



Rising meningitis in USA and Mexico: insights from the fatal outbreak

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Abstract

Meningitis, an inflammatory disease affecting the meningeal layers of the brain and the spinal cord, poses a significant public health concern globally. Most meningitis cases are caused by viral infections, bacterial infections being the second most common cause, while fungal or parasitic infections are deemed rare. Despite the decrease in bacterial meningitis because of vaccination and treatment, a recent meningitis outbreak in the United States and Mexico highlighted ongoing challenges. The current meningitis outbreak is caused by a pathogenic fungus and is associated with surgical procedures performed under spinal anaesthesia as reported by the Centers for Disease Control and Prevention (CDC) on the 11 May of 2023. Around 20 cases with clinical suspicion of meningitis, including two fatalities, have been attributed to this rampant outbreak. Timely diagnosis, utilising diagnostic modalities such as lumbar puncture and pathogen detection methods, is crucial for appropriate management. Iatrogenic meningitis must be avoided by enhancing surveillance, infection control procedures, and adherence to aseptic practices. To lessen the effects of meningitis and enhance patient outcomes, the WHO's roadmap and preventive interventions, such as targeted immunisations, are essential.

Keywords: fungal infections, lumbar puncture, meningitis outbreak, meningitis, spinal anaesthesia

Introduction

Meningitis is an inflammatory disorder affecting the meningeal layers enveloping the spinal cord and brain. It affects individuals of all age groups and is primarily attributed to bacterial infection, although viral, fungal, and parasitic agents can also incite this condition. Furthermore, non-infectious etiologies encompass factors such as specific medications, cranial trauma, iatrogenic occurrences after neurosurgical interventions, and underlying conditions including systemic lupus erythematosus and malignancies^[1,3]. Despite the availability of effective vaccination and treatment, meningitis specifically the bacterial type still poses a major public health concern and a threat to people's lives, with

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article

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Annals of Medicine & Surgery (2024) 86:279–283

Received 7 August 2023; Accepted 21 October 2023

Published online 7 November 2023

<https://dx.doi.org/10.1097/MS9.0000000000001463>

HIGHLIGHTS

- With a fatality rate of over 30%, meningitis continues to pose serious hazards to neurological health and life worldwide, including in Northern America.
- In the United States, there are ~75 000 instances of enteroviral meningitis annually, with viral meningitis accounting for over half of all meningitis cases. Approximately 4100 individuals are affected by bacterial meningitis each year in the United States, with an overall yearly occurrence of 1.33 cases per 100 000 individuals.
- The most recent documented outbreak of fungal meningitis occurred in May 2023. A total of five cases were found in the USA on 11 May 2023, by the CDC. This was also communicated via the International Health Regulations National Focal Point (IHR NFP) to Mexico. These five cases had previously undergone spinal anaesthesia-related surgical procedures at two private clinics in the Mexican state of Tamaulipas's capital city of Matamoros which borders the USA.
- To lessen the effects of meningitis and enhance patient outcomes, the WHO's roadmap and preventive interventions, such as targeted immunisations, are essential.

high mortality and morbidity rates. In 2019, the global incidence of meningitis was estimated to be 2.51 million new cases, with a 95% uncertainty interval ranging from 2.11 to 2.99 million. Among these cases, 1.28 million were reported in individuals under the age of five^[3]. Several epidemics and outbreaks still occur yearly, with the most recent outbreak happening now in the United States of America (USA) and in Mexico^[4]. On 11 May 2023, the Centers for Disease Control and Prevention (CDC)

informed Mexico's Directorate General of Epidemiology (DGE) through International Health Regulations National Focal Point (IHR NFP) about five female cases with central nervous system infections in the USA. These cases were associated with prior surgical procedures under spinal anaesthesia at clinics in a Mexican border city^[5]. This paper aims to address the current Fungal Meningitis Outbreak in the USA and Mexico, assess the current efforts to mitigate this meningitis outbreak, determine the challenges & obstacles in fighting meningitis in the American Continent, and provide evidence-based recommendations for public health interventions.

Epidemiology

Global meningitis epidemiology is highly dynamic, changes over the past 25 years among adults and children have been influenced by the widespread use of conjugate vaccines, the HIV-1 epidemic, the introduction of antiretroviral and antibacterial treatment, including prevention of mother-to-child transmission, and significant advancements in development and poverty reduction strategies, including improved maternal and neonatal care^[5]. Between 2006 and 2016, there was a significant increase in instances of bacterial meningitis reported to worldwide surveillance sites being associated with poverty^[5]. In the United States, there are ~75 000 instances of enteroviral meningitis annually, with viral meningitis accounting for over half of all meningitis cases^[6]. Approximately 4100 individuals are affected by bacterial meningitis each year in the United States, with an overall yearly occurrence of 1.33 cases per 100 000 people^[6]. In Mexico, meningitis continues to be a significant factor contributing to illness, neurological sequelae, and death^[7]. However, there is a lack of comprehensive information regarding the epidemiology and microbiology of this disease among both children and adults. The most recent documented outbreak of fungal meningitis occurred in May 2023. A total of five cases were found in the USA on 11 May 2023, by the CDC. This was also communicated via the International Health Regulations National Focal Point (IHR NFP) to Mexico. These five cases had previously undergone spinal anaesthesia-related surgical procedures at two private clinics in the Mexican state of Tamaulipas's capital city of Matamoros which borders the USA. Around 20 cases with clinical suspicion of meningitis, including two fatalities, have been attributed to this rampant outbreak. The Mexico Epidemiological Diagnosis and Reference Institute has played a paramount role in the diagnostic surveillance of the suspected cases^[4]. With a fatality rate of over 30%, meningitis continues to pose serious hazards to neurological health and life worldwide, including in Northern America and Mexico^[8].

Aetiology of meningitis and reasons for upsurge in cases

Most meningitis cases are caused by viral infections, bacterial infections being the second most common cause, while fungal or parasitic infections are deemed rare. Determining the origin of bacterial meningitis is essential since viral meningitis is sometimes mistaken for aseptic meningitis when testing for bacteria provides negative results. Aseptic meningitis now refers to a variety of symptoms brought on by different infectious agents, the majority of which are viral but also include mycoplasma, Q fever, and other rickettsia diseases^[6]. Targeting the most prevalent

microorganisms causing the disease, conjugate vaccines significantly reduce the prevalence of bacterial meningitis^[5]. Approximately 10% of individuals affected by bacterial meningitis succumb to the disease worldwide. Among the various pathogens, *Streptococcus pneumoniae* is responsible for the highest mortality rate, resulting in the death of 20–30% of adults and 10% of children^[6]. In the USA, an estimated 500 cases of bacterial meningitis prove fatal each year. Males make up ~60% of the cases, with adults aged 25–34 accounting for 20% of the total. The most current meningeal outbreaks in the USA and Mexico are outlined in the table below (Table 1)^[4–9].

Recent advances in diagnosis of meningeal infections

Several diagnostic modalities are available for the detection of meningitis. Lumbar puncture (LP) is the gold standard modality of investigation. LP is recommended within 1 hour of hospital admission, and before starting antibiotics. However, it is important to denote any contraindication to LP such as signs and symptoms of sepsis, skin infections over the site of injection, cardiac or respiratory compromise, patients on antiplatelet or anticoagulant therapy, or those with thrombocytopenia or other types of clotting diseases.^[10] Moreover, some patients may require brain imaging before an LP due to risk of herniation. Imaging is indicated if there are any signs of focal neurological deficits, papilledema, uncontrolled or ongoing seizures, and in patients with a Glasgow Coma Scale (GCS) of 12 or less. The cerebrospinal spinal fluid (CSF) analysis from an LP in patients with meningitis may show leukocytosis and increased neutrophil counts (mainly in cases of bacterial meningitis), lymphocytosis (in viral meningitis)^[11].

The overall sensitivities and specificities of latex agglutination and enzyme immunoassay conducted on blood and CSF samples were 93% to 100% and 93% to 98%, respectively. More recently, a lateral flow test with sensitivity and specificity of more than 98% for both specimen types (including whole blood from finger stick samples) and 85% for urine was authorised for use in serum and CSF. In some circumstances (such as those involving bone or soft tissue involvement) or when a preliminary diagnosis cannot be made due to a low suspicion score, histology may be useful. Ultimately, molecular approaches are mostly employed for research and have not yet been implemented in clinical practice around the world^[12]. Moreover, CSF Biochemistry helps in differentiating meningitis etiologies as shown in the Figure below (Fig. 1)^[11,12].

Table 1

Aetiological causes of meningitis in USA and Mexico 2013–2023

Region/country	Area	Year of outbreak	Aetiology
USA	New York	2018	<i>Neisseria meningitidis</i>
USA	California	2020	<i>Streptococcus pneumoniae</i>
USA	Texas	2013	<i>Listeria monocytogenes</i>
USA	Massachusetts	2014	<i>Neisseria meningitidis</i>
Mexico	Tamaulipas	2023	<i>Fusarium solani</i>
Mexico	Veracruz	2019	<i>Neisseria meningitidis</i>
Mexico	Jalisco	2022	<i>Haemophilus influenzae</i>
Mexico	Baja California	2015	<i>Streptococcus pneumoniae</i>
Mexico	Chiapas	2017	<i>Neisseria meningitidis</i>

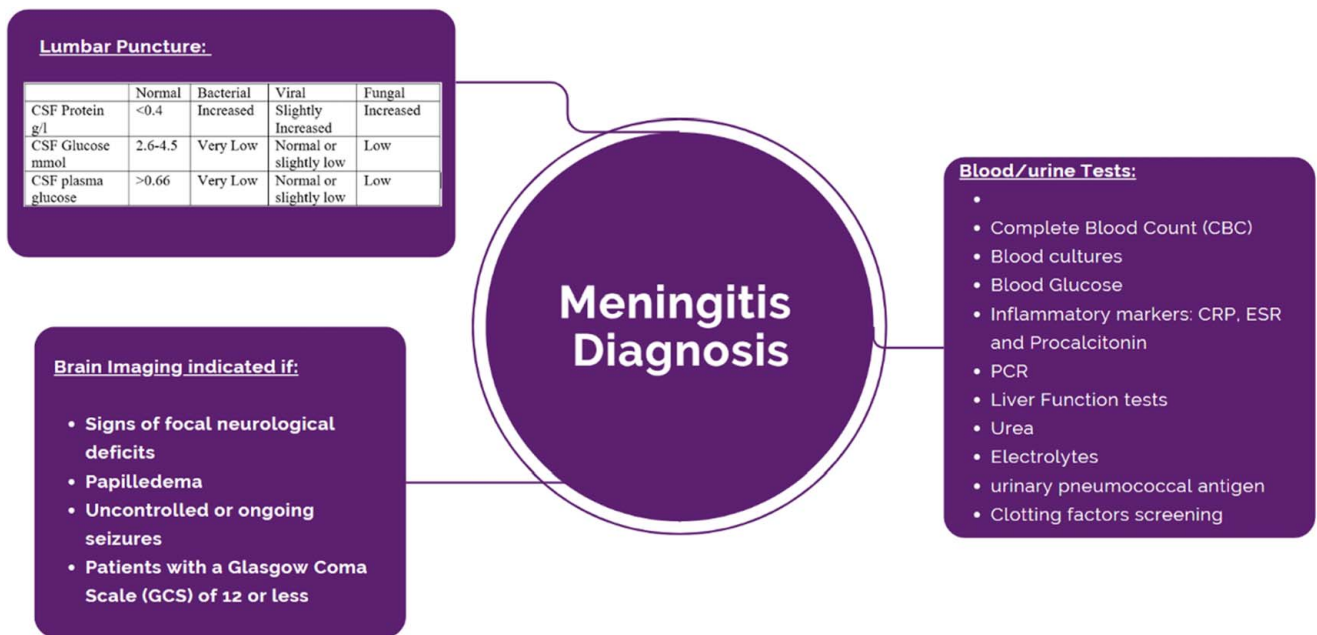


Figure 1. The meningitis diagnostic algorithm. CRP indicates C-reactive protein; ESR erythrocyte sedimentation rate; PCR, polymerase chain reaction.

Current challenges and efforts to mitigate meningitis

Significant strides have been made in diminishing the impact of infectious meningitis since 1990. Nevertheless, this progress has been unevenly distributed, with countries in the African meningitis belt and South Asia still grappling with a substantial disease burden^[13].

In the United States, the CDC reported unusual meningitis cases in Mexico. State and local health departments are contacting and following up on affected patients, advising MRI and lumbar puncture. In the current context, the source, transmission route, and vehicle for the current outbreak of fungal meningitis following medical/surgical procedures are still unknown, and investigations are ongoing^[5,14]. In Mexico, ongoing epidemiological investigations are strengthening surveillance for meningitis. Two healthcare facilities where the procedures took place have been closed. WHO recommends continued laboratory analysis, case identification and outbreak investigation to identify the cause, source, and transmission route. Infection prevention and control measures, including safe injection practices, should be reinforced. No travel restrictions are advised, but symptomatic travellers should seek medical attention and disclose their travel history^[5].

Immediate evaluation, even without symptoms, is urged, with suspected cases reported to local health departments. Clinicians caring for patients in Matamoros, Mexico, should refer to detailed CDC recommendations^[2].

Individuals are advised to consider postponing elective procedures involving epidurals until the risk of infection is better understood. Due to the significant morbidity and mortality associated with meningitis despite the availability of medical care, the majority of efforts should be focused on preventing occurrences through regular immunisation regimens. In addition, monitoring patients, carrying out epidemiological research, and

controlling infections are essential measures in reducing the spread of meningitis in the currently affected regions^[14].

Iatrogenic meningitis can arise as a result of a breach in sterility or aseptic approaches when an offending agent is introduced into the subarachnoid space during spinal anaesthesia. Contamination can originate from diverse origins, encompassing surgical instrumentation, pharmaceuticals, and potential droplet transmission facilitated by healthcare personnel. The assurance of procedural sterility, along with meticulous adherence to personal protective measures and aseptic protocols, assumes paramount importance. This is underscored by assertions challenging the adequacy of sterility protocols^[15]. Medical tourism draws participation from over one million individuals annually originating from the United States, thus emphasising the relevance of these concerns within a substantial population^[5,14]. Although invasive fungal infections causing meningitis, such as *Candida* and *Cryptococcus*, are relatively uncommon, *Histoplasma capsulatum* poses a higher risk to immunocompromised individuals. Diagnosis of these infections can be challenging and requires careful evaluation along with supportive serological testing^[16].

Recommendations

Fungal meningitis represents a relatively rare yet serious medical condition. Several predisposing factors, encompassing specific health conditions and medication regimens, heighten the susceptibility to developing meningitis^[17]. Notably, the Southern United States exhibits a particular vulnerability to fungal lung infections that can ultimately culminate in meningitis^[9,17].

In the ongoing fight against meningitis, a multifaceted approach is imperative. Prevention is of paramount importance, to combat the spread of this disease it is necessary to introduce preventive measures such as antifungal prophylaxis, immunisations, particularly for high-risk groups, including asymptomatic

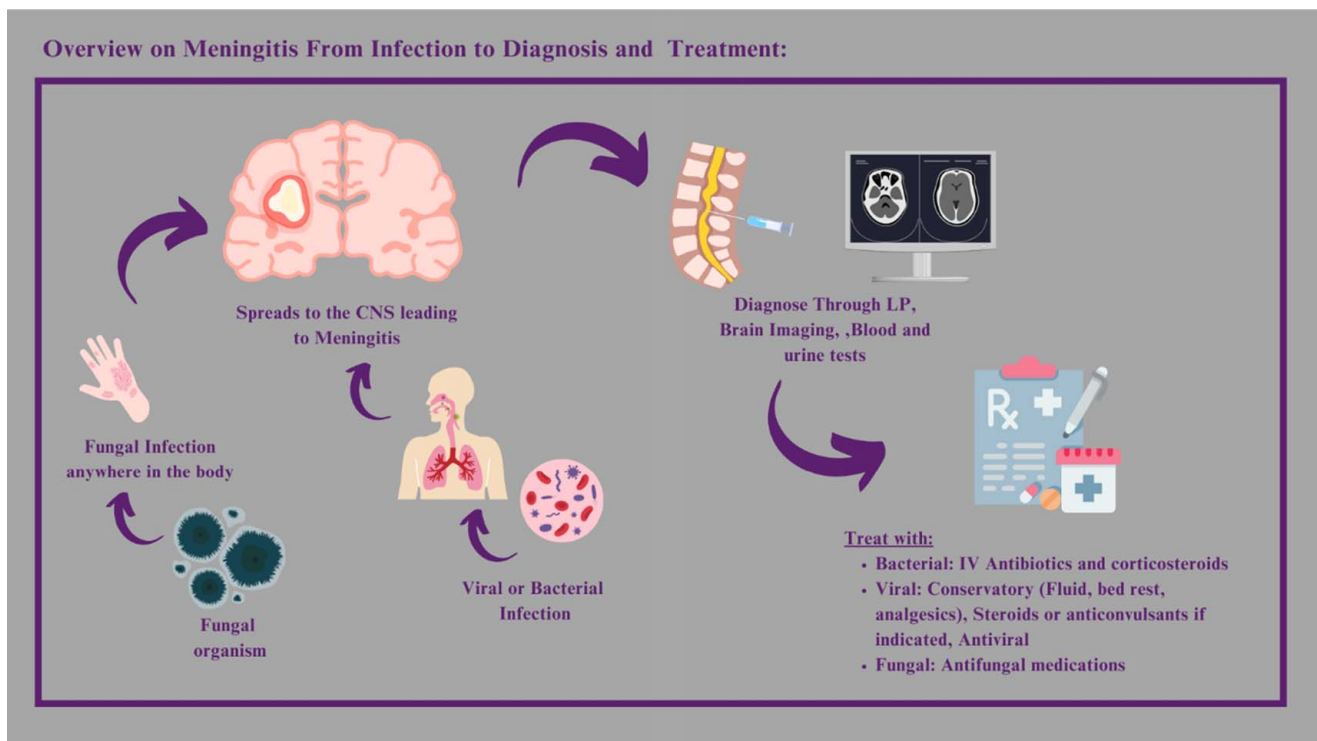


Figure 2. Overview of meningitis infection. CNS, central nervous system. LP, Lumbar puncture.

carriers such as babies, young children, and teenagers. In addition, close contacts of meningococcal disease patients may receive antibiotics, and children with fungal meningitis should stay home from school until fever-free. Moreover, early diagnosis is the key to initiating early treatment and containing the spread of the disease^[3–6,18].

On a global scale, initiatives like the World Health Organization's (WHO) "Defeating Meningitis by 2030" roadmap offer hope for a future free from the scourge of meningitis. This ambitious initiative aims to not only eliminate epidemics of bacterial meningitis but also reduce the overall number of cases and associated fatalities. Furthermore, it strives to enhance the quality of life for individuals affected by this ailment, promising a brighter tomorrow^[18].

In the clinical context, it is crucial for healthcare providers to exercise vigilance when administering certain medications, such as epidural steroid injections, as these can potentially lead to infections that may, in turn, trigger meningitis^[19].

Proactive measures, targeted vaccinations, and prompt diagnosis and treatment play a crucial role in preventing meningitis^[19] (See Fig. 2).

Conclusion

With several infectious agents creating outbreaks and epidemics, meningitis continues to be a serious public health issue worldwide. A fungal meningitis outbreak tied to epidural anaesthesia in Tamaulipas, Mexico, from 1 January to 13 May 2023, has prompted a coordinated response from the CDC, Mexican Ministry of Health, and U.S. health departments. This study

centres on Mexico and the USA due to recent outbreaks, offering insights into diverse demographics and international implications, underscoring ongoing impact on the American continent. Various diagnostic techniques, including lumbar puncture, are essential for early and accurate diagnosis. Current efforts in the USA and Mexico include patient follow-up, epidemiological investigations, and infection control, stressing the need for close collaboration and information sharing. The source of the fungal meningitis outbreak remains unknown, highlighting the need for strict aseptic practices during medical procedures. Challenges also arise from medical tourism and regional risk factors. Preventive measures like antifungal prophylaxis, vaccinations, and early diagnosis are vital in combating meningitis. Global initiatives like the WHO's "Defeating Meningitis by 2030" roadmap offer hope for a meningitis-free future.

Ethics approval

Not applicable.

Consent

Informed consent was not required for this article.

Source of funding

We have not received any financial support for this manuscript.

Author contribution

O.U.: conceptualization, project administration, writing—review and designing. H.A.: conceptualization, writing the first draft and revising, reviewing and editing. All authors approved the final manuscript and submission.

Conflicts of interest disclosure

The author declared no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Abubakar Nazir.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Data availability statement

Not applicable.

Acknowledgement

The authors appreciate the Journal Editors's valuable feedback.

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