Published in final edited form as:

Clin Infect Dis. 2024 June 14; 78(6): 1554–1558. doi:10.1093/cid/ciad570.

Update on Outbreak of Fungal Meningitis Among US Residents Who Received Epidural Anesthesia at Two Clinics in Matamoros, Mexico

Dallas J. Smith[1], **Jeremy A. W. Gold**[1], **Tom Chiller**[1], **Nirma D. Bustamante**[2], **Maria Julia Marinissen**[3,4], **Gabriel Garcia Rodriquez**[5], **Vladimir Brian Gonzalez Cortes**[5], **Celida Duque Molina**[6], **Samantha Williams**[1], **Axel A. Vazquez Deida**[7,8], **Katrina Byrd**[2,7], **Peter G. Pappas**[9], **Thomas F. Patterson**[10], **Nathan P. Wiederhold**[11], **George R. Thompson III**[12,13], **Luis Ostrosky-Zeichner**[14], **Fungal Meningitis Response Team**

[1]Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[2]Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[3]Health Attache, U.S. Embassy, Mexico City, Mexico

[4]U.S. Section, U.S.-Mexico Border Health Commission, U.S. Department of Health and Human Services, Washington D.C., USA

[5]General Director of Epidemiology, Ministry of Health Mexico, México City, México

[6]Director of Medical Services, Mexican Social Security Institute, México City, México

[7]Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[8]Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[9]Division of Infectious Diseases, Department of Internal Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA

[10]Division of Infectious Diseases, Department of Medicine, The University of Texas Health Science Center, San Antonio, Texas, USA

[11]Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center, San Antonio, Texas, USA

[12]Division of Infectious Diseases, Department of Internal Medicine, University of California, Davis Medical Center, Sacramento, California, USA

[13]Department of Medical Microbiology and Immunology, University of California, Davis, Davis, California, USA

[14]Division of Infectious Diseases, McGovern Medical School, Houston, Texas, USA

Correspondence: D. J. Smith, Mycotic Diseases Branch, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Mailstop: H24-10, Atlanta, GA 30329 (rhq8@cdc.gov); J. A. W. Gold, Mycotic Diseases Branch, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Mailstop: H24-10, Atlanta, GA 30329 (leo3@cdc.gov).

Abstract

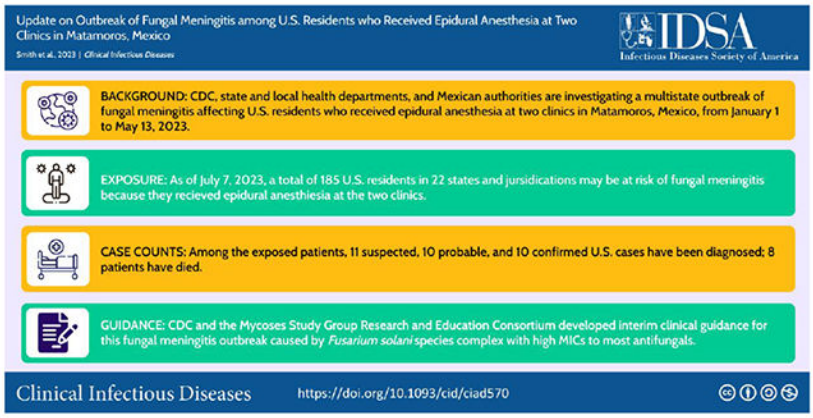
Background.—Public health officials are responding to an outbreak of fungal meningitis among patients who received procedures under epidural anesthesia at 2 clinics (River Side Surgical Center and Clinica K-3) in Matamoros, Mexico, during 1 January to 13 May 2023. This report describes outbreak epidemiology and outlines interim diagnostic and treatment recommendations.

Methods.—Interim recommendations for diagnosis and management were developed by the Mycoses Study Group Research Education and Consortium (MSGERC) based on the clinical experience of clinicians caring for patients during the current outbreak or during previous outbreaks of healthcare-associated fungal meningitis in Durango, Mexico, and the United States.

Results.—As of 7 July 2023, the situation has evolved into a multistate and multinational fungal meningitis outbreak. A total of 185 residents in 22 US states and jurisdictions have been identified who might be at risk of fungal meningitis because they received epidural anesthesia at the clinics of interest in 2023. Among these patients, 11 suspected, 10 probable, and 10 confirmed US cases have been diagnosed, with severe vascular complications and 8 deaths occurring. *Fusarium solani* species complex has been identified as the causative agent, with antifungal susceptibility testing of a single isolate demonstrating poor in vitro activity for most available antifungals. Currently, triple therapy with intravenous voriconazole, liposomal amphotericin B, and fosmanogepix is recommended.

Conclusions.—Efforts to understand the source of this outbreak and optimal treatment approaches are ongoing, but infectious diseases physicians should be aware of available treatment recommendations. New information will be available on the Centers for Disease Control and Prevention's (CDC's) website.

Graphical Abstract



This graphical abstract is also available at Tidbit: https://tidbitapp.io/tidbits/update-on-outbreak-of-fungal-meningitis-among-u-s-residents-who-received-epidural-anesthesia-at-two-clinics-in-matamoros-mexico-4ac506e4-c163-4f4a-b2f7-c96223f2a045

Keywords

fungal meningitis; Fusarium; epidural; healthcare-associated infection; medical tourism

On 8 May 2023, the Centers for Disease Control and Prevention (CDC) learned through the Emerging Infections Network of 2 patients in Texas who developed suspected fungal meningitis after receiving procedures under epidural anesthesia in Matamoros, Tamaulipas, Mexico, a city located on the southern border of Texas, United States [1]. Over the following days, CDC and Texas Department of Health and Human Services identified additional suspected fungal meningitis cases in Texas residents. This prompted an investigation, performed in partnership with Mexican Health Authorities, that led to the closure of 2 Matamoros clinics (River Side Surgical Center and Clinica K-3) on 13 May 2023 [1].

As of 7 July 2023, the situation has evolved into a multistate and multinational fungal meningitis outbreak. A total of 185 residents in 22 US states and jurisdictions have been identified who might be at risk of fungal meningitis because they received epidural anesthesia at the clinics of interest in 2023. Among these patients, 11 suspected, 10 probable, and 10 confirmed US cases have been diagnosed (see case definitions: Table 1); 8 patients (1 probable and 7 confirmed cases) have died.

ILLUSTRATIVE PATIENT CASE

On 19 April 2023, a 30-year-old Hispanic woman with a past medical history of Hashimoto's thyroiditis and irritable bowel syndrome received liposuction under spinal epidural anesthesia at Riverside Clinic in Matamoros, Mexico. On 8 May 2023, she began experiencing neck pain, headache, and chills associated with the pain. She presented on 6 June 2023, to the emergency department. There she received a lumbar puncture with opening pressure of 10 cm H_2O, glucose 23 mg/dL, protein 166 mg/dL, red blood cells (RBC) 20 cells/mcL, white blood cells (WBC) 940 cells/mcL (60% neutrophils, 19% lymphocytes). Her cerebrospinal fluid (CSF) grain stain showed rare fungal forms and the β-D-glucan level exceeded >500 pg/mL, but culture results and DNA sequencing of 28S rDNA were ultimately negative. She was started on intravenous liposomal amphotericin B and voriconazole. Her Initial computed tomography (CT) brain, magnetic resonance imaging (MRI) brain, and CT angiography (CTA) head and neck were unremarkable.

On 15 June 2023, a repeat lumbar puncture showed an opening pressure of 20 cm H_20, glucose 34 mg/dL, protein 118 mg/dL, RBC 117 cells/mcL, and WBC 63 cells/mcL. She reported continued headaches, and because of worsening cerebrospinal fluid (CSF) pressure and symptoms, she was started on intra-thecal liposomal amphotericin B (10 mg daily) in addition to the systemic antifungals. Despite aggressive antifungal therapy and corticosteroids, her repeat MRI brain on 3 July 2023, showed interval development of thick nodular leptomeningeal enhancement in the prepontine cistern, with nodules in the vicinity of the right fifth cranial nerve and to the left of the basilar artery and with arterial narrowing. In the treating clinicians' experience, these imaging findings could precede a vascular rupture and subarachnoid hemorrhage. Terbinafine was added as a desperate measure, with no further improvement.

The patient received a “pipeline stent” of the left basilary artery, a ventriculo-peritoneal shunt, and was eventually started on compassionate use fosmanogepix, with good clinical and CSF parameter response, including a decrease in CSF β-D-glucan level levels. The patient was discharged home on fosmanogepix monotherapy and is still being monitored by clinicians.

OUTBREAK SOURCE AND IDENTIFICATION OF *FUSARIUM SOLANI* SPECIES COMPLEX AS AN ETIOLOGIC AGENT

Although the outbreak has been linked to epidural anesthesia at the 2 implicated clinics in Matamoros, the precise source of the outbreak remains unknown. The outbreak might be due to contaminated medications or poor infection control practices used while administering epidural anesthesia.

A fungal etiology was suspected early in the investigation because of elevated CSF β-D-glucan levels in multiple patients. On 19 May 2023, Mexican public health officials from the Mexican Institute of Social Security reported the first positive *Fusarium solani* result from a *Fusarium*-specific polymerase chain reaction (PCR) test from a patient’s CSF sample; the PCR result was validated by the Mexico’s National Institute for Epidemiological Diagnosis and Reference. Subsequently, metagenomic next-generation sequencing and pan-fungal PCR testing of CSF samples from 9 affected US patients have since identified *F. solani* species complex; however, it is possible that patients could be affected by >1 fungus or that other fungi not yet identified could be implicated in this outbreak. Blood and CSF cultures from affected patients have been negative to date, for fungi and other pathogens. However, *F. solani* was isolated from 1 patient’s tissue culture on 3 July 2023.

RESEMBLANCE TO THE RECENT *F. SOLANI* FUNGAL MENINGITIS OUTBREAK IN DURANGO, MEXICO

Notably, in November 2022, Mexican public health officials reported a similar outbreak in Durango, Mexico, which is located over 500 miles from Matamoros, Tamaulipas, Mexico [2]. Patients in the Durango outbreak had also developed *F. solani* fungal meningitis after receipt of epidural anesthesia, although an *Alternaria* sp. was found in a single patient. Although the outbreak investigation by Mexican public health officials is still ongoing, preliminary data published by the México Ministry of Health shows 1801 patients were potentially exposed; 80 were diagnosed with fungal meningitis, of whom 40 died [2]. The outbreak in Durango is being attributed by Mexican authorities to lapses in infection prevention and control practices by clinics and anesthesiologists. Additional details on the Durango outbreak are pending publication by Mexican authorities.

CLINICAL FEATURES AND LABORATORY TESTING RESULTS

As of 7 July 2023, central nervous system (CNS) infection-related symptoms (eg, headache, photophobia, fever, nausea, vomiting, neck stiffness, and altered mental status) have been reported a mean of 22 days (range 2–58 days) following epidural anesthesia. CSF findings have been consistent with fungal infection: white blood cells/μL (mean 671, range 24–1761),

protein mg/dL (mean 96, range 1–254), and glucose mg/dL (mean 33, range 19–57). Ten probable and confirmed patients have had highly positive CSF μ-D-glucan results (mean 454 pg/mL, range 51–500). Antifungal susceptibility testing of a single *F. solani* isolate, which was obtained from a tissue culture from 1 patient, exhibited high minimum inhibitory concentrations (MICs) to multiple antifungal drugs (suggesting resistance), although *F. solani* has no established breakpoints (Table 2).

INTERIM CONSIDERATIONS FOR DIAGNOSIS AND CLINICAL MANAGEMENT

Optimal therapy for patients with *F. solani* fungal meningitis infections has not been established, likely varies among patients and may be complex and prolonged. Interim recommendations on the diagnosis and management of patients with suspected fungal meningitis were developed by the MSGERC based on the clinical experience of clinicians caring for patients during the current outbreak or during previous outbreaks of healthcare-associated fungal meningitis in Durango, Mexico, and the United States [3, 4].

Current recommendations encourage all patients (including asymptomatic patients) who received epidural anesthesia at 1 of the implicated clinics in Matamoros after 1 January 2023 to seek urgent evaluation at their nearest emergency department for potential infection. Even in asymptomatic patients, evaluation should involve a lumbar puncture unless contraindicated. This recommendation is based on the high mortality (50%) associated with *Fusarium* CNS infections and the fact that during the Durango and the 2012 US fungal meningitis outbreak some patients were found on CSF examination to have fungal meningitis in the absence of symptoms (data not published) [2]. CSF diagnostic testing should include opening pressure, WBC count with differential, protein, glucose, and fungal stains and culture. Additional CSF should be saved for further testing if CSF WBC count is elevated, in which case CSF β-D-glucan should tested and metagenomic or pan-fungal PCR testing should be considered. *F. solani* is generally difficult to treat with currently available antifungals; all attempts should be made to culture the fungus and perform antifungal susceptibility testing. Information on how to obtain recommended testing is available in the interim recommendations posted by MSGERC [3].

Asymptomatic patients with normal CSF results (ie, <5 WBC/μL after correction for RBC) should not receive antifungal therapy. It is unclear if repeated evaluation of the CSF in asymptomatic patients is needed; however, repeat assessment after two weeks from the initial results seems prudent if suspicions remain. If patients develop symptoms that are concerning for potential CNS infection following initial negative results, a lumbar puncture and CSF assessment should be repeated.

For patients with an elevated CSF WBC count, empiric treatment with antifungal therapy is recommended while awaiting specific diagnostic results. Management should ideally be guided by consultation with an infectious disease specialist and a neurologist. MRI of the brain with and without contrast should be performed to assess for meningeal enhancement or nodularity, vasculitis, brain edema, ventriculitis, hemorrhage, or ischemia if patients have abnormal CSF results.

Regarding antifungal treatment, *F. solani* is a difficult-to-treat environmental fungal pathogen against which most currently available antifungals have little to no in vitro activity [5]. Experience with invasive infections has been almost exclusively in heavily immunocompromised patients [5]. The recommended treatment in the ongoing outbreak is triple therapy with intravenous voriconazole (6 mg/kg every 12 hours), intravenous liposomal amphotericin B (initial dosing: 10 mg/kg/day), and fosmanogepix (highest dose allowed from Pfizer's compassionate use protocol) [6]. Liposomal amphotericin B is preferred over other amphotericin B formulations because of better CNS penetration [7]. Kidney function and electrolyte disturbance should be monitored closely given the well-known toxicity of this agent. Voriconazole therapeutic drug monitoring should be performed (day 5 of therapy and weekly thereafter) and the dose of voriconazole adjusted dependent upon the serum concentration (goal trough in *Fusarium* CNS infections 4–5 μg/mL or a higher trough level if the patient can tolerate it). Drug-drug interactions, hepatotoxicity, and visual disturbances (eg, blurred vision, changes in color perception, photopsia) are common during voriconazole administration and should be continuously monitored during patient treatment. Intrathecal therapy with amphotericin B is associated with toxicity (eg, arachnoiditis) and requires considerable expertise; however, it has been used in several patients with refractory cases during the current outbreak [8]. If intrathecal therapy is being considered for refractory cases, discussions with those highly experienced with this treatment practice are recommended. Fosmanogepix has been shown to have in vitro activity against *Fusarium* species and experimental models of fusariosis both alone and in combination with other antifungals [9–11]. Fosmanogepix has been shown to have a similar concentration in plasma compared with its concentration in the meninges, cerebrum, cerebellum, and spinal cord; considering the antifungal susceptibility results (Table 2) from a single isolate in this outbreak, fosmanogepix has the potential to improve patient outcomes [12]. The optimal dose is unknown, and fosmanogepix is only available under a compassionate use protocol with Pfizer. Patients intolerant to voriconazole should not receive posaconazole or isavuconazole given their high MICs from the single isolate from this outbreak (Table 2).

Repeated CNS MRIs will likely be needed for periodic reassessment or if new CNS symptoms develop. Acute complications such as hydrocephalus, hemorrhage, vasculitis, or stroke may develop, even in those receiving appropriate antifungal therapy. These complications may occur because of continued spread of infection, or, in those receiving effective antifungal therapy, potentially because of the host response to fungal antigens expressed following fungal cell death. Therefore, careful consideration of serial imaging findings and discussion with infectious diseases experts, neurologists, and radiologists experienced in CNS imaging should be undertaken before making therapeutic changes.

Antifungal therapy is expected to be prolonged given the severity of complications and requires careful periodic reassessment of patient symptoms, laboratory values including CSF assessment, and radiographic findings. A minimum of 3–6 months of therapy should be considered, with the duration tailored to individual patients. Patients with more extensive disease or immunosuppression should receive longer courses of therapy (>6 months). Decreasing CSF β -D-glucan levels can suggest the infection is improving. Following

cessation of therapy, patients should be periodically monitored for potential relapse of infection, maintaining a low threshold for repeating CNS imaging and CSF analysis.

COMPLICATIONS, MANAGEMENT, AND CONTROVERSIES

Patients in this outbreak are experiencing high rates of neurovascular complications, including mycotic aneurysms, vasculitis, aneurysms, intra-cranial hemorrhage, and stroke. These vascular events have generally been localized to the basilar circulation, brain stem, and cerebellum. Patients have also experienced intra-cranial hypertension and brain edema, often requiring osmotic therapy, frequent lumbar punctures, and/or placement of lumbar drains, external ventriculostomy devices, or ventriculo-peritoneal shunts. In some patients who have experienced neurovascular complications, corticosteroids and/or endovascular procedures have been used, but the utility and ideal timing of these measures is unknown. Because of the high frequency of these complications and the advanced management strategies required, it is suggested that patients be cared for in hospitals and units that have access to advanced neuroimaging and neurological intensive care units.

ONGOING CHALLENGES AND NEXT STEPS

Several challenges remain regarding the ongoing fungal meningitis outbreak. First, reaching patients has been difficult because of missing or incorrect contact information. In addition, some patients in the United States have avoided or delayed evaluation because they do not have health insurance or have limited coverage to cover the cost of testing. Management of fungal meningitis in this outbreak has been challenging because of a lack of data to guide optimal therapy and because the causative organism(s) have high MICs to most antifungals. The utility and timing of steroids, advanced neurological and neurosurgical procedures, and the role of intra-thecal amphotericin B or experimental antifungals remain unknown. Public health officials are continuing to investigate the origins of this outbreak. Updated information about the outbreak will continue to be provided on CDC’s website.

Acknowledgments.

The authors would like to thank the state and local health departments who have responded to this fungal meningitis outbreak.

Disclaimer.

The findings and conclusions of this article are those of the authors and do not necessarily represent the official position of the US Department of Health and Human Services and the US Centers for Disease Control and Prevention (CDC). The findings and conclusions of this article are those of the authors and do not necessarily represent the official position of the Texas Department of State Health Services (DSHS). The findings and conclusions of this article are those of the authors and do not necessarily represent the official position of the Ministry of Health of México.

Potential conflicts of interest.

L. O.-Z. is the president of the MSG-ERC, Vice-President of ICHS, and has received research funding, consulting and/or speaking honoraria from the following entities: Scynexis, Pulmocide, Gilead, Astellas, NIH, Pfizer, T2 biosystems, F2G, GSK, Melinta, Viracor, and Cidara. P. G. P. has received research funding from F2G, Cidara, CDC, Astellas, Melinta, Gilead, Mayne, Scynexis, participated on Data Safety Monitoring or Advisory Board for Melinta, Matinas, Cidara, and Scynexis; and serves as a consultant for Melinta, F2G, Matinas, and Scynexis. T. F. P. has served as a consultant, on data safety monitoring/data review committees, on a Scientific Advisory Board, or received research support from: Cidara, F2G, Gilead, Scynexis, and Sfunga, outside of the submitted work and

royalties from Wolters Klower. A. N. M. serves as a consultant to the Michigan Department of Health & Human Services and is a shareholder of Pfizer pharmaceuticals. N. P. W. has received research support from bioMerieux, Bruker, F2G, Maxwell Biosciences, Mycovia, Scynexis, and Sfunga; payment or honoraria for speaking or educational events and travel support from American Society for Microbiology; a leadership or fiduciary role at Clinical and Laboratory Standards Institute; receipt of antifungal powders from F2G, Pfizer, and Scynexis; and has served as a consultant for F2G. G. R. T. reports grants or contracts and consulting fees from Astellas, Cidara, F2G, Mayne, Mundipharma, and Melinta; and participation on a Data Safety Monitoring or Advisory Board for Pfizer. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Fungal meningitis response team:

Anurag N. Malani, Division of Infectious Diseases, Trinity Health Michigan, Ann Arbor, Michigan; Carol A. Kauffman, Veterans Affairs Medical Center, University of Michigan Medical School, Ann Arbor, Michigan; John R. Perfect, Division of Infectious Diseases, Department of Medicine, Duke University Medical Center, Durham, North Carolina; Meghan Lyman, Shawn R. Lockhart, and Anastasia P. Litvintseva, Centers for Disease Control and Prevention, Atlanta, Georgia; Victoria Parada, Valley Baptist Medical Center-Harlingen, Harlingen, Texas; James W. Castillo, Cameron County Public Health, San Benito, Texas; Jose Campo Maldonado, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas; JulieAnna Rivas, Arizona Department of Health Services, Phoenix, Arizona; Karen Zabel, Maricopa County Department of Public Health, Phoenix, Arizona; Lori Koenecke, South Dakota Department of Health, Pierre, South Dakota; Simone Godwin, Tennessee Department of Health, Nashville, Tennessee; Christopher D. Wilson, Tennessee Department of Health, Nashville, Tennessee; Nicole Evert, Thi Dang, and Emilie Prot, Texas Department of State Health Services, Austin, Texas; Raquel Castillo, Ameera Khan, Layda Rincon, and Ashley Ruiz, Cameron County Public Health, San Benito, Texas; Charlene Offiong, Houston Department of Health, Houston, Texas; Ana Zangeneh, Harris County Public Health, Houston, Texas; Jessica Pearson, Missouri Department of Health and Senior Services, Raytown, Missouri; Karen Van Fleet, Jackson County Public Health, Lee’s Summit, Missouri.

References

1. CDC Health Alert Network. Outbreak of suspected fungal meningitis in U.S. patients who underwent surgical procedures under epidural anesthesia in Matamoros, Mexico. 17 May 2023. Available at: https://emergency.cdc.gov/han/2023/han00491.asp. Accessed 10 July 2023.
2. Mexico Ministry of Health. Comunicado técnico semanal. Meningitis, Durango. Available at: https://www.gob.mx/salud/documentos/comunicado-tecnico-semanal-meningitis. Accessed 10 July 2023.
3. Fungus Education Hub. Interim recommendations for diagnosis and management of cases of fungal meningitis associated with epidural anesthesia administered in Matamoros, Mexico. Available at: https://funguseducationhub.org/interim-guidance-matamoros-fm-outbreak-5_20_23/. Accessed 27 June 2023.
4. Chiller TM, Roy M, Nguyen D, et al. Clinical findings for fungal infections caused by methylprednisolone injections. N Engl J Med 2013; 369:1610–9. [PubMed: 24152260]
5. Al-Hatmi AMS, Meis JF, de Hoog GS. Fusarium: molecular diversity and intrinsic drug resistance. PLoS Pathog 2016; 12:e1005464. [PubMed: 27054821]
6. Perfect JR, Marr KA, Walsh TJ, et al. Voriconazole treatment for less-common, emerging, or refractory fungal infections. Clin Infect Dis 2003; 36:1122–31. [PubMed: 12715306]

7. Ashley ED. Antifungal drugs: special problems treating central nervous system infections. J Fungi (Basel) 2019; 5:97. [PubMed: 31614505]
8. Ho J, Fowler P, Heidari A, Johnson RH. Intrathecal amphotericin B: a 60-year experience in treating coccidioidal meningitis. Clin Infect Dis 2017; 64:519–24. [PubMed: 27927853]
9. Alkhazraji S, Gebremariam T, Alqarihi A, et al. Fosmanogepix (APX001) is effective in the treatment of immunocompromised mice infected with invasive pulmonary scedosporiosis or disseminated fusariosis. Antimicrob Agents Chemother 2020; 64:e01735–19. [PubMed: 31818813]
10. Gebremariam T, Gu Y, Alkhazraji S, Youssef E, Shaw KJ, Ibrahim AS. The combination treatment of fosmanogepix and liposomal amphotericin B is superior to monotherapy in treating experimental invasive mold infections. Antimicrob Agents Chemother 2022; 66:e00380–22. [PubMed: 35670592]
11. Badali H, Patterson HP, Sanders CJ, et al. Manogepix, the active moiety of the investigational agent fosmanogepix, demonstrates *in vitro* activity against members of the Fusarium oxysporum and Fusarium solani species complexes. Antimicrob Agents Chemother 2021; 65:e02343–20. [PubMed: 33722886]
12. Petraitiene R, Petraitis V, Maung BBW, et al. Efficacy and pharmacokinetics of fosmanogepix (APX001) in the treatment of *Candida* endophthalmitis and hematogenous meningoencephalitis in nonneutropenic rabbits. Antimicrob Agents Chemother 2021; 65:e01795–20. [PubMed: 33361304]

Table 1.

Case Definitions in Use for Outbreak of Fungal Meningitis Among US Residents Who Received Epidural Anesthesia at Two Clinics in Matamoros, Mexico[a]

Term	Criteria
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 (eg, 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 (ie, 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: CSF, cerebrospinal fluid; LP, lumbar puncture; mNGS, metagenomic next-generation sequencing; PCR, polymerase chain reaction; RBC, red blood cells; WBC, white blood cell.

[a]Cases definitions apply to persons who received procedures with epidural anesthesia in Matamoros, Mexico, at Clinica K-3 or River Side Surgical Center, since 1 January 2023.

Table 2.

Antifungal Susceptibility Testing Results of One *Fusarium solani* Isolate From the Outbreak of Fungal Meningitis Among U.S. Residents Who Received Epidural Anesthesia at Two Clinics in Matamoros, Mexico[a]

Antifungal	Results (mcg/mL)
Amphotericin B	2
Anidulafungin	>8
Caspofungin	>8
Micafungin	>8
Ibrexafungerp	>8
Rezafungin	8
Itraconazole	>16
Posaconazole	>16
Voriconazole	8
Isavuconazole	>16
Olorofim	>4
Manogepix	≤0.008
Terbinafine	>2

[a]Methodology used: Clinical and Laboratory Standards Institute's reference method for broth dilution antifungal susceptibility testing of filamentous fungi. Testing was performed at UT Health San Antonio's Fungus Testing Laboratory. Minimum inhibitory concentrations (MICs, amphotericin B, azoles, and olorofim) and minimum effective concentrations (MECs, echinocandins, ibrexafungerp, and manogepix) are reported.