Multidisciplinar (Montevideo). 2025; 3:191
doi: 10.62486/agmu2025191
ISSN: 3046-4064

REVIEW

Current perspectives in the diagnosis and management of bacterial meningitis. Literature review and update

Perspectivas actuales en el diagnóstico y tratamiento de la meningitis bacteriana. Revisión y actualización de la literatura

Jhossmar Cristians Auza-Santivañez[1], Blas Apaza Huanca[1], Carlos Alberto Paz Roman[2], Paul Cardozo Gil[3], Jose Bernardo Antezana-Muñoz[4], Freddy Ednildon Bautista-Vanegas[5], Jorge Márquez-Molina[6], Mildred Ericka Kubatz La Madrid[7], Eloy Paycho Anagua[7]

[1]Ministerio de Salud y Deportes. Instituto Académico Científico Quispe-Cornejo. La Paz, Bolivia.
[2]Hospital de Niños Dr. Mario Ortíz Suárez.
[3]Hospital Obrero Nro 3. Caja Nacional de Salud. Santa Cruz. Bolivia.
[4]Hospital Elizabeth Seton. Caja Petrolera de Salud. Cochabamba.
[5]Kliniken Beelitz GmbH - Brandenburg Deutschland. Germany.
[6]Hospital Seguro Social Universitario. Departamento de emergencias. Cochabamba, Bolivia.
[7]Hospital de Tercer Nivel Dr. Hernán Messuti Ribera. Pando, Bolivia.

Cite as: Auza-Santivañez JC, Apaza Huanca B, Paz Roman CA, Cardozo Gil P, Antezana-Muñoz JB, Bautista-Vanegas FE, et al. Current perspectives in the diagnosis and management of bacterial meningitis. Literature review and update. Multidisciplinar (Montevideo).2025; 3:191. https://doi.org/10.62486/agmu2025191

Submitted: 07-05-2024 **Revised:** 20-08-2024 **Accepted:** 16-02-2025 **Published:** 17-02-2025

Editor: Prof. Dr. Javier Gonzalez-Argote

Corresponding author: Jhossmar Cristians Auza-Santivañez

ABSTRACT

Introduction: bacterial meningitis is a serious and potentially fatal disease that has represented a significant challenge to medicine since its identification in the 19th century. Despite advances in antimicrobial treatment, it remains a major cause of morbidity and mortality worldwide. This review aims to update current perspectives on the diagnosis and management of bacterial meningitis, focusing on its pathogenesis, clinical manifestations, diagnostic methods, and therapeutic strategies.
Method: a search for information was carried out in the period August-December 2024 in the SciELO, LILACS, Scopus, PubMed-MedLine databases, the Google Scholar search engine, as well as in the ClinicalKeys services. For the recovery of information, an advanced search strategy was used and the terms "meningitis or bacterial meningitis" were used, as well as their translations into the English language. To combine the terms, Boolean operators were used, with search formulas according to the syntax requested by each database. Furthermore, in order to achieve a review based on the best possible evidence, only studies of the type case series, original articles or systematic reviews were selected.
Results and discussion: bacterial meningitis develops when pathogens overcome the host's defense mechanisms, colonizing mucous membranes, invading the bloodstream and penetrating the subarachnoid space. The main pathogens include Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae. The most common clinical manifestations are fever, headache, stiff neck and altered mental status. Diagnosis is based on analysis of cerebrospinal fluid (CSF), which shows pleocytosis, increased protein and decreased glucose. Empirical treatment includes antibiotics such as cefotaxime, ceftriaxone and vancomycin, together with dexamethasone as adjuvant therapy to reduce inflammation.
Conclusions: bacterial meningitis is a serious infection of the central nervous system, a medical emergency whose mortality and sequelae can be reduced with timely diagnosis and treatment. The key is to start treatment immediately and without delay. Prevention is the cornerstone of its control. Only through multidisciplinary management, which could include an expert infectious disease specialist, an intensive

care physician, a specialized nurse and adequate laboratory equipment, can the impact of this devastating disease be mitigated.

Keywords: Bacterial Meningitis; Diagnosis; Treatment; Epidemiology; Prevention; Cerebrospinal Fluid; Antibiotics; Dexamethasone.

RESUMEN

Introducción: la meningitis bacteriana es una enfermedad grave y potencialmente mortal que ha representado un desafío significativo para la medicina desde su identificación en el siglo XIX. A pesar de los avances en el tratamiento antimicrobiano, sigue siendo una causa importante de morbilidad y mortalidad en todo el mundo. Esta revisión tiene como objetivo actualizar las perspectivas actuales en el diagnóstico y manejo de la meningitis bacteriana, enfocándose en su patogenia, manifestaciones clínicas, métodos diagnósticos y estrategias terapéuticas.
Método: se realizó una búsqueda de información en el periodo agosto-diciembre de 2024 en las bases de datos SciELO, LILACS, Scopus, PubMed-MedLine, el buscador Google Académico, así como en los servicios ClinicalKeys. Para la recuperación de la información se utilizó una estrategia de búsqueda avanzada y se empleó los términos "meningitis o meningitis bacteriana", así como sus traducciones al idioma inglés. Para combinar los términos se emplearon operadores booleanos, con fórmulas de búsqueda según la sintaxis solicitada por cada base de datos. Además, con el objetivo de lograr una revisión basada en la mejor evidencia posible, solo se seleccionaron aquellos estudios de tipo serie de casos, artículos originales o revisiones sistemáticas.
Resultados y discusión: la meningitis bacteriana se desarrolla cuando los patógenos superan los mecanismos de defensa del huésped, colonizando las membranas mucosas, invadiendo el torrente sanguíneo y penetrando en el espacio subaracnoideo. Los principales patógenos incluyen *Streptococcus pneumoniae*, *Neisseria meningitidis* y *Haemophilus influenzae*. Las manifestaciones clínicas más comunes son fiebre, cefalea, rigidez de nuca y alteración del estado mental. El diagnóstico se basa en el análisis del líquido cefalorraquídeo (LCR), que muestra pleocitosis, aumento de proteínas y disminución de glucosa. El tratamiento empírico incluye antibióticos como cefotaxima, ceftriaxona y vancomicina, junto con dexametasona como terapia adyuvante para reducir la inflamación.
Conclusiones: la meningitis bacteriana es una infección grave del sistema nervioso central, es una emergencia médica cuya mortalidad y secuelas pueden reducirse con un diagnóstico y tratamiento oportunos. La clave es iniciar el tratamiento de inmediato y sin demora. La prevención es la piedra angular en su control. Solo mediante un manejo multidisciplinario lo cual pudiera incluir un experto infectólogo, un médico en cuidados intensivos, un enfermero especializado y un equipo de laboratorio adecuado podrán mitigar el impacto de esta enfermedad devastadora.

Palabras clave: Meningitis Bacteriana; Diagnóstico; Tratamiento; Epidemiología; Prevención; Líquido Cefalorraquídeo; Antibióticos, Dexametasona.

INTRODUCTION

From its original recognition in 1805 until the beginning of the 20th century, bacterial meningitis caused by Haemophilus influenzae and Streptococcus pneumoniae was practically 100 % fatal. In 1913, the introduction of intrathecal meningococcal antiserum by Simon Flexner reduced the mortality rate of meningococcal meningitis from 75 % to 31 %. Still, the clinical outcome did not drastically improve for the three meningeal pathogens until the arrival of systemic antimicrobial therapy in the 1930s.[1] Despite the efficacy of antibiotics in eliminating bacteria from cerebrospinal fluid (CSF), bacterial meningitis in adults continues to cause significant morbidity and mortality worldwide.[2] The pathogenesis and pathophysiology of bacterial meningitis involve a complex interaction between the virulence factors of the pathogens and the host immune response.[3,4] It is believed that much of the damage caused by this infection results from toxins released into the cerebrospinal fluid when the host develops an inflammatory response. Meningitis is an inflammatory disease of the leptomeninges and the tissues surrounding the brain and spinal cord. It is characterized by an abnormal number of white blood cells (WBCs) in most patients' cerebrospinal fluid (CSF).[1] The meninges consist of three parts: the pia mater, the arachnoid mater, and the dura mater. Bacterial meningitis reflects an infection of the arachnoid and the CSF in both the subarachnoid space and the cerebral ventricles. This review analyzes the clinical and laboratory manifestations, as well as an update on the management of acute bacterial meningitis in adults.

METHOD

A search for information was carried out in August-December 2024 in the databases SciELO, LILACS, Scopus,

PubMed-MedLine, the search engine Google Scholar, and ClinicalKeys services. To retrieve the information, an advanced search strategy was used, employing the terms "meningitis," "bacterial meningitis," and "acute bacterial meningitis," as well as their translations into English. Boolean operators combined the terms with search formulas according to the syntax requested by each database. Letters to the editor and conference proceedings were excluded to ensure the quality and relevance of the selected information. In addition, only case series studies, original articles, or systematic reviews were selected to achieve a review based on the best possible evidence.

RESULTS AND DISCUSSION

Pathogenesis and Pathophysiology

Bacterial meningitis develops when the pathogen's virulence factors overcome the host's defense mechanisms.[3,5] The pathogenesis of this disease for the most common meningeal pathogens (Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, Streptococcus group B [GBS], and Escherichia coli) involves four main processes: colonization of the respiratory, gastrointestinal or lower genital tract; invasion of the bloodstream; survival in the bloodstream and entry into the subarachnoid space.[3,4]

Colonization of mucous membranes

Many meningeal pathogens possess surface components such as fimbriae that facilitate mucosal colonization. Invasion of the bloodstream. This process depends on environmental factors (for example, previous viral infections such as influenza, smoking, and alcohol abuse) and host factors (such as asplenia, complement deficiency, antibody deficiency, and immunosuppression).the duration and intensity of bacteremia influence.[4,6] Bacterial penetration into the subarachnoid space. This process involves interactions between the bacteria and the endothelial cells of the blood-brain barrier in the post-capillary veins.[6]

In Haemophilus influenzae and Streptococcus pneumoniae, the choroid plexus may be the initial site of entry of bacteria into the ventricle, allowing their subsequent spread through the cerebrospinal fluid (CSF).[7,8] Adhesion to laminin receptors on brain endothelial cells is mediated by specific bacterial adhesins, such as the pneumococcal surface protein for S. pneumoniae and the outer membrane protein porin A for N. meningitidis.[9] This process also involves the platelet-activating factor receptor (PAFR) on the surfaces of endothelial cells, facilitating invasion by S. pneumoniae through the transcellular mechanism and by N. meningitidis through the paracellular pathway.[10]

Once adhered, N. meningitidis uses its type IV pili to activate beta-2 adrenergic receptors, organizing cortical plaques that prevent complement-mediated lysis and facilitate the opening of the interendothelial junctions, allowing the paracellular migration of the bacteria towards the CSF.[11] After successfully invading the CSF, the bacteria can multiply rapidly, reaching concentrations of up to 10^7 organisms per milliliter in hours due to inadequate humoral immunity in the CSF.[3] The low concentrations of immunoglobulins and complement in human CSF (generally 1000 times lower than in serum) result in deficient opsonic activity, favoring bacterial replication and the subsequent development of inflammation.[12] Despite an early influx of leukocytes during bacterial meningitis, the host defenses in the CSF remain suboptimal due to the lack of functional opsonic and bactericidal activity. The clinical disease observed after the entry of bacteria into the CSF results from a complex interaction between the bacterial components and the host's inflammatory response, which affects both the integrity of the blood-brain barrier and neuronal health.

Contribution of cell wall components

As the bacteria begin to die, especially after antibiotic exposure, bacterial fragments interact with pattern recognition receptors in the host, triggering an immune response.[13] Generation of inflammatory cytokines: Inhibiting several steps in the inflammatory cascade, such as neutrophil recruitment, can improve clinical outcomes in cases of meningitis by reducing neuronal loss.[5] Dexamethasone is The only clinically proven adjunctive therapy that improves this inflammatory response and reduces mortality in high-income countries with pneumococcal meningitis.[14,15]

Epidemiology

Bacterial meningitis can be community-acquired or healthcare-associated. The leading causes of community-acquired bacterial meningitis in adults in developed countries are Streptococcus pneumoniae, Neisseria meningitidis, and, especially in patients over 50 years of age or those with deficiencies in cell-mediated immunity, Listeria monocytogenes. On the other hand, the most common causes of healthcare-associated ventriculitis and meningitis tend to be different, generally involving staphylococci and aerobic gram-negative bacilli. These infections most commonly occur following neurosurgical procedures, such as craniotomies, ventriculoperitoneal shunts, external ventricular drains, or head injuries, such as skull base fractures with or without clinical evidence of cerebrospinal fluid leakage.[2]

Risk factors

In community-acquired meningitis, the organism responsible for acute bacterial meningitis depends partly on the acquisition route and the host's underlying factors. There are three main mechanisms for the development of meningitis: Colonization of the nasopharynx. This colonization can lead to an invasion of the bloodstream, followed by an invasion of the central nervous system (CNS). Invasion of the Central Nervous System (CNS). This can occur following bacteremia of localized origin, as in the case of infective endocarditis. Direct entry into the CNS: This can happen from contiguous infections (for example, sinuses or mastoids), trauma, or cerebrospinal fluid leakage.[17] Host factors that may predispose to meningitis include asplenia, complement deficiency, excessive use of glucocorticoids, diabetes mellitus, alcoholism, hypogammaglobulinemia, and human immunodeficiency virus (HIV) infection. Furthermore, it is essential to question patients with suspected meningitis about other predisposing factors, such as recent infection (especially respiratory or ear infection), recent exposure to someone with meningitis, injection drug use, recent head trauma, otorrhoea or rhinorrhoea and recent travel.[18]

Clinical manifestations

The classic triad of acute bacterial meningitis, which occurs in approximately 41 % of patients, consists of fever, neck stiffness, and altered mental state, usually with a sudden onset.[3,4] Patients over 60 present this triad more frequently than younger patients (58 % versus 36 %).[5] The most common clinical characteristics include severe headache (84 %), fever above 38°C (74 %), neck stiffness (74 %), Glasgow Coma Scale score below 14 (71 %), and nausea (62 %).[3,4,6] In a prospective study carried out in 2004 with 696 cases of bacterial meningitis acquired in the community, almost all the patients (95 %) presented at least two of the four classic symptoms: headache, fever, neck stiffness, and altered mental state.[4] The absence of these findings practically excludes the presence of bacterial meningitis.[7] In addition to the classic symptoms, less common manifestations are observed, such as convulsions (23 %), aphasia or hemiparesis (22 %), coma (13 %), cranial nerve palsies (9 %), skin rash (8 %) and paralysis (4 %). [3,4,8,9] Concomitant infections may include sinusitis or otitis (34 %), pneumonia (9 %), and endocarditis (1 %).[3]

Physical examination

Although patients may not specifically complain of neck stiffness, it is essential to assess for meningeal irritation. Passive or active neck flexion generally results in the inability to touch the chin to the chest. Difficulty in lateral neck movement is a less reliable finding.[18] Tests to evaluate meningitis, such as the Kernig and Brudzinski signs, were initially developed for patients with advanced stages of untreated bacterial and tuberculous meningitis. The Brudzinski sign refers to spontaneous flexion of the hips during an attempt at passive neck flexion. In contrast, the Kernig sign refers to the inability or reluctance to allow full knee extension when the hip is flexed at 90 degrees. This test is generally carried out in the supine position, although it can also be done with the patient seated.[18] Stiff Neck and the Kernig and Brudzinski signs were described over a century ago. However, their sensitivity may be lower in current cases of bacterial meningitis acquired in the community. For example, in a well-designed prospective study involving 297 patients with suspected meningitis, the sensitivity was extremely low: 5 % for each sign and 30 % for neck stiffness, while the specificity was 95 % for each sign and 68 % for neck stiffness.[18] Accentuating the headache with jolts can be a more sensitive diagnostic maneuver. A positive test consists of intensifying the pain by making rapid horizontal rotations of the head at a frequency of two to three times per second. The diagnostic value of this maneuver has been evaluated in several studies with mixed results.[19,20] Although one study showed a sensitivity of 97 % for this test in the diagnosis of meningitis, other studies have revealed lower sensitivities and specificities, highlighting the limited predictive value of this maneuver.[19,20]

Laboratory studies

Initial analyses should include a complete blood count with differential and platelet count and two aerobic blood cultures in adequate volume, preferably before the start of antimicrobial therapy. Serum electrolytes and glucose, blood urea nitrogen, and creatinine concentrations should also be evaluated to determine the relationship between glucose in the cerebrospinal fluid (CSF) and serum glucose. To obtain a reliable ratio, it is crucial to extract the serum glucose sample within an hour of the lumbar puncture.[12] However, this is only achieved in 13 % of patients with meningitis. In addition, coagulation studies may be necessary, mainly if petechiae or purpuric lesions are observed.[21] The white blood cell count is usually elevated, with a tendency towards immature forms; however, leukopenia may be present in severe infections. The platelet count may also be reduced. Both leukopenia and thrombocytopenia have been associated with an unfavorable prognosis in patients with bacterial meningitis.[22,23] Coagulation studies may indicate disseminated intravascular coagulation. Serum chemistry results often reflect the severity of the pathological process and may show metabolic acidosis with anion gap or hyponatremia. In one case series, hyponatremia was observed in 30 % of patients, although

it was generally mild and did not require specific treatment.[24]

Blood cultures

These are usually positive and are useful when CSF cannot be obtained before starting antimicrobial treatment. Approximately 50 % to 90 % of patients with bacterial meningitis have positive blood cultures.[3,4,6] However, some studies have reported lower yields in patients with meningococcal infection.[25] Cultures obtained after antimicrobial therapy are much less likely to be positive, particularly for meningococcus.[25,26] In healthcare-associated ventriculitis and meningitis, prior antibiotic therapy may significantly reduce the sensitivity of gram stain and CSF culture.[26] Serum and urine tests for bacterial antigens and cultures of mucosal surfaces for the causative pathogen are generally not useful.

Examination of cerebrospinal fluid

It is recommended that cerebrospinal fluid (CSF) be extracted from all patients with suspected meningitis unless there are contraindications for lumbar puncture. CSF examination is essential to establish the diagnosis of bacterial meningitis, identify the causative organism, and perform in vitro susceptibility tests.[27]

Precautions

Although there are no absolute contraindications for lumbar puncture, certain precautions should be considered: Possible increase in intracranial pressure with risk of cerebral herniation due to obstructive hydrocephalus, cerebral edema, or space-occupying lesions—Thrombocytopenia or other hemorrhagic diathesis, including ongoing anticoagulant treatment and suspected spinal epidural abscess.

Indications for computed axial tomography (CAT) before lumbar puncture

A crucial decision is determining whether a CAT scan of the head should be performed before lumbar puncture to rule out massive lesions or increased intracranial pressure. These conditions can cause cerebral hernias during the extraction of the CSF and have devastating consequences.[28,29] A CT scan should be performed on adults with suspected bacterial meningitis who present one or more risk factors: immunocompromised state (for example, HIV infection, immunosuppressive therapy, transplantation), history of central nervous system disease (massive lesions, cerebrovascular accidents), recent convulsions (within a week), capillary edema, abnormal level of consciousness and focal neurological deficit.

Analysis of cerebrospinal fluid

This is an essential component for the diagnosis of bacterial meningitis, and the CSF should be sent for cell count and differential, glucose concentration, protein concentration, Gram staining and bacterial culture, and other appropriate tests (e.g., rapid tests or polymerase chain reaction (PCR)), according to clinical suspicion. The characteristic findings in bacterial meningitis include a CSF glucose concentration <40 mg/dL, a CSF/serum glucose ratio ≤0,4, a protein concentration >200 mg/dL, and a cell count greater than 1000 cells/µL, predominantly neutrophils.[3,30,31] However, doctors need to recognize that there are exceptions and that empirical antimicrobial therapy is justified in the face of clinical suspicion, even if the CSF abnormalities are not diagnostic. It is possible to observe a false increase in the leukocyte count in the CSF after a traumatic lumbar puncture or in cases of intracerebral or subarachnoid hemorrhage where red blood cells and leukocytes are introduced into the subarachnoid space.[32]

Gram stain

Whenever bacterial meningitis is suspected, a Gram stain should be performed. This test can suggest bacterial etiology a day or more before the culture results.[25] Typical findings include gram-positive diplococci suggesting pneumococcal infection, gram-negative diplococci suggesting meningococcal infection, pleomorphic gram-negative coccobacilli suggesting H. influenzae infection, and gram-positive bacilli and coccobacilli suggesting Listeria infection. The reported sensitivity for Gram staining in bacterial meningitis varies between 50 % and 90 %, while its specificity is close to 100 %.[4,11,32]

Diagnosis

Acute bacterial meningitis should be suspected immediately in adults presenting with fever, headache, neck stiffness, and/or altered mental status. A delayed diagnosis is associated with a delay in antimicrobial therapy, less use of adjuvant steroids, and an increase in mortality.[33] The isolation of a bacterial pathogen in the cerebrospinal fluid (CSF) by culture or other diagnostic techniques confirms the diagnosis of bacterial meningitis. Likewise, isolating bacteria in blood cultures in a patient with CSF pleocytosis also validates the diagnosis, even if the CSF culture is negative. Establishing a definitive diagnosis can be complicated in patients who have received antibiotics before lumbar puncture, as this decreases the sensitivity of the culture and Gram stain. This is especially problematic in healthcare-associated meningitis, where concomitant antibiotics

are frequently administered. The management of patients with negative cultures but with suspected bacterial meningitis is detailed in other studies.

Treatment

Personal and family history information should be collected before starting antimicrobial therapy in cases of bacterial meningitis. Some relevant aspects may suggest the causative organism: Severe drug allergies and recent exposure to people with meningitis (e.g., Neisseria meningitidis). Recent sinusitis or otitis media (e.g., Streptococcus pneumoniae). Recent use of antibiotics (e.g., resistance to S. pneumoniae). Recent travel, such as Hajj or Umrah pilgrimages (e.g., N. meningitidis). recent injection drug use (e.g., Staphylococcus aureus). progressive petechial or ecchymotic rash (e.g., N. meningitidis). History of recent or remote head injury (e.g., S. pneumoniae). HIV infection or associated risk factors (e.g., S. pneumoniae, Listeria monocytogenes, Cryptococcus neoformans). Any other condition that compromises the immune system.

Avoid delays

Antimicrobial therapy should be started immediately after the lumbar puncture (LP) or, if a CAT scan is required before the LP, immediately after obtaining the blood cultures.[2,8]

General Measures

Maintaining an adequate fluid and electrolyte balance is essential, as both overhydration and dehydration can be associated with adverse outcomes. Evidence suggests that intravenous maintenance fluids are preferable to fluid restriction during the first 48 hours, especially in settings with high mortality rates and when patients present in an advanced state. However, there is insufficient evidence to guide practice in other contexts.

Antimicrobial therapy

The selection of antimicrobials should be empirical and performed immediately after obtaining cerebrospinal fluid (CSF) or when lumbar puncture is delayed. In these cases, therapy should be directed at the most likely pathogens based on the patient's age and any underlying disease or comorbidity.[2,8] It is also essential to know local susceptibility patterns. The empirical regimens are described in detail below. Once the CSF Gram stain results are available, the antimicrobial regimen should be adjusted to cover the most likely pathogen.

Route of administration and duration

Due to the generally limited penetration of antimicrobials into the CSF, all patients should be treated with intravenous antimicrobial agents. Oral antimicrobials should be avoided, as the doses and tissue concentrations are usually considerably lower than those obtained with parenteral agents. The duration of antimicrobial treatment for bacterial meningitis will depend on the causative pathogen.

Requirements in the choice of antimicrobial

There are three general requirements for antimicrobial therapy in bacterial meningitis[2,19]: the use of bactericidal drugs effective against the infecting organism, the use of drugs that can penetrate the CSF, given that the blood-brain barrier prevents the entry of macromolecules, and the structuring of the regimen to optimize bactericidal efficacy according to the pharmacodynamic characteristics of the agent or agents used.

Causal organisms

Streptococcus pneumoniae and Neisseria meningitidis are the two most commonly isolated pathogens in community-acquired bacterial meningitis, accounting for 0,306 and 0,123 cases per 100 000 people, respectively, in the United States.[22] In a prospective study of 1412 episodes of community-acquired bacterial meningitis in the Netherlands, S. pneumoniae was responsible for 51 % of cases, N. meningitidis for 37 %, and Listeria monocytogenes for 4 %.[12] It is important to note that, in adults, the incidence of bacterial meningitis caused by L. monocytogenes increases with age.[23] Therefore, it is recommended that adults over 50 years of age receive an antimicrobial agent active against L. monocytogenes (e.g., ampicillin) as part of the empirical regimen.[23]

Empirical treatment with beta-lactams

The beta-lactams selected include cefotaxime and ceftriaxone. These drugs have adequate penetration into the cerebrospinal fluid (CSF) and potent activity against the primary pathogens that cause bacterial meningitis, although there are notable exceptions such as L. monocytogenes and some penicillin-resistant strains of S. pneumoniae.[20]

With the global increase in penicillin-resistant pneumococci, adding vancomycin to the empirical regimen should be considered in countries where the prevalence of resistance is greater than 1 % (for example, the United States) until culture and susceptibility results are obtained.[2,24,25]

Therapeutic alternatives

Ceftazidime is a third-generation cephalosporin with broad in vitro activity against gram-negative bacteria, including Pseudomonas aeruginosa. Still, it is less effective against penicillin-resistant pneumococci than cefotaxime or ceftriaxone.[20] However, cefepime, a fourth-generation cephalosporin, is safe and therapeutically equivalent to cefotaxime for the treatment of bacterial meningitis in infants and children; it is also a suitable alternative when broad activity against Pseudomonas and other gram-negative bacteria is required.[35]

Table 1. Recommended doses of antimicrobial therapy for adults with bacterial meningitis

Antimicrobial agent	Dose (adult)
Amikacin	5 mg/kg every 8 hours *
Ampicillin	2 g every 4 hours
Aztreonam	2 g every 6 to 8 hours
Cefepime	2 g every 8 hours
Cefotaxime	2 g every 4 to 6 hours
Ceftazidime	2 g every 8 hours
Ceftriaxone	2 g every 12 hours
Chloramphenicol	1 to 1,5 g every 6 hours
Ciprofloxacin	400 mg every 8 to 12 hours
Gentamicin	1,7 mg/kg every 8 hours
Levofloxacin	750 mg once a day
Meropenem	2 g every 8 hours
Moxifloxacin	400 mg every 24 hours
Nafcillin	2 g IV every 4 hours
Oxacillin	2 g IV every 4 hours
Potassium penicillin G	4 million units every 4 hours
Rifampicin	600 mg every 24 hours
Tobramycin	1,7 mg/kg every 8 hours
Trimethoprim-sulfamethoxazole (co-trimoxazole)	5 mg/kg every 8 hours
Vancomycin	15 to 20 mg/kg every 8 to 12 hours

Source: tomado de la IDSA: Sociedad Americana de Enfermedades Infecciosas.
*Dosis basada en el peso corporal ideal o peso para dosificación; ajustar según sea necesario en pacientes con bajo peso.

Selection of antibiotics

The most likely pathogens causing community-acquired bacterial meningitis are S. pneumoniae, N. meningitidis, and, less frequently, H. influenzae and group B streptococci in healthy adults under 60 years of age.[23] People over this age have an increased risk of meningitis caused by L. monocytogenes.[23,36]

These patients without evidence of renal failure should be treated empirically with the following regimen until culture and susceptibility data are obtained:[8,24,25]

- Ceftriaxone: 2 g IV every 12 hours.
- Cefotaxime: 2 g IV every four to six hours.

Immunocompromised patients

In immunocompromised individuals, empirical antibiotic coverage should include activity against L. monocytogenes, in addition to the standard treatment for S. pneumoniae, regardless of age.[19] These patients include those with underlying conditions that compromise their immune system (for example, AIDS or lymphoma) or those undergoing immunosuppressive treatments such as cytotoxic chemotherapy or systemic glucocorticoids.

An appropriate regimen for immunocompromised patients with normal renal function includes:

- Vancomycin: 15 to 20 mg/kg IV every eight to twelve hours (without exceeding two grams per dose or a daily dose greater than sixty mg/kg; adjust to achieve minimum serum concentrations between fifteen and twenty mcg/mL).

- Ampicillin: Two grams IV every four hours.

Alternatives may include:

- Cefepime: Two grams IV every eight hours.
- Meropenem: Two grams IV every eight hours (if meropenem is used, starting treatment with ampicillin is unnecessary as it has activity against Listeria).[37]
- Dexamethasone: It is recommended to administer dexamethasone as an adjuvant (0,15 mg/kg IV every six hours) as part of the empirical treatment for adults with suspected bacterial meningitis acquired in the community.[8]

In patients receiving dexamethasone as an adjunctive treatment, it is not necessary to adjust the dose of vancomycin or routinely add other additional agents (such as rifampicin or fluoroquinolone). Although the inflammatory response of the cerebrospinal fluid (CSF) after the administration of dexamethasone can temporarily reduce the penetration of the drug into the CSF and delay its sterilization, significant concentrations can be reached with an adequate dosage.[8]

Prevention: Bacterial meningitis can be prevented mainly through effective vaccination. In some intances, temporary protection can be provided through antimicrobial prophylaxis.[8]

Vaccines: Vaccines against Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae are essential for preventing some leading causes of adult bacterial meningitis. Vaccination against S. pneumoniae and N. meningitidis is recommended for adults with specific risk factors. However, routine immunization against H. influenzae type b is not recommended, except in patients who have undergone splenectomy. The indications for vaccination are discussed separately.[8] Skull base fracture and cerebrospinal fluid leak: Prophylactic antimicrobials are not recommended in patients with skull base fracture and cerebrospinal fluid leakage, as there is no evidence to support their benefit.[8] Neurosurgery: Perioperative antimicrobial prophylaxis is indicated in patients undergoing neurosurgery, including procedures to place cerebrospinal fluid shunts or other devices.[37]

CONCLUSIONS

Bacterial meningitis is a severe central nervous system infection, a medical emergency whose mortality and sequelae can be reduced with timely diagnosis and treatment. The key is to start treatment immediately and without delay. Prevention is the cornerstone of its control and will depend on combined strategies that include adequate vaccination in at-risk populations, precise identification of risk factors, and the judicious use of evidence-based prophylactic measures. Only through multidisciplinary management, which could consist of an expert dialectologist, an intensive care physician, a specialized nurse, and an adequate laboratory team, will it be possible to mitigate the impact of this devastating disease.

REFERENCES

1. Erdem H, Ozturk-Engin D, Cag Y, Senbayrak S, Inan A, Kazak E, et al. Central nervous system infections in the absence of cerebrospinal fluid pleocytosis. International Journal of Infectious Diseases. 2017 Dec 1;65:107–9. Availe in: https://doi.org/10.1016/j.ijid.2017.10.011

2. Ranzenigo M, van Soest TM, Hensen EF, Cinque P, Castagna A, Brouwer MC, van de Beek D. Otitis in Patients With Community-Acquired Bacterial Meningitis: A Nationwide Prospective Cohort Study. Clin Infect Dis. 2024 Aug 15;79(2):329-335. Availe in: https://doi.org/10.1093/cid/ciae221

3. McGill F, Heyderman RS, Panagiotou S, Tunkel AR, Solomon T. Acute bacterial meningitis in adults. The Lancet. 2016 Dec 17;388(10063):3036–47. Availe in: https://doi.org/10.1016/S0140-6736(16)30654-7

4. van de Beek D, Brouwer M, Hasbun R, Koedel U, Whitney CG, Wijdicks E. Community-acquired bacterial meningitis. Nature Reviews Disease Primers. 2016 Nov 3;2(1):16074. Availe in: https://doi.org/10.1038/nrdp.2016.74

5. Doran KS, Fulde M, Gratz N, Kim BJ, Nau R, Prasadarao N, et al. Host–pathogen interactions in bacterial meningitis. Acta Neuropathol. 2016 Feb;131(2):185–209. Availe in: https://doi.org/10.1007/s00401-015-1531-z

6. Kim KS. Investigating Bacterial Penetration of the Blood–Brain Barrier for the Pathogenesis, Prevention, and Therapy of Bacterial Meningitis. ACS Infect Dis. 2020 Jan 10;6(1):34–42. Availe in: https://pubs.acs.org/doi/10.1021/acsinfecdis.9b00319

7. Daum RS, Scheifele DW, Syriopoulou VPh, Averill D, Smith AL. Ventricular involvement in experimental Hemophilus influenzae meningitis. The Journal of Pediatrics. 1978 Dec;93(6):927–30. Availe in: https://doi.org/10.1016/s0022-3476(78)81213-x

8. Prager O, Friedman A, Nebenzahl YM. Role of neural barriers in the pathogenesis and outcome of Streptococcus pneumoniae meningitis. Experimental and Therapeutic Medicine. 2017 Mar;13(3):799–809. Availe in: https://doi.org/10.3892/etm.2017.4082

9. Orihuela CJ, Mahdavi J, Thornton J, Mann B, Wooldridge KG, Abouseada N, et al. Laminin receptor initiates bacterial contact with the blood brain barrier in experimental meningitis models. J Clin Invest. 2009 Jun 1;119(6):1638–46. Availe in: https://doi.org/10.1172/jci36759

10. Bernard SC, Simpson N, Join-Lambert O, Federici C, Laran-Chich MP, Maïssa N, et al. Pathogenic Neisseria meningitidis utilizes CD147 for vascular colonization. Nat Med. 2014 Jul;20(7):725–31. Availe in: https://doi.org/10.1038/nm.3563

11. Coureuil M, Bourdoulous S, Marullo S, Nassif X. Invasive meningococcal disease: a disease of the endothelial cells. Trends in Molecular Medicine. 2014 Oct;20(10):571–8. Availe in: https://doi.org/10.1016/j.molmed.2014.08.002

12. Koedel U, Scheld WM, Pfister HW. Pathogenesis and pathophysiology of pneumococcal meningitis. The Lancet Infectious Diseases. 2002 Dec;2(12):721–36. Availe in: https://doi.org/10.1016/s1473-3099(02)00450-4

13. Chiavolini D, Pozzi G, Ricci S. Animal Models of Streptococcus pneumoniae Disease. Clin Microbiol Rev. 2008 Oct;21(4):666–85. Availe in: https://doi.org/10.1128/CMR.00012-08

14. Brouwer MC, Heckenberg SGB, De Gans J, Spanjaard L, Reitsma JB, Van De Beek D. Nationwide implementation of adjunctive dexamethasone therapy for pneumococcal meningitis. Neurology. 2010 Oct 26;75(17):1533–9. Availe in: https://doi.org/10.1212/WNL.0b013e3181f96297

15. Brouwer MC, Heckenberg SGB, De Gans J, Spanjaard L, Reitsma JB, Van De Beek D. Nationwide implementation of adjunctive dexamethasone therapy for pneumococcal meningitis. Neurology. 2010 Oct 26;75(17):1533–9. Availe in: https://doi.org/10.1212/WNL.0b013e3181f96297

16. Durand ML, Calderwood SB, Weber DJ, Miller SI, Southwick FS, Caviness VS, et al. Acute Bacterial Meningitis in Adults -- A Review of 493 Episodes. N Engl J Med. 1993 Jan 7;328(1):21–8. Availe in: https://doi.org/10.1056/NEJM199301073280104

17. Yezli S. The threat of meningococcal disease during the Hajj and Umrah mass gatherings: A comprehensive review. Travel Medicine and Infectious Disease. 2018 Jul;24:51–8. Availe in: https://doi.org/10.1016/j.tmaid.2018.05.003

18. Thomas KE, Hasbun R, Jekel J, Quagliarello VJ. The Diagnostic Accuracy of Kernig's Sign, Brudzinski's Sign, and Nuchal Rigidity in Adults with Suspected Meningitis. CLIN INFECT DIS. 2002 Jul;35(1):46–52. Availe in: https://doi.org/10.1086/340979

19. Uchihara T, Tsukagoshi H. Jolt Accentuation of Headache: The Most Sensitive Sign of CSF Pleocytosis. Headache. 1991 Mar;31(3):167–71. Availe in: https://doi.org/10.1111/j.1526-4610.1991.hed3103167.x

20. Tamune H, Takeya H, Suzuki W, Tagashira Y, Kuki T, Nakamura M. Absence of jolt accentuation of headache cannot accurately rule out meningitis in adults. The American Journal of Emergency Medicine. 2013 Nov;31(11):1601–4. Availe in: https://doi.org/10.1016/j.ajem.2013.08.028

21. 1. Thomas AE, Baird SF, Anderson J. Purpuric and petechial rashes in adults and children: initial assessment. BMJ. 2016 Mar 22;i1285. Availe in: https://doi.org/10.1136/bmj.i1285

22. Kaplan SL. CLINICAL PRESENTATIONS, DIAGNOSIS, AND PROGNOSTIC FACTORS OF BACTERIAL MENINGITIS. Infectious Disease Clinics of North America. 1999 Sep;13(3):579–94. Availe in: https://doi.org/10.1016/s0891-5520(05)70095-7

23. Kornelisse RF, Westerbeek CML, Spoor AB, Van Der Heijde B, Spanjaard L, Neijens HJ, et al. Pneumococcal Meningitis in Children: Prognostic Indicators and Outcome. Clinical Infectious Diseases. 1995 Dec 1;21(6):1390–7. Availe in: https://doi.org/10.1093/clinids/21.6.1390

24. Brouwer MC, Van De Beek D, Heckenberg SGB, Spanjaard L, De Gans J. Hyponatraemia in adults with community-acquired bacterial meningitis. QJM. 2006 Dec 17;100(1):37–40. Availe in: https://doi.org/10.1093/qjmed/hcl131

25. Geiseler PJ, Nelson KE, Levin S, Reddi KT, Moses VK. Community-Acquired Purulent Meningitis: A Review of 1,316 Cases During the Antibiotic Era, 1954-1976. Clinical Infectious Diseases. 1980 Sep 1;2(5):725–45. Availe in: https://doi.org/10.1093/clinids/2.5.725

26. Rogers T, Sok K, Erickson T, Aguilera E, Wootton SH, Murray KO, et al. Impact of Antibiotic Therapy in the Microbiological Yield of Healthcare–Associated Ventriculitis and Meningitis. Open Forum Infectious Diseases. 2019 Mar 1;6(3):ofz050. Availe in: https://doi.org/10.1093/ofid/ofz050

27. Brouwer MC, Thwaites GE, Tunkel AR, Van De Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. The Lancet. 2012 Nov;380(9854):1684–92. Availe in: https://doi.org/10.1016/S0140-6736(12)61185-4

28. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed Tomography of the Head before Lumbar Puncture in Adults with Suspected Meningitis. N Engl J Med. 2001 Dec 13;345(24):1727–33. Availe in: https://doi.org/10.1056/NEJMoa010399

29. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice Guidelines for the Management of Bacterial Meningitis. Clinical Infectious Diseases. 2004 Nov 1;39(9):1267–84. Availe: https://doi.org/10.1086/425368

30. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice Guidelines for the Management of Bacterial Meningitis. Clinical Infectious Diseases. 2004 Nov 1;39(9):1267–84. Availe in: https://doi.org/10.1086/425368

31. Van De Beek D, Brouwer M, Hasbun R, Koedel U, Whitney CG, Wijdicks E. Community-acquired bacterial meningitis. Nat Rev Dis Primers. 2016 Nov 3;2(1):16074. Availe in: https://doi.org/10.1038/nrdp.2016.74

32. Fitch MT, Van De Beek D. Emergency diagnosis and treatment of adult meningitis. The Lancet Infectious Diseases. 2007 Mar;7(3):191–200. Availe in: https://doi.org/10.1016/S1473-3099(07)70050-6

33. Bodilsen J, Brandt CT, Sharew A, Dalager-Pedersen M, Benfield T, Schønheyder HC, et al. Early versus late diagnosis in community-acquired bacterial meningitis: a retrospective cohort study. Clinical Microbiology and Infection. 2018 Feb;24(2):166–70. Availe in: https://doi.org/10.1016/j.cmi.2017.06.021

34. Sinner SW, Tunkel AR. Antimicrobial agents in the treatment of bacterial meningitis. Infectious Disease Clinics of North America. 2004 Sep;18(3):581–602. Availe in: https://doi.org/10.1016/j.idc.2004.04.005

35. Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar puncture in pediatric bacterial meningitis: defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. Pediatrics. 2001 Nov;108(5):1169–74. Availe in: https://doi.org/10.1542/peds.108.5.1169

36. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed Tomography of the Head before Lumbar Puncture in Adults with Suspected Meningitis. N Engl J Med. 2001 Dec 13;345(24):1727–33. Availe in: http://www.nejm.org/doi/abs/10.1056/NEJMoa010399

37. Hasbun R. Healthcare-associated ventriculitis: current and emerging diagnostic and treatment strategies. Expert Review of Anti-infective Therapy. 2021 Aug 3;19(8):993–9. Availe in: https://doi.org/10.1080/14787210.2021.1866544

FINANCING

The authors did not receive funding for the implementation of this study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

CONTRIBUTION OF AUTHORSHIP

Conceptualization: Jhossmar Cristians Auza-Santivañez.
Formal analysis: Mildred Ericka Kubatz La Madrid.
Research: Paul Cardozo Gil, Jorge Márquez-Molina, Jose Bernardo Antezana-Muñoz.
Methodology: Jhossmar Cristians Auza-Santivañez, Freddy Ednildon Bautista-Vanegas.
Project administration: Jhossmar Cristians Auza-Santivañez.
Supervision: Mildred Ericka Kubatz La Madrid.
Visualization: Jorge Márquez-Molina.
Writing - original draft: Jhossmar Cristians Auza-Santivañez, Blas Apaza Huanca, Paul Cardozo Gil, Jose Bernardo Antezana-Muñoz, Freddy Ednildon Bautista-Vanegas, Jorge Márquez-Molina, Mildred Ericka Kubatz La Madrid, Eloy Paycho Anagua, Carlos Alberto Paz Roman.
Writing - review and editing: Jhossmar Cristians Auza-Santivañez, Blas Apaza Huanca, Paul Cardozo Gil, Jose Bernardo Antezana-Muñoz, Freddy Ednildon Bautista-Vanegas, Jorge Márquez-Molina, Mildred Ericka Kubatz La Madrid, Eloy Paycho Anagua, Carlos Alberto Paz Roman.