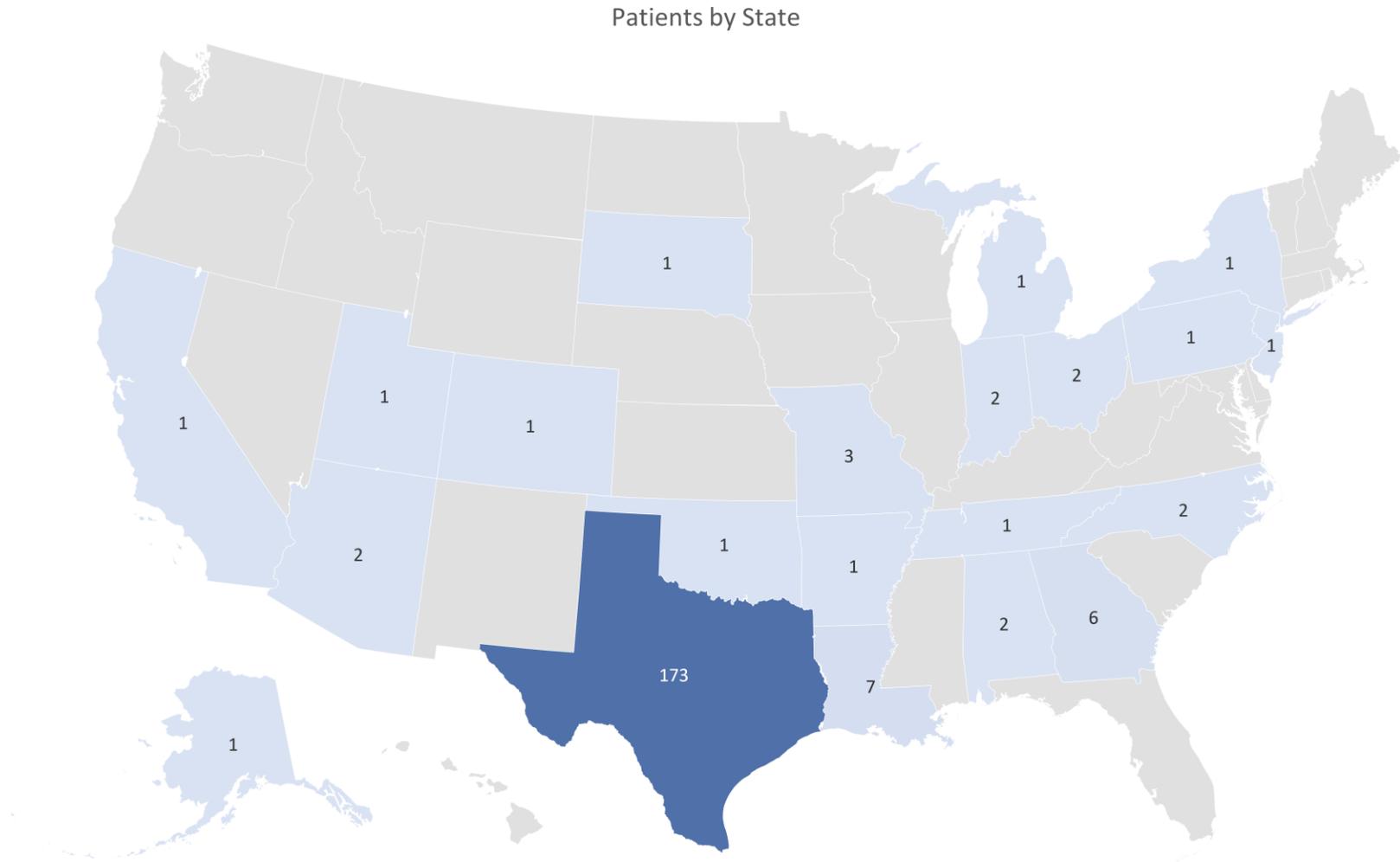
Demographic characteristics of exposed U.S. residents

Patients, by Clinic	
Clinica K-3	117
River Side Surgical Center	94

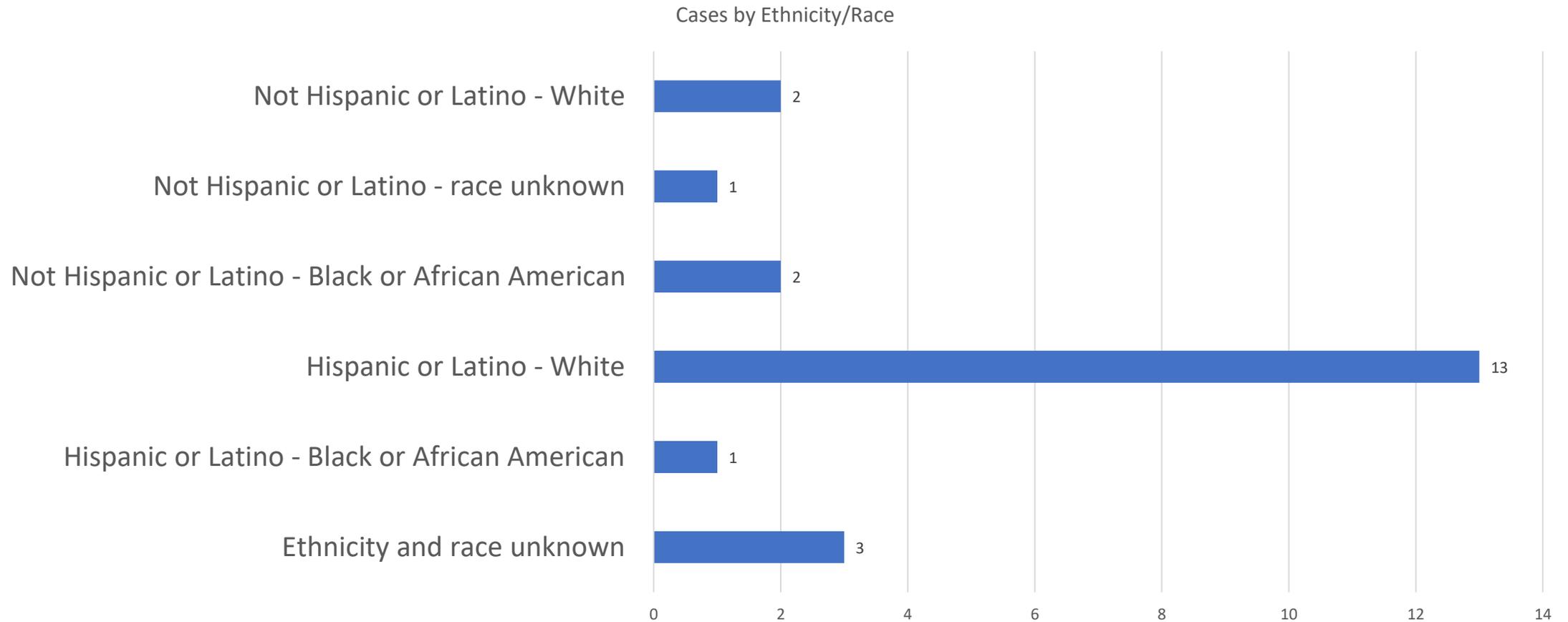
Patients, by Sex	
Female	190
Male	18

Age	
Mean	34 (14–69)

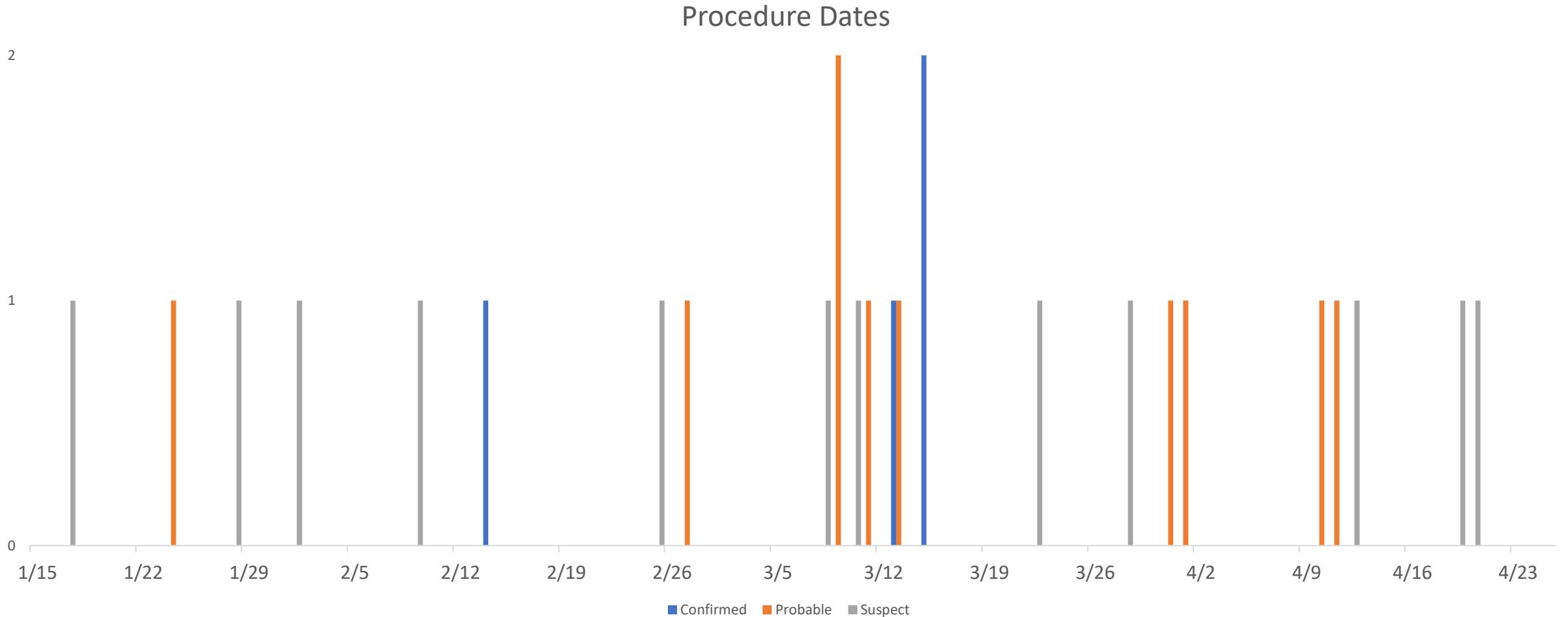
Patients are from 23 U.S. states, D.C., and Puerto Rico



Fungal meningitis has been diagnosed most frequently in Hispanic and Latino patients

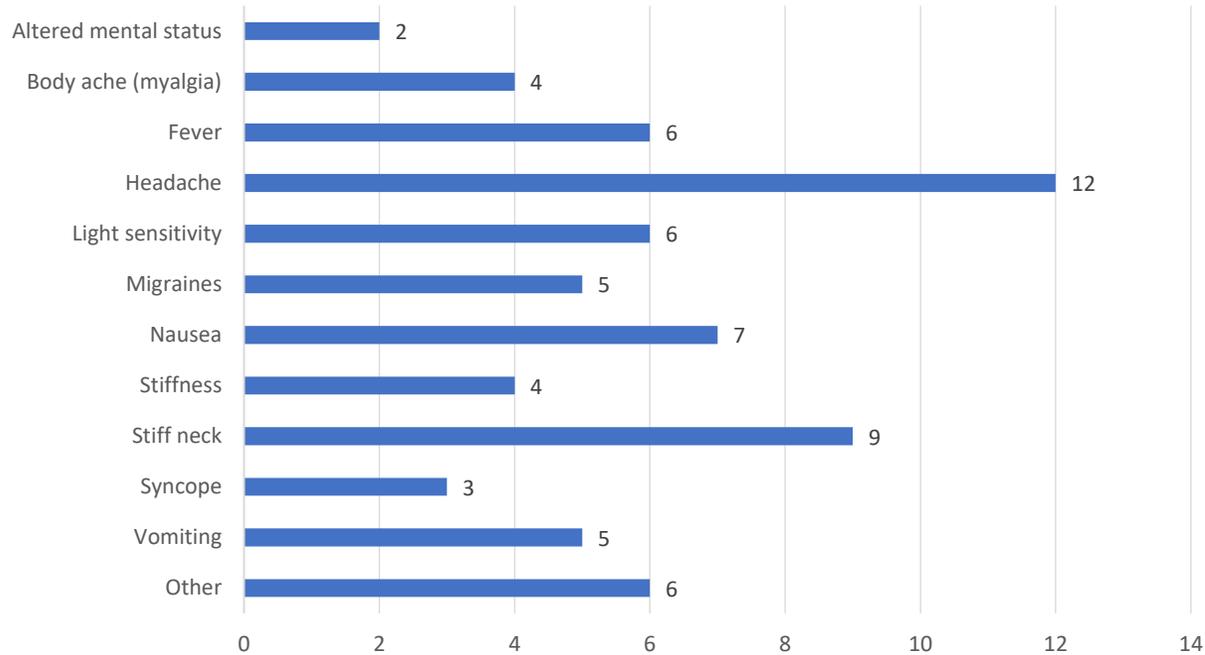


Procedure dates for suspected, probable, and confirmed cases ranged from 1/17/23 to 4/28/23



Clinical summary

Symptom Frequency



Time frame	Average	Median	Min	Max
# Days from Procedure to Onset	19	18	2	32
# Days from Procedure to Hospitalization	56	56	14	106

Laboratory summary

LP Results	Average	Min	Max
Glucose (mg/dL)	32	19	57
WBC (K/ μ L)	757	24	1761
Protein (mg/dL)	109	34	254

- 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

Compilation of resources

- **Fungal Meningitis Outbreak Webpage**

- [Suspected Fungal Meningitis Outbreak Associated with Procedures Performed under Epidural Anesthesia in Matamoros, Mexico | HAI | CDC](#)
- <https://www.cdc.gov/hai/outbreaks/es/meningitis-epidural-anesthesia.html>

- **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>

- **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

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Chief Epidemiology Officer

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DISCLOSURES

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



INTERIM GUIDANCE PROCESS

**Multidisciplinary
group convened on
5/19/23**

**Groups
represented (boots
on the ground and
experts):**

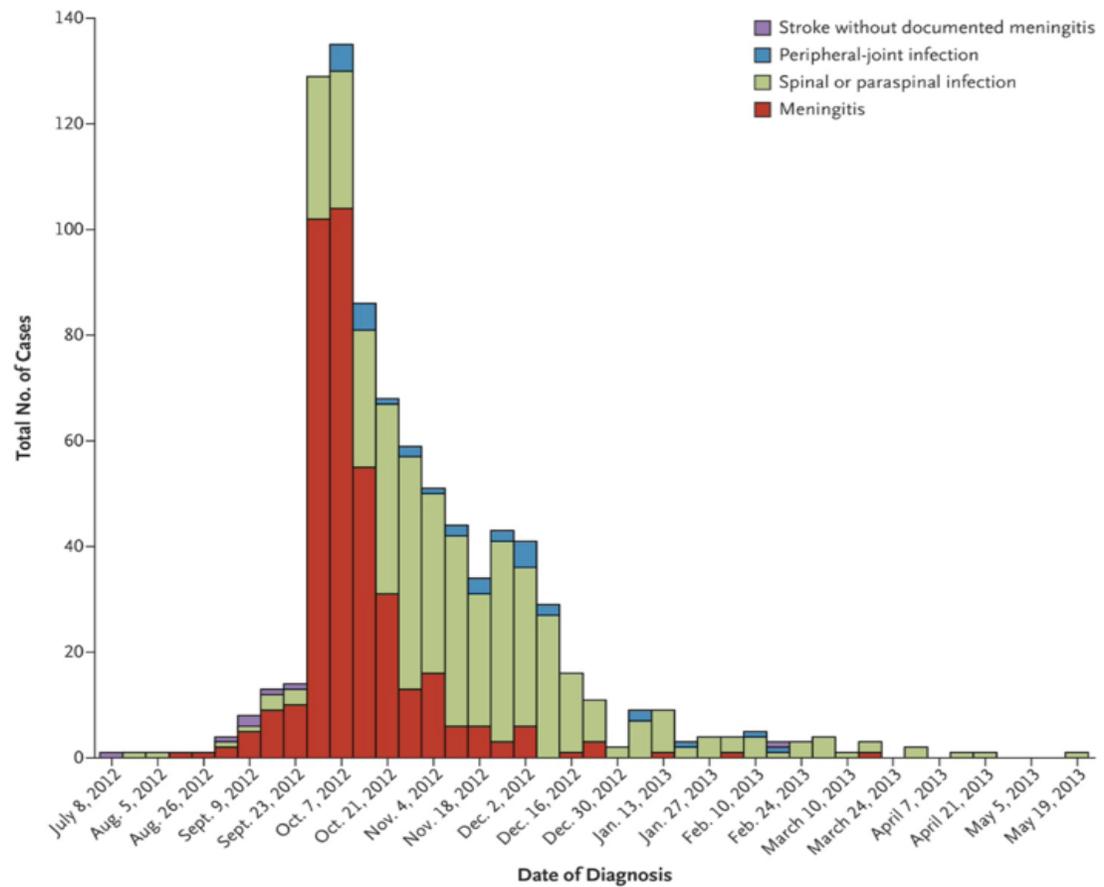
Epidemiology
Local health authority
Pharmacy
Medical Mycology
Neurology

**Experience from
recent outbreaks,
literature, expert
opinion**

**End product hosted in
msgerc.org and
funguseducationhub.org**

**Updated as
information
becomes available**





Smith et al., NEJM, 2013

THE EXSEROHILUM OUTBREAK

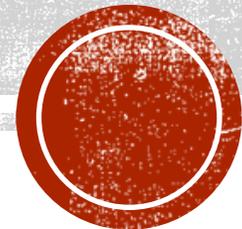
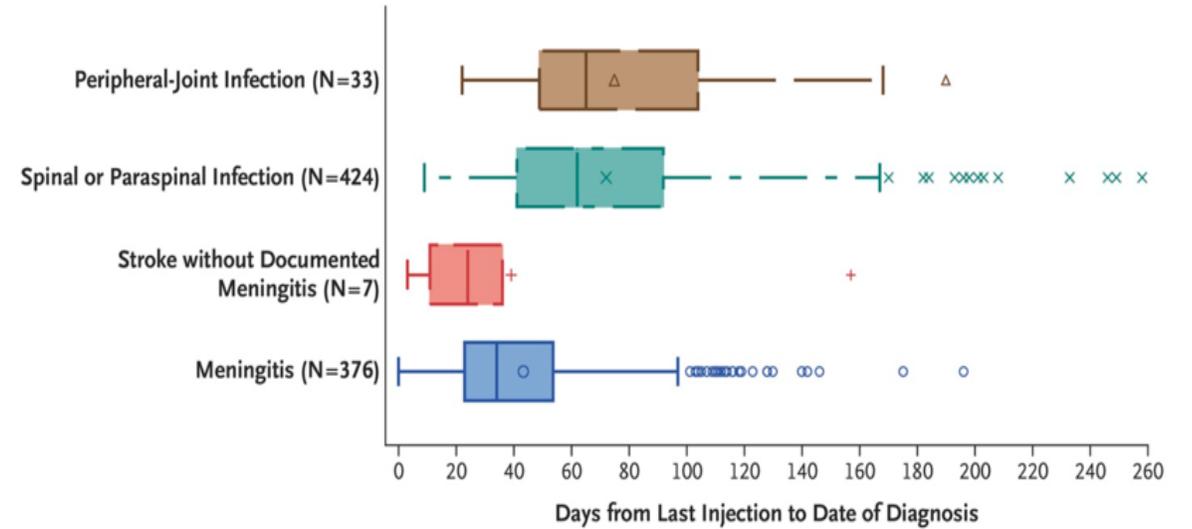
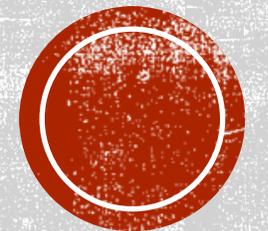


Table 2. National Attack Rates for All Infections and National and State-Specific Attack Rates for Meningitis and Spinal or Paraspinal Infections, as of July 1, 2013.*

Description	No. of Cases	Persons Potentially Exposed [†]	No. of Cases/100 Persons Potentially Exposed (95% CI)
National attack rate, all infections	749	13,534	5.5 (5.1–5.9)
National attack rate, meningitis and spinal or paraspinal infections [‡]	716	12,068	5.9 (5.5–6.4)
State-specific attack rate, meningitis and spinal or paraspinal infections ^{‡§}			
Florida	25	1,034	2.4 (1.6–3.5)
Georgia	1	180	0.6 (0.03–2.7)
Idaho	1	47	2.1 (0.1–10.5)
Illinois	2	238	0.8 (0.1–2.8)
Indiana	91	1,362	6.7 (5.4–8.2)
Maryland	26	1,057	2.5 (1.6–3.5)
Michigan	239	1,727	13.8 (12.3–15.5)
Minnesota	12	843	1.4 (0.8–2.4)
New Hampshire	9	601	1.5 (0.7–2.8)
New Jersey	50	638	7.8 (5.9–10.1)
New York	1	405	0.2 (0.01–1.2)
North Carolina	18	100	18 (11.4–26.5)
Ohio	20	328	6.1 (3.9–9.1)
Pennsylvania	1	720	0.1 (0.01–0.7)
Rhode Island	3	266	1.1 (0.3–3.1)
South Carolina	3	231	1.3 (0.3–3.5)
Tennessee	151	1,010	14.9 (12.7–17.5)
Texas	2	58	3.5 (0.6–11.4)
Virginia	54	645	8.4 (6.4–10.7)
West Virginia	7	121	5.8 (2.6–11.1)



EXSEROHILUM LESSONS



DURANGO OUTBREAK



- November 2022
- 1801 exposures, 80 cases, 39 deaths, 31 cases with + Fusarium PCR



Tabla 2. Distribución de casos de meningitis por días transcurridos entre la exposición y el inicio de síntomas, Durango, 09 de mayo de 2023

Días	Casos	Porcentaje
0 a 7	45	58
8 a 14	7	9
15 a 28	7	9
Más de 28	19	24
TOTAL	78	100

*Dos de los casos se reportaron asintomáticos.



Tabla 3. Síntomas más frecuentes entre pacientes con meningitis, Durango, 09 de mayo de 2023

Síntomas más frecuentes	Casos	Porcentaje
Dolor de cabeza	75	94
Náuseas	30	38
Rigidez de nuca	26	33
Vómito	24	30
Alteraciones visuales	21	26
Fiebre	19	24

*Dos de los casos se reportaron como asintomáticos.

https://www.gob.mx/cms/uploads/attachment/file/825329/COMUNICADO_TECNICO_SEMANAL_09MAYO2023.pdf



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



**ASYMPTOMATIC
PATIENTS
W/NORMAL LP**

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

AND

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**



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



FUNGAL MENINGITIS GUIDANCE WRITING GROUP

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THANK YOU!

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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
https://emergency.cdc.gov/coca/calls/2023/callinfo_060823.asp

**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/> 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.

Thank you for joining us today!



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