WHO guidelines on meningitis diagnosis, treatment and care

World Health Organization

WHO guidelines on meningitis diagnosis, treatment and care

World Health Organization

WHO guidelines on meningitis diagnosis, treatment and care

ISBN 978-92-4-010804-2 (electronic version)

ISBN 978-92-4-010805-9 (print version)

Suggested citation. WHO guidelines on meningitis diagnosis, treatment and care. Geneva: World Health Organization; 2025. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at https://iris.who.int/.

Design and layout: Green Ink Publishing Services Ltd.

Contents

Acknowledgements

The World Health Organization (WHO) gratefully acknowledges the contributions and collaborative efforts of all those involved in the development of this publication.

As part of *Defeating meningitis by 2030: a global road map*, these guidelines were prepared by the Department of Mental Health, Brain Health and Substance Use under the leadership of Devora Kestel and Tarun Dua in collaboration with the Health Emergencies Programme (Department of Epidemic and Pandemic Threat Management) and the Department of Immunization, Vaccines and Biologicals.

The guideline development was coordinated by the WHO Technical Team: Nicoline Schiess (Brain Health Unit), Nicolò Binello (Emerging Zoonoses and High Impact Epidemics Unit), Francesco Venuti (Brain Health Unit) and Elaine Brohan (Brain Health Unit).

WHO is grateful for support from the guideline methodologist Ani Movsisyan, Ludwig-Maximilians-Universität München, Germany. Special thanks are extended to the Guideline Development Group (GDG) co-chairs, Satinder Aneja (Lady Hardinge Medical College, India) and Matt Coldiron (Médecins Sans Frontières, Epicentre, United States of America). Thanks are also due to the members of the GDG: Taoufik Alsaadi (American Center for Psychiatry and Neurology, United Arab Emirates), Action Amos (person with lived experience, International Bureau for Epilepsy, Malawi), Matthijs Brouwer (Amsterdam University Medical Centers, the Kingdom of the Netherlands), Chahnez Charfi Triki (University of Sfax, Tunisia), Adam Cohen (Centers for Disease Control and Prevention, USA), Isabel Elicer (Hospital Dr Sótero del Río, Chile), Nora Groce (University College London, United Kingdom of Great Britain and Northern Ireland), Mariam Hassan (Shaukat Khanum Memorial Cancer Hospital and Research Centre, Pakistan), Robert Heyderman (University College London, United Kingdom), Angelina Kakooza (Makerere University, Uganda), Hanan Khalil (Qatar University, Qatar), Andy Marso (person with lived experience, American Academy of Family Physicians, USA), Kate Milner (University of Melbourne, Australia), Charles Newton (University of Oxford, United Kingdom), Njideka Okubadejo (African Academy of Neurology, Nigeria), Pierre Ongolo Zogo, (University of Yaounde, Cameroon), Armel Poda (University Nazi Boni, Burkina Faso), Kameshwar Prasad (All India Institute of Medical Sciences, India), Paula Reges (Oswaldo Cruz Foundation/Fiocruz, Brazil), James Sejvar (Centers for Disease Control and Prevention, USA), Pratibha Singhi (Amrita Hospital, India), Tom Solomon (University of Liverpool, United Kingdom), Kevin Tan (Duke–NUS Medical School, Singapore) and Mekonnen Teferi (Armauer Hansen Research Institute, Ethiopia).

For their contributions to the guidelines, WHO would also like to thank the members of the systematic review teams: Nina Groeneveld (Amsterdam University Medical Centers, the Kingdom of the Netherlands), Daniel Munblit (King's College London, United Kingdom), Netravathi M (National Institute of Mental Health and Neurosciences, India), Manya Prasad (Institute of Liver and Biliary Sciences, India), Priscilla Rupali (Christian Medical College Vellore, India) and Kiran Thakur (Columbia University, USA). Special thanks are also due to the WHO librarian, Kavita Kothari (WHO Library and Digital Information Networks).

WHO is grateful to the members of the External Review Group (ERG): Melody Asukile (University Teaching Hospitals, Zambia), Gidu Said Bakhit (Juba Teaching Hospital, South Sudan), Matthew Broom (Auckland City Hospital, New Zealand), Dominique Andree Yvette Caugant (Norwegian Institute of Public Health, Norway), Lindsey Enajet (person with lived experience, ItsME Foundation, the Kingdom of the Netherlands), Brian Greenwood (London School of Hygiene &

Tropical Medicine, United Kingdom), Jean Luc Kagayo (United Nations Children's Fund [UNICEF], USA), Brenda Kwambana (Liverpool School of Tropical Medicine, United Kingdom), Bruce Langoulant (Meningitis Centre Australia, Australia), Lucy McNamara (Centers for Disease Control and Prevention, USA), Zomer Sardar (Shalamar Medical and Dental College, Pakistan) and Miklos Szolics (Tawam Hospital, United Arab Emirates).

Appreciation is also due to WHO staff across headquarters and regional offices.

From the Secretariat of *Defeating meningitis by 2030: a global road map* at WHO headquarters: Lorenzo Pezzoli, Katya Fernandez, Joaquin Baruch Monza (Department of Epidemic and Pandemic Threat Management); Marie-Pierre Preziosi, Antoine Durupt, Virginia Benassi, Heidi Soeters, Carole Tevi Benissan (Department of Immunization, Vaccines and Biologicals). From the Division of Antimicrobial Resistance: Silvia Bertagnolio, Benedikt Huttner, Chad Centner (Department of Surveillance, Prevention and Control). From the Health Emergencies Programme: Janet Diaz, Jamie Rylance (Department of Country Readiness Strengthening). From the Division of Universal Health Coverage/Communicable and Noncommunicable Diseases: Shelly Chadha, Antony Dutine, Stuart Keel, Alexandra Rauch, Carolina Der Mussa (Department of Noncommunicable Diseases); Ajay Rangaraj (Global HIV, Hepatitis and Sexually Transmitted Infections Programmes); and Medea Gegia (Global Tuberculosis Programme). From the Division of Universal Health Coverage/ Life Course: Teri Reynolds, Emilie Calvello Hynes (Department of Integrated Health Services); Wilson Were (Department of Maternal, Newborn, Child and Adolescent Health and Ageing); and Shamsuzzoha Syed (Special Programme on Primary Health Care).

From the WHO Regional Office for Africa: Florence Baingana, Chido Rwafa Madzvamutse (Department of Mental Health and Substance Use); Anderson Latt, Clement Lingani (Department of Epidemic Preparedness and Response); and André Bita Fouda (Department of Vaccine-Preventable Diseases).

From the Regional Office for the Americas, also known as the Pan American Health Organization: Renato Oliveira e Souza, Claudina Cayetano, Francisco Varela (Department of Noncommunicable Diseases and Mental Health); Angel Rodriguez, Marc Rondy (Health Emergencies Programme); Pilar Ramon-Pardo and Nathalie El Omeiri (Department of Communicable Diseases Prevention, Control and Elimination).

From the Regional Office for the Eastern Mediterranean: Khalid Saeed (Department of Noncommunicable Diseases and Mental Health); Chiori Kodama (Health Emergencies Programme); and Quamrul Hasan (Department of Immunization, Vaccine-Preventable Diseases and Polio Transition).

From the Regional Office for Europe: Ledia Lazeri (Department of Mental Health and Substance Use); Marc-Alain Widdowson (Health Emergencies Programme); Jose Hagan, Roberta Pastore and Liudmila Mosina (Department of Vaccine-Preventable Diseases and Immunization).

From the Regional Office for South-East Asia: Andrea Bruni (Department of Mental Health and Substance Use); Manish Kakkar (Health Emergencies Programme); and Tondo Njambe Emmanuel (Department of Immunization and Vaccine Development).

From the Regional Office for the Western Pacific: Martin Vandendyck, Jasmine Vergara (Department of Mental Health and Substance Use); Gina Samaan (Health Emergencies Programme); and Xiaojun Wang (Department of Vaccine-Preventable Diseases and Immunization).

Financial support for the development of the guidelines was provided by the Ministry for Europe and Foreign Affairs, France.

Abbreviations

ASM	anti-seizure medicine(s)
AST	antimicrobial susceptibility testing
AWaRe	WHO Access, Watch and Reserve classification of antibiotics
CI	confidence interval
CLSI	Clinical and Laboratory Standards Institute
CRP	C-reactive protein
CRPD	United Nations Convention on the Rights of Persons with Disabilities
CSF	cerebrospinal fluid
CT	computed tomography
DIC	disseminated intravascular coagulation
DOI	declarations of interest
ERG	External Review Group
EtD	Evidence-to-Decision
EUCAST	European Committee on Antimicrobial Susceptibility Testing
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GBS	Group B *Streptococcus*
HIC	high-income country
HSV	herpes simplex virus
LMIC	low- and middle-income country
NGO	nongovernmental organization
OR	odds ratio
PCR	polymerase chain reaction
PCT	procalcitonin
PIR	Package of interventions for rehabilitation
RBC	red blood cell
RCT	randomized controlled trial
RR	risk ratio
TNF	tumour necrosis factor
UHC	universal health coverage
UI	unit interval
WBC	white blood cell
WHO	World Health Organization

Executive summary

Meningitis continues to pose a public health threat globally, despite successful efforts to control the disease in several regions of the world. The burden of mortality and morbidity from meningitis, including the risk of neurological and physical sequelae, remains high, particularly in low- and middle-income countries (LMICs) and in settings experiencing large-scale, disruptive epidemics. Furthermore, the financial burden related to meningitis care and aftercare contributes to significant health inequities among the most vulnerable, marginalized and disadvantaged populations.

In 2017, representatives from governments, global health organizations, public health bodies, academia, the private sector and civil society organizations united in a call to action to eliminate meningitis as a public health problem. As a result, the World Health Organization (WHO) together with global partners and experts, coordinated the development of *Defeating meningitis by 2030: a global road map*, which was approved by the Seventy-third World Health Assembly (resolution WHA73.9). While several causes of meningitis can be prevented by vaccination, the defeating meningitis road map strongly emphasizes the need to improve the clinical management and long-term care of people with meningitis, in an effort to reduce mortality, minimize the incidence of sequelae and disability, mitigate the risk of antimicrobial resistance and improve the quality of life of affected individuals, families and communities.

The *WHO guidelines on meningitis diagnosis, treatment and care* provide evidence-based, quality-assured recommendations for the clinical management of children over 1 month of age, adolescents and adults with acute, community-acquired meningitis. Due to the similarities in clinical presentation, initial diagnostic approach and treatment strategies, both bacterial and viral causes are considered within the scope of this document. The guidelines provide recommendations applicable worldwide and are primarily intended for health-care professionals working in first or second-level health-care facilities, including emergency, inpatient and outpatient services. Additionally, the guidelines are directed at policy-makers, health-care planners and programme managers operating at national and international levels (e.g. ministries of health, national public health bodies, non-governmental organizations). Since resource-limited settings bear the highest burden of meningitis globally, this document was specifically developed to provide technical guidance suitable for implementation in LMICs.

The guidelines were developed in accordance with the *WHO handbook for guideline development* and meet international standards for evidence-based guidelines. Conflicts of interest from all individual contributors were declared, assessed and managed in line with WHO procedures. In collaboration with the Guideline Development Group (GDG) and the guideline methodologist, the WHO Steering Group identified priority questions and outcomes to determine the scope of the guidelines. Overall, 20 guideline questions were formulated using the PICO (population, intervention, comparator, outcome) format, addressing different areas of meningitis diagnosis, treatment and long-term care. For each guideline question, a systematic evidence review was conducted and subsequently used to develop the Evidence-to-Decision frameworks, according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

The GDG formulated the recommendations while considering a range of domains, including the certainty of evidence, the balance between desirable and undesirable effects, values and preferences of intended users, resource requirements and cost-effectiveness, health equity, equality and non-discrimination, feasibility, human rights and sociocultural acceptability.

A strong recommendation was issued when GDG members were confident that the desirable effects of adhering to the recommendation outweighed the undesirable effects. A conditional recommendation was made when GDG members concluded that the desirable effects of adhering to the recommendation probably outweighed the undesirable effects, but they were not confident about the trade-offs or identified specific conditions under which the recommendation applies. When guideline questions addressed the same topic but involved different populations (e.g. children and adults), they were discussed together by the GDG, resulting in single recommendations. The guidelines also include good practice statements, reflecting a consensus within the GDG that the net benefits of adhering to the statement are large and unequivocal, and that the implications of the statement are common sense. The GDG reached unanimous agreement on all the recommendations and ratings.

The recommendations are organized into three sections: A. Diagnosis, B. Treatment and C. Management of sequelae, and are presented along with the remarks in the Summary of Recommendations.

Summary of recommendations

A. Diagnosis

Lumbar puncture

Good practice statement

In individuals with suspected acute meningitis, lumbar puncture should be performed as soon as possible, preferably before the initiation of antimicrobial treatment, unless there are specific contraindications or reasons for deferral.

Cerebrospinal fluid investigations

Strong recommendation for

In individuals with suspected acute meningitis, Gram stain should be performed on cerebrospinal fluid samples.

Strong recommendation. Moderate certainty of evidence.

Strong recommendation for

In individuals with suspected acute meningitis, cerebrospinal fluid investigations should be performed to determine white blood cell count (total and differential), protein concentration, glucose concentration and the cerebrospinal fluid to blood glucose ratio.

Strong recommendation. Moderate certainty of evidence.

Conditional recommendation for

In individuals with suspected acute meningitis, cerebrospinal fluid lactate levels should be considered when antibiotic therapy has not yet been administered.

Conditional recommendation. Moderate certainty of evidence.

Remarks

Cerebrospinal fluid (CSF) Gram stain, white blood cell (WBC) count (total and differential), and protein and glucose concentration have varying sensitivity and specificity. However, none of these tests can be used alone to confirm or rule out a diagnosis of meningitis.

A combined, integrated approach to the interpretation of CSF findings is required to mitigate and minimize the risks associated with the diagnostic performance of individual tests (i.e. risk of false negatives and/or false positives).

The diagnostic yield of these CSF laboratory investigations may decrease when antimicrobial treatment is initiated prior to lumbar puncture.

Normal WBC count and protein concentration may be higher in infants and young children than in older age groups, emphasizing the importance of using age-appropriate threshold values.

When performing a Gram stain on CSF samples, the following results may be observed and inform clinical decision-making:

- Gram-positive diplococci suggest pneumococcal infection.
- Gram-negative diplococci suggest meningococcal infection.
- Gram-negative coccobacilli are consistent with *Haemophilus influenzae* infection.
- Gram-positive bacilli or coccobacilli suggest *Listeria* infection.

Classic CSF characteristics of acute bacterial meningitis caused by pyogenic pathogens include WBC pleocytosis with neutrophilic predominance, low glucose concentration, low CSF-to-serum glucose ratio and high protein concentration.

CSF lactate levels may contribute to differentiating between bacterial and viral meningitis. However, the diagnostic value and clinical applications of CSF lactate are limited after the initiation of antibiotic administration or in the presence of other central nervous system diseases in the differential diagnosis.

The presence of red blood cells in CSF samples should be investigated as it may indicate traumatic lumbar puncture or acute subarachnoid haemorrhage.

Cerebrospinal fluid culture

Good practice statement

In individuals with suspected acute meningitis, cerebrospinal fluid culture and antimicrobial susceptibility testing remain the gold standard for bacterial pathogen identification.

Cerebrospinal fluid molecular testing

Strong recommendation for

In individuals with suspected acute meningitis, PCR-based molecular tests for relevant pathogens should be performed on cerebrospinal fluid samples.

Strong recommendation. Low certainty of evidence.

Remarks

Results of polymerase chain reaction (PCR)-based tests on CSF should be interpreted in the context of clinical presentation (i.e. medical history, symptoms and signs) and additional laboratory findings (e.g. CSF characteristics, Gram stain and culture).

The diagnostic yield of CSF PCR tests for bacterial pathogens may decrease when antimicrobial treatment is initiated prior to lumbar puncture or sample transportation and preservation practices are suboptimal.

CSF culture and antimicrobial susceptibility testing (AST) should not be replaced by PCR and should be routinely performed as the gold standard tests for pathogen identification and characterization of antibiotic resistance profiles. Where resources permit, blood cultures and AST should also be performed in individuals with suspected acute meningitis.

Blood culture

Good practice statement

In individuals with suspected acute meningitis, blood cultures should be obtained as soon as possible, preferably before the initiation of antibiotic therapy.

Blood markers of bacterial infection

Conditional recommendation for

In individuals with suspected acute meningitis, peripheral white blood cell count (total and differential) should be considered where resources allow.

Conditional recommendation. Low certainty of evidence.

Conditional recommendation for

In individuals with suspected acute meningitis, C-reactive protein or procalcitonin should be considered where resources allow.

Conditional recommendation. Moderate certainty of evidence.

Remarks

None of the included peripheral blood tests can be used to confirm or exclude the diagnosis of bacterial meningitis and lumbar puncture should not be deferred or delayed based on their results.

WBC count (absolute and differential), C-reactive protein or procalcitonin should not be performed in isolation and results should be interpreted in the context of clinical presentation (i.e. medical history, symptoms and signs) and CSF characteristics.

Both C-reactive protein and procalcitonin may have a role in differentiating acute bacterial meningitis from other forms of meningitis. Given the lack of evidence comparing C-reactive protein to procalcitonin for the diagnosis of acute bacterial meningitis or regarding the incremental diagnostic value of C-reactive protein and procalcitonin when used in combination, these tests may be used individually.

The decision on whether to choose C-reactive protein or procalcitonin (or both) should be based on resources and local availability. When C-reactive protein is measured, quantitative C-reactive protein assays should be preferred over qualitative assays, since serum levels can be monitored and used as a marker of clinical response to treatment.

Cranial imaging

Strong recommendation against

In individuals with suspected acute meningitis, cranial imaging should not be performed routinely.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

Where cranial imaging is readily accessible:

Cranial imaging should be performed prior to lumbar puncture to rule out cerebral space-occupying lesions with midline shift, if any of the following features are identified at time of presentation:

- Glasgow Coma Score below 10
- focal neurological signs
- cranial nerve deficits
- papilloedema
- new-onset seizures (in adults)
- severe immunocompromised state.

Strong recommendation. Very low certainty of evidence.

Strong recommendation against

Where cranial imaging is not readily accessible:

Lumbar puncture should be deferred if any of the following features are identified at time of presentation and until they have resolved:

- Glasgow Coma Score below 10
- focal neurological signs
- cranial nerve deficits
- papilloedema
- new-onset seizures (in adults)
- severe immunocompromised state.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

Treatment should not be delayed for cranial imaging or when lumbar puncture is deferred.

Strong recommendation. Very low certainty of evidence.

Remarks

When lumbar puncture is deferred, blood samples (including blood cultures) should be collected, and antimicrobial treatment started as soon as possible, prior to cranial imaging.

Seizures are a common finding in febrile children suspected of having acute meningitis. New-onset isolated seizures in children do not require cranial imaging prior to lumbar puncture when they occur in the absence of any other at-risk features.

Severe immunocompromised state (e.g. organ transplantation) should warrant lumbar puncture deferral. However, for people living with HIV suspected of having a first episode of cryptococcal meningitis, prompt lumbar puncture with measurement of opening pressure and rapid cryptococcal antigen assay is recommended as the preferred diagnostic approach.

B. Treatment

General management

Good practice statement

Children and adults with suspected acute meningitis should be immediately admitted or urgently transferred to an appropriate health-care facility for further management.

Timing of empiric antimicrobial treatment

Conditional recommendation for

In children and adults presenting with suspected acute meningitis, empiric parenteral antimicrobial treatment before admission or transfer to an appropriate health-care facility should be considered.

Conditional recommendation. Very low certainty of evidence.

Strong recommendation for

In children and adults with suspected acute meningitis admitted to an appropriate health-care facility, empiric intravenous antimicrobial treatment should be administered as early as possible.

Strong recommendation. Very low certainty of evidence.

Remarks

Before admission or transfer to an appropriate health-care facility:

- Parenteral antimicrobial treatment may be beneficial where acute bacterial meningitis is strongly suspected and a clinically significant delay in transfer or referral is considered likely.
- Antimicrobial treatment should be administered intravenously. If intravenous administration is not possible and/or an intravenous line is not secured, intramuscular administration should be pursued.

After admission or transfer to an appropriate health-care facility:

- Intravenous antimicrobial treatment should be given as soon as acute bacterial meningitis is suspected. The "1-hour window" is generally regarded as the golden time period to initiate empiric antibiotic therapy.
- Lumbar puncture, in the absence of contraindications or reasons for deferral, and blood tests should be performed prior to initiating empiric antimicrobial treatment. However, any delay in diagnostic investigations should not delay therapy administration.
- In the absence of contraindications or reasons for deferral, individuals who have received antimicrobial treatment before admission should undergo lumbar puncture as soon as possible once they are admitted in an appropriate health-care facility.

- Adequate clinical monitoring within an appropriate health-care facility is warranted when antimicrobial treatment is administered to an individual with known severe antibiotic allergy.

Empiric antimicrobial treatment regimens

Strong recommendation for

In children and adults with suspected or probable acute bacterial meningitis, intravenous ceftriaxone or cefotaxime should be administered as empiric treatment.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

In the presence of one or more risk factors for *Listeria monocytogenes* infection (i.e. age over 60 years, pregnancy, immunocompromised state), intravenous ampicillin or amoxicillin should be administered in addition to the initial antimicrobial regimen.

Strong recommendation. Very low certainty of evidence.

Conditional recommendation for

In areas with high prevalence of penicillin or third-generation cephalosporin resistance of *Streptococcus pneumoniae*, intravenous vancomycin should be considered in addition to the initial antimicrobial regimen.

Conditional recommendation. Very low certainty of evidence.

Remarks

Ceftriaxone or cefotaxime are equally recommended as first-line agents for empiric treatment among suspected and probable cases of acute bacterial meningitis. However, intravenous ceftriaxone should be preferred over cefotaxime during meningococcal and pneumococcal disease epidemics.

Ampicillin or amoxicillin should be added to the initial empiric antimicrobial regimen in the presence of any of the following risk factors for *Listeria monocytogenes* infection:

- age over 60 years
- pregnancy
- immunosuppressive therapy
- organ transplantation
- malignancy
- advanced HIV disease
- diabetes mellitus
- end-stage kidney disease
- liver cirrhosis
- alcohol use disease.

Prevalence thresholds to define settings at risk for penicillin or cephalosporin resistance of *Streptococcus pneumoniae* should be defined at the national and/or sub-national level. In areas with known high prevalence of penicillin or cephalosporin resistance of *S. pneumoniae*, intravenous vancomycin would provide adequate antimicrobial coverage against resistant strains. In setting with low tuberculosis burden, rifampicin can be used as an alternative to vancomycin. In settings with high tuberculosis burden, rifampicin can be used only when vancomycin is not readily available or contraindicated.

As soon as a bacterial pathogen is isolated and AST results are known, antibiotic therapy should be reviewed and optimized accordingly.

To mitigate the risk of antimicrobial resistance and ensure appropriate use of second-line antibiotic agents, beta-lactam allergies should be thoroughly investigated before making a treatment decision. Cephalosporins can be safely used in most cases of non-severe penicillin allergy, and vice versa. In cases of previous life-threatening reactions caused by the exposure to beta-lactams, any use of beta-lactams should be avoided.

Conditional recommendation for

In children and adults with suspected or probable acute bacterial meningitis, intravenous chloramphenicol with benzylpenicillin, ampicillin or amoxicillin should only be considered for empiric treatment when ceftriaxone or cefotaxime are not immediately available.

Conditional recommendation. Very low certainty of evidence.

Remarks

In settings with low vaccination coverage for *H. influenzae* type b, intravenous amoxicillin or ampicillin should be preferred over benzylpenicillin for combined empiric treatment (i.e. in association with chloramphenicol).

As soon as a bacterial pathogen is isolated and AST results are known, antibiotic therapy should be reviewed and optimized accordingly.

To mitigate the risk of antimicrobial resistance and ensure appropriate use of second-line antibiotic agents, beta-lactam allergies should be thoroughly investigated before making a treatment decision. In cases of previous life-threatening reactions caused by the exposure to beta-lactams, any use of beta-lactams should be avoided.

Duration of empiric antimicrobial treatment

Conditional recommendation for

In non-epidemic settings, in children and adults with suspected or probable acute bacterial meningitis and no pathogen identification, discontinuation of empiric antibiotic therapy may be considered after 7 days if the person has clinically recovered.

Conditional recommendation. Very low certainty of evidence.

Remarks

All efforts should be made to identify and characterize the causative pathogen on blood and CSF samples through culture and molecular tests (e.g. PCR).

When the pathogen remains unknown, empiric antibiotic therapy can be discontinued after 7 days, provided that the person has clinically recovered. Clinical recovery may be indicated by the presence of *all* of the following for at least 48 hours:

- resolution of fever
- resolution of vital sign abnormalities (blood pressure, heart rate, respiratory rate, oxygen saturation)
- resolution of altered consciousness
- normal mental status.

In the absence of clinical recovery within one week of empiric treatment, antibiotic therapy should be extended and accompanied by an appropriate diagnostic work-up, including a repeat lumbar puncture provided there are no contraindications.

Strong recommendation for

During meningococcal disease epidemics, empiric treatment with parenteral ceftriaxone should be administered for 5 days to children and adults with suspected or probable meningococcal meningitis.

Strong recommendation. Very low certainty of evidence.

Conditional recommendation for

During pneumococcal disease epidemics, empiric treatment with parenteral ceftriaxone for 10 days should be considered for children and adults with suspected or probable pneumococcal meningitis.

Conditional recommendation. Very low certainty of evidence.

Remarks

During meningococcal and pneumococcal disease epidemics, intravenous ceftriaxone is the preferred administration option. If intravenous administration is not immediately feasible, intramuscular ceftriaxone should be given.

During meningococcal and pneumococcal disease epidemics, in the absence of clinical recovery, empiric treatment can be extended, and further diagnostic investigations should be performed.

Post-exposure antimicrobial prophylaxis

Strong recommendation for

In the presence of sporadic disease, antibiotic prophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin should be provided to close contacts of laboratory-confirmed cases of meningococcal disease, in accordance with known antimicrobial susceptibility patterns.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

During large-scale epidemics, antibiotic prophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin should be provided to close contacts of clinically suspected cases of meningococcal disease, in accordance with known antimicrobial susceptibility patterns.

Strong recommendation. Very low certainty of evidence.

Conditional recommendation for

Rifampicin should be considered when ceftriaxone or ciprofloxacin cannot be administered.

Conditional recommendation. Very low certainty of evidence.

Remarks

Vaccination remains the primary control intervention against meningococcal disease. All efforts should be undertaken to ensure the highest vaccination coverage in the target population, including routine immunization, mass preventive campaigns and reactive campaigns implemented as part of outbreak response.

Considering the increasing incidence of cases caused by ciprofloxacin-resistant isolates worldwide, the choice of antibiotic should be guided by the antimicrobial susceptibility patterns prevalent within the community and potentially adjusted as necessary based on susceptibility testing results from index cases.

Antibiotic prophylaxis should be provided to close contacts as soon as possible. Administration later than 14 days after case identification likely has limited or no benefit.

Close contacts should be defined based on context-specific considerations and available resources. In the presence of an index case, during the 7 days before symptom onset and until 24 hours after initiation of appropriate antibiotic therapy, people at increased risk of infection include:

- individuals with prolonged exposure while in close proximity (less than 1 metre) to the index case (e.g. household contacts);
- individuals directly exposed to oral secretions of the index case (e.g. via kissing, mouth-to-mouth resuscitation, endotracheal intubation).

In the presence of small-scale outbreaks, antibiotic prophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin should be provided to close contacts of laboratory-confirmed or clinically suspected cases of meningococcal disease, depending on available resources.

- If laboratory confirmation is expected to be obtained for all suspected cases, antibiotic prophylaxis should be provided to close contacts of laboratory-confirmed cases.
- If laboratory confirmation is not expected to be obtained for most suspected cases, antibiotic prophylaxis can also be provided to close contacts of strongly suspected cases.

Adjunctive corticosteroids

Strong recommendation for

In non-epidemic settings where lumbar puncture can be performed, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should be initiated with the first dose of antibiotics in children and adults with suspected acute bacterial meningitis.

If cerebrospinal fluid characteristics are not consistent with bacterial meningitis, intravenous corticosteroids should be discontinued.

Strong recommendation. Low certainty of evidence.

Conditional recommendation for

In non-epidemic settings where lumbar puncture cannot be performed, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) may be initiated with the first dose of antibiotics when acute bacterial meningitis is strongly suspected in children and adults and no concurrent condition contraindicates their use.

Conditional recommendation. Very low certainty of evidence.

Strong recommendation against

During meningococcal disease epidemics, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should not be routinely used in children and adults with suspected or probable meningococcal meningitis.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

During pneumococcal disease epidemics, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should be initiated with the first dose of antibiotics in children and adults with suspected or probable pneumococcal meningitis.

Strong recommendation. Very low certainty of evidence.

Remarks

Corticosteroids should be administered intravenously in an inpatient setting.

The beneficial effects of corticosteroids are likely to decrease as the delay in administration increases. Therefore, corticosteroids should be administered with the first dose of antibiotics or as soon as possible after the initial antibiotic dose.

Dexamethasone should be considered the corticosteroid of choice for children and adults. However, the dexamethasone 6-hourly administration schedule can be resource-consuming and its accessibility across different settings is variable. When dexamethasone cannot be administered, intravenous hydrocortisone or methylprednisolone may be used as alternatives, at equivalent dosage and with an appropriate administration schedule.

Upon initial administration, the duration of corticosteroid use should be informed by CSF characteristics and pathogen isolation.

- If CSF characteristics are considered consistent with or suggestive of bacterial meningitis, intravenous corticosteroids should be continued for a maximum duration of 4 days.
- If CSF characteristics are consistent with bacterial meningitis and *S. pneumoniae* or *H. influenzae* type b is detected through culture or molecular testing, intravenous corticosteroids should be continued for a maximum duration of 4 days.
- If CSF characteristics are consistent with bacterial meningitis and a bacterial pathogen other than *S. pneumoniae* or *H. influenzae* type b is detected through culture or molecular testing, intravenous corticosteroids can be discontinued.

Intravenous corticosteroids should not be administered when the benefits do not outweigh the risks.

Corticosteroids should not be administered to individuals with cerebral malaria as their use is associated with prolonged coma resolution times when compared to placebo.

The above recommendations on the use of corticosteroids as adjunctive treatment for suspected acute bacterial meningitis also apply to people living with HIV who are on antiretroviral therapy and have undetectable viral load (less than 50 copies/µl).

Intravenous corticosteroids administered as adjunctive treatment for suspected acute bacterial meningitis in children and adults with advanced HIV disease has not proven to be beneficial in reducing mortality or morbidity.

The recommendations on the use of corticosteroids during meningococcal and pneumococcal disease epidemics are applicable if the causative agent of the epidemic is identified via culture or PCR.

Osmotic agents

Conditional recommendation against

Glycerol should not be used routinely as adjunctive therapy in children and adults with suspected, probable or confirmed acute bacterial meningitis.

Conditional recommendation. Low certainty of evidence.

Remarks

Osmotic agents other than glycerol, such as mannitol, sorbitol and hypertonic saline can be used as a temporary measure for the management of increased intracranial pressure, including in children and adults with bacterial meningitis and signs of impending brain herniation (e.g. rapid change in level of consciousness, hypertension, bradycardia, loss of pupillary reaction).

Interventions with a more durable effect on intracranial pressure (e.g. ventilatory support, decompressive craniectomy) may be required in people with increased intracranial pressure.

Fluid management

Conditional recommendation against

Fluid intake should not be routinely restricted in children and adults with suspected, probable or confirmed acute bacterial meningitis.

Conditional recommendation. Very low certainty of evidence.

Remarks

Maintenance fluids are preferably administered orally or by enteric tube (e.g. nasogastric tube). Among infants and young children, breastfeeding is the ideal method of hydration.

When fluids cannot be administered orally or by enteric tube, isotonic solutions (e.g. Ringer's lactate, normal saline) should be routinely used as maintenance intravenous fluids.

In accordance with clinical judgement, moderate fluid restriction can be implemented in individuals without signs of shock or hypovolemia who present with clinical manifestations suggestive of syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Anti-seizure medicines

Conditional recommendation for

In children and adults with acute symptomatic seizures from meningitis, anti-seizure medicines should be continued for no longer than three months, in the absence of any recurring seizures.

Conditional recommendation. Very low certainty of evidence.

Remarks

The choice of anti-seizure medicines is affected by several factors, including seizure semiology, comorbidities, availability, cost and side-effects. Specific considerations are also in place for older adults, individuals with HIV, people with learning difficulties, and women and girls with childbearing potential.

Recommendations for the diagnosis and management of epilepsy and seizures in children and adults are presented in the *WHO mental health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders*.

C. Management of sequelae

Clinical assessment

Strong recommendation for

Children and adults with acute meningitis from any cause should be reviewed for sequelae by a health-care provider prior to discharge and at follow-up.

Strong recommendation. Very low certainty of evidence.

Remarks

A clinical assessment at follow-up should be performed at least once within four weeks of discharge.

When sequelae are detected, referral to the appropriate services should be arranged.

When available, psychological support should be offered to both the person with meningitis and their caregivers.

Rehabilitation

Strong recommendation for

In children and adults with sequelae due to acute meningitis from any cause, rehabilitation should be provided as soon as possible.

Strong recommendation. Very low certainty of evidence.

Remarks

The WHO *Package of interventions for rehabilitation* (PIR) outlines interventions for rehabilitation of 20 health conditions, spanning seven disease areas, including musculoskeletal, neurological, neurodevelopmental and sensory disorders. Interventions are organized into functioning domains, relevant to people with different health conditions, including individuals with sequelae following acute meningitis.

Hearing loss

Strong recommendation for

In children and adults with acute meningitis from any cause, formal audiological screening should be conducted before discharge.

If audiological screening is not possible before discharge, it should be conducted within four weeks of discharge.

Strong recommendation. Very low certainty of evidence.

Remarks

When hearing loss is detected, urgent referral for hearing rehabilitation or evaluation for cochlear implantation should be arranged. This is crucial to prevent the rapid impairment of speech due to the loss of auditory feedback and to avoid cochlear ossification in individuals eligible for cochlear implantation.

Individuals screened before discharge and found to have no hearing loss should undergo a second formal audiological screening test, as a small number may still develop hearing loss at a later stage.

Strong recommendation for

In children and adults with hearing loss from acute meningitis from any cause, hearing rehabilitation should be provided as soon as possible.

Strong recommendation. Very low certainty of evidence.

Remarks

The WHO PIR (Module 6) outlines assessments and interventions for hearing loss. Rehabilitation interventions for hearing impairment include the provision of, and training in, the use of hearing technologies (hearing aids, cochlear implants and middle ear implants), and speech and language therapy to enhance perceptive skills and develop communication and linguistic abilities. Rehabilitation also includes training in the use of sign language and other means of sensory substitution, such as speech reading, use of print on palm or Tadoma signed communication.

1. Introduction

1. Introduction

1.1 Global burden of meningitis

Meningitis continues to pose a significant public health threat globally, despite successful efforts to control the disease in several countries and regions of the world. The burden of morbidity and mortality from meningitis remains high, particularly in low- and middle-income countries (LMICs) and in settings experiencing large-scale, disruptive epidemics. In 2019, there were an estimated 2.51 million cases (95% unit interval [UI] 2.11–2.99 million) and 236 000 deaths (95% UI 204 000–277 000) due to meningitis worldwide *(1)*. The burden was greatest among children younger than 5 years of age, with 1.28 million cases (95% UI 0.95–1.71 million) and 112 000 deaths (95% UI 87 400–145 000) *(1)*.

Approximately one in five individuals affected by bacterial meningitis incurs long-term complications, including physical and neuropsychological sequelae, which may result in disability and have a profound impact on the quality of life *(2)*. In 2021, the burden of premature mortality and disability caused by meningitis was estimated to exceed 15 million disability adjusted life years worldwide *(3)*.

Furthermore, meningitis care imposes a significant financial burden on affected individuals, their families and communities. In resource-limited settings, families caring for children with long-term neurological complications may struggle to afford the necessary medical expenses *(2)*. With limited disposable income, households may be forced to sacrifice basic necessities to cover the costs of long-term care.

1.2 Defeating meningitis by 2030: a global road map

Although several causes of meningitis can be prevented by vaccination, gaps persist in ensuring adequate diagnosis, treatment and follow-up care for affected individuals, especially in LMICs. In 2017, representatives from governments, global health organizations, public health bodies, academia, the private sector and civil society organizations united in a call to action to defeat meningitis. As a result, the World Health Organization (WHO), together with global partners and experts, coordinated the development of *Defeating meningitis by 2030: a global road map*, with the vision of eliminating meningitis as a public health problem by 2030 *(2)*.

In November 2020, the defeating meningitis road map was approved by the Seventy-third World Health Assembly (resolution WHA73.9). With a view towards a world free of meningitis, the road map outlines three visionary goals:

- eliminate epidemics of bacterial meningitis
- reduce cases of vaccine-preventable bacterial meningitis by 50% and deaths by 70%
- reduce disability and improve quality of life after meningitis of any cause.

To achieve these objectives, the defeating meningitis road map sets out strategic goals, key activities and specific milestones, which are organized into five interconnected pillars: Prevention and epidemic control; Diagnosis and treatment; Surveillance; Support and care; and Advocacy and engagement. Within this context, two strategic goals emphasize the need to improve the clinical management and long-term care of people with meningitis:

- Strategic Goal 9 (Diagnosis and treatment pillar): Provide and implement appropriate, context-specific, quality-assured guidelines and tools for treatment and supportive care to reduce the risk of mortality, sequelae and antimicrobial resistance.
- Strategic Goal 13 (Support and care pillar): Strengthen early recognition and management of sequelae from meningitis in health-care and community settings.

1.3 Objective of the guidelines and target audience

The *WHO guidelines on meningitis diagnosis, treatment and care*, referred to as the guidelines, were developed to provide evidence-based recommendations for the clinical management of people with meningitis, including acute and long-term care.

In line with the WHO's goal to achieve universal health coverage (UHC), the guidelines are primarily intended for health-care professionals working in first- or second-level health-care facilities, including emergency, inpatient and outpatient services. Quality improvement teams across all levels of the health system will also benefit from this work. Moreover, the guidelines are directed at policy-makers, health-care planners and programme managers operating at national and international levels (e.g. ministries of health, national public health bodies). Finally, the guidelines aim to serve as a tool for academic institutions and non-governmental and civil society organizations to inform their research, teaching and capacity-building agendas.

The recommendations are applicable worldwide. As low-resource settings bear the highest burden of meningitis globally, this document was specifically developed to provide clinical guidance that can be implemented in LMICs.

1.4 Scope of the guidelines

The guidelines address the diagnosis, treatment and long-term care of acute-onset, community-acquired meningitis in adults, adolescents and children aged more than 1 month. Throughout the publication, the term "children" encompasses infants (aged more than 1 month), toddlers and adolescents, unless otherwise specified. The guidelines include recommendations for epidemic and non-epidemic settings, with the former superseding previous WHO recommendations on treatment and post-exposure prophylaxis from 2014 *(4)*.

Due to the similarities in clinical presentation, initial diagnostic approach, and some treatment strategies across different forms of acute community-acquired meningitis, both bacterial and viral causes are considered within the scope of these guidelines. The clinical presentation of acute community-acquired meningitis, along with the public health importance and epidemiology of the most common causative pathogens, is outlined below.

1.5 Clinical presentation

Acute meningitis is characterized by the rapid onset of fever, neck stiffness, headache, photophobia and/or altered mental status, ranging from sensory obtundation to confusion, lethargy and coma *(5)*. The classic triad of fever, neck stiffness and altered mental status or headache should prompt a strong clinical suspicion of *bacterial* meningitis but is reported only in approximately half of affected individuals *(5)*. Conversely, the absence of all four manifestations significantly reduces the probability of a bacterial cause.

Constitutional symptoms, including malaise, fatigue, nausea and/or vomiting, are common, nonspecific complaints. Seizures, focal neurological deficits (e.g. aphasia, hemiparesis or monoparesis), and cranial nerve palsies occur in a proportion of cases. These neurologic symptoms often reflect concurrent involvement of the brain parenchyma (meningoencephalitis) and are more common in bacterial disease. In addition to nuchal rigidity, classical signs of meningeal irritation, including Brudzinski and Kernig's signs, should always be investigated, but their sensitivity is limited, and their absence cannot be used to rule out meningitis *(6)*.

In infants, the clinical presentation is variable and less characteristic as neck stiffness and headache are less frequent or harder to identify. Common manifestations include fever or hypothermia, bulging fontanel, lethargy and/or irritability, reduced feeding, abnormal cry (continuous, weak or high-pitched), signs of respiratory distress (e.g. apnoea, tachypnoea, grunting) and seizures *(7)*.

Some individuals with meningitis may develop symptoms and signs of increased intracranial pressure, which is caused by the presence of cerebral oedema, hydrocephalus or a space-occupying lesion (e.g. brain abscess, subdural empyema). The most severe complication of intracranial hypertension is cerebral herniation.

In some forms of bacterial meningitis, sepsis may also ensue as part of the natural course of the disease. In severe cases, septic shock, multiorgan failure and/or disseminated intravascular coagulation (DIC) can occur. Finally, certain clinical manifestations can provide critical insights into the underlying cause of meningitis and indicate the most likely pathogen. In individuals with meningococcal sepsis (meningococcaemia), a characteristic haemorrhagic, non-blanching skin rash may appear as petechial or purpuric lesions, most frequently on the trunk and lower portions of the body. The rash correlates with the degree of thrombocytopenia and may precede devastating haemorrhagic complications (e.g. purpura fulminans).

1.6 Etiology

Among the different forms of acute community-acquired meningitis, bacterial disease is associated with the greatest morbidity and mortality burden worldwide and constitutes the primary focus of the guidelines. The most common causative pathogens of bacterial meningitis primarily depend on age, immune status and the presence of concurrent risk factors (Table 1.1) *(8, 9)*.

1.6.1 *Streptococcus pneumoniae*

Streptococcus pneumoniae, also known as pneumococcus, is the most frequent cause of acute bacterial meningitis in adults *(1)*. Routine administration of the pneumococcal conjugate vaccine, targeting the most prevalent of over 100 identified serotypes, has significantly reduced the incidence of invasive pneumococcal disease in several countries *(10)*. However, pneumococcal meningitis still occurs worldwide, particularly among individuals with predisposing conditions, including a contiguous infectious focus (e.g. otitis media, mastoiditis, sinusitis), head trauma with skull base fracture, functional or anatomical asplenia, and immunocompromised state *(11-15)*. In addition, pneumococcal meningitis outbreaks have been reported in Central and West Africa for the past 20 years. Primarily caused by serotype 1, they typically demonstrate lower peak attack rates, but higher case fatality rates compared to meningococcal meningitis outbreaks *(19)*.

1.6.2 *Neisseria meningitidis*

Neisseria meningitidis, also known as meningococcus, is a leading cause of bacterial meningitis in children *(1)*. Six serogroups (A, B, C, W, X and Y) are responsible for over 95% of invasive meningococcal disease cases worldwide *(1)*. Meningococcal disease can present as a sporadic or epidemic-prone infection with varying degrees of endemicity. Outbreaks and epidemics of meningococcal disease are more likely to occur in settings that facilitate infection transmission, including regions with low vaccination coverage, overcrowded living conditions and mass gatherings, and areas with limited or disrupted access to health services (e.g. conflict-afflicted areas, refugee camps) *(19)*.

The incidence is particularly high in the African meningitis belt, a geographical region stretching from Senegal in the west to Ethiopia in the east, where outbreaks and epidemics are most common during the dry season (from December to June) *(20)*. Before the introduction of serogroup A conjugate meningococcal vaccination in routine immunization programmes, serogroup A was the most frequent causative agent, accounting for large-scale, recurrent epidemics every 8–12 years. Since 2017, serogroups C, W and X have been predominant, with seasonal epidemics generally smaller in size. In the Middle East, meningococcal disease outbreaks often occur in conflict settings or in relation to the Hajj and Umrah mass gatherings *(21, 22)*. In high-income countries (HICs) across North America, Europe and Oceania, serogroups B, C, W and Y are responsible for sporadic cases and small-scale outbreaks, with peak incidence in later winter and early spring *(23, 24)*.

Colonization of the nasopharynx is a prerequisite condition for the development of systemic infection. Additional risk factors for invasive disease include anatomical or functional asplenia, complement component deficiencies or inhibitors, and HIV infection *(25-30)*.

1.6.3 *Haemophilus influenzae*

Haemophilus influenzae remains a major cause of bacterial meningitis in children worldwide. Invasive disease, including meningitis, most frequently occurs in children under 5 years of age and is typically caused by encapsulated (or typable) strains *(1)*. Among the six serotypes identified, serotype b remains one of the most commonly associated with meningitis, although the widespread introduction of a serotype b conjugate vaccine in routine immunization programmes has led to a drastic decline in the incidence of invasive disease in the paediatric population. However, a growing number of cases caused by non-b serotypes and non-typeable strains have been reported *(31, 32)*.

1.6.4 *Streptococcus agalactiae*

Streptococcus agalactiae, also known as Group B *Streptococcus* (GBS), is part of the normal commensal bacterial flora of the gastrointestinal and genitourinary tracts. With 10 serotypes currently identified (Ia, Ib and II–IX), GBS is responsible for severe infections, including meningitis, in neonates and infants aged less than 3 months, pregnant and postpartum women, elderly individuals and people with underlying chronic conditions *(33)*.

1.6.5 *Listeria monocytogenes*

Listeria monocytogenes is a relatively common cause of meningitis and meningoencephalitis in immunocompromised individuals, pregnant women, people aged over 60 years and neonates. The bacterium is ubiquitous in nature, can be found in soil, water and animal digestive tracts, and is well known for its characteristic ability to survive and grow at refrigeration temperatures, which facilitates foodborne transmission (e.g. ready-to-eat food, dairy products, prepared salads, fresh vegetables and fruits) *(34)*.

1.6.6 Non-typhoidal salmonellae

Non-typhoidal salmonellae cause a broad range of clinical infections in humans through faecal–oral transmission, including bacteraemia, sepsis and meningitis. The greatest morbidity and mortality burden is in sub-Saharan Africa, where bacteraemia can occur in the form of sporadic or epidemic disease, with outbreaks more common during or immediately after the rainy season *(35)*. The risk of meningitis is higher among infants, individuals with HIV infection, and children with severe malarial anaemia, malnutrition, sickle cell disease or other hemoglobinopathies *(36)*.

1.6.7 Other bacteria

While not traditionally regarded as common causes of acute community-acquired meningitis, other bacterial infections may be considered in the differential diagnosis for individuals who live in endemic areas and/or have specific epidemiological risk factors. These include tuberculosis, brucellosis, leptospirosis, Lyme disease, syphilis and several rickettsioses (e.g. scrub typhus, epidemic typhus, endemic typhus, Rocky Mountain spotted fever).

Table 1.1 Etiology of acute bacterial meningitis, in descending order of frequency

Children (over 1 month) and adolescents	Non-immunocompromised adults	Immunocompromised adults or adults over 60 years
Neisseria meningitidis[a]	*Streptococcus pneumoniae*	*Streptococcus pneumoniae*
Streptococcus pneumoniae[a]	*Neisseria meningitidis*	*Neisseria meningitidis*
Haemophilus influenzae		*Listeria monocytogenes*
Non-typhoidal *Salmonella*		

[a] The relative prevalence of *N. meningitidis* and *S. pneumoniae* in children varies across geographic regions.

1.6.8 Viruses

Acute viral meningitis is usually associated with a better clinical prognosis and lower mortality compared to bacterial disease.

Enteroviruses, including Coxsackieviruses, echoviruses, non-polio enteroviruses and parechoviruses are the most common cause of viral meningitis *(37)*. Enteroviral meningitis may show a seasonal pattern, with incidence peaks in summer and fall in temperate regions and year-round transmission in tropical settings.

Herpes simplex virus (HSV), particularly HSV-2, is also a frequent agent of viral meningitis, followed by other herpesviruses, including varicella-zoster virus and, less commonly, Epstein-Barr virus and cytomegalovirus.

Moreover, sporadic cases and outbreaks of meningitis or meningoencephalitis worldwide can be caused by arboviruses. These include but are not limited to West Nile virus, Japanese encephalitis virus, tick-borne encephalitis virus, Toscana virus, St Louis encephalitis virus, La Crosse encephalitis virus, eastern equine encephalitis virus and western equine encephalitis virus.

Finally, acute meningitis can occur as a clinical manifestation with variable incidence of primary HIV infection, measles, mumps, influenza, COVID-19 and lymphocytic choriomeningitis.

1.7 Exclusion criteria

Given the significant differences in clinical manifestations and management strategies, the following disease categories are not addressed by the guidelines and are considered outside the scope of this publication:

- meningitis in newborns (0–28 days);
- hospital-acquired, nosocomial and health-care-associated meningitis;
- subacute and chronic meningitis, including tuberculous, cryptococcal and eosinophilic meningitis;
- non-infectious meningitis, including meningitis associated with drugs, malignancy and autoimmune diseases.

Guidance on the management of neonates with acute meningitis is provided in the *WHO pocket book of hospital care for children: guidelines for the management of common childhood illnesses (38).*

1.8 Related WHO publications and resources

The guidelines were developed in close conceptual and strategic synergy with related WHO guidelines, action plans, technical products and strategic initiatives (Box 1.1).

Box 1.1 WHO publications and resources

Pocket book of hospital care for children: guidelines for the management of common childhood illnesses, second edition (2013)

Meningitis outbreak response in sub-Saharan Africa (2014)

Managing meningitis epidemics in Africa (2015)

Framework on integrated, people-centred health services: report by the Secretariat (2016)

Priority assistive products list (2016)

mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings (Version 2.0) (2016)

Basic emergency care: approach to the acutely ill and injured: participant workbook (2018)

Roadmap for access to medicines, vaccines and health product 2019–2023: comprehensive support for access to medicines, vaccines and other health products (2019)

Defeating meningitis by 2030: a global road map (2021)

Hearing screening: considerations for implementation (2021)

World report on hearing (2021)

Global report on health equity for persons with disabilities (2022)

The WHO Aware (Access, Watch, Reserve) antibiotic book (2022)

WHO consolidated guidelines on tuberculosis: module 4: treatment: drug-susceptible tuberculosis treatment (2022)

WHO consolidated guidelines on tuberculosis: module 4: treatment: drug-resistant tuberculosis treatment, 2022 update

Intersectoral global action plan on epilepsy and other neurological disorders, 2022–2031 (2023)

Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders (2023)

Fourth WHO model list of essential in vitro diagnostics (2023)

WHO model lists of essential medicines [website] (2023)

Package of interventions for rehabilitation (2023)

Universal health coverage – fact sheet (2023)

WHO guidelines for malaria (2024)

2. Methodology

2. Methodology

The *WHO guidelines on meningitis diagnosis, treatment and care* were prepared in accordance with the WHO standards and methods for guideline development. Details of this approach can be found in the *WHO handbook for guideline development (39)*.

2.1 Guideline contributors

Full details for all contributors are provided in Annex 1.

2.1.1 WHO Steering Group

The WHO Steering Group was established to guide and oversee the guideline development process. The WHO Steering Group included WHO staff members from the Department of Mental Health, Brain Health and Substance Use, the Health Emergencies Programme, the Department of Immunization, Vaccines and Biologicals, and other relevant Divisions and Departments from WHO Headquarters and Regional Offices. The Steering Group suggested the scope of the guidelines; identified priority research areas; prepared the planning proposal; drafted the guideline questions; and determined the composition of the Guideline Development Group (GDG) and External Review Group (ERG).

2.1.2 Guideline Development Group

The GDG was assembled to be a diverse group of individuals with a wide range of expertise, including members with extensive relevant experience in clinical practice, research, health policy and guideline development, as well as people with lived experience. The GDG members were selected by the WHO Steering Group, with careful consideration of gender and geographic balance. Since these guidelines are primarily intended for low-resource settings, particularly in LMICs, information on country income (based on World Bank classification) was included to ensure that this aspect was adequately represented within the GDG membership.

Two co-chairs of the GDG were nominated by the WHO Steering Group and confirmed by the members of the GDG before the start of the first meeting. They were selected based on their previous experience with WHO GDGs as well as their understanding of WHO guideline development processes.

Specific tasks of the GDG included supporting the definition of the scope of the guidelines, examining and interpreting the evidence, formulating the recommendations and reviewing the draft document.

2.1.3 Systematic review teams

Six systematic review teams were selected based on their thematic and technical expertise. They conducted qualitative and quantitative systematic reviews and, to the extent possible, assessed the certainty of the evidence using standard systematic review and grading processes, as detailed in the *WHO handbook for guideline development (39)*. A WHO librarian assisted each team with their search to ensure consistency across all systematic reviews.

2.1.4 Guideline methodologist

A guideline methodologist was identified by the WHO Steering Group, ensuring expertise in the prioritization of questions and outcomes, evidence synthesis, rating the certainty of evidence through the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, translation of evidence into recommendations, and overall guideline development processes. The methodologist supported the planning, scoping and development of guideline questions and assisted the GDG in formulating evidence-informed recommendations in a transparent and explicit manner.

2.1.5 External Review Group

The ERG included individuals with technical expertise in clinical practice, research and health policy as well as people with lived experience. The proposed members were identified by the WHO Steering Group, with careful consideration of gender, geographic and country-level income representation. The ERG reviewed the draft guidelines to identify errors or gaps in evidence and to provide feedback on clarity, context-specific issues and implementation implications. The group was not expected to change the recommendations formulated by the GDG. Comments from external reviewers were incorporated as appropriate and the final draft was circulated to the GDG.

2.2 Declarations of interest and confidentiality agreements

In accordance with the WHO procedures for declarations of interests (DOIs), all members of the GDG and ERG were asked to declare in writing any competing interests (academic, financial or other) at the time of the invitation to participate in the guideline development process. The standard WHO DOI form and confidentiality agreement forms were completed, signed by each expert and sent electronically to the WHO Technical Team prior to participation in the guideline development process. Biographies of proposed GDG members were also displayed on the WHO website for public consultation.

In addition to the DOI forms, curriculum vitae and short biographies were received and reviewed by the WHO Technical Team to determine if any conflict of interest existed and a note for the record was prepared. The list of declared interests and relevant notes was updated throughout the process to reflect any newly declared interests. A summary of declared interests of GDG and ERG members is available in Annex 2.

2.3 Evidence retrieval, appraisal and synthesis

Evidence retrieval, appraisal and synthesis followed the methods outlined in the *WHO handbook for guideline development (39)*.

2.3.1 Systematic review methods

Evidence supporting the content of the guidelines was extracted from several sources by the systematic review teams and the guideline methodologist, in collaboration with the WHO Technical Team and the WHO librarian. The systematic review teams developed standard

protocols for each guideline question, set criteria for identification of studies (including search strategies for different bibliographic databases), outlined methods for assessing the risk of bias and defined a data analysis plan before embarking on evidence retrieval and appraisal. The protocols were reviewed by the guideline methodologist, the WHO Technical Team and members of the WHO Steering Group. The evidence from the reviews was retrieved according to standard operating procedures, format and timelines provided by the WHO Steering Group and the guideline methodologist. The systematic review methods used for each guideline question are detailed in the quantitative evidence reports in Web Annex A and in the qualitative and economic evidence reports in Web Annex B.

2.3.2 Evidence appraisal

Quantitative evidence

A briefing note as well as report templates were provided by the WHO Technical Team to ensure a consistent approach to quantitative evidence appraisal across the systematic review teams. The GRADE approach to rating the certainty of quantitative evidence was used for all critical outcomes identified in the guideline questions, and a GRADE evidence profile was prepared for each outcome *(40)*.

The certainty of the evidence for each outcome was rated as "high", "moderate", "low" or "very low", as defined in Table 2.1. A body of evidence based on randomized controlled trials (RCTs) was rated as being of high certainty at the outset, while evidence from non-randomized trials and observational studies was considered of low certainty. For both types of studies, the initial ratings could be downgraded based on five factors: limitations in study design and execution (risk of bias); indirectness; imprecision; inconsistency; and publication bias. The risk of bias was assessed at the level of the individual study and across studies, while the other four factors were assessed for each outcome across all included studies.

For RCTs, the Cochrane Risk of Bias 2 (RoB 2) tool was used by the systematic review teams to assess the risk of bias *(41)*. The following characteristics were considered the distinguishing features of the RCTs that yield the best quality evidence:

- random sequence generation
- concealment of allocation to treatment group
- blinding of participants and investigators
- reporting of data on all study participants, including attrition and exclusions from analysis
- complete reporting of all study outcomes that were specified *a priori*.

For observational studies, different tools were used to assess the risk of bias based on the study design (e.g. ROBINS-I for prospective cohort studies with comparator and QUADAS-2 for diagnostic accuracy studies). The main features yielding the best quality results were categorized as follows:

- application of appropriate eligibility criteria
- use of an unbiased approach to measurement of exposure and outcomes
- adequate control for confounding
- documentation and consideration of differential withdrawals of study participants across treatment groups.

Table 2.1 The certainty of evidence used in GRADE

High	High level of confidence that the true effect lies close to the estimate of the effect.
Moderate	Moderate level of confidence in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Limited confidence in the effect estimate: the true effect may be substantially different from the estimate of the effect.
Very low	Very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.

Qualitative evidence

A qualitative evidence synthesis focused on end users' values and experiences of diagnosis, treatment and long-term care for meningitis and addressed factors influencing the uptake of related health services. The qualitative evidence synthesis team used the GRADE CERQual (Confidence in the Evidence from Reviews of Qualitative Research) tool to assess the confidence in qualitative review findings *(42)*.

Economic evidence

A scoping review was undertaken to compile information regarding costs and resource utilization associated with the diagnosis, treatment and management of sequelae of acute community-acquired meningitis associated with the diagnosis, treatment and management of sequelae of acute community-acquired meningitis.

2.3.3 Evidence synthesis

For each guideline question, the systematic review team produced an evidence report, which summarized the relevant findings from the systematic review and qualitative evidence synthesis (Web Annex A and Web Annex B). Where possible, outcomes were presented as a meta-analysis. If this was not possible, a narrative description of findings was provided. The WHO Technical Team reviewed the evidence reports and developed the relevant sections of the GRADE Evidence-to-Decision (EtD) frameworks, in collaboration with the guideline methodologist (Web Annex C).

Evidence-to-Decision framework

The GRADE EtD frameworks include explicit and systematic considerations of evidence on interventions across specified domains *(39, 40)*. The domains on desirable effects, undesirable effects, certainty of the evidence of effects, and balance between desirable and undesirable effects were primarily informed by the quantitative evidence reviews. By contrast, the qualitative evidence synthesis and the scoping economic review were used for the domains of values and preferences of intended users, resource requirements, certainty of the evidence of resource requirements, cost-effectiveness, impact on health equity, equality and non-discrimination, feasibility, and alignment with human rights principles and sociocultural acceptability. The evidence reports and the EtD frameworks were subsequently presented to the GDG (section 2.4).

2.4 Decision-making during GDG meetings

2.4.1 GDG meetings

Four GDG meetings were conducted between May 2023 and June 2024. The first GDG meeting was held in person in Geneva, Switzerland on 15–17 May 2023, and was followed by a virtual meeting on 16 June 2023. During the first meeting, the GDG agreed on the scope of the guidelines and formulated 20 guideline questions according to the PICO (population, intervention, comparator, outcome) format *(39)*. The guideline questions covered several aspects of meningitis diagnosis, antimicrobial therapy, adjunctive treatment, supportive care and sequelae management, and informed the work of the systematic review teams in the following months.

The next in-person GDG meeting took place in Geneva between 30 April and 3 May 2024, and was followed by an online meeting on 15 May 2024. In advance of the meeting, the evidence reports, the EtD frameworks and additional relevant materials for each guideline question were provided to the GDG members. During the meeting, the systematic review teams presented the summary of findings for each question. Under the leadership of the GDG co-chairs, the GDG members came to a consensus on the judgement for each domain of the EtD framework while providing additional input and technical considerations. Based on available evidence as well as their knowledge and experience, the GDG formulated the recommendations and agreed on the strength of the recommendations and overall certainty of evidence. The draft of each recommendation was made by consensus, defined as full agreement among all GDG participants, when possible. If GDG members were unable to reach a consensus, the decision was put to a vote. A recommendation or decision stood if a large majority (more than two thirds of the participants) voted in support of it. Voting was done by a show of hands (physical and/or electronic depending on the meeting format). The WHO Steering Group, systematic review teams, guideline methodologist and meeting observers did not participate in the voting process.

2.4.2 Types of recommendations

Two types of guidance are presented in the guidelines.

- Recommendations: These recommendations were formulated by the GDG using the GRADE approach and are supported by systematic reviews of the evidence, with a formal assessment of the certainty of evidence.
- Good practice statements: These statements reflect a consensus within the GDG that the net benefits of adhering to the statement are large and unequivocal, and that the implications of the statement are common sense. They typically represent situations in which a large body of indirect evidence, often composed of several bodies of evidence linked together in the causal pathway, unequivocally demonstrates the net benefit of the recommended action. Systematic reviews of the evidence were therefore not conducted.

2.4.3 Strength of recommendation

In addition to considering the certainty of evidence on benefits and harms and their relative effect, the strength of the recommendation was influenced by the contextual factors considered in the EtD framework. Each recommendation was classified as strong or conditional, for or against an intervention, according to the GRADE approach *(39)*.

- Strong recommendation: A strong recommendation is one for which the GDG was confident that the desirable effects of adhering to the recommendation outweighed the undesirable effects. A strong recommendation for an intervention indicates that most individuals should receive the intervention and it can be adopted as policy in most circumstances. The same rationale applies in reverse for strong recommendations against an intervention.
- Conditional recommendation: A conditional recommendation is one for which the GDG concluded that the desirable effects of adhering to the recommendation probably outweighed the undesirable effects, but the GDG was not confident about these trade-offs or identified specific conditions under which the recommendation applies. A conditional recommendation for an intervention indicates that different choices would be appropriate for different individuals and policy-making would require substantial debate among different stakeholders.

Strong recommendations when the evidence is of low or very low certainty

The GDG used caution and provided thorough justifications when formulating strong recommendations based on low- or very-low-certainty evidence. In accordance with the *WHO handbook for guideline development*, the GDG considered five specific situations in which strong recommendations may be indicated despite low or very low confidence in effect estimates *(39)*:

- life-threatening situation
- uncertain benefit, certain harm
- potentially equivalent options, one clearly less risky or costly than the other
- high confidence in benefits being similar, but one option potentially more risky or costly than the other
- potential catastrophic harm.

2.5 Document preparation and peer review

Following the outlined processes, the WHO Technical Team circulated proposed recommendations to the GDG members and the WHO Steering Group for additional input and feedback. The WHO Technical Team drafted the guideline document, including recommendations and supporting evidence, and circulated it electronically to the ERG for review. The full draft was subsequently shared with the GDG and WHO Steering Group. All comments from the GDG, WHO Steering Group and ERG were collated and incorporated as appropriate.

The recommendations are presented in separate sections within Chapter 3, in line with the thematic categories of the guidelines: A. Diagnosis, B. Treatment and C. Management of sequelae.

3. Recommendations

3. Recommendations

A. Diagnosis

The diagnosis of acute meningitis is established through a combination of clinical features, cerebrospinal fluid (CSF) and blood test results. Lumbar puncture and CSF examination remain the mainstay of meningitis diagnosis.

A.1 Lumbar puncture

Good practice statement

In individuals with suspected acute meningitis, lumbar puncture should be performed as soon as possible, preferably before the initiation of antimicrobial treatment, unless there are specific contraindications or reasons for deferral.

Justification

Examination of the CSF provides crucial information for the differential diagnosis of meningitis, allows the identification of the causative pathogen and guides therapeutic decisions.

A lumbar puncture can be performed safely in most cases. Nevertheless, some complications may occur, even when the standard technique is used and adequate infection prevention and control measures are undertaken *(43, 44)*. The most serious yet rare complication of lumbar puncture is cerebral herniation in the presence of increased intracranial pressure. Other complications include headache, infection, bleeding, back pain, radicular pain, intracranial hypotension and pneumocephalus *(43, 44)*.

A.1.1 Contraindications and deferral

Certain conditions are associated with an increased risk of complications following lumbar puncture. Lumbar puncture should not be performed in the presence of any of the following:

- known or suspected bleeding diathesis or disorder;
- skin or soft tissue infection or suspected spinal epidural abscess overlying or localized within close proximity to the lumbar puncture site;
- hemodynamic or respiratory compromise that requires clinical stabilization.

Furthermore, lumbar puncture can increase the risk of cerebral herniation and incur harm in individuals with raised intracranial pressure, including those with severe cerebral oedema and/or a space-occupying lesion with midline shift (e.g. brain abscess, subdural empyema, large cerebral infarction, brain neoplasm or metastasis) *(45)*. The incidence of cerebral herniation can be reduced by identifying individuals who are at particular risk and deferring lumbar puncture accordingly. This topic is further addressed in section A.4.

A.2 Cerebrospinal fluid investigations

A.2.1 Opening pressure and macroscopic appearance

CSF pressure is generally measured when performing lumbar puncture in the lateral decubitus position. Some forms of meningitis, including acute bacterial meningitis, can lead to an increased CSF opening pressure due to cerebral oedema and/or impaired CSF secretion or reabsorption.

When a lumbar puncture is performed, the appearance of the CSF should be visually inspected. Acute bacterial meningitis most often presents with a turbid or cloudy CSF, primarily due to the abundant presence of white blood cells (WBCs). A clear CSF can be observed in normal conditions, but it is also consistent with a wide range of infectious diseases, including viral meningitis.

A.2.2 Initial laboratory investigations

Laboratory investigations of CSF specimens are crucial to support or confirm the clinical suspicion of acute meningitis. Initial tests include Gram stain, cell count, glucose, protein and lactate concentration.

Gram stain on CSF samples is a well-known, validated test that can indicate the presence of a bacterial pathogen before culture results are available. However, the quality of the exam depends primarily on laboratory capacity and available infrastructural resources.

Normally, the CSF is acellular. In adults, up to five leukocytes per microlitre (µl) are considered normal, while thresholds are higher for infants and young children. The presence of an abnormal increase in the CSF WBC concentration usually indicates the underlying presence of an inflammatory state. Moreover, up to five red blood cells (RBCs) per µl are considered normal in adults, with higher thresholds among infants and young children. The presence of an abnormal increase of RBCs may indicate recent bleeding.

Glucose concentration in the CSF is variable and strictly depends on the glucose concentration in the peripheral blood (or serum). The normal CSF-to-blood glucose ratio ranges between 0.5 and 0.8, while values equal to or lower than 0.4 are considered abnormally low *(46, 47).*

Proteins are not normally present in high concentrations in the CSF. However, in the context of pathologic alterations that disrupt the blood–brain barrier, proteins can gain access to the CSF. Elevations of protein concentration (over 45 mg/dl) can be found in acute meningitis as well as in other inflammatory, obstructive and bleeding central nervous system disorders.

Lactate concentration in the CSF may be elevated in several central nervous system disorders, including infectious meningitis, and has been proposed as a tool to distinguish between bacterial and viral meningitis.

In individuals with suspected acute meningitis, should cerebrospinal fluid tests (i.e. Gram stain, white blood cell count and differential, glucose, total protein, lactate) be performed?

Strong recommendation for

In individuals with suspected acute meningitis, Gram stain should be performed on cerebrospinal fluid samples.

Strong recommendation. Moderate certainty of evidence.

Strong recommendation for

In individuals with suspected acute meningitis, cerebrospinal fluid investigations should be performed to determine white blood cell count (total and differential), protein concentration, glucose concentration and the cerebrospinal fluid to blood glucose ratio.

Strong recommendation. Moderate certainty of evidence.

Conditional recommendation for

In individuals with suspected acute meningitis, cerebrospinal fluid lactate levels should be considered when antibiotic therapy has not yet been administered.

Conditional recommendation. Moderate certainty of evidence.

Justification

The GDG indicated that lumbar puncture and CSF investigations including Gram stain, cellularity and biochemical analyses are paramount for meningitis diagnosis and emphasized their role in differentiating acute bacterial meningitis from other forms of acute meningitis, including viral meningitis.

Overall, 27 studies addressing the diagnostic accuracy of initial CSF investigations were included in the systematic review of the evidence *(5, 48-73)*. The majority of CSF tests showed at least moderate sensitivity and specificity for the diagnosis of acute bacterial meningitis.

- CSF Gram stain likely has moderate to high sensitivity (85%, 95% confidence interval [CI] 55–96%; 6 studies; high-certainty evidence) and very high specificity (99%; 1 study; moderate-certainty evidence) for the diagnosis of acute bacterial meningitis. Additional evidence showed excellent specificity and varying sensitivity, depending on the bacterial pathogen.
- CSF WBC count has moderate sensitivity (77%, 95% CI 74–81%; 12 studies; high-certainty evidence) and moderate to high specificity (83%, 95% CI 75–92%; 12 studies; high-certainty evidence).
- CSF neutrophil count likely has moderate to high sensitivity (82%, 95% CI 70–94%; 10 studies; moderate-certainty evidence) and moderate to high specificity (84%, 95% CI 77–90%; 10 studies; high-certainty evidence).
- CSF total protein concentration has moderate to high sensitivity (86%, 95% CI 80–92%, 12 studies; high-certainty evidence) and moderate specificity (79%, 95% CI 70–88%, 12 studies; high-certainty evidence).

- CSF glucose concentration may have moderate to low sensitivity (66%, 95% CI 52–79%; 8 studies; low-certainty evidence), while it has moderate to high specificity (85%, 95% CI 72–98%; 8 studies; high-certainty evidence).
- CSF-to-blood glucose ratio has moderate to high sensitivity (88%, 95% CI 83–93%; 6 studies; high-certainty evidence), while it likely has moderate specificity (78%, 95% CI 52–100%; 6 studies; moderate-certainty evidence).
- CSF lactate concentration has high sensitivity (94%, 95% CI 91–98%; 6 studies; high-certainty evidence) and moderate to high specificity (86%, 95% CI 74–98%; 6 studies; high-certainty evidence).

While the systematic review focused on the diagnostic performance of individual CSF tests, the GDG highlighted the need to advocate for widespread, combined use of CSF Gram stain, WBC count, and glucose and protein levels, which can assist the differential diagnosis with results available in a relatively short turnaround time. Based on their clinical knowledge, the GDG also agreed to recommend the simultaneous measurement of blood glucose concentration to enable calculation of CSF-to-blood glucose ratio.

The GDG emphasized that the use of CSF lactate is strongly affected by the prior use of antibiotics. In resource-limited settings, people often receive antibiotic therapy before presenting to a health-care facility, thus limiting the clinical value of CSF lactate. As a result, the GDG issued a conditional recommendation for the use of CSF lactate only when no prior antibiotic therapy is administered.

Finally, the GDG discussed the variability in comparator groups across studies. Most studies used CSF culture, CSF polymerase chain reaction (PCR) and/or clinical characteristics as reference standards. While concerns about the heterogeneity of comparator groups across studies were raised, the GDG considered the overall certainty of evidence as moderate.

Full details of the evidence are provided in Web Annex A (1. Initial cerebrospinal fluid investigations). The EtD framework for this guideline question is available in Web Annex C.

Remarks

CSF Gram stain, WBC count (total and differential), and protein and glucose concentration have varying sensitivity and specificity. However, none of these tests can be used alone to confirm or rule out a diagnosis of meningitis.

A combined, integrated approach to the interpretation of CSF findings is required to mitigate and minimize the risks associated with the diagnostic performance of individual tests (i.e. risk of false negatives and/or false positives).

The diagnostic yield of these CSF laboratory investigations may decrease when antimicrobial treatment is initiated prior to lumbar puncture.

Normal WBC count and protein concentration may be higher in infants and young children than in older age groups, emphasizing the importance of using age-appropriate threshold values.

When performing a Gram stain on CSF samples, the following results may be observed and inform clinical decision-making:

- Gram-positive diplococci suggest pneumococcal infection.
- Gram-negative diplococci suggest meningococcal infection.

- Gram-negative coccobacilli are consistent with *H. influenzae* infection.
- Gram-positive bacilli or coccobacilli suggest *Listeria* infection.

Classic CSF characteristics of acute bacterial meningitis caused by pyogenic pathogens include WBC pleocytosis with neutrophilic predominance, low glucose concentration, low CSF-to-serum glucose ratio and high protein concentration (Table 3.1).

CSF lactate levels may contribute to differentiating between bacterial and viral meningitis. However, the diagnostic value and clinical applications of CSF lactate are limited after the initiation of antibiotic administration or in the presence of other central nervous system diseases in the differential diagnosis.

The presence of RBCs in CSF samples should be investigated as it may indicate traumatic lumbar puncture or acute subarachnoid haemorrhage.

Table 3.1 Typical CSF abnormalities in bacterial and viral meningitis

Bacterial meningitis	Viral meningitis
Increased opening pressure	Normal or mildly elevated opening pressure
Turbid or cloudy appearance	Clear appearance
Marked leukocyte pleocytosis	Moderate leukocyte pleocytosis
Neutrophilic predominance	Lymphocytic predominance
Low CSF-to-blood glucose	Normal CSF-to-blood glucose
Markedly increased protein	Normal or mildly increased protein
Increased lactate (prior to antibiotics)	Normal lactate

Implementation considerations

CSF Gram stain, leukocyte count (absolute and differential), and protein and glucose concentration are included in the *WHO model list of essential in vitro diagnostics (74)*.

The availability of adequate clinical capacity (e.g. trained health workforce) and laboratory infrastructure across all levels of the health system is required to facilitate access to lumbar puncture and meningitis diagnostic tests.

A context-appropriate laboratory testing strategy with well-defined pathways for sample collection, storage and analysis should be established and implemented. In resource-limited settings, CSF laboratory investigations should be widely accessible in peripheral health facilities. Where not available, CSF samples should be collected and appropriately transported to higher-level laboratories.

Research gaps

Given the increasing availability of point-of-care tests in resource-limited settings, more studies should be conducted to assess and evaluate their diagnostic performance and clinical role in meningitis diagnosis.

The GDG highlighted the need for further research to investigate the additive or incremental value of each CSF test and understand which test should be given priority in resource-constrained settings.

Antigen detection tests, including latex agglutination tests and lateral flow assays, are not included as part of these recommendations (Box 3.1). They can support meningitis diagnosis by providing results quickly, although a positive test should always be confirmed with culture or molecular testing to establish a definitive diagnosis with pathogen identification. Further studies are needed to evaluate their diagnostic performance, particularly in field conditions, and support their widespread use in clinical settings.

Additional evidence on the clinical applications of novel diagnostics, including host biomarkers and metagenomic techniques, is required to improve prompt and accurate identification of meningitis and overcome current diagnostic challenges in low-resource settings, such as the need for an invasive procedure or long turnaround times.

Box 3.1 Antigen detection tests

Antigen detection tests for meningitis include latex agglutination tests and lateral flow assays and generally provide results within 20–30 minutes against a subset of potential causative pathogens. A positive test result from any antigen detection test should be confirmed with culture or molecular testing to establish a definitive diagnosis.

A.2.3 Culture

Good practice statement

In individuals with suspected acute meningitis, cerebrospinal fluid culture and antimicrobial susceptibility testing remain the gold standard for bacterial pathogen identification.

Justification

Based on their clinical knowledge and experience, the GDG agreed that culture on CSF specimens should be regarded as the gold standard test for the diagnosis of bacterial meningitis and should always be accompanied by antimicrobial susceptibility testing (AST).

CSF collection should ideally be performed as soon as possible, as the diagnostic yield of culture decreases when CSF is collected after the initiation of antimicrobial treatment *(75)*. Culture-based tests require good-quality laboratory infrastructure for isolation and biosafety and are usually conducted on blood agar and/or chocolate agar plates *(76)*.

AST methods should be performed as described in internationally recognized guidelines, such as those provided by the Clinical and Laboratory Standards Institute (CLSI) (https://clsi.org) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (http://www.eucast.org/) *(76)*. Notably, CLSI and EUCAST provide specific breakpoints for certain antimicrobials targeting pathogens that cause meningitis, including *S. pneumoniae*, *N. meningitidis*, *H. influenzae*, *L. monocytogenes* and *S. agalactiae*. This accounts for the generally reduced penetration of antimicrobials across the blood–CSF barrier, even in the presence of inflammation *(77)*. Therefore, when interpreting AST results, breakpoints relevant to the treatment of bacterial meningitis should be specifically considered *(78, 79)*.

CSF culture and AST are included in the *WHO model list of essential in vitro diagnostics (74)*.

A.2.4 Molecular testing

PCR methods have emerged as highly sensitive and specific tests that can be used to detect bacterial or viral DNA and identify the causative pathogen. Available PCR platforms include single-target (singleplex) or multitarget (multiplex) panels, with several tests providing results in less than two hours. Molecular tests require electrically powered instruments, advanced laboratory infrastructure and skilled laboratory technicians.

In individuals with suspected acute meningitis, should cerebrospinal fluid PCR be performed?

Strong recommendation for

In individuals with suspected acute meningitis, PCR-based molecular tests for relevant pathogens should be performed on cerebrospinal fluid samples.

Strong recommendation. Low certainty of evidence.

Justification

Individual PCR testing is highly sensitive and specific across the most common bacterial pathogens, including *S. pneumoniae*, *N. meningitidis* and *H. influenzae* type b, while the diagnostic performance is lower for enteroviruses. Multiplex PCR testing demonstrates an overall high diagnostic yield, but sensitivity and specificity may vary substantially based on the causative pathogen and setting. The potential for false positives and false negatives remains, especially for certain bacterial pathogens.

Based on available evidence and their clinical knowledge and experience, the GDG agreed to make a strong recommendation for the use of PCR-based tests. They also highlighted that both singleplex and multiplex PCR should be considered, and the choice should be made based on available technical and infrastructural resources. In addition, given the varying diagnostic performance of PCR, they highlighted the importance of interpreting results based on the concurrent clinical presentation and laboratory findings.

Full details of the evidence are provided in Web Annex A (2a and 2b. Cerebrospinal fluid molecular testing). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Results of PCR-based tests on CSF should be interpreted in the context of clinical presentation (i.e. medical history, symptoms and signs) and additional laboratory findings (e.g. CSF characteristics, Gram stain and culture).

The diagnostic yield of CSF PCR tests for bacterial pathogens may decrease when antimicrobial treatment is initiated prior to lumbar puncture or sample transportation and preservation practices are suboptimal.

CSF culture and AST should not be replaced by PCR and should be routinely performed as the gold standard tests for pathogen identification and characterization of antibiotic resistance profiles. Where resources permit, blood cultures along with AST should also be performed in individuals with suspected acute meningitis.

Implementation considerations

The availability of adequate clinical capacity (e.g. trained health workforce) and laboratory infrastructure across all levels of the health system is required to facilitate access to lumbar puncture and diagnostic tests for meningitis.

In resource-limited settings, molecular testing, including PCR, may only be performed in one or few reference or specialized laboratories nationwide. As a result, in peripheral health facilities where such testing is not routinely available, CSF samples should be collected and appropriately transported to higher-level laboratories in a timely manner. For this purpose, a context-appropriate laboratory network and testing strategy should be established and implemented.

Research gaps

The GDG highlighted the importance of enhancing global efforts to develop quality-assured molecular assays that can inform clinical decision-making and improve access to meningitis diagnosis worldwide.

The GDG emphasized the need for further research on the diagnostic performance of CSF PCR for multiple pathogens using a combination of clinical judgment, CSF characteristics and CSF culture as the reference standard.

The majority of studies identified by the systematic review were conducted in resource-rich settings. Further research on the clinical applications and diagnostic performance of molecular tests for meningitis diagnosis should be conducted in resource-limited contexts.

Loop-mediated isothermal amplification (LAMP) assays are an alternative nucleic acid amplification method, known for their ease of use and short turnaround time *(80)*. While LAMP-based assays for *S. pneumoniae*, *N. meningitidis* and *H. influenzae* have been established, this is an area of active research and development *(81-84)*.

A.3 Blood investigations

Blood tests can serve as a valuable tool to support or corroborate the diagnosis of meningitis in addition to CSF investigations or when lumbar puncture cannot be performed.

A.3.1 Culture

Good practice statement

In individuals with suspected acute meningitis, blood cultures should be obtained as soon as possible, preferably before the initiation of antibiotic therapy.

Justification

Blood cultures serve as a confirmatory laboratory test for identifying causative bacterial pathogens and determining their antimicrobial susceptibility patterns. Therefore, when bacterial meningitis is suspected, blood cultures should be performed immediately, preferably before antibiotic treatment.

The sensitivity of blood culture among individuals with bacterial meningitis varies depending on the bacterial species and is higher in cases of pneumococcal meningitis *(85)*. In addition, the diagnostic yield of blood culture may be substantially reduced when blood culture is obtained after the initiation of antibiotic therapy *(75, 86)*.

Furthermore, blood culture and AST can be particularly useful if CSF cannot be collected before the administration of antibiotics or lumbar puncture is contraindicated.

Blood cultures and AST are included in the *WHO model list of essential in vitro diagnostics (74)*.

A.3.2 Markers of bacterial infection

In the presence of an acute-onset infectious disease, including meningitis, serum levels of inflammatory markers, such as C-reactive protein (CRP), are often increased. In addition, an elevated count of peripheral WBCs with neutrophil predominance and high serum procalcitonin (PCT) levels can suggest an underlying bacterial infection.

In individuals with suspected acute meningitis, should white blood cell count, C-reactive protein and/or procalcitonin be performed on peripheral blood samples?

Conditional recommendation for

In individuals with suspected acute meningitis, peripheral white blood cell count (total and differential) should be considered where resources allow.

Conditional recommendation. Low certainty of evidence.

Conditional recommendation for

In individuals with suspected acute meningitis, C-reactive protein or procalcitonin should be considered where resources allow.

Conditional recommendation. Moderate certainty of evidence.

Justification

Based on available evidence and their clinical knowledge and experience, the GDG highlighted that peripheral WBC count, CRP and PCT may serve as important diagnostic tools in settings where resources permit.

Overall, 22 studies addressing the diagnostic accuracy of peripheral WBC count, CRP and/or PCT were included in the systematic review of the evidence *(52-55, 57, 59-64, 66, 68, 87-95)*. Specifically, low-certainty evidence showed that WBC count may have moderate to low sensitivity (68%, 95% CI 59–78%; 12 studies) and moderate specificity (74%, 95% CI 69–79%; 12 studies) for the diagnosis of acute bacterial meningitis. By contrast, neutrophil count was associated with higher sensitivity (89%, 95% CI 84–92%; 2 studies; moderate-certainty evidence) and lower specificity (58%, 95% CI 33–84%; 2 studies; low-certainty evidence). High-certainty evidence showed that CRP has moderate to high sensitivity (82%, 95% CI 74–89%; 15 studies) and specificity (84%, 95% CI 77–92%;

15 studies). Similarly, PCT has moderate to high sensitivity (87%, 95% CI 75–98%; 13 studies) and specificity (86%, 95% CI 79–93%; 13 studies).

The GDG acknowledged that most studies included in the systematic review used non-bacterial meningitis as a comparator, whereas other bacterial systemic infections without central nervous system involvement were not considered.

Full details of the evidence are provided in Web Annex A (3. Blood markers of bacterial infection). The EtD framework for this guideline question is available in Web Annex C.

Remarks

None of the included peripheral blood tests can be used to confirm or exclude the diagnosis of bacterial meningitis and lumbar puncture should not be deferred or delayed based on their results.

WBC count (total and differential), CRP or PCT should not be performed in isolation and results should be interpreted in the context of clinical presentation (i.e. medical history, symptoms and signs) and CSF characteristics.

Both CRP and PCT may have a role in differentiating acute bacterial meningitis from other forms of meningitis. Given the lack of evidence comparing C-reactive protein to procalcitonin for the diagnosis of acute bacterial meningitis or regarding the incremental diagnostic value of C-reactive protein and procalcitonin when used in combination, these tests may be used individually.

The decision on whether to choose CRP or PCT (or both) should be based on resources and local availability. When CRP is measured, quantitative CRP assays should be preferred over qualitative assays, since serum levels can be monitored and used as a marker of clinical response to treatment.

Implementation considerations

Complete blood count, CRP and PCT are included in the *WHO model list of essential in vitro diagnostics (74)*.

Where feasible, these tests can be conducted in primary health-care settings. However, the GDG acknowledged that resource constraints may constitute an important barrier to their implementation. These tests should only be performed when resources allow and should not be regarded as alternatives to CSF investigations.

Research gaps

Further research is required comparing the diagnostic performance of serum CRP and PCT. In addition, the incremental diagnostic value of performing both serum CRP and PCT should be investigated.

Moreover, studies on the clinical applications of novel diagnostics, including host biomarkers, are needed to differentiate among different central nervous system disorders. In this context, research on biomarkers with short turnaround times and minimal implementation barriers in resource-limited settings should be prioritized.

A.3.3 Additional testing

Blood (or serum) glucose measurement is required immediately before lumbar puncture to accurately determine the CSF-to-blood (or CSF-to-serum) glucose ratio.

Coagulation studies, including platelet count, prothrombin time and activated partial thromboplastin time may be useful in the presence of purpuric or petechial lesions or when DIC is suspected (e.g. purpura fulminans).

Serum electrolytes and organ function tests, including creatinine, blood urea nitrogen, bilirubin and transaminases may be helpful as part of the initial assessment or when septic shock and/or multiorgan failure are suspected. In the *WHO model list of essential in vitro diagnostics*, whole blood lactate is also recommended to assess metabolic acidosis, sepsis and/or hypovolemia *(74)*.

In malaria-endemic settings, cerebral malaria may present with clinical features similar to acute meningitis. According to the *WHO guidelines for malaria*, all cases of suspected malaria should have a parasitological test (microscopy or rapid diagnostic test) to confirm the diagnosis *(96)*. However, in settings with moderate to high malaria transmission and areas with intensely seasonal transmission, symptomatic malaria is usually confined to young children, whereas adolescents and adults rarely exhibit severe clinical manifestations, despite being infected with low parasite densities *(96)*. Therefore, while a positive test for malaria confirms malaria infection and warrants antimalarial treatment, it does not necessarily rule out a concurrent diagnosis of meningitis.

HIV infection is a cause of acute meningitis, serves as a risk factor for invasive pneumococcal and meningococcal disease and may be considered in individuals with suspected meningitis *(28, 30, 97, 98)*. In the presence of advanced HIV disease, the clinical management of individuals with meningitis requires a tailored approach, taking into consideration the most common causative agents, including *Cryptococcus neoformans* and *Mycobacterium tuberculosis*. According to WHO's *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring,* HIV testing should be offered to all populations in settings with high HIV burden *(99)*. Conversely, HIV testing should be offered to selected populations in settings with low HIV burden, including children and adults with symptoms and signs that could indicate HIV infection, HIV-exposed children, key populations and their partners, as well as pregnant women *(99)*.

Disease-specific serology testing on blood and/or CSF samples is particularly useful when certain bacterial or viral infections are suspected (e.g. syphilis, Lyme disease, leptospirosis, brucellosis, rickettsioses, and several arboviral diseases).

Molecular tests performed on whole-blood specimens are an area of current research and development. Although the evidence on blood PCR tests was not appraised as part of these guidelines, they may be included in the battery of blood tests performed when acute bacterial meningitis is suspected (where resources allow). However, when lumbar puncture is not contraindicated, all tests performed on blood should be considered as an adjunct to CSF investigations (rather than an alternative) and not contribute to lumbar puncture delays.

A.4 Cranial imaging

In individuals with meningitis, a causal association between lumbar puncture and cerebral herniation is difficult to ascertain because the latter may occur as a disease complication, regardless of lumbar puncture. Nonetheless, the risk of cerebral herniation following lumbar

puncture is higher in the presence of severe cerebral oedema and/or space-occupying lesions with midline shift, which can be detected through cranial imaging (e.g. computed tomography [CT] scan) *(45)*.

In individuals with suspected acute meningitis, should clinical characteristics be used to predict the presence on cranial imaging of intracranial abnormalities associated with increased risk of adverse events secondary to lumbar puncture?

Strong recommendation against

In individuals with suspected acute meningitis, cranial imaging should not be performed routinely.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

Where cranial imaging is readily accessible:

Cranial imaging should be performed prior to lumbar puncture to rule out cerebral space-occupying lesions with midline shift, if any of the following features are identified at time of presentation:

- Glasgow Coma Score below 10
- focal neurological signs
- cranial nerve deficits
- papilloedema
- new-onset seizures (in adults)
- severe immunocompromised state.

Strong recommendation. Very low certainty of evidence.

Strong recommendation against

Where cranial imaging is not readily accessible:

Lumbar puncture should be deferred if any of the following features are present at time of presentation and until they have resolved:

- Glasgow Coma Score below 10
- focal neurological signs
- cranial nerve deficits
- papilloedema
- new-onset seizures (in adults)
- severe immunocompromised state.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

Treatment should not be delayed for cranial imaging or when lumbar puncture is deferred.

Strong recommendation. Very low certainty of evidence.

Justification

The GDG highlighted that a causal relationship between lumbar puncture and subsequent severe adverse events may be challenging to define since brain herniation can also occur among individuals with acute bacterial meningitis who do not undergo lumbar puncture. However, it was emphasized that lumbar puncture may be associated with an increased risk of brain herniation in the presence of severe cerebral oedema and/or space-occupying lesions (e.g. brain abscess, subdural empyema) with midline shift, which can be detected on cranial imaging. Therefore, the identification of clinical characteristics that can be associated with these intracranial abnormalities may contribute to reducing the risk of brain herniation following lumbar puncture.

One prospective cohort study was considered as indirect evidence *(100)*. Conducted in adults with clinically suspected meningitis, the study indicated that several factors may be associated with *any* abnormal finding on cranial imaging, including age of 60 years or older (risk ratio [RR] 4.3, 95% CI 2.9–6.4), an immunocompromised state (RR 1.8, 95% CI 1.1–2.8), a history of central nervous system disease (RR 4.8, 95% CI 3.3–6.9), seizures within one week before presentation (RR 3.2, 95% CI 2.1–5.0), an abnormal level of consciousness (RR 3.3, 95% CI 2.2–4.4), inability to answer two consecutive questions correctly (RR 3.8, 95% CI 2.5–5.8), gaze palsy (RR 3.2, 95% CI 1.9–5.4), abnormal visual fields (RR 4.0, 95% CI 2.7–5.9), facial palsy (RR 4.9, 95% CI 3.8–6.3), arm drift (RR 4.0, 95% CI 2.7–5.8), leg drift (RR 4.4, 95% CI 3.0–6.5) and abnormal language (i.e. aphasia, dysarthria or extinction; RR 4.3, 95% CI 2.9–6.5).

Based on this study, as well as the GDG's clinical knowledge and experience, a set of clinical criteria was defined to select at-risk individuals (children and adults) who require cranial imaging before lumbar puncture to rule out the presence of cerebral space-occupying lesions with midline shift. These criteria include Glasgow Coma Score below 10, focal neurological signs, cranial nerve deficits, papilloedema, new-onset seizures (in adults) and/or severe immunocompromised state. Where cranial imaging is not readily accessible, lumbar puncture should be deferred until these features have resolved.

The GDG emphasized that cranial imaging should not be routinely performed in individuals who are not at risk, given its limited added value in determining the risk of brain herniation combined with the potential for significant delays in treatment initiation, especially in resource-limited settings. Furthermore, the GDG also considered additional indirect evidence showing that lumbar puncture without a prior CT was associated with lower rates of mortality, neurological and/or hearing deficits, and functional impairment as compared with lumbar puncture after CT.

Finally, based on their clinical expertise, the GDG further highlighted that lumbar puncture deferral and cranial imaging should not contribute to any delays in treatment initiation.

Full details of the evidence are provided in Web Annex A (4. Cranial imaging). The EtD framework for this guideline question is available in Web Annex C.

Remarks

When lumbar puncture is deferred, blood samples (including blood cultures) should be collected and antimicrobial treatment started as soon as possible, prior to cranial imaging.

Seizures are a common finding in febrile children suspected of having acute meningitis. New-onset isolated seizures in children do not require cranial imaging prior to lumbar puncture when they occur in the absence of any other at-risk features.

Severe immunocompromised state (e.g. organ transplantation) should warrant lumbar puncture deferral. However, for people living with HIV suspected of having a first episode of cryptococcal meningitis, prompt lumbar puncture with measurement of opening pressure and rapid cryptococcal antigen assay is recommended as the preferred diagnostic approach *(99)*.

Implementation considerations

Most clinical characteristics for at-risk individuals can be assessed through a medical history, physical examination and fundoscopy (where available).

Cranial imaging modalities (e.g. CT scan) and specialized clinical expertise (e.g. neurologists, radiologists) are required to accurately detect cerebral space-occupying lesions with midline shift and determine the associated risk of brain herniation following lumbar puncture. Multisectoral interventions for strengthening health systems should therefore be planned and implemented at the national level to enhance access to cranial imaging.

Research gaps

Well-designed observational studies are required to investigate whether additional clinical characteristics can be used in children and adults with suspected acute meningitis to predict the presence of intracranial abnormalities on cranial imaging associated with brain herniation following lumbar puncture.

B. Treatment

B.1 General management

Good practice statement

Children and adults with suspected acute meningitis should be immediately admitted or urgently transferred to an appropriate health-care facility for further management.

Justification

Acute meningitis is a medical emergency that requires prompt diagnosis and urgent care. Individuals where acute meningitis is suspected are managed based upon the initial evaluation, including clinical history, physical examination, CSF characteristics and blood test results. Therefore, the GDG agreed that children and adults with suspected acute meningitis should be immediately admitted or urgently transferred to an appropriately equipped health-care facility where lumbar puncture can be performed and adequate monitoring and management of severe illness can be ensured. The term "health-care facility" was preferred over "hospital" to better capture the differences in service provision and levels of care across countries and regions.

The most appropriate setting for inpatient care (general medical or paediatric ward versus intensive care unit) is determined by the severity of illness, available resources and clinical capacity. Intensive care units may be indicated for people with hemodynamic or respiratory compromise, seizures, altered mental status or other life-threatening complications, including DIC, septic shock or multiorgan failure.

Establishment of a reliable vascular access among hospitalized children and adults is a critical step to ensure appropriate supportive measures and intravenous drug administration. Supportive measures may be required, depending on disease severity and level of care, including adequate hemodynamic support for individuals presenting with shock (e.g. septic shock), prompt respiratory support (e.g. oxygen therapy) for individuals with hypoxemia or respiratory failure, and treatment of metabolic disturbances (e.g. hypoglycaemia, electrolyte abnormalities). Fluid management and treatment of acute symptomatic seizures are discussed below (sections B.5 and B.6, respectively).

B.2 Antimicrobial treatment

Acute bacterial meningitis is a medical emergency. Therefore, empiric antimicrobial treatment is warranted when a bacterial origin is suspected based on the epidemiological risk, medical history, clinical manifestations and initial CSF characteristics.

B.2.1 General principles

Individuals requiring antimicrobial therapy for acute bacterial meningitis should be treated with parenteral antibiotics (in line with the guideline recommendations). Once admitted to an appropriate health-care facility, intravenous administration is the recommended option. Oral antimicrobials should be avoided since the CSF concentrations achieved tend to be significantly lower compared to parenteral agents *(101, 102)*.

Antimicrobial penetration into the CSF largely depends on the status of the blood–brain barrier *(103)*. Maximal intravenous doses are required throughout the therapeutic course to achieve and maintain appropriate drug concentrations in the CSF. Specific dosing recommendations are used for the treatment of bacterial meningitis, with higher doses often required compared to other infections.

Given the impaired humoral immune response in the CSF, optimal microbiologic cure requires antimicrobial agents that can exert a bactericidal effect locally. Clinical observations underscore the significance of this approach, with poor outcomes associated with bacteriostatic treatment regimens *(101, 102)*.

In individuals with suspected acute meningitis, should empiric antimicrobial treatment be provided as soon as possible?

Conditional recommendation for

In children and adults presenting with suspected acute meningitis, empiric parenteral antimicrobial treatment before admission or transfer to an appropriate health-care facility should be considered.

Conditional recommendation. Very low certainty of evidence.

Strong recommendation for

In children and adults with suspected acute meningitis admitted to an appropriate health-care facility, empiric intravenous antimicrobial treatment should be administered as early as possible.

Strong recommendation. Very low certainty of evidence.

Justification

As antibiotics remain the mainstay of treatment, the GDG agreed on the critical importance of formulating recommendations on the timing of empiric therapy, including before and after admission or transfer to an appropriate health-care facility. The terms "pre-hospital" and "early in-hospital" were employed further below to reflect the settings of studies included in the systematic review. However, while formulating the recommendations, "health-care facility" was preferred over "hospital" to better capture the differences in service provision and levels of care across countries and regions. In line with the rest of the guidelines, an appropriate health-care facility was defined as an appropriately equipped health-care facility where lumbar puncture can be performed and adequate monitoring and management of severe illness can be ensured.

Before admission or transfer to an appropriate health-care facility:

- Two prospective cohort studies assessed the effect of antimicrobial treatment prior to hospital admission (pre-hospital therapy) *(104, 105)*. Very-low-certainty evidence showed that the effect of pre-hospital therapy is uncertain on mortality (RR 0.68, 95% CI 0.29–1.63; 2 studies), hearing loss (RR 2.98, 95% CI 1.09–8.13; 1 study), and paresis (RR 2.21, 95% CI 0.93–5.25; 1 study). However, the GDG acknowledged that the estimates favouring no pre-hospital treatment are probably linked to admission delays in the pre-hospital treatment group (median of 3 days in the intervention arm versus median of 1 day in the comparator).

- Based on the overall body of direct and indirect evidence and their clinical knowledge and experience, the GDG agreed to issue a conditional recommendation on empiric therapy prior to admission or transfer to an appropriate health-care facility. Specifically, they emphasized that the benefits of parenteral antibiotics may outweigh the undesirable consequences in selected settings, especially where bacterial meningitis is strongly suspected and a clinically significant delay in admission, transfer or referral is considered likely. On the other hand, the GDG clearly indicated that antibiotic therapy should never delay hospital admission or transfer and referral efforts.
- While the optimal route of antibiotic administration is intravenous, the GDG highlighted that intramuscular administration should be used when intravenous options are not available.

After admission or transfer to an appropriate health-care facility:

- One prospective cohort study conducted in adults assessed the effect of early in-hospital antimicrobial treatment (3 hours or less) compared to delayed treatment (more than 3 hours) *(106)*. Low-certainty evidence showed that early in-hospital antimicrobial treatment is associated with lower mortality rates (RR 0.34, 95% CI 0.20–0.58).
- Based on the overall body of direct and indirect evidence and their clinical knowledge and experience, the GDG recommended that intravenous antibiotic therapy be given as early as possible upon admission, transfer or referral to an appropriate health-care facility. They also highlighted that empiric antimicrobial treatment should ideally be initiated after lumbar puncture and blood sampling but any delay in or deferral of diagnostic investigations should not delay therapy administration.
- The opportunity to specify a time point for intravenous antibiotic administration upon admission was also discussed. Given the inconsistency of time points used across studies, the GDG decided to recommend treatment initiation as soon as possible and acknowledged that the "1-hour window" is often considered the golden hour for medical emergencies, including acute bacterial meningitis.

Full details of the evidence are provided in Web Annex A (5. Timing of empiric antimicrobial treatment). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Before admission or transfer to an appropriate health-care facility:

- Parenteral antimicrobial treatment may be beneficial where acute bacterial meningitis is strongly suspected and a clinically significant delay in transfer or referral is considered likely.
- Antimicrobial treatment should be administered intravenously. If intravenous administration is not possible and/or an intravenous line is not secured, intramuscular administration should be pursued.

After admission or transfer to an appropriate health-care facility:

- Intravenous antimicrobial treatment should be given as soon as acute bacterial meningitis is suspected. The "1-hour window" is generally regarded as the golden time period to initiate empiric antibiotic therapy.
- Lumbar puncture, in the absence of contraindications or reasons for deferral, and blood tests should be performed prior to initiating empiric antimicrobial treatment. However, any delay in diagnostic investigations should not delay therapy administration.

- In the absence of contraindications or reasons for deferral, individuals who have received antimicrobial treatment before admission should undergo lumbar puncture as soon as possible once they are admitted in an appropriate health-care facility.
- Adequate clinical monitoring within an appropriate health-care facility is warranted when antimicrobial treatment is administered to an individual with known severe antibiotic allergy.

Recommendations on the choice of empiric antimicrobial regimen are provided in section B.2.2.

B.2.2 Empiric treatment regimens

In individuals with suspected or probable acute bacterial meningitis, should empiric treatment with parenteral ceftriaxone or cefotaxime combined with additional antimicrobials be used rather than monotherapy with ceftriaxone or cefotaxime?

Strong recommendation for

In children and adults with suspected or probable acute bacterial meningitis, intravenous ceftriaxone or cefotaxime should be administered as empiric treatment.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

In the presence of one or more risk factors for *Listeria monocytogenes* infection (i.e. age over 60 years, pregnancy, immunocompromised state), intravenous ampicillin or amoxicillin should be administered in addition to the initial antimicrobial regimen.

Strong recommendation. Very low certainty of evidence.

Conditional recommendation for

In areas with high prevalence of penicillin or third-generation cephalosporin resistance of *Streptococcus pneumoniae*, intravenous vancomycin should be considered in addition to the initial antimicrobial regimen.

Conditional recommendation. Very low certainty of evidence.

Justification

Acute bacterial meningitis is a life-threatening disease associated with high rates of morbidity and mortality, including long-term complications and disability. As antibiotic therapy remains the mainstay of treatment, the GDG emphasized the critical importance of formulating recommendations on empiric treatment, even in the absence of comparative studies addressing the guideline question. Thus, the GDG agreed to make recommendations primarily based on available indirect evidence as well as their clinical knowledge and experience.

The GDG indicated that antibiotic selection in individuals with suspected or probable acute bacterial meningitis should be tailored to the most likely causative pathogens based on the person's age and specific risk factors.

The most common causative agents in various age groups were discussed, including *S. pneumoniae*, *N. meningitidis*, *H. influenzae* and, among children aged 1–3 months, *S. agalactiae*. Selected third-generation cephalosporins generally possess potent activity against these pathogens and have adequate cerebrospinal fluid penetration. Therefore, intravenous ceftriaxone or cefotaxime were recommended as the initial empiric treatment regimen for children aged over 1 month and adults.

The GDG emphasized some practical benefits of using ceftriaxone over cefotaxime, including its wider availability in resource-limited settings and longer half-life, which allows twice daily administration and resource optimization. In addition, ceftriaxone was shown to be effective in eradicating nasopharyngeal carriage of *N. meningitidis* and to contribute to reducing infection transmission during meningococcal and pneumococcal meningitis epidemics *(107)*. Therefore, ceftriaxone was indicated as first-line agent for empiric monotherapy among suspected and probable cases of meningitis during epidemics of meningococcal and pneumococcal disease.

Listeria monocytogenes is a Gram-positive pathogen that shows intrinsic resistance to third-generation cephalosporins, including ceftriaxone and cefotaxime, and can cause meningitis or meningoencephalitis, especially among people with one or more risk factors *(108, 109)*. Based on available evidence, people at risk comprise individuals aged over 60 years, pregnant women and immunocompromised hosts. These include people who receive long-term corticosteroid therapy or other immunosuppressive treatment, have undergone organ transplantation, are affected by hematologic or solid malignancies, advanced HIV disease, diabetes mellitus, end-stage kidney disease, advanced chronic liver disease and/or alcohol use disease. Thus, in the presence of any of these risk factors, intravenous ampicillin or amoxicillin should be part of the initial antimicrobial regimen (e.g. in addition to ceftriaxone or cefotaxime), in order to provide adequate antimicrobial coverage against *Listeria* infection.

The GDG discussed the clinical and public health importance of penicillin-resistant or third-generation cephalosporin-resistant strains of *S. pneumoniae* and agreed to recommend that intravenous vancomycin be added to the initial antimicrobial regimen in settings with demonstrated high prevalence of penicillin or cephalosporin resistance among pneumococcal isolates. The GDG also considered the variability in clinical practice, especially in high-resource environments, where rifampicin or linezolid may be used in place of vancomycin. Given the risk of antimicrobial resistance among individuals with tuberculosis infection or disease following rifampicin exposure, the GDG agreed that in contexts with high tuberculosis burden, rifampicin can be used only when vancomycin is not available or contraindicated.

Full details of the evidence are provided in Web Annex A (6. Empiric antimicrobial treatment regimen, Part 1). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Ceftriaxone or cefotaxime are equally recommended as first-line agents for empiric treatment among suspected and probable cases of acute bacterial meningitis. However, intravenous ceftriaxone should be preferred over cefotaxime during meningococcal and pneumococcal disease epidemics.

Ampicillin or amoxicillin should be added to the initial empiric antimicrobial regimen in the presence of any of the following risk factors for *L. monocytogenes* infection:

- age over 60 years
- pregnancy
- immunosuppressive therapy
- organ transplantation
- malignancy
- advanced HIV disease
- diabetes mellitus
- end-stage kidney disease
- liver cirrhosis
- alcohol use disease.

Prevalence thresholds to define settings at risk for penicillin or cephalosporin resistance of *S. pneumoniae* should be defined at the national and/or sub-national level. In areas with known high prevalence of penicillin or cephalosporin resistance of *S. pneumoniae*, intravenous vancomycin would provide adequate antimicrobial coverage against resistant strains. In settings with low tuberculosis burden, rifampicin can be used as an alternative to vancomycin. In settings with high tuberculosis burden, rifampicin can be used only when vancomycin is not readily available or contraindicated.

To mitigate the risk of antimicrobial resistance and ensure appropriate use of second-line antibiotic agents, beta-lactam allergies should be thoroughly investigated before making a treatment decision. Cephalosporins can be safely used in most cases of non-severe penicillin allergy, and vice versa. In cases of previous life-threatening reactions caused by the exposure to beta-lactams, any use of beta-lactams should be avoided.

Implementation considerations

All recommended antibiotics are included in the *WHO model list of essential medicines*, which provides a list of safe and effective antimicrobial drugs that should be available and affordable everywhere (https://list.essentialmeds.org/) *(110)*.

All recommended antibiotics are included in the *WHO AWaRe (access, watch, reserve) antibiotic book*, which provides guidance on the best use and dosing of antibiotics for bacterial meningitis based on the principles of the AWaRe classification of antibiotics *(8)*.

Research gaps

Epidemiological studies on penicillin or cephalosporin resistance of *S. pneumoniae*, including prevalence trends and patterns, are urgently required, especially in resource-limited settings and in the African meningitis belt region.

In individuals with suspected or probable acute bacterial meningitis, should parenteral antimicrobial regimens (penicillin [i.e. benzylpenicillin, ampicillin, amoxicillin] or chloramphenicol alone or in combination) be used rather than monotherapy with ceftriaxone or cefotaxime?

Conditional recommendation for

In children and adults with suspected or probable acute bacterial meningitis, intravenous chloramphenicol with benzylpenicillin, ampicillin or amoxicillin should only be considered for empiric treatment when ceftriaxone or cefotaxime are not immediately available.

Conditional recommendation. Very low certainty of evidence.

Justification

Third-generation cephalosporins are the mainstay of empiric treatment for acute bacterial meningitis. However, the GDG acknowledged that ceftriaxone and cefotaxime might not be immediately available, accessible or affordable in some resource-limited settings and agreed to make a recommendation on alternative antibiotic regimens for suspected and probable cases.

Overall, 20 RCTs compared alternative parenteral antimicrobial regimens (i.e. penicillins and/or chloramphenicol) to ceftriaxone or cefotaxime monotherapy in children and adults *(111-130)*. Very-low-certainty evidence showed that the effect of alternative parenteral antibiotics compared to ceftriaxone or cefotaxime is uncertain on mortality (RR 1.02, 95% CI 0.68–1.53; 13 RCTs), time to fever resolution (MD 0.75 days, 95% CI 0.26–1.24; 12 RCTs), neurological sequelae (RR 1.11, 95% CI 0.88–1.41; 13 RCTs) and adverse events (RR 0.70, 95% CI 0.46–1.04; 10 RCTs). No data were available on the subgroups of interest, including pregnant women, elderly or immunocompromised individuals.

The GDG highlighted that most included studies were conducted up to four decades before publication of these guidelines and compared ceftriaxone or cefotaxime to combinations of alternative antibiotics (i.e. chloramphenicol and one of the following: benzylpenicillin, ampicillin or amoxicillin). Given the changes over time in the resistance profiles among the most common bacterial pathogens, the GDG highlighted the limited applicability of these results to current clinical practices and expressed concern about the use of benzylpenicillin, ampicillin or amoxicillin monotherapy in settings with high prevalence of *N. meningitidis* isolates with reduced penicillin susceptibility, penicillin-resistant *S. pneumoniae* or beta-lactamase-producing *H. influenzae*. Similarly, the GDG was concerned about the use of chloramphenicol alone where resistance among *S. pneumoniae* or *N. meningitis* isolates is common. They therefore decided to make a conditional recommendation on combined antibiotic therapy (i.e. chloramphenicol and one of the following: benzylpenicillin, ampicillin or amoxicillin) in cases where ceftriaxone or cefotaxime are not immediately available.

Full details of the evidence are provided in Web Annex A (7. Empiric antimicrobial treatment regimen, Part 2). The EtD framework for this guideline question is available in Web Annex C.

Remarks

In settings with low vaccination coverage for *H. influenzae* type b, intravenous amoxicillin or ampicillin should be preferred over benzylpenicillin for combined empiric treatment (i.e. in association with chloramphenicol).

To mitigate the risk of antimicrobial resistance and ensure appropriate use of second-line antibiotic agents, beta-lactam allergies should be thoroughly investigated before making a treatment decision. In cases of previous life-threatening reactions caused by the exposure to beta-lactams, any use of beta-lactams should be avoided.

Implementation considerations

All recommended antibiotics are included in the *WHO model list of essential medicines*, which provides a list of safe and effective antimicrobial drugs that should be available and affordable everywhere (https://list.essentialmeds.org/) *(110)*.

All recommended antibiotics are included in the *WHO AWaRe (access, watch, reserve) antibiotic book*, which provides guidance on the best use and dosing of antibiotics for bacterial meningitis based on the principles of the WHO AWaRe classification of antibiotics *(8)*.

During large-scale meningococcal disease epidemics, when ceftriaxone is not available and a longer treatment course is considered impractical or not feasible, one or two intramuscular injections of long-acting chloramphenicol might be used for suspected cases aged over 2 years (where available). In these circumstances, however, the person should be reviewed at 24 and 48 hours and treatment should be extended in the absence of clinical improvement.

In settings where allergy testing, specialist advice or treatment for anaphylaxis are not available, pragmatic decisions should be based on a detailed history of any reported possible penicillin allergy *(8)*. People with a definite history of immediate collapse, breathing difficulties or severe facial swelling within a few minutes to 1–2 hours of taking an antibiotic of the penicillin class are likely to have had a true anaphylactic reaction. If any alternative antibiotics are available, they are preferred. Individuals who have only had gastrointestinal symptoms or a rash appearing a few days after receiving an antibiotic of the penicillin group and who have shown no signs of becoming seriously unwell are generally less likely to develop severe anaphylaxis if they are administered such antibiotics again in the future. Therefore, if one of these antibiotics is the most appropriate and available treatment option, it can be given with the advice to stop if the person develops a new skin rash, especially if the onset is rapid, the rash is raised and itchy and/or accompanying symptoms are present, such as shortness of breath.

Research gaps

Epidemiological studies on penicillin or chloramphenicol resistance of most common bacterial pathogens are required, especially in resource-limited settings and in the African meningitis belt region.

B.2.3 Empiric treatment duration

The overall treatment duration may depend upon the isolated pathogen (section B.2.4). However, if the causative agent remains unknown, the treatment duration varies based on the epidemiological setting as well as several host factors, as outlined below.

In non-epidemic settings, in individuals with suspected or probable acute bacterial meningitis, in the absence of pathogen identification, should empiric antimicrobial treatment be administered for 10 days compared to a shorter or longer treatment course?

Conditional recommendation for

In non-epidemic settings, in children and adults with suspected or probable acute bacterial meningitis and no pathogen identification, discontinuation of empiric antibiotic therapy may be considered after 7 days if the person has clinically recovered.

Conditional recommendation. Very low certainty of evidence.

Justification

Overall, two RCTs conducted in children addressed the guideline question and compared a 10-day antibiotic therapy regimen to shorter regimens *(131, 132)*. Low-certainty evidence indicated that empiric antibiotic treatment for 10 days compared to empiric treatment for less than 10 days may result in little to no difference on all-cause mortality (RR 0.96, 95% CI 0.28–3.27; 1 study), disease relapse (RR 0.86, 95% CI 0.31–2.38; 1 study) and disease complications, including neurological sequelae, hearing loss and hydrocephalus (RR 0.85, 95% CI 0.58–1.23; 2 studies).

No studies comparing 10 days of treatment with longer regimens were included in the systematic review. However, based on the body of indirect evidence as well as their clinical knowledge and experience, the GDG emphasized that longer treatment regimens may be more likely associated with adverse events, including drug toxicity, hospital-acquired infections and other complications of hospitalization.

Using the available evidence and their expertise, the GDG decided to make a recommendation suggesting a 7-day antibiotic regimen for empiric treatment, conditional upon clinical recovery. While the RCTs were conducted only in children, the GDG highlighted that the duration of antimicrobial treatment for most infectious diseases does not vary depending on age (except for neonates) and agreed that the above-mentioned evidence could be extrapolated to formulate a recommendation for adults while considering the certainty of evidence as very low.

Full details of the evidence are provided in Web Annex A (8. Duration of empiric antimicrobial treatment in non-epidemic settings). The EtD framework for this guideline question is available in Web Annex C.

Remarks

All efforts should be made to identify and characterize the causative pathogen on blood and CSF samples through culture and molecular tests (e.g. PCR).

When the pathogen remains unknown, empiric antibiotic therapy can be discontinued after 7 days, provided that the person has clinically recovered. Clinical recovery may be indicated by the presence of *all* of the following for at least 48 hours:

- resolution of fever
- resolution of vital sign abnormalities (blood pressure, heart rate, respiratory rate, oxygen saturation)

- resolution of altered consciousness
- normal mental status.

In the absence of clinical recovery within one week of empiric treatment, antibiotic therapy should be extended and accompanied by an appropriate diagnostic work-up, including a repeat lumbar puncture if there are no contraindications.

Research gaps

Further studies are needed to investigate and evaluate the compliance with and effectiveness of recommended empiric treatment in high- and low-resource settings.

In epidemic settings, in cases with suspected or probable acute bacterial meningitis, should empiric treatment with parenteral ceftriaxone be administered for 5 days compared to an alternative treatment course duration?

Strong recommendation for

During meningococcal disease epidemics, empiric treatment with parenteral ceftriaxone should be administered for 5 days to children and adults with suspected or probable meningococcal meningitis.

Strong recommendation. Very low certainty of evidence.

Conditional recommendation for

During pneumococcal disease epidemics, empiric treatment with parenteral ceftriaxone for 10 days should be considered for children and adults with suspected or probable pneumococcal meningitis.

Conditional recommendation. Very low certainty of evidence.

Justification

The epidemiological landscape of epidemic-prone meningitis has changed over the past decade, with non-serogroup A *N. meningitidis* and, less often, *S. pneumoniae* responsible for the majority of epidemics within and outside the African meningitis belt region. Therefore, the GDG emphasized the critical importance of providing specific recommendations for meningococcal and pneumococcal epidemics, including antibiotic treatment duration for suspected and probable cases. Given the absence of studies directly addressing the guideline question, the GDG agreed to make recommendations primarily based on the body of indirect evidence, as well as their clinical knowledge and experience.

During invasive meningococcal disease epidemics, the currently recommended antibiotic treatment for suspected and probable cases of meningococcal meningitis is a 5-day course with parenteral ceftriaxone for both children and adults aged 2 months and older *(4)*. Although single-dose ceftriaxone can be effective, a minority, albeit significant proportion (5–15%) of laboratory-confirmed cases during meningococcal meningitis outbreaks is often caused by *S. pneumoniae*

and/or *H. influenzae*, which are generally associated with a higher risk of mortality and long-term neurological complications *(4)*. In line with previous recommendations, the GDG thus highlighted the benefits of a 5-day antibiotic regimen over single-dose therapy, including decreased mortality, morbidity and risk of antimicrobial resistance. In addition, the GDG considered these benefits to outweigh the risk of adverse effects, complications due to hospitalization and higher costs, and they agreed to issue a strong recommendation despite the very-low-certainty evidence.

During invasive pneumococcal disease epidemics, the duration of antibiotic treatment for suspected and probable cases of pneumococcal meningitis should reflect the duration generally recommended for laboratory-confirmed cases (i.e. 10–14 days). While considering the potential challenges in operationalizing relatively longer treatment regimens in resource-limited settings during outbreaks, the GDG agreed to issue a conditional recommendation indicating 10 days as probably the most appropriate default duration. This treatment course would also provide adequate coverage against other common bacterial pathogens, including *N. meningitidis* and *H. influenzae*.

Full details of the evidence are provided in Web Annex A (9. Duration of empiric antimicrobial treatment in epidemic settings). The EtD framework for this guideline question is available in Web Annex C.

Remarks

During meningococcal and pneumococcal disease epidemics, intravenous ceftriaxone is the preferred administration option. If intravenous administration is not immediately feasible, intramuscular ceftriaxone should be given.

During meningococcal and pneumococcal disease epidemics, in the absence of clinical recovery, empiric treatment can be extended, and further diagnostic investigations should be performed.

Implementation considerations

Ceftriaxone should be used at maximum dosage and administered every 12 hours in an inpatient setting. When this is not feasible or considered impractical (e.g. during large-scale epidemics), once daily administration is acceptable provided that the same daily dosage is maintained. If the person is clinically stable and can return to the health facility every day, they can be discharged and given parenteral ceftriaxone at full dose once daily to complete treatment in an outpatient setting.

During large-scale meningococcal disease epidemics in settings with weak infrastructure or health services stretched to capacity, it may not be feasible to maintain a 5-day treatment regimen for all suspected cases. Under these circumstances, single-dose treatment protocols may be implemented, provided that there is laboratory confirmation that the epidemic is caused by *N. meningitidis,* and the person can be reviewed after 24 and 48 hours. In the absence of clinical recovery, the person should be hospitalized, and empiric treatment extended (at least 5 days in adults and children aged over 1 month).

During meningococcal or pneumococcal disease epidemics, antibiotic treatment should be provided free of charge in government health services *(4, 20)*.

Surveillance and monitoring of resistance trends and patterns, including among asymptomatic nasopharyngeal carriers, should be implemented during outbreaks.

Research gaps

Further studies are needed to investigate and evaluate the compliance with and effectiveness of recommended treatment protocols for outbreak response.

Box 3.2 WHO case definition

Throughout the guidelines, the term "case" has a clinical implication and refers to an individual with suspected, probable or confirmed meningitis as determined by the treating clinician.

On the other hand, standard case definitions of bacterial meningitis, meningococcal disease and pneumococcal disease are used for surveillance purposes and are not intended to be employed by health-care providers as the sole basis for establishing a clinical diagnosis or guiding clinical management. However, they may be used to streamline clinical operations in very resource-limited settings, during large-scale epidemics and in humanitarian emergencies.

When formulating the recommendations for outbreak and epidemic settings, the GDG strongly emphasized the urgent need to revise and update the WHO standard case definitions. While this task falls outside the scope of these guidelines, WHO is actively undertaking efforts to address this need and develop a derivative technical product.

B.2.4 Specific treatment

In accordance with the *WHO AWaRe Antibiotic Book*, the antimicrobial treatment regimen should be reviewed and modified according to culture and antimicrobial susceptibility results *(8)*. This approach aims to prevent or minimize the inappropriate use of broad-spectrum antibiotics and the emergence of drug-resistant pathogens. To this end, the spectrum of antimicrobial coverage may be narrowed or changed as appropriate and unnecessary components of the initial empiric regimen discontinued (Table 3.2). Moreover, antibiotic therapy should be optimized when the clinical presentation and results of the CSF Gram stain are unequivocal (e.g. if Gram-negative diplococci are seen, *N. meningitidis* is the likely pathogen).

Box 3.3 Appropriate use of antibiotics

As soon as a bacterial pathogen is isolated and antimicrobial susceptibility testing results are known, antibiotic therapy should be reviewed and optimized accordingly.

If a viral pathogen is confirmed as the causative agent through molecular tests or serology, empiric antib iotic treatment can generally be discontinued. Most common viral infections do not require specific therapy, except herpes virus and HIV meningitis *(99, 133, 134)*.

Notably, the overall treatment duration, including empiric and specific therapy, partially depends on the pathogen, although it may substantially vary based on the local epidemiology, clinical characteristics, disease severity and underlying chronic conditions (e.g. immunosuppression) *(8)*. The advised duration of treatment illustrated in Table 3.2 is primarily based on empiric data and routine clinical practice standards.

Table 3.2 Specific antibiotic therapy for the most common causes of community-acquired acute bacterial meningitis[a]

Pathogen	Specific therapy	Overall duration
Streptococcus pneumoniae		10–14 days
Penicillin-susceptible	Penicillin G *or* ampicillin *or* amoxicillin	
Penicillin-resistant	Ceftriaxone *or* cefotaxime	
Cephalosporin-resistant	Vancomycin + rifampicin, *or*	
	Vancomycin + ceftriaxone/cefotaxime, *or*	
	Rifampicin + ceftriaxone/cefotaxime	
Neisseria meningitidis		5–7 days
Penicillin-susceptible	Penicillin G *or* ampicillin *or* amoxicillin	
Penicillin-resistant	Ceftriaxone *or* cefotaxime	
Haemophilus influenzae		7–10 days
Beta-lactamase-negative	Ampicillin *or* amoxicillin	
Beta-lactamase-positive	Ceftriaxone *or* cefotaxime	
Streptococcus agalactiae	Penicillin G *or* ampicillin *or* amoxicillin	14–21 days
Listeria monocytogenes	Penicillin G *or* ampicillin *or* amoxicillin	21 days

[a] The choice of antibiotic regimen must be based on antimicrobial susceptibility test results.

B.2.5 Post-exposure prophylaxis

The risk of meningococcal infection is increased 400- to 800-fold in individuals in close contact to an index case, with the highest risk for household contacts *(107)*. Although the definition of "close contact" has not been universally established and may vary across different settings, post-exposure antibiotic prophylaxis is widely used to prevent secondary cases and/or decrease asymptomatic nasopharyngeal carriage of meningococcal infection *(135)*.

Should antibiotic prophylaxis be provided to close contacts of cases of meningococcal disease?

Strong recommendation for

In the presence of sporadic disease, antibiotic prophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin should be provided to close contacts of laboratory-confirmed cases of meningococcal disease, in accordance with known antimicrobial susceptibility patterns.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

During large-scale epidemics, antibiotic prophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin should be provided to close contacts of clinically suspected cases of meningococcal disease, in accordance with known antimicrobial susceptibility patterns.

Strong recommendation. Very low certainty of evidence.

Conditional recommendation for

Rifampicin should be considered when ceftriaxone or ciprofloxacin cannot be administered.

Conditional recommendation. Very low certainty of evidence.

Justification

A systematic review was conducted to investigate the efficacy and safety of antibiotic prophylaxis among close contacts of cases of meningococcal disease. A cluster randomized trial and a prospective cohort study directly addressed the guideline question *(136, 137)*. The cluster randomized trial was conducted in Niger during a meningococcal disease outbreak and used single-dose ciprofloxacin in the intervention arms *(136)*. The prospective cohort study was conducted in the USA and used rifampicin, minocycline or sulphonamide *(137)*.

Very-low-certainty evidence from both studies showed that the effect of antibiotic prophylaxis for close contacts on secondary cases of meningococcal disease is uncertain (RR 0.47, 95% CI 0.10–2.15). When considering only the trial conducted in the African meningitis belt, very-low-certainty evidence suggested that the effect of chemoprophylaxis for household contacts with single-dose ciprofloxacin remains uncertain (RR 0.85, 95% CI 0.65–1.12).

Given the study design, the intervention used, the target population and the study setting, the GDG underscored the critical relevance of additional findings from the cluster randomized trial *(136)*. While acknowledging the uncertain effect of chemoprophylaxis on the prevention of secondary cases when given to household contacts, they highlighted the protective effect when administered village-wide (adjusted attack rate ratio 0.40, 95% CI 0.19–0.87). Moreover, individual-level protective effectiveness of 82% (crude attack rate ratio 0.18, 95% CI 0.10–0.33) was demonstrated when comparing all persons in the study area who received ciprofloxacin (in-household and village-wide prophylaxis arms) to all persons who did not receive ciprofloxacin.

The GDG agreed that the potential clinical benefit of chemoprophylaxis may also be derived from studies that address the eradication of nasopharyngeal carriage through antimicrobials. Therefore, they discussed the evidence from the systematic review by Zalmanovici et al. (2013), which assessed the effect of chemoprophylaxis on carriage eradication *(107)*. Specifically, rifampicin (RR 0.20, 95% CI 0.14–0.29) and ciprofloxacin (RR 0.03, 95% CI 0.00–0.42) were shown to be effective in eradicating carriage compared to placebo at 1–2 weeks. In addition, ceftriaxone was shown to be more effective than rifampicin (RR 5.93, 95% CI 1.22–28.68) in eradicating carriage after 1–2 weeks of follow-up. Eleven trials reported the susceptibility of persistent isolates to at least one of the studied antibiotics, with no development of resistance detected for any antibiotic, except for rifampicin in three studies *(107)*.

Based on available evidence and their knowledge and experience, the GDG agreed to recommend chemoprophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin for close contacts of meningococcal disease cases. However, the increasing incidence of cases caused by ciprofloxacin-resistant strains in several regions worldwide raises concerns about potential prophylaxis failure, particularly in areas with high levels of ciprofloxacin resistance. Consequently, antibiotic selection should be guided by the antimicrobial susceptibility patterns prevalent within the community and potentially adjusted as necessary based on susceptibility testing results from index cases. Finally, the GDG agreed that rifampicin should be considered an alternative option when ceftriaxone or ciprofloxacin are contraindicated or not available.

The potential benefits of chemoprophylaxis are possibly larger when antimicrobials are administered to close contacts of laboratory-confirmed cases, underscoring the need to obtain laboratory confirmation in the presence of sporadic disease. Conversely, the GDG acknowledged that the majority of cases during large-scale epidemics are non-laboratory confirmed and recommended that close contacts of strongly suspected cases receive chemoprophylaxis. In the presence of small-scale outbreaks, the GDG agreed that antimicrobials be provided to close contacts of laboratory-confirmed or strongly suspected cases of meningococcal disease, depending on laboratory capacity and available resources.

Full details of the evidence are provided in Web Annex A (10. Post-exposure antimicrobial prophylaxis). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Vaccination remains the primary control intervention against meningococcal disease. All efforts should be undertaken to ensure the highest vaccination coverage in the target population, including routine immunization, mass preventive campaigns and reactive campaigns implemented as part of outbreak response.

Considering the increasing incidence of cases caused by ciprofloxacin-resistant isolates worldwide, the choice of antibiotic should be guided by antimicrobial susceptibility patterns prevalent within the community and potentially adjusted as necessary based on susceptibility testing results from index cases.

Antibiotic prophylaxis should be provided to close contacts as soon as possible. Administration later than 14 days after case identification probably has limited or no benefit.

Close contacts should be defined based on context-specific considerations and available resources. In the presence of an index case, during the 7 days before symptom onset and until 24 hours after initiation of appropriate antibiotic therapy, people at increased risk of infection include:

- individuals with prolonged exposure while in close proximity (less than 1 metre) to the index case (e.g. household contacts);
- individuals directly exposed to oral secretions of the index case (e.g. via kissing, mouth-to-mouth resuscitation, endotracheal intubation).

In the presence of small-scale outbreaks, antibiotic prophylaxis with single-dose parenteral ceftriaxone or oral ciprofloxacin should be provided to close contacts of laboratory-confirmed or clinically suspected cases of meningococcal disease, depending on available resources.

- If laboratory confirmation is expected to be obtained for all suspected cases, antibiotic prophylaxis should be provided to close contacts of laboratory-confirmed cases.

- If laboratory confirmation is not expected to be obtained for most suspected cases, antibiotic prophylaxis can also be provided to close contacts of strongly suspected cases.

Implementation considerations

The definition of close contact may have an impact on the rollout of chemoprophylaxis. In high-income settings, close contacts generally refer to individuals with prolonged exposure while in close proximity to one case or directly exposed to their oral secretions. Therefore, close contacts may include household members, roommates, intimate partners, contact persons at childcare centres, schools or dormitories, military recruits in training centres and at-risk health-care providers. However, while such a broad definition may be appropriate in the presence of sporadic disease, it may require some context-specific adaptations for large-scale epidemics, especially in settings that are densely populated and/or subject to large population movements. For example, depending on the setting's characteristics, antibiotic prophylaxis may be limited to household contacts or extended more broadly within the affected community.

During meningococcal disease epidemics, antibiotic prophylaxis should be provided free of charge in government health services and carefully integrated with the primary control measures, including reactive vaccination and clinical case management.

The feasibility of administering a single dose of ceftriaxone may vary based on the setting, available resources and trained personnel. Additionally, during large-scale epidemics, access to ceftriaxone may be limited, and its use should be prioritized for antimicrobial treatment of individuals with meningococcal disease.

Surveillance and monitoring of resistance trends and patterns, including among asymptomatic nasopharyngeal carriers, is required. Settings where large-scale antibiotic prophylaxis has been used should be prioritized.

Research gaps

Further studies are needed to investigate the effectiveness and safety of antibiotic prophylaxis for close contacts in preventing secondary cases of meningococcal disease. Additional research should be conducted in settings experiencing sporadic disease as well as during epidemics (e.g. outside the African meningitis belt and in urban settings within the meningitis belt).

Further studies are required to evaluate the available evidence on the use of village-wide prophylaxis during meningococcal disease epidemics.

Future evaluations of large-scale antibiotic prophylaxis should continue investigating antimicrobial resistance patterns among respiratory and gastrointestinal bacteria.

B.3 Adjunctive corticosteroids

Early intravenous administration of systemic corticosteroids (e.g. dexamethasone) has been used as part of the initial management strategy to reduce the risk of death and neurological complications among individuals with acute bacterial meningitis. Animal studies suggest that some disease outcomes, including hearing loss and other neurological complications, might be related to host inflammatory responses and the presence of cerebral oedema rather than the infection itself *(138-140)*. These observations have led to the use of intravenous corticosteroids as anti-inflammatory agents to decrease CSF proinflammatory cytokines and cerebral oedema and reduce the risk of poor outcome *(141)*.

In individuals with suspected, probable or confirmed acute bacterial meningitis, should adjunctive corticosteroids (dexamethasone, hydrocortisone, methylprednisolone) be administered?

Strong recommendation for

In non-epidemic settings where lumbar puncture can be performed, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should be initiated with the first dose of antibiotics in children and adults with suspected acute bacterial meningitis.

If cerebrospinal fluid characteristics are not consistent with bacterial meningitis, intravenous corticosteroids should be discontinued.

Strong recommendation. Low certainty of evidence.

Conditional recommendation for

In non-epidemic settings where lumbar puncture cannot be performed, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) may be initiated with the first dose of antibiotics when acute bacterial meningitis is strongly suspected in children and adults and no concurrent condition contraindicates their use.

Conditional recommendation. Very low certainty of evidence.

Strong recommendation against

During meningococcal disease epidemics, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should not be routinely used in children and adults with suspected or probable meningococcal meningitis.

Strong recommendation. Very low certainty of evidence.

Strong recommendation for

During pneumococcal disease epidemics, intravenous corticosteroids (dexamethasone, hydrocortisone or methylprednisolone) should be initiated with the first dose of antibiotics in children and adults with suspected or probable pneumococcal meningitis.

Strong recommendation. Very low certainty of evidence.

Justification

The GDG considered the evidence from 26 RCTs comparing intravenous corticosteroids to placebo in children and adults *(142-166)*. Notably, one RCT in which the prevalence of HIV infection in the study population was higher than 90% was excluded from the systematic review to prevent heterogeneity in study populations and was considered as additional evidence *(167)*.

- Overall, the evidence suggested that intravenous corticosteroids may have beneficial effects compared to placebo in terms of lower rates of mortality (RR 0.80, 95% CI 0.65–0.98; 26 RCTs; moderate-certainty evidence), short-term neurological sequelae (RR 0.77, 95% CI 0.61–0.99; 12 RCTs; low-certainty evidence), hearing loss (RR 0.66, 95% CI 0.51–0.86; 19 RCTs; high-certainty evidence) and post-meningitis epilepsy (RR 0.55, 95% CI 0.34–0.89; 8 RCTs; low-certainty evidence).
- In the subgroup analyses based on the causative pathogen, low-certainty evidence from five RCTs suggested that the effect of intravenous corticosteroids on mortality in pneumococcal meningitis may result in little to no difference when compared to placebo (RR 0.58, 95% CI 0.32–1.08). High-certainty evidence from four RCTs showed that corticosteroids result in a mild reduction of mortality in *H. influenzae* type b meningitis (RR 0.71, 95% CI 0.50–1.00). Moderate-certainty evidence from five RCTs suggested that corticosteroids probably result in little to no effect on mortality in meningococcal meningitis (RR 0.83, 95% CI 0.44–1.57).
- In the subgroup analyses based on age, low-certainty evidence suggested that intravenous corticosteroids may reduce mortality (RR 0.61, 95% CI 0.42–0.88; 8 RCTs) and the risk of short-term neurological sequelae (RR 0.48, 95% CI 0.27–0.84; 2 RCTs) in adults. In addition, corticosteroids may reduce the risk of hearing loss in both adults (RR 0.68, 95% CI 0.49–0.96; 4 RCTs; low-certainty evidence) and children (RR 0.71, 95% CI 0.53–0.95; 15 RCTs; moderate-certainty evidence).
- In the subgroup analyses based on World Bank income classification, there was no evidence of a difference in mortality between HICs and LMICs (P = 0.64). Nonetheless, moderate-certainty evidence indicated that intravenous corticosteroids likely reduce the risk of short-term neurological sequelae in HICs (RR 0.62, 95% CI 0.46–0.84; 9 RCTs), while having little to no effect in LMICs (RR 1.09, 95% CI 0.82–1.45; 3 RCTs).
- Low certainty of evidence from 21 RCTs showed that intravenous corticosteroids may result in little to no difference in adverse events compared to placebo (RR 1.26, 95% CI 0.93–1.70). However, the GDG emphasized that the studies were not adequately designed to detect adverse events of corticosteroids and stressed the importance of reporting side-effects to the relevant surveillance systems.

Based on available evidence, the GDG recognized the beneficial effects of corticosteroids on multiple critical outcomes and agreed on issuing a strong recommendation for their use in settings where lumbar puncture can be performed. They also indicated that CSF characteristics should inform the use of corticosteroids prior to, or in the absence of, pathogen identification. Therefore, they recommended corticosteroid treatment be discontinued if acute bacterial meningitis is considered unlikely based on initial CSF findings. Conversely, they agreed on the potential net benefits of continuing corticosteroids when CSF characteristics suggest a bacterial infection.

The GDG also emphasized that there is some evidence of a beneficial effect of corticosteroids for *H. influenzae* type b meningitis. A similar direction of effect, though not statistically significant, was found for pneumococcal meningitis. Conversely, neither a similar direction nor precision of effect estimates were observed in the meningococcal meningitis subgroup. These findings are also consistent with a previous Cochrane systematic review, in which a subgroup analysis by causative organism showed a favourable effect of corticosteroids only in pneumococcal and *H. influenzae* type b meningitis *(168)*.

The GDG acknowledged that all studies presented in the systematic review included individuals who underwent a lumbar puncture and highlighted the limited applicability of these findings to settings where lumbar puncture is contraindicated or deferred or cannot be performed due to the lack of human and/or infrastructural resources. Based on their clinical knowledge and expertise, the GDG emphasized the potential harm of withholding corticosteroids among individuals where acute bacterial meningitis is strongly suspected. At the same time, they also recognized that a strong clinical suspicion based on clinical findings has suboptimal sensitivity and specificity. Therefore, they agreed that intravenous corticosteroids may be initiated with the first dose of antibiotics when acute bacterial meningitis is strongly suspected, provided there are no concurrent conditions that contraindicate their use.

The GDG also formulated recommendations on the use of corticosteroids among suspected and probable cases during laboratory-confirmed epidemics. First, in line with previous recommendations, all efforts should be made to obtain CSF and blood samples from suspected cases and identify the causative pathogen. Based on available evidence as well as resource and feasibility considerations, the GDG agreed that corticosteroids should not be routinely given to suspected or probable cases of meningococcal meningitis during laboratory-confirmed invasive meningococcal disease epidemics. Conversely, they highlighted the potential benefits of intravenous corticosteroids in suspected and probable cases of pneumococcal meningitis during a confirmed invasive pneumococcal disease epidemic and issued a strong recommendation accordingly.

Full details of the evidence are provided in Web Annex A (11. Adjunctive corticosteroids). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Corticosteroids should be administered intravenously in an inpatient setting.

The beneficial effects of corticosteroids are likely to decrease as the delay in administration increases. Therefore, corticosteroids should be administered with the first dose of antibiotics or as soon as possible after the initial antibiotic dose.

Dexamethasone should be considered the corticosteroid of choice for children and adults. However, the dexamethasone 6-hourly administration schedule can be resource-consuming and its accessibility across different settings is variable. When dexamethasone cannot be administered, intravenous hydrocortisone or methylprednisolone may be used as alternatives, at the equivalent dosage and with an appropriate administration schedule.

Upon initial administration, the duration of corticosteroid use should be informed by CSF characteristics and pathogen isolation.

- If CSF characteristics are consistent with or suggestive of bacterial meningitis, intravenous corticosteroids should be continued for a maximum duration of 4 days.
- If CSF characteristics are consistent with bacterial meningitis and *S. pneumoniae* or *H. influenzae* type b is detected through culture or molecular testing, intravenous corticosteroids should be continued for a maximum duration of 4 days.
- If CSF characteristics are consistent with bacterial meningitis and a bacterial pathogen other than *S. pneumoniae* or *H. influenzae* type b is detected through culture or molecular testing, intravenous corticosteroids can be discontinued.

Intravenous corticosteroids should not be administered when the benefits do not outweigh the risks.

Corticosteroids should not be administered to individuals with cerebral malaria as their use is associated with prolonged coma resolution times when compared to placebo *(96)*.

The above recommendations on the use of corticosteroids as adjunctive treatment for suspected acute bacterial meningitis also apply to people living with HIV who are on antiretroviral therapy and have undetectable viral load (less than 50 copies/µl).

Intravenous corticosteroids administered as adjunctive treatment for suspected acute bacterial meningitis in children and adults with advanced HIV disease has not proven to be beneficial in reducing mortality or morbidity *(99)*.

The recommendations on the use of corticosteroids during meningococcal and pneumococcal disease epidemics are applicable if the causative agent of the epidemic is identified via culture or PCR.

Implementation considerations

Among children and adults with suspected acute bacterial meningitis, all efforts should be undertaken to ensure immediate admission or urgent transfer to a health-care facility with lumbar puncture capability, where adequate monitoring and management of severe illness and drug side-effects can be ensured.

In the absence of contraindications or reasons for deferral, lumbar puncture should be performed prior to initiating antibiotic and adjunctive treatment. However, any delay in diagnostic investigations should not delay therapy administration.

The use of intravenous corticosteroids for tuberculous meningitis is considered outside the scope of these guidelines. Relevant clinical guidance on corticosteroid treatment in tuberculous meningitis is provided in the *WHO consolidated guidelines on tuberculosis: drug-susceptible tuberculosis treatment (169)*.

Research gaps

Additional studies with a longer follow-up period are needed to investigate the burden of sequelae in children and adults with acute bacterial meningitis who received intravenous corticosteroids.

Further research is required among people living with HIV without advanced HIV disease but with a detectable viral load (e.g. newly diagnosed individuals, people with suboptimal adherence to therapy), to assess the effectiveness and safety of intravenous corticosteroids in the presence of suspected acute bacterial meningitis.

Implementation studies are needed to investigate and evaluate compliance with the recommendations, assess their effectiveness in reducing mortality and neurological sequelae, and monitor adverse events.

B.4 Treatment of increased intracranial pressure

Increased intracranial pressure is a potentially life-threatening complication of meningitis and a medical emergency, which may occur as a result of cerebral oedema, hydrocephalus and/or space-occupying lesions (e.g. brain abscess, subdural empyema). Successful management of individuals with elevated intracranial pressure requires prompt diagnosis and the appropriate use of invasive monitoring in intensive care units (where resources and capacities are available).

In addition to general supportive measures, some interventions associated with a low risk of adverse events can be used to manage intracranial hypertension *(170, 171)*. These include elevation of the head of the bed by 15–30 degrees, maintaining normal body temperature using antipyretics or cooling blankets as needed, and treating hypoxia, hypercapnia and hypotension.

Osmotic agents are commonly used to treat increased intracranial pressure. Their effectiveness and safety in the context of acute bacterial meningitis were reviewed as part of the process of developing the guidelines.

B.4.1 Osmotic agents

In individuals with suspected, probable or confirmed acute bacterial meningitis, should osmotic agents be used?

Conditional recommendation against

Glycerol should not be used routinely as adjunctive therapy in children and adults with suspected, probable or confirmed acute bacterial meningitis.

Conditional recommendation. Low certainty of evidence.

Justification

Four RCTs on the role of osmotic therapy in children and adolescents with acute bacterial meningitis were considered *(154, 164, 165, 172)*. Glycerol was the only osmotic agent evaluated in these studies and compared against standard care.

Low-certainty evidence suggested that glycerol may result in little to no difference in mortality at one-month follow-up (RR 0.84, 95% CI 0.62–1.15; 4 RCTs) and neurological sequelae at two-months follow-up (RR 0.77, 95% CI 0.38–1.53; 4 RCTs). Neurological sequelae included hemiplegia, quadriparesis, ataxia, blindness, hearing loss, seizures, developmental delay, severe psychomotor retardation and hydrocephalus requiring a shunt.

Low-certainty evidence also showed that glycerol may result in little to no difference in hearing loss at 1.5-months follow-up (RR 0.70, 95% CI 0.47–1.04; 4 RCTs) and post-meningitis epilepsy or symptomatic seizures at one-month follow-up (RR 0.89, 95% CI 0.71–1.12; 3 RCTs).

In subgroup analyses based on causative pathogens and adjunctive corticosteroids, there was no evidence of a difference between osmotic therapy and placebo on mortality or hearing loss across all groups.

Although all studies were conducted in children and adolescents up to 16 years of age, their findings were considered generalizable to adults, though downgraded for indirectness.

Based on available evidence and their clinical knowledge and experience, the GDG recommended that oral glycerol not be used as part of the routine management of people with acute bacterial meningitis. However, they acknowledged that some osmotic agents (but not glycerol) may be used as a temporary intervention in selected individuals to treat increased intracranial pressure and avert impending brain herniation.

Two studies conducted in resource-limited settings with high HIV prevalence were not included in the systematic review but considered as additional evidence by the GDG *(173, 174)*. With glycerol independently associated with mortality, the GDG agreed that the recommendation against the routine use of glycerol for bacterial meningitis is applicable to all settings.

Full details of the evidence are provided in Web Annex A (12. Osmotic agents). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Osmotic agents other than glycerol, such as mannitol, sorbitol and hypertonic saline can be used as a temporary measure for the management of increased intracranial pressure, including in children and adults with bacterial meningitis and signs of impending brain herniation (e.g. rapid change in level of consciousness, hypertension, bradycardia, loss of pupillary reaction).

Interventions with a more durable effect on intracranial pressure (e.g. ventilatory support, decompressive craniectomy) may be required in people with increased intracranial pressure.

Implementation considerations

People with increased intracranial pressure require intensive care monitoring and management. Therefore, adequate health-care infrastructure and workforce capacity are required.

Mannitol is included in the *WHO model list of essential medicines*, which provides a list of safe and effective antimicrobial drugs that should be available and affordable everywhere (https://list.essentialmeds.org/) *(110)*.

Research gaps

Further studies are required to investigate the effect of osmotic agents other than glycerol, including mannitol, sorbitol and hypertonic saline, in children and adults with bacterial meningitis.

Studies with a longer follow-up period among individuals with acute bacterial meningitis would be of value to better assess the effect of osmotic agents on neurological sequelae.

B.5 Fluid management

In individuals with suspected, probable or confirmed acute bacterial meningitis, should fluid restriction be implemented?

Conditional recommendation against

Fluid intake should not be routinely restricted in children and adults with suspected, probable or confirmed acute bacterial meningitis.

Conditional recommendation. Very low certainty of evidence

Justification

Two RCTs examining the role of fluid restriction in children with acute bacterial meningitis were considered *(175, 176)*. Notably, both studies were conducted in LMICs more than two decades ago and used maintenance fluids in the comparator arms that are no longer considered the standard of care (fifth-normal saline and half-normal saline, respectively, with 5% dextrose).

Very-low-certainty evidence suggested that the effect of fluid restriction compared with normal fluid maintenance is uncertain on mortality (RR 1.19, 95% CI 0.77–1.85) and neurological sequelae (RR 1.31, 95% CI 0.74–2.30). Neurological sequelae included spasticity, hypotonia, hemiplegia, sensory deficit, cranial neuropathy, seizures and coma.

While adverse events related to fluid restriction were not reported, the GDG considered the direction of the relative and absolute effect for the critical outcomes, suggesting a lower risk of death and neurological sequelae in the comparator arm (no fluid restriction).

Although both studies were only conducted in children up to 12 years of age, their findings were considered generalizable to adults.

Based on available evidence and their clinical knowledge and experience, the GDG expressed concern that fluid restriction might cause harm in both children and adults with acute bacterial meningitis and recommended that fluid intake not be systematically restricted beyond routine maintenance. In settings where dehydration is commonly observed (e.g. during the dry season in the African meningitis belt), fluid restriction can be further detrimental to disease management.

Full details of the evidence are provided in Web Annex A (13. Fluid management). The EtD framework for this guideline question is available in Web Annex C.

Remarks

Maintenance fluids are preferably administered orally or by enteric tube (e.g. nasogastric tube). Among infants and young children, breastfeeding is the ideal method of hydration.

When fluids cannot be administered orally or by enteric tube, isotonic solutions (e.g. Ringer's lactate, normal saline) should be routinely used as maintenance intravenous fluids.

In accordance with clinical judgement, moderate fluid restriction can be implemented in individuals without signs of shock or hypovolemia who present with clinical manifestations suggestive of syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Implementation considerations

Monitoring of volume status and electrolyte abnormalities in people with acute bacterial meningitis requires adequate health workforce capacity and laboratory infrastructure.

Guidance on fluid management of children with shock is provided in the *WHO pocket book of hospital care for children: guidelines for the management of common childhood illnesses (38)*.

Research gaps

Randomized clinical trials should be conducted in adults, including elderly populations, to assess the effectiveness and safety of fluid restriction for acute bacterial meningitis.

Further studies are required to evaluate the effectiveness and safety of restricting or administering maintenance fluids in HICs, where individuals generally have earlier access to health services and mortality rates are lower compared to resource-limited settings.

B.6 Treatment of acute symptomatic seizures

Management of acute symptomatic seizures aims to stop seizures as soon as possible to prevent progression to status epilepticus, cardiorespiratory failure and cerebral damage. The 2023 *mental health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders* and the 2016 *mhGAP intervention guide* provide comprehensive recommendations on the management of seizures and the use of anti-seizure medicines (ASM) *(177, 178)*.

B.6.1 Anti-seizure medicines

The decision to start ASM immediately after a first symptomatic seizure among individuals with meningitis depends on multiple factors, including the clinical stability of the person and the estimated risk of recurrent seizure.

In children and adults with acute symptomatic seizures from meningitis, should anti-seizure medicines be stopped before three months?

Conditional recommendation for

In children and adults with acute symptomatic seizures from meningitis, anti-seizure medicines should be continued for no longer than three months, in the absence of any recurring seizures.

Conditional recommendation. Very low certainty of evidence.

Justification

Acute symptomatic seizures frequently occur as a complication of meningitis, and ASM is commonly prescribed to prevent recurrent episodes. Even in the absence of comparative studies, the GDG emphasized the critical importance of formulating a recommendation on ASM treatment duration based on indirect evidence and their clinical knowledge and experience.

Very-low-certainty evidence from one RCT in 60 children with acute encephalitis syndrome (48% presenting with aseptic meningitis or meningoencephalitis) showed that the effect of four weeks of ASM treatment on seizure recurrence at 12 months is uncertain when compared with 12 weeks (RR 1.00, 95% CI 0.06–16.68) *(179)*. Very-low-certainty evidence from one cohort study in 141 adults with acute symptomatic first-ever seizure (7% with meningitis or meningoencephalitis) indicated that the effect of less than 100 days of ASM on seizure recurrence at 12 months is uncertain when compared with more than 100 days (RR 1.20, 95% CI 0.21–6.84) *(180)*.

The GDG considered the uncertain balance of potential benefits and harms in an indirect population (meningoencephalitis) where the recurrence of seizures is generally higher than in individuals with meningitis. It was also emphasized that the inappropriate and prolonged use of ASM may expose people to unnecessary side-effects and drug interactions, and lead to increased health-care costs. Conversely, premature ASM discontinuation might result in recurrent seizures, with short-term and long-term medical, social and economic consequences. Based on these considerations, the GDG agreed to issue a conditional recommendation, indicating that treatment should be continued for no longer than three months in people with acute meningitis in the absence of recurrent seizures.

Full details of the evidence are provided in Web Annex A (14. Anti-seizure medicines). The EtD framework for this guideline question is available in Web Annex C.

Remarks

The choice of ASM is affected by several factors, including seizure semiology, comorbidities, availability, cost and side-effects. Specific considerations are also in place for older adults, individuals with HIV, people with learning difficulties, and women and girls with childbearing potential.

Recommendations for the diagnosis and management of epilepsy and seizures in children and adults are presented in the *WHO mental health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders* and the related intervention guide *(177, 178)*.

Implementation considerations

Adequate risk communication and health education messages should be used when interacting with affected people and their caregivers, to ensure full understanding of the rationale of early discontinuation of ASM.

Research gaps

RCTs and cohort studies are required to compare different time points for a clinical assessment aimed at detecting sequelae.

Standardized outcome measures are needed to assess the efficacy of discontinuation of ASM in individuals with acute symptomatic seizures and/or epilepsy due to acute meningitis. These measures should include timing of discontinuation, seizure recurrence rates, neurological outcomes, mortality and adverse effects.

Further research targeting potential risk factors, including age, disease severity, causative pathogens and comorbidities, could help identify specific populations that may benefit differently from variable timing of ASM discontinuation.

The lack of cost-effectiveness analyses comparing variable timing of ASM discontinuation in people with acute meningitis highlights the need to evaluate the economic implications of different strategies, considering health-care resource utilization and long-term outcomes.

C. Management of sequelae

Acute meningitis may result in the development of long-term complications and sequelae, leading to profound disability, limitations in functioning, and decreased participation in life and the community. Major sequelae include but are not limited to hearing loss, focal neurological deficits, neuropsychological impairment (cognitive impairment in adults, intellectual disability and/or behavioural changes in children), hydrocephalus, seizure recurrence and epilepsy, limb or digit amputation and skin scarring. Some people may also experience a range of after-effects that may not be immediately apparent, including social and emotional difficulties, which contribute to a lower quality of life.

The incidence of neurological sequelae is highly variable based on causative pathogen, geographical region and presence of comorbidities *(181)*. Bacterial meningitis is more frequently associated with sequelae, with pneumococcal infection posing the highest risk *(182)*. Additionally, the risk of sequelae is nearly three times higher in Africa and Asia compared to Europe *(183)*.

Along with inequities in health outcomes, people with sequelae due to acute meningitis may experience gaps in formal social support mechanisms and are frequently reliant on support from family members, often female, to access health services and engage in community activities. The WHO *Global report on health equity for persons with disability* calls on Member States to take action to advance health equity for individuals with disabilities, including those that result from meningitis *(184)*.

C.1 General management

Early recognition of sequelae while the person is still in hospital is a crucial first step in assessing, addressing and commencing care, including rehabilitation, as soon as possible. Neurological examination and screening for easily missed or subtle sequelae, such as hearing, vision or neurocognitive impairment, and psychological after-effects, can be conducted while the person is still admitted in an inpatient setting. This is also an opportunity to provide the person and family members with resources for further medical follow-up and relevant information on the rights of people with disabilities as well as social and economic support that may be available through government.

Due to the complex needs and high levels of dependency and morbidity of people with sequelae from neurological infections, a range of coordinated health and social care is essential, in particular including the involvement of parents as partners in the dialogue with clinicians. Assisting parents and families in the coordination and planning of follow-up care is particularly important for the parents of a child with physical and intellectual disabilities. Continuity of care can often be optimized using digital health solutions that foster greater information-sharing between providers, people with neurological disorders and their carers, and allow for remote consultation through telehealth *(185)*.

After discharge from hospital, people with meningitis may need long-term follow-up care and rehabilitation, often requiring the use of assistive technology (Box 3.4). These services can be provided in outpatient hospital settings, outpatient physiotherapy or occupational therapy practices, and community environments, such as home, school or workplace.

Box 3.4 Assistive technology

Assistive technology, including hearing aids, wheelchairs, spectacles and prostheses, enables and promotes inclusion and participation, especially of people with disabilities, thereby playing a crucial role in the management of physical and neurological sequelae due to meningitis.

To enhance access to high-quality, affordable assistive products globally, WHO launched the *Priority assistive products list* (APL) in 2016 *(186)*. The APL includes priority assistive products, selected on the basis of widespread need and impact on a person's life, and provides support to Member States in fulfilling their commitment to improving access to assistive technology, in accordance with the United Nations Convention on the Rights of Persons with Disabilities (CRPD) *(187)*.

C.2 Clinical assessment

Should children with acute meningitis from any cause be reviewed by a health-care provider before discharge from hospital or at follow-up to identify sequelae?

Should adults with acute meningitis from any cause be reviewed by a health-care provider before discharge from hospital or at follow-up to identify sequelae?

Strong recommendation for

Children and adults with acute meningitis from any cause should be reviewed for sequelae by a health-care provider prior to discharge and at follow-up.

Strong recommendation. Very low certainty of evidence.

Justification

The unaddressed burden of meningitis sequelae can significantly impact the quality of life of affected children and adults, leading to increased morbidity and mortality. Therefore, the GDG emphasized the critical importance of performing clinical assessments of individuals with acute meningitis to detect and manage sequelae. Despite the lack of comparative studies, they agreed to issue a strong recommendation for both children and adults, based on available indirect evidence as well as their clinical knowledge and experience.

The GDG highlighted that a review by a health-care provider can facilitate early identification of sequelae, enable prompt initiation of rehabilitation, and reduce the risk of further complications and death. They therefore agreed that children and adults with a diagnosis of meningitis from any cause should be reviewed by a health-care provider before discharge and at follow-up.

The GDG also recognized that sequelae may be a life-long condition that can be associated with mental health problems and highlighted the importance of offering psychological support whenever available. Further WHO guidance on mental health can be found in the *mhGAP intervention guide (178)*.

Full details of the evidence are provided in Web Annex A (15. Clinical assessment of sequelae). The EtD framework for this guideline question is available in Web Annex C.

Remarks

A clinical assessment at follow-up should be performed at least once within four weeks of discharge.

When sequelae are detected, referral to the appropriate services should be arranged.

When available, psychological support should be offered to both the person with meningitis and their caregivers.

Implementation considerations

Regular follow-up visits should be provided after four weeks from discharge for people who are found to have persistent sequelae. However, timing can vary significantly based on individual characteristics, the type of sequela and available resources.

Health-care providers should inform individuals and their families about potential sequelae following acute meningitis, including behavioural changes.

The WHO *Package of interventions for rehabilitation* (PIR) provides information on clinical assessments for 20 health conditions, including musculoskeletal, neurological and sensory disorders, which may be relevant to the management of meningitis sequelae *(188)*.

Strengthening health systems is essential to ensure adequate and timely provision of follow-up care for sequelae. This includes implementing community-based surveillance of sequelae and fostering multisectoral collaboration with civil society, including associations of people with lived experience. Such efforts are aimed at developing an integrated, person-centred approach to the follow-up of sequelae.

Community awareness about sequelae is crucial to increasing acceptability of follow-up care, reducing stigmatization and discrimination, and facilitating better detection outside of hospital settings. This is particularly important in schools and the workplace.

Research gaps

There is a need for RCTs and cohort studies comparing different time points for a clinical assessment to identify sequelae.

Implementation studies are crucial to investigate compliance with the current recommendation. These studies should assess the effectiveness of improving sequelae detection and reducing the time to access health care and rehabilitation services.

The large variability of outcomes measured in observational studies underscores the need for the development of a core outcome set to guide research efforts on screening for sequelae following acute meningitis.

C.3 Rehabilitation

Rehabilitation plays a vital role in the management of meningitis sequelae. By working with the person and their family, modifying the environment to better suit their needs, using assistive products, educating to strengthen self-management, and adapting tasks so that they can be performed more safely and independently, rehabilitation strategies can help an individual with meningitis sequelae to overcome difficulties with independence in daily activities and perform meaningful life roles through a person-centred approach.

To address the significant unmet need for rehabilitation, particularly in LMICs, and assist Member States in planning and budgeting for the integration of rehabilitation services into their health systems, WHO released the WHO PIR in 2023 *(188)*. The package consists of eight modules and outlines the most essential interventions and related assessments for rehabilitation for 20 health conditions, including amputation (Module 2), neurological conditions (Module 3), neurodevelopmental disorders (Module 5) and sensory conditions (Module 6) *(189-192)*.

In children with sequelae following acute meningitis from any cause (excluding isolated hearing loss), should rehabilitation for sequelae be provided?

In adults with sequelae following acute meningitis from any cause (excluding isolated hearing loss), should rehabilitation for sequelae be provided?

Strong recommendation for

In children and adults with sequelae due to acute meningitis from any cause, rehabilitation should be provided as soon as possible.

Strong recommendation. Very low certainty of evidence.

Justification

The GDG emphasized that rehabilitation plays a crucial role in addressing the diverse range of meningitis sequelae, particularly in the earliest years, when the brain develops rapidly, and children are the most sensitive to such interventions. Thus, they highlighted the importance of formulating a strong recommendation on rehabilitation for both children and adults based on available evidence as well as their clinical knowledge and experience.

Given the lack of comparative studies addressing the guideline question, the GDG primarily discussed the indirect evidence from a systematic review of rehabilitation intervention outcomes of children and adults with infectious encephalitis and the evidence from the WHO PIR *(193, 194)*. While rehabilitation interventions described in the PIR are not specifically targeted at sequelae resulting from acute meningitis, the GDG concurred that interventions for other conditions with neurological and musculoskeletal (i.e. amputation) damage are also applicable to this population.

The GDG agreed that the beneficial effects of rehabilitation for meningitis sequelae is larger when initiated as soon as possible. Early intervention allows for the rapid reacquisition of functionality or the avoidance of further functional loss (when possible), facilitates neuroplasticity and prevents complications. The GDG also highlighted the long-term benefits of rehabilitation in reducing the burden on families and caregivers of affected individuals.

Finally, while acknowledging the critical role of rehabilitation services outside epidemics, the GDG indicated that rehabilitation interventions should be an integral part of the outbreak response.

Full details of the evidence are provided in Web Annex A (16a and 16b. Rehabilitation for sequelae). The EtD framework for these guideline questions is available in Web Annex C.

Remarks

The WHO PIR outlines interventions for rehabilitation of 20 health conditions, spanning seven disease areas, including musculoskeletal, neurological, neurodevelopmental and sensory disorders *(188)*. Interventions are organized into functioning domains, relevant to people with different health conditions, including individuals with sequelae following acute meningitis (Table 3.3).

A description of the functioning domains and interventions relevant to the sequelae following acute meningitis, extracted from the PIR modules for musculoskeletal, neurological and sensory conditions, and neurodevelopmental disorders, is available in Annex 3.

Table 3.3 Overview of functioning interventions for rehabilitation

Intervention type	Intervention category	Examples
Pharmacological	Medicines	Analgesics
Non-pharmacological	Therapeutic techniques and procedures, exercises and training	Manual therapy Cognitive behavioural therapy Range of motion exercises Communication skills training
	Physical modalities	Neuromuscular electrical stimulation
	Assistive products	Provision of and training in the use of assistive products for self-care
	Environmental modifications	Installation of ramps Lighting control
	Self-management interventions	Education and advice on self-directed training
		Carer and family training and support

Source: WHO, 2023 (*193*).

Implementation considerations

Rehabilitation services should be integrated into the comprehensive management of people with sequelae from acute meningitis. Fragmented services may contribute to frustration for the person

with the limitations and functioning or long-term disability and their caregivers, potentially limiting access to rehabilitation.

The period spanning intrauterine life to 3 years of age is critical, as the brain grows faster than at any other time. Approximately 80% of a child's brain is formed by this age. For healthy brain development in these years, children need a safe, secure and loving environment, with the right nutrition and stimulation from parents and caregivers or medical interventions, such as rehabilitation. The WHO *Nurturing care for early childhood development* framework serves as guidance for governments to strengthen policies and services and deliver essential interventions with quality and equity, while supporting caregivers to provide children with the care they need, particularly when affected by stressors, such as meningitis and meningitis sequelae *(195)*.

Strengthening health systems is essential to ensure the adequate and timely provision of rehabilitation for sequelae. This includes the training of specialized personnel and the establishment of rehabilitation centres as well as interventions aimed at increasing awareness regarding sequelae among health-care providers and the general population.

Research gaps

The lack of observational studies on sequelae rehabilitation following acute meningitis as well as RCTs comparing different rehabilitation options, highlights a neglected area of research within meningitis management and care that should be prioritized.

Implementation studies are needed to investigate and evaluate compliance with the recommendations from the WHO PIR and assess their effectiveness in improving quality of life, functioning and participation of people with sequelae and reducing caregiver burden.

Sequelae can cause permanent disability and affect the entire life course, highlighting the need for studies with prolonged follow-up time (greater than five years) to evaluate the long-term effects of rehabilitation on sequelae and quality of life.

Cost analyses and cost-effectiveness studies should be conducted, particularly in LMICs, to identify rehabilitation interventions that need to be prioritized in settings with limited resources.

The large variability of outcomes measured in rehabilitation studies underscores the need for the development of a core outcome set to guide studies on rehabilitation following acute meningitis.

C.4 Hearing loss

Hearing loss is probably the most common long-term effect of acute bacterial meningitis and occurs in a significant proportion of children and adults. It is more frequently associated with pneumococcal meningitis than any other form of bacterial meningitis and may occur at admission or during the disease course *(181, 182)*. Transient hearing loss is generally caused by a conductive disorder, while permanent hearing loss is associated with the involvement of the eighth cranial nerve, cochlea or labyrinth.

In children and adults with acute meningitis from any cause, should a formal audiological screening test be conducted before discharge or within four weeks of discharge?

Strong recommendation for

In children and adults with acute meningitis from any cause, formal audiological screening should be conducted before discharge.

If audiological screening is not possible before discharge, it should be conducted within four weeks of discharge.

Strong recommendation. Very low certainty of evidence.

Justification

Formal audiological screening at the appropriate time allows for early diagnosis, reduces the time to access hearing rehabilitation services and contributes to mitigating the impact of long-term complications. In individuals potentially eligible for cochlear implants, unnecessary delays may increase the likelihood of cochlear ossification, affecting the feasibility and auditory performance of cochlear implants.

The GDG emphasized the critical importance of formulating a strong recommendation in favour of timely formal audiological screening, even in the absence of comparative studies addressing the guideline question. This recommendation is based on available indirect evidence as well as the GDG's experience and clinical expertise.

The GDG emphasized that conducting formal audiological screening before discharge constitutes a "window of opportunity" for clinicians. It increases the likelihood of timely detection of hearing loss following acute meningitis and allows for the early initiation of hearing rehabilitation (particularly cochlear implantation). However, as formal audiological screening cannot always be performed before discharge (e.g. due to lack of resources or suboptimal clinical recovery), the GDG agreed that it should be conducted at least within four weeks of discharge. This interval was considered adequate to provide clinicians with the flexibility to organize follow-up arrangements while not substantially increasing the risk of loss to follow-up.

Full details of the evidence are provided in Web Annex A (17. Hearing loss screening). The EtD framework for this guideline question is available in Web Annex C.

Remarks

When hearing loss is detected, urgent referral for hearing rehabilitation or evaluation for cochlear implantation should be arranged. This is crucial to prevent the rapid impairment of speech due to the loss of auditory feedback and to avoid cochlear ossification in individuals eligible for cochlear implantation.

Individuals screened before discharge and found to have no hearing loss should undergo a second formal audiological screening test, as a small number may still develop hearing loss at a later stage.

Implementation considerations

Formal audiological screening is an essential health service to which countries should guarantee universal access as part of UHC.

When formal audiological screening cannot be conducted before discharge, details about the follow-up appointment (including place and time) within four weeks should be provided before the person leaves the health-care facility.

Audiological screening services should not be provided in isolation but integrated within the comprehensive management of individuals with sequelae due to meningitis. Fragmented services may contribute to frustration for the person with the disability and their caregivers, potentially limiting access to health care.

Strengthening of health systems is crucial to ensure an adequate and timely audiological assessment. This includes the training of specialized personnel and the establishment of the necessary infrastructure dedicated to audiological screening within health-care facilities.

The WHO handbook *Hearing screening: considerations for implementation* provides technical guidance for establishing evidence-based programmes for hearing screening in different target age-groups and facilitating early interventions for ear diseases and hearing loss *(196)*.

Research gaps

RCTs and cohort studies are required to compare different time points for a formal audiological screening or to compare different screening tests.

Further research is needed to measure the burden of hearing loss due to acute meningitis, including the proportion of people experiencing conductive and sensorineural hearing loss as well as transient or permanent deficits.

Most observational studies identified were conducted in HICs, highlighting the need for further evidence on formal audiological screening in LMICs.

Implementation studies are needed to investigate compliance with the current recommendation, to assess its effectiveness in improving detection of hearing loss and time to access hearing rehabilitation services.

Based on the large variability of audiological screening tests used in the observational studies, further research is needed to evaluate hearing impairment through validated screening tests, such as those recommended by the WHO handbook *Hearing screening: considerations for implementation (196)*.

In children and adults with hearing loss following acute meningitis, should hearing rehabilitation be provided?

Strong recommendation for

In children and adults with hearing loss from acute meningitis from any cause, hearing rehabilitation should be provided as soon as possible.

Strong recommendation. Very low certainty of evidence.

Justification

The GDG emphasized the critical importance of formulating a strong recommendation on hearing rehabilitation, even in the absence of comparative studies addressing the guideline question,

and they agreed to use the available additional evidence as well as their clinical knowledge and experience.

The majority of the identified case series on cochlear implantation were conducted in HICs, involving children with variable follow-up periods and outcomes measured. However, the GDG acknowledged that these studies provide useful information regarding the significant beneficial effect of cochlear implants on auditory performance in people with severe hearing loss.

The GDG agreed that the high costs associated with hearing rehabilitation and hearing devices may constitute a significant barrier to their widespread implementation, particularly in resource-limited settings. However, based on existing evidence and their technical expertise, the GDG agreed that hearing rehabilitation interventions are likely to be cost-effective overall.

Finally, the GDG agreed that the beneficial effects of hearing rehabilitation are likely to be larger when initiated early. This consideration also applies to cochlear implants because early cochlear ossification can affect feasibility and auditory performance post-intervention.

Full details of the evidence are provided in Web Annex A (18. Rehabilitation for hearing loss). The EtD framework for this guideline question is available in Web Annex C.

Remarks

The WHO PIR (Module 6) outlines assessments and interventions for hearing loss *(192)*. Rehabilitation interventions for hearing impairment include the provision of, and training in, the use of hearing technologies (hearing aids, cochlear implants and middle ear implants), and speech and language therapy to enhance perceptive skills and develop communication and linguistic abilities (Table 3.4). Rehabilitation also includes training in the use of sign language and other means of sensory substitution, such as speech reading, use of print on palm and Tadoma signed communication.

Table 3.4 Overview of rehabilitation interventions for hearing loss

Functioning domain	Intervention categories	Interventions for hearing loss
Hearing	Assistive products	Provision of and training in the use of assistive products for hearing
Speech, language, communication	Therapeutic techniques and procedures, exercises and training	Auditory training Speech and language therapy Verbal and/or sign language training Communication skills training
	Assistive products	Provision of and training in the use of assistive products for communication
Education, vocation	Therapeutic techniques and procedures, exercises and training	Educational or vocational counselling, training and support

Community, social life	Therapeutic techniques and procedures, exercises and training	Participation-focused interventions
Self-management	Self-management interventions	Education, advice and support for self-management of the health condition
Carer and family support	Self-management interventions	Carer and family training and support

Implementation considerations

Hearing rehabilitation services should be integrated into the comprehensive management of individuals with sequelae from acute meningitis. Fragmented services may contribute to frustration for the person with the disability and their caregivers, potentially limiting access to rehabilitation.

Strengthening of health systems is crucial to ensure adequate and timely provision of hearing rehabilitation and hearing aids. This includes the training of specialized personnel and the establishment of rehabilitation centres dedicated to hearing loss rehabilitation. Moreover, interventions aimed at increasing awareness regarding hearing loss and hearing rehabilitation need to be implemented among health-care workers and the general population.

Research gaps

Implementation studies are needed to investigate and evaluate compliance with the recommendations from the WHO PIR and assess their effectiveness in improving quality of life, functioning and participation of people with hearing loss, and reducing caregiver burden.

Cost analyses and cost-effectiveness studies should be conducted, particularly in LMICs, to identify hearing rehabilitation interventions that need to be prioritized in settings with limited resources.

Hearing loss can cause permanent disability and affect the entire life course, highlighting the need for studies with prolonged follow-up time to evaluate the long-term effects of rehabilitation on hearing loss and quality of life.

The large variability of outcomes measured in the case series on cochlear implants underscores the need for the development of a core outcome set to guide studies on hearing rehabilitation following acute meningitis.

Further research on new technologies to develop affordable, widely accessible hearing aids is needed.

4. Conclusion and next steps

4. Conclusion and next steps

4.1 Publication and dissemination

While the guidelines were developed in English, the executive summary and the summary of recommendations will be translated into all six official United Nations languages, contingent upon available resources. The guidelines and related resources are available online and can be found on the WHO website. All research evidence and references are available in Web Annexes A, B and C, which can be downloaded from the web platform.

WHO headquarters will work closely with regional and country offices to notify relevant departments within ministries of health and national public health bodies about these published guidelines and ensure their wide dissemination globally. A briefing package will be prepared for WHO technical officers outside of WHO headquarters, including an executive summary and a questions-and-answers document related to policy and programme implications.

As part of the implementation of WHO's *Defeating meningitis by 2030: a global road map (2)*, the *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (185)* and the *Package of interventions for rehabilitation (PIR) (188)*, relevant capacity-building activities will be undertaken through meetings, workshops and training initiatives at regional, subregional and national levels. Upon publication, Member States will be supported to adapt, use and implement these guidelines.

4.2 Derivative technical products

As part of the scaling-up strategy in countries, clinical tools and job aids will be developed based on the guidelines to translate the evidence-based recommendations into case management protocols and algorithms on meningitis diagnosis and treatment. These tools aim to streamline clinical operations and facilitate decision-making for front-line health-care professionals working at primary- and secondary-level health-care facilities. Additional clinical considerations and details considered beyond the scope of the guidelines will be incorporated into these products.

4.3 Updating of WHO resources

The *WHO model list of essential medicines (110)*, the *WHO model list of essential in vitro diagnostics (197)* and the *WHO AWaRe (access, watch, reserve) antibiotic book (8)* will be updated based on the recommendations in these guidelines.

Furthermore, as the GDG strongly emphasized the urgent need for WHO to revise and update the WHO standard case definitions when formulating the recommendations for outbreak and epidemic settings, WHO is actively undertaking efforts to address this need at the time of publication and develop a derivative technical product.

4.4 Monitoring and evaluation

Following the publication of the guidelines, WHO will continue to gather regular feedback from implementation activities to assess their usefulness and impact. Additionally, WHO will solicit ongoing input from international experts and health-care providers who have extensive experience in meningitis, other brain infections and their sequelae. This feedback will be used to evaluate the guidelines' effects on health-care processes and outcomes, ensuring their quality and identifying areas for improvement. Where possible, this effort will leverage existing WHO resources, including the defeating meningitis road map and the indicators provided as part of WHO's *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (2, 185)*.

4.5 Updating the evidence

The WHO Steering Group will continue to monitor research developments in the field of meningitis and its sequelae, with particular attention to areas where no evidence was found or where recommendations were based on low- or very-low-certainty evidence. In these cases, new research may warrant the introduction of new recommendations or changes to existing ones. Following the publication and dissemination of the guidelines, any concerns regarding the validity of a recommendation will be promptly communicated to the implementers, along with plans for updating the recommendation if necessary.

References

1. Global Burden of Disease 2019 Meningitis Antimicrobial Resistance Collaborators. Global, regional, and national burden of meningitis and its aetiologies, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2023;22:685-711 (https://doi.org/10.1016/S1474-4422(23)00195-3).

2. Defeating meningitis by 2030: a global road map. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/342010).

3. World Health Organization. Global Health Estimates 2021: DALY Global. 2021 (https://cdn.who.int/media/docs/default-source/gho-documents/global-health-estimates/ghe2021_daly_global_new.xlsx).

4. Meningitis outbreak response in sub-Saharan Africa: WHO guideline. Geneva: World Health Organization; 2014 (https://iris.who.int/handle/10665/144727).

5. van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. N Engl J Med. 2004;351:1849-59 (https://doi.org/10.1056/NEJMoa040845).

6. 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;35:46-52. (https://doi.org/10.1086/340979).

7. Curtis S, Stobart K, Vandermeer B, Simel DL, Klassen T. Clinical features suggestive of meningitis in children: a systematic review of prospective data. Pediatrics. 2010;126:952-60 (https://doi.org/10.1542/peds.2010-0277).

8. The WHO AWaRe (access, watch, reserve) antibiotic book. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/365237).

9. Defeating meningitis 2030: baseline situation analysis. Geneva: World Health Organization; 2019 (https://www.who.int/publications/m/item/defeating-meningitis-2030-baseline-situation-analysis).

10. Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper – February 2019 – Vaccins antipneumococciques conjugués chez les nourrissons et les enfants de moins de 5 ans: note de synthèse de l'OMS – février 2019. Weekly Epidemiological Record. Geneva: World Health Organization; 2019;94:85-103 (https://iris.who.int/handle/10665/310970).

11. Bijlsma MW, Brouwer MC, Kasanmoentalib ES, Kloek AT, Lucas MJ, Tanck MW et al. Community-acquired bacterial meningitis in adults in the Netherlands, 2006–14: a prospective cohort study. Lancet Infect Dis. 2016;16:339-47 (https://doi.org/10.1016/S1473-3099(15)00430-2).

12. Durand ML, Calderwood SB, Weber DJ, Miller SI, Southwick FS, Caviness VS, Jr. et al. Acute bacterial meningitis in adults. A review of 493 episodes. N Engl J Med. 1993;328:21-8 (https://doi.org/10.1056/NEJM199301073280104).

13. Theilacker C, Ludewig K, Serr A, Schimpf J, Held J, Bogelein M et al. Overwhelming postsplenectomy infection: a prospective multicenter cohort study. Clin Infect Dis. 2016;62:871-8 (https://doi.org/10.1093/cid/civ1195).

14. Overturf GD, Powars D, Baraff LJ. Bacterial meningitis and septicemia in sickle cell disease. Am J Dis Child. 1977;131:784-7 (https://doi.org/10.1001/archpedi.1977.02120200066014).

15. Picard C, Puel A, Bustamante J, Ku CL, Casanova JL. Primary immunodeficiencies associated with pneumococcal disease. Curr Opin Allergy Clin Immunol. 2003;3:451-9 (https://doi.org/10.1097/00130832-200312000-00006).

16. Twomey JJ. Infections complicating multiple myeloma and chronic lymphocytic leukemia. Arch Intern Med. 1973;132:562-5. (https://www.ncbi.nlm.nih.gov/pubmed/4542660).

17. Redd SC, Rutherford GW, 3rd, Sande MA, Lifson AR, Hadley WK, Facklam RR et al. The role of human immunodeficiency virus infection in pneumococcal bacteremia in San Francisco residents. J Infect Dis. 1990;162:1012-7 (https://doi.org/10.1093/infdis/162.5.1012).

18. Franklin K, Kwambana-Adams B, Lessa FC, Soeters HM, Cooper L, Coldiron ME et al. Pneumococcal meningitis outbreaks in Africa, 2000–2018: systematic literature review and Meningitis Surveillance Database analyses. J Infect Dis. 2021;224:S174-S83 (https://doi.org/10.1093/infdis/jiab105).

19. Vaccination in acute humanitarian emergencies: a framework for decision making. Geneva: World Health Organization; 2017 (https://iris.who.int/handle/10665/255575).

20. Managing meningitis epidemics in Africa: a quick reference guide for health authorities and health-care workers. Geneva: World Health Organization; 2015 (https://iris.who.int/handle/10665/154595).

21. Al-Abri SS, Abuhasan MY, Albayat SSA, Bai X, Bastaki H, Borrow R et al. Meningococcal disease in the Middle East: a report from the Global Meningococcal Initiative. J Infect. 2024;88:71-6 (https://doi.org/10.1016/j.jinf.2023.10.011).

22. Yezli S. The threat of meningococcal disease during the Hajj and Umrah mass gatherings: a comprehensive review. Travel Med Infect Dis. 2018;24:51-8 (https://doi.org/10.1016/j.tmaid.2018.05.003).

23. Cohn AC, MacNeil JR, Harrison LH, Hatcher C, Theodore J, Schmidt M et al. Changes in *Neisseria meningitidis* disease epidemiology in the United States, 1998–2007: implications for prevention of meningococcal disease. Clin Infect Dis. 2010;50:184-91 (https://doi.org/10.1086/649209).

24. Rosenstein NE, Perkins BA, Stephens DS, Popovic T, Hughes JM. Meningococcal disease. N Engl J Med. 2001;344:1378-88 (https://doi.org/10.1056/nejm200105033441807).

25. Ellison RT, 3rd, Kohler PF, Curd JG, Judson FN, Reller LB. Prevalence of congenital or acquired complement deficiency in patients with sporadic meningococcal disease. N Engl J Med. 1983;308:913-6 (https://doi.org/10.1056/NEJM198304213081601).

26. Densen P. Complement deficiencies and meningococcal disease. Clin Exp Immunol. 1991;86 Suppl 1:57-62 (https://doi.org/10.1111/j.1365-2249.1991.tb06209.x).

27. Applegate AO, Fong VC, Tardivel K, Lippold SA, Zarate S. Notes from the field: meningococcal disease in an international traveler on eculizumab therapy – United States, 2015. MMWR Morb Mortal Wkly Rep. 2016;65:696-7 (https://doi.org/10.15585/mmwr.mm6527a3).

28. Miller L, Arakaki L, Ramautar A, Bodach S, Braunstein SL, Kennedy J et al. Elevated risk for invasive meningococcal disease among persons with HIV. Ann Intern Med. 2014;160:30-7 (https://doi.org/10.7326/0003-4819-160-1-201401070-00731).

29. Stephens DS, Hajjeh RA, Baughman WS, Harvey RC, Wenger JD, Farley MM. Sporadic meningococcal disease in adults: results of a 5-year population-based study. Ann Intern Med. 1995;123:937-40 (https://doi.org/10.7326/0003-4819-123-12-199512150-00007).

30. Cohen C, Singh E, Wu HM, Martin S, de Gouveia L, Klugman KP et al. Increased incidence of meningococcal disease in HIV-infected individuals associated with higher case-fatality ratios in South Africa. Aids. 2010;24:1351-60 (https://doi.org/10.1097/QAD.0b013e32833a2520).

31. Langereis JD, de Jonge MI. Invasive disease caused by nontypeable *Haemophilus influenzae*. Emerg Infect Dis. 2015;21:1711-8. (https://doi.org/10.3201/eid2110.150004).

32. Chekrouni N, Koelman DLH, Brouwer MC, van der Ende A, van de Beek D. Community-acquired *Haemophilus influenzae* meningitis in adults. J Infect. 2021;82:145-50 (https://doi.org/10.1016/j.jinf.2021.03.016).

33. Slotved HC, Kong F, Lambertsen L, Sauer S, Gilbert GL. Serotype IX, a proposed new *Streptococcus agalactiae* serotype. J Clin Microbiol. 2007;45:2929-36 (https://doi.org/10.1128/JCM.00117-07).

34. World Health Organization, Food and Agriculture Organization of the United Nations (FAO). Risk assessment of *Listeria monocytogenes* in ready-to-eat foods: technical report. Rome: FAO; 2004 (https://iris.who.int/handle/10665/42875).

35. Uche IV, MacLennan CA, Saul A. A systematic review of the incidence, risk factors and case fatality rates of invasive nontyphoidal salmonella (iNTS) disease in Africa (1966 to 2014). PLoS Negl Trop Dis. 2017;11:e0005118 (https://doi.org/10.1371/journal.pntd.0005118).

36. Global Burden of Disease 2017 Non-Typhoidal Salmonella Invasive Disease Collaborators. The global burden of non-typhoidal salmonella invasive disease: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis. 2019;19:1312-24 (https://doi.org/10.1016/S1473-3099(19)30418-9).

37. Kupila L, Vuorinen T, Vainionpää R, Hukkanen V, Marttila RJ, Kotilainen P. Etiology of aseptic meningitis and encephalitis in an adult population. Neurology. 2006;66:75-80 (https://doi.org/10.1212/01.wnl.0000191407.81333.00).

38. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses, second edition. Geneva: World Health Organization; 2013 (https://iris.who.int/handle/10665/81170).

39. WHO handbook for guideline development. 2nd ed. Geneva: World Health Organization; 2014 (https://iris.who.int/handle/10665/145714).

40. Moberg J, Oxman AD, Rosenbaum S, Schunemann HJ, Guyatt G, Flottorp S et al. The GRADE Evidence to Decision (EtD) framework for health system and public health decisions. Health Res Policy Syst. 2018;16:45 (https://doi.org/10.1186/s12961-018-0320-2).

41. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898 (https://doi.org/10.1136/bmj.l4898).

42. Lewin S, Booth A, Glenton C, Munthe-Kaas H, Rashidian A, Wainwright M et al. Applying GRADE-CERQual to qualitative evidence synthesis findings: introduction to the series. Implement Sci. 2018;13:2 (https://doi.org/10.1186/s13012-017-0688-3).

43. Williams J, Lye DC, Umapathi T. Diagnostic lumbar puncture: minimizing complications. Intern Med J. 2008;38:587-91 (https://doi.org/10.1111/j.1445-5994.2008.01631.x).

44. Evans RW. Complications of lumbar puncture. Neurol Clin. 1998;16:83-105 (https://doi.org/10.1016/s0733-8619(05)70368-6).

45. Brouwer MC, Thwaites GE, Tunkel AR, van de Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. Lancet. 2012;380:1684-92 (https://doi.org/10.1016/s0140-6736(12)61185-4).

46. Nigrovic LE, Kimia AA, Shah SS, Neuman MI. Relationship between cerebrospinal fluid glucose and serum glucose. N Engl J Med. 2012;366:576-8. (https://doi.org/10.1056/NEJMc1111080).

47. Leen WG, Willemsen MA, Wevers RA, Verbeek MM. Cerebrospinal fluid glucose and lactate: age-specific reference values and implications for clinical practice. PLoS One. 2012;7:e42745 (https://doi.org/10.1371/journal.pone.0042745).

48. Bohr V, Rasmussen N, Hansen B, Kjersem H, Jessen O, Johnsen N et al. 875 cases of bacterial meningitis: diagnostic procedures and the impact of preadmission antibiotic therapy. Part III of a three-part series. J Infect. 1983;7:193-202 (https://doi.org/10.1016/s0163-4453(83)96980-3).

49. Nigrovic LE, Kuppermann N, Malley R, Bacterial Meningitis Study Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of P. Children with bacterial meningitis presenting to the emergency department during the pneumococcal conjugate vaccine era. Acad Emerg Med. 2008;15:522-8 (https://doi.org/10.1111/j.1553-2712.2008.00117.x).

50. Shameem S, Vinod Kumar CS, Neelagund YF. Bacterial meningitis: rapid diagnosis and microbial profile: a multicentered study. J Commun Dis. 2008;40:111-20. (https://www.ncbi.nlm.nih.gov/pubmed/19301695).

51. Sigurdardottir B, Bjornsson OM, Jonsdottir KE, Erlendsdottir H, Gudmundsson S. Acute bacterial meningitis in adults. A 20-year overview. Arch Intern Med. 1997;157:425-30 (https://doi.org/10.1001/archinte.1997.00440250077009).

52. Taniguchi T, Tsuha S, Shiiki S, Narita M. Point-of-care cerebrospinal fluid Gram stain for the management of acute meningitis in adults: a retrospective observational study. Ann Clin Microbiol Antimicrob. 2020;19:59 (https://doi.org/10.1186/s12941-020-00404-9).

53. Alnomasy SF, Alotaibi BS, Mujamammi AH, Hassan EA, Ali ME. Microbial aspects and potential markers for differentiation between bacterial and viral meningitis among adult patients. PLoS One. 2021;16:e0251518 (https://doi.org/10.1371/journal.pone.0251518).

54. Babenko D, Seidullayeva A, Bayesheva D, Turdalina B, Omarkulov B, Almabayeva A et al. Ability of procalcitonin and C-reactive protein for discriminating between bacterial and enteroviral meningitis in children using decision tree. Biomed Res Int. 2021;2021:5519436 (https://doi.org/10.1155/2021/5519436).

55. Chaudhary S, Bhatta NK, Lamsal M, Chaudhari RK, Khanal B. Serum procalcitonin in bacterial & non-bacterial meningitis in children. BMC Pediatr. 2018;18:342 (https://doi.org/10.1186/s12887-018-1314-5).

56. Domingues RB, Fernandes GBP, Leite F, Senne C. Performance of lactate in discriminating bacterial meningitis from enteroviral meningitis. Rev Inst Med Trop Sao Paulo. 2019;61:e24 (https://doi.org/10.1590/s1678-9946201961024).

57. Dubos F, Korczowski B, Aygun DA, Martinot A, Prat C, Galetto-Lacour A et al. Serum procalcitonin level and other biological markers to distinguish between bacterial and aseptic meningitis in children: a European multicenter case cohort study. Arch Pediatr Adolesc Med. 2008;162:1157-63 (https://doi.org/10.1001/archpedi.162.12.1157).

58. Giulieri S, Chapuis-Taillard C, Jaton K, Cometta A, Chuard C, Hugli O et al. CSF lactate for accurate diagnosis of community-acquired bacterial meningitis. Eur J Clin Microbiol Infect Dis. 2015;34:2049-55 (https://doi.org/10.1007/s10096-015-2450-6).

59. Gowin E, Wysocki J, Avonts D, Januszkiewicz-Lewandowska D, Michalak M. Usefulness of inflammatory biomarkers in discriminating between bacterial and aseptic meningitis in hospitalized children from a population with low vaccination coverage. Arch Med Sci. 2016;12:408-14 (https://doi.org/10.5114/aoms.2016.59269).

60. Kalchev Y, Petkova T, Raycheva R, Argirova P, Stoycheva M, Murdjeva M. Combined testing of cerebrospinal fluid IL-12 (p40) and serum C-reactive protein as a possible discriminator of acute bacterial neuroinfections. Cytokine. 2021;140:155423 (https://doi.org/10.1016/j.cyto.2021.155423).

61. Morales-Casado MI, Julián-Jiménez A, Lobato-Casado P, Cámara-Marín B, Pérez-Matos JA, Martínez-Maroto T. Factores predictores de meningitis bacteriana en los pacientes atendidos en urgencias [Predictive factors of bacterial meningitis in the patients seen in emergency departments]. Enferm Infecc Microbiol Clin. 2017;35:220-8 (https://doi.org/10.1016/j.eimc.2016.02.007) (in Spanish).

62. Pormohammad A, Lashkarbolouki S, Azimi T, Gholizadeh P, Bostanghadiri N, Safari H et al. Clinical characteristics and molecular epidemiology of children with meningitis in Tehran, Iran: a prospective study. New Microbes New Infect. 2019;32:100594 (https://doi.org/10.1016/j.nmni.2019.100594).

63. Sanaei Dashti A, Alizadeh S, Karimi A, Khalifeh M, Shoja SA. Diagnostic value of lactate, procalcitonin, ferritin, serum-C-reactive protein, and other biomarkers in bacterial and viral meningitis: a cross-sectional study. Medicine (Baltimore). 2017;96:e7637 (https://doi.org/10.1097/md.0000000000007637).

64. Sormunen P, Kallio MJ, Kilpi T, Peltola H. C-reactive protein is useful in distinguishing Gram stain-negative bacterial meningitis from viral meningitis in children. J Pediatr. 1999;134:725-9 (https://doi.org/10.1016/s0022-3476(99)70288-x).

65. Staal SL, Olie SE, Ter Horst L, van Zeggeren IE, van de Beek D, Brouwer MC. Granulocytes in cerebrospinal fluid of adults suspected of a central nervous system infection: a prospective study of diagnostic accuracy. Infection. 2024 (https://doi.org/10.1007/s15010-024-02200-5).

66. Tamune H, Takeya H, Suzuki W, Tagashira Y, Kuki T, Honda H et al. Cerebrospinal fluid/blood glucose ratio as an indicator for bacterial meningitis. Am J Emerg Med. 2014;32:263-6 (https://doi.org/10.1016/j.ajem.2013.11.030).

67. Wang Y, Cao M, Zhu X, Ni Q, Liu X. The cerebrospinal fluid neutrophil to lymphocyte ratio is a sensitive biomarker for bacterial meningitis in children. Child's Nerv Syst. 2022;38:1165-71 (https://doi.org/10.1007/s00381-022-05501-y).

68. Fouad R, Khairy M, Fathalah W, Gad T, El-Kholy B, Yosry A. Role of clinical presentations and routine CSF analysis in the rapid diagnosis of acute bacterial meningitis in cases of negative Gram stained smears. J Trop Med. 2014;2014:213762 (https://doi.org/10.1155/2014/213762).

69. Mentis AF, Kyprianou MA, Xirogianni A, Kesanopoulos K, Tzanakaki G. Neutrophil-to-lymphocyte ratio in the differential diagnosis of acute bacterial meningitis. Eur J Clin Microbiol Infect Dis. 2016;35:397-403 (https://doi.org/10.1007/s10096-015-2552-1).

70. Viallon A, Zeni F, Lambert C, Pozzetto B, Tardy B, Venet C et al. High sensitivity and specificity of serum procalcitonin levels in adults with bacterial meningitis. Clin Infect Dis. 1999;28:1313-6 (https://doi.org/10.1086/514793).

71. Mekitarian Filho E, Horita SM, Gilio AE, Nigrovic LE. Cerebrospinal fluid lactate level as a diagnostic biomarker for bacterial meningitis in children. Int J Emerg Med. 2014;7:14 (https://doi.org/10.1186/1865-1380-7-14).

72. Nasir H, Afzal MF, Hamid MH, Laeeq A. Diagnostic accuracy of cerebrospinal fluid lactate in confirmed cases of acute bacterial meningitis in children. Pak J Med Sci. 2020;36:1558-61 (https://doi.org/10.12669/pjms.36.7.1682).

73. Nazir M, Wani WA, Malik MA, Mir MR, Ashraf Y, Kawoosa K et al. Cerebrospinal fluid lactate: a differential biomarker for bacterial and viral meningitis in children. J Pediatr (Rio J). 2018;94:88-92 (https://doi.org/10.1016/j.jped.2017.03.007).

74. The selection and use of essential in vitro diagnostics: report of the third meeting of the WHO Strategic Advisory Group of Experts on In Vitro Diagnostics, 2020 (including the third WHO model list of essential in vitro diagnostics). Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/339064).

75. Nigrovic LE, Malley R, Macias CG, Kanegaye JT, Moro-Sutherland DM, Schremmer RD et al. Effect of antibiotic pretreatment on cerebrospinal fluid profiles of children with bacterial meningitis. Pediatrics. 2008;122:726-30. (https://doi.org/10.1542/peds.2007-3275).

76. World Health Organization, United States Centers for Disease Control Prevention. Laboratory methods for the diagnosis of meningitis caused by *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*: WHO manual, 2nd edition. Geneva: World Health Organization; 2011 (https://iris.who.int/handle/10665/70765).

77. Nau R, Sorgel F, Eiffert H. Penetration of drugs through the blood-cerebrospinal fluid/blood-brain barrier for treatment of central nervous system infections. Clin Microbiol Rev. 2010;23:858-83 (https://doi.org/10.1128/CMR.00007-10).

78. CLSI M100. Performance standards for antimicrobial susceptibility testing, 34th edition 2024 (https://clsi.org/standards/products/microbiology/documents/m100/).

79. Breakpoint tables for interpretation of MICs and zone diameters, version 14.0, 2024. In: EUCAST [website]. The European Committee on Antimicrobial Susceptibility Testing; 2025 (http://www.eucast.org/).

80. Hassan MM, Grist LF, Poirier AC, La Ragione RM. JMM profile: Loop-mediated isothermal amplification (LAMP): for the rapid detection of nucleic acid targets in resource-limited settings. J Med Microbiol. 2022;71 (https://doi.org/10.1099/jmm.0.001522).

81. Kim DW, Kilgore PE, Kim EJ, Kim SA, Anh DD, Seki M. Loop-mediated isothermal amplification assay for detection of *Haemophilus influenzae* type b in cerebrospinal fluid. J Clin Microbiol. 2011;49:3621-6 (https://doi.org/10.1128/JCM.00515-11).

82. McKenna JP, Fairley DJ, Shields MD, Cosby SL, Wyatt DE, McCaughey C et al. Development and clinical validation of a loop-mediated isothermal amplification method for the rapid detection of *Neisseria meningitidis*. Diagn Microbiol Infect Dis. 2011;69:137-44 (https://doi.org/10.1016/j.diagmicrobio.2010.10.008).

83. Kim DW, Kilgore PE, Kim EJ, Kim SA, Anh DD, Dong BQ et al. The enhanced pneumococcal LAMP assay: a clinical tool for the diagnosis of meningitis due to *Streptococcus pneumoniae*. PLoS One. 2012;7:e42954 (https://doi.org/10.1371/journal.pone.0042954).

84. Lee D, Kim EJ, Kilgore PE, Kim SA, Takahashi H, Ohnishi M et al. Clinical evaluation of a loop-mediated isothermal amplification (LAMP) assay for rapid detection of *Neisseria meningitidis* in cerebrospinal fluid. PLoS One. 2015;10:e0122922 (https://doi.org/10.1371/journal.pone.0122922).

85. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. Clin Microbiol Rev. 2010;23:467-92 (https://doi.org/10.1128/CMR.00070-09).

86. Geiseler PJ, Nelson KE, Levin S, Reddi KT, Moses VK. Community-acquired purulent meningitis: a review of 1316 cases during the antibiotic era, 1954–1976. Rev Infect Dis. 1980;2:725-45 (https://doi.org/10.1093/clinids/2.5.725).

87. Lembo RM, Marchant CD. Acute phase reactants and risk of bacterial meningitis among febrile infants and children. Ann Emerg Med. 1991;20:36-40 (https://doi.org/10.1016/s0196-0644(05)81115-1).

88. Morales Casado MI, Moreno Alonso F, Juárez Belaunde AL, Heredero Gálvez E, Talavera Encinas O, Julián-Jiménez A. Ability of procalcitonin to predict bacterial meningitis in the emergency department. Neurologia. 2016;31:9-17 (https://doi.org/10.1016/j.nrl.2014.07.003).

89. Morales-Casado MI, Julián-Jiménez A, Moreno-Alonso F, Valente-Rodríguez E, López-Muñoz D, Saura-Montalbán J et al. Rendimiento diagnóstico de la procalcitonina y la proteína C reactiva para predecir meningitis bacteriana en los ancianos en urgencias. [Diagnostic usefulness of procalcitonin and C-reactive protein in the emergency department for predicting bacterial meningitis in the elderly]. Enferm Infecc Microbiol Clin. 2016;34:8-16 (https://doi.org/10.1016/j.eimc.2015.02.019).

90. Umran RM, Radhi NH. Diagnostic value of serum procalcitonin level in differentiating bacterial from nonbacterial meningitis in children. Iran J Pediatr. 2014;24:739-44 (https://pubmed.ncbi.nlm.nih.gov/26019780/).

91. Ahmed MA, Askar GA, Farghaly HS, Ahmed AO, Kamal DT, Ahmed SS et al. Accuracy of cerebrospinal fluid C-reactive protein and multiplex polymerase chain reaction and serum procalcitonin in diagnosis of bacterial and viral meningitis in children. Acta Neurol Taiwan. 2022;31(2):61-71 (https://pubmed.ncbi.nlm.nih.gov/35266132/).

92. Santotoribio JD, Cuadros-Muñoz JF, García-Casares N. Comparison of C reactive protein and procalcitonin levels in cerebrospinal fluid and serum to differentiate bacterial from viral meningitis. Ann Clin Lab Sci. 2018;48:506-10 (https://pubmed.ncbi.nlm.nih.gov/30143494/).

93. El Shorbagy HH, Barseem NF, Abdelghani WE, Suliman HA, Al-Shokary AH, Elsadek AE et al. The value of serum procalcitonin in acute meningitis in children. J Clin Neurosci. 2018;56:28-33 (https://doi.org/10.1016/j.jocn.2018.08.012).

94. Shen HY, Gao W, Cheng JJ, Zhao SD, Sun Y, Han ZJ et al. Direct comparison of the diagnostic accuracy between blood and cerebrospinal fluid procalcitonin levels in patients with meningitis. Clin Biochem. 2015;48:1079-82 (https://doi.org/10.1016/j.clinbiochem.2015.06.017).

95. Zhang L, Ma L, Zhou X, Meng J, Wen J, Huang R et al. Diagnostic value of procalcitonin for bacterial meningitis in children: a comparison analysis between serum and cerebrospinal fluid procalcitonin levels. Clin Pediatr. 2019;58:159-65 (https://doi.org/10.1177/0009922818809477).

96. WHO guidelines for malaria, 16 October 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/373339).

97. Nuorti JP, Butler JC, Gelling L, Kool JL, Reingold AL, Vugia DJ. Epidemiologic relation between HIV and invasive pneumococcal disease in San Francisco County, California. Ann Intern Med. 2000;132:182-90 (https://doi.org/10.7326/0003-4819-132-3-200002010-00003).

98. Marcus JL, Baxter R, Leyden WA, Muthulingam D, Yee A, Horberg MA et al. Invasive pneumococcal disease among HIV-infected and HIV-uninfected adults in a large integrated healthcare system. AIDS Patient Care STDS. 2016;30:463-70 (https://doi.org/10.1089/apc.2016.0165).

99. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, 2021 update edition. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/342899).

100. 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;345:1727-33 (https://doi.org/10.1056/NEJMoa010399).

101. Quagliarello VJ, Scheld WM. Treatment of bacterial meningitis. N Engl J Med. 1997;336:708-16 (https://doi.org/10.1056/NEJM199703063361007).

102. van de Beek D, Brouwer M, Hasbun R, Koedel U, Whitney CG, Wijdicks E. Community-acquired bacterial meningitis. Nat Rev Dis Primers. 2016;2:16074 (https://doi.org/10.1038/nrdp.2016.74).

103. Hieber JP, Nelson JD. A pharmacologic evaluation of penicillin in children with purulent meningitis. N Engl J Med. 1977;297:410-3 (https://doi.org/10.1056/NEJM197708252970802).

104. Kaplan SL, Smith EO, Wills C, Feigin RD. Association between preadmission oral antibiotic therapy and cerebrospinal fluid findings and sequelae caused by *Haemophilus influenzae* type b meningitis. Pediatr Infect Dis. 1986;5:626-32 (https://doi.org/10.1097/00006454-198611000-00005).

105. Roznovsky L, Krizova P, Struncova V, Dostal V, Plisek S, Kasal E et al. Administration of antibiotics before admission in patients with meningococcal disease. Cent Eur J Public Health. 2003;11:14-8 (https://www.ncbi.nlm.nih.gov/pubmed/12690797).

106. Auburtin M, Wolff M, Charpentier J, Varon E, Le Tulzo Y, Girault C et al. Detrimental role of delayed antibiotic administration and penicillin-nonsusceptible strains in adult intensive care unit patients with pneumococcal meningitis: the PNEUMOREA prospective multicenter study. Crit Care Med. 2006;34:2758-65 (https://doi.org/10.1097/01.CCM.0000239434.26669.65).

107. Zalmanovici Trestioreanu A, Fraser A, Gafter-Gvili A, Paul M, Leibovici L. Antibiotics for preventing meningococcal infections. Cochrane Database Syst Rev. 2013;2013:CD004785 (https://doi.org/10.1002/14651858.CD004785.pub5).

108. Charlier C, Perrodeau É, Leclercq A, Cazenave B, Pilmis B, Henry B et al. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. Lancet Infect Dis. 2017;17:510-9 (https://doi.org/10.1016/s1473-3099(16)30521-7).

109. Koopmans MM, Brouwer MC, Vázquez-Boland JA, van de Beek D. Human listeriosis. Clin Microbiol Rev. 2023;36:e0006019 (https://doi.org/10.1128/cmr.00060-19).

110. The selection and use of essential medicines 2023: web annex A: World Health Organization model list of essential medicines: 23rd list (2023). Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/371090).

111. Aronoff SC, Reed MD, O'Brien CA, Blumer JL. Comparison of the efficacy and safety of ceftriaxone to ampicillin/chloramphenicol in the treatment of childhood meningitis. J Antimicrob Chemother. 1984;13:143-51 (https://doi.org/10.1093/jac/13.2.143).

112. Barson WJ, Miller MA, Brady MT, Powell DA. Prospective comparative trial of ceftriaxone vs. conventional therapy for treatment of bacterial meningitis in children. Pediatr Infect Dis. 1985;4:362-8. (https://doi.org/10.1097/00006454-198507000-00006).

113. Bryan JP, Rocha H, da Silva HR, Taveres A, Sande MA, Scheld WM. Comparison of ceftriaxone and ampicillin plus chloramphenicol for the therapy of acute bacterial meningitis. Antimicrob Agents Chemother. 1985;28:361-8 (https://doi.org/10.1128/AAC.28.3.361).

114. Congeni BL. Comparison of ceftriaxone and traditional therapy of bacterial meningitis. Antimicrob Agents Chemother. 1984;25:40-4 (https://doi.org/10.1128/AAC.25.1.40).

115. del Rio MA, Chrane D, Shelton S, McCracken GH, Jr., Nelson JD. Ceftriaxone versus ampicillin and chloramphenicol for treatment of bacterial meningitis in children. Lancet. 1983;1:1241-4 (https://doi.org/10.1016/s0140-6736(83)92696-x).

116. Girgis NI, Abu el Ella AH, Farid Z, Woody JN, Lissner C. Ceftriaxone compared with a combination of ampicillin and chloramphenicol in the treatment of bacterial meningitis in adults. Drugs Exp Clin Res. 1987;13:497-500. (https://www.ncbi.nlm.nih.gov/pubmed/3428132).

117. Girgis NI, Abu el-Ella AH, Farid Z, Haberberger RL, Woody JN. Ceftriaxone alone compared to ampicillin and chloramphenicol in the treatment of bacterial meningitis. Chemotherapy. 1988;34(Suppl 1):16-20 (https://doi.org/10.1159/000238642).

118. Haffejee IE. Cefotaxime versus penicillin-chloramphenicol in purulent meningitis: a controlled single-blind clinical trial. Ann Trop Paediatr. 1988;8:225-9 (https://doi.org/10.1080/02724936.1988.11748576).

119. Jacobs RF, Wells TG, Steele RW, Yamauchi T. A prospective randomized comparison of cefotaxime vs ampicillin and chloramphenicol for bacterial meningitis in children. J Pediatr. 1985;107:129-33 (https://doi.org/10.1016/s0022-3476(85)80634-x).

120. Marhoum el Filali K, Noun M, Chakib A, Zahraoui M, Himmich H. Ceftriaxone versus penicillin G in the short-term treatment of meningococcal meningitis in adults. Eur J Clin Microbiol Infect Dis. 1993;12:766-8 (https://doi.org/10.1007/BF02098465).

121. Narciso P, De Mori P, Giannuzzi R, Tocci G, Visco G. Ceftriaxon versus ampicillin therapy for purulent meningitis in adults. Drugs Exp Clin Res. 1983;9:717-19.

122. Nathan N, Borel T, Djibo A, Evans D, Djibo S, Corty JF et al. Ceftriaxone as effective as long-acting chloramphenicol in short-course treatment of meningococcal meningitis during epidemics: a randomised non-inferiority study. Lancet. 2005;366:308-13. (https://doi.org/10.1016/S0140-6736(05)66792-X).

123. Odio CM, Faingezicht I, Salas JL, Guevara J, Mohs E, McCracken GH, Jr. Cefotaxime vs. conventional therapy for the treatment of bacterial meningitis of infants and children. Pediatr Infect Dis. 1986;5:402-7 (https://doi.org/10.1097/00006454-198607000-00005).

124. Peltola H, Anttila M, Renkonen OV; The Finnish Study Group. Randomised comparison of chloramphenicol, ampicillin, cefotaxime, and ceftriaxone for childhood bacterial meningitis. Lancet. 1989;1:1281-7 (https://doi.org/10.1016/s0140-6736(89)92685-8).

125. Pichler H, Diridl G, Jeschko E, Wolf D. Ceftriaxone vs piperacillin in patients with bacterial meningitis. J Chemother. 1989;1:682-3. (https://www.ncbi.nlm.nih.gov/pubmed/16312591).

126. Sharma PR, Adhikari RK, Joshi MP, Lal M, Chodon T, Pokhrel BM et al. Intravenous chloramphenicol plus penicillin versus intramuscular ceftriaxone for the treatment of pyogenic meningitis in Nepalese children. Trop Doct. 1996;26:84-5. (https://doi.org/10.1177/004947559602600215).

127. Steele RW, Bradsher RW. Comparison of ceftriaxone with standard therapy for bacterial meningitis. J Pediatr. 1983;103:138-41 (https://doi.org/10.1016/s0022-3476(83)80801-4).

128. Tuncer AM, Gur I, Ertem U, Ece A, Turkmen S, Deniz B et al. Once daily ceftriaxone for meningococcemia and meningococcal meningitis. Pediatr Infect Dis J. 1988;7:711-3 (https://doi.org/10.1097/00006454-198810000-00009).

129. Wells TG, Trang JM, Brown AL, Marmer BC, Jacobs RF. Cefotaxime therapy of bacterial meningitis in children. J Antimicrob Chemother. 1984;14(Suppl B):181-9 (https://doi.org/10.1093/jac/14.suppl_b.181).

130. Zavala I, Barrera E, Nava A. Ceftriaxone in the treatment of bacterial meningitis in adults. Chemotherapy. 1988;34 Suppl 1:47-52 (https://doi.org/10.1159/000238647).

131. Molyneux E, Nizami SQ, Saha S, Huu KT, Azam M, Bhutta ZA et al. 5 versus 10 days of treatment with ceftriaxone for bacterial meningitis in children: a double-blind randomised equivalence study. Lancet. 2011;377:1837-45 (https://doi.org/10.1016/S0140-6736(11)60580-1).

132. Vaswani ND, Gupta N, Yadav R, Nadda A. Seven versus ten days antibiotics course for acute pyogenic meningitis in children: a randomized controlled trial. Indian J Pediatr. 2021;88:246-51 (https://doi.org/10.1007/s12098-020-03454-1).

133. Noska A, Kyrillos R, Hansen G, Hirigoyen D, Williams DN. The role of antiviral therapy in immunocompromised patients with herpes simplex virus meningitis. Clin Infect Dis. 2015;60:237-42 (https://doi.org/10.1093/cid/ciu772).

134. Shalabi M, Whitley RJ. Recurrent benign lymphocytic meningitis. Clin Infect Dis. 2006;43:1194-7 (https://doi.org/10.1086/508281).

135. Gardner P. Clinical practice. Prevention of meningococcal disease. N Engl J Med. 2006;355:1466-73 (https://doi.org/10.1056/NEJMcp063561).

136. Coldiron ME, Assao B, Page AL, Hitchings MDT, Alcoba G, Ciglenecki I et al. Single-dose oral ciprofloxacin prophylaxis as a response to a meningococcal meningitis epidemic in the African meningitis belt: a 3-arm, open-label, cluster-randomized trial. PLoS Med. 2018;15:e1002593 (https://doi.org/10.1371/journal.pmed.1002593).

137. Analysis of endemic meningococcal disease by serogroup and evaluation of chemoprophylaxis. J Infect Dis. 1976;134:201-4 (https://doi.org/10.1093/infdis/134.2.201).

138. Bhatt SM, Lauretano A, Cabellos C, Halpin C, Levine RA, Xu WZ et al. Progression of hearing loss in experimental pneumococcal meningitis: correlation with cerebrospinal fluid cytochemistry. J Infect Dis. 1993;167:675-83 (https://doi.org/10.1093/infdis/167.3.675).

139. Lutsar I, Friedland IR, Jafri HS, Wubbel L, Ahmed A, Trujillo M et al. Factors influencing the anti-inflammatory effect of dexamethasone therapy in experimental pneumococcal meningitis. J Antimicrob Chemother. 2003;52:651-5 (https://doi.org/10.1093/jac/dkg417).

140. van Furth AM, Roord JJ, van Furth R. Roles of proinflammatory and anti-inflammatory cytokines in pathophysiology of bacterial meningitis and effect of adjunctive therapy. Infect Immun. 1996;64:4883-90 (https://doi.org/10.1128/iai.64.12.4883-4890.1996).

141. Saez-Llorens X, Jafari HS, Severien C, Parras F, Olsen KD, Hansen EJ et al. Enhanced attenuation of meningeal inflammation and brain edema by concomitant administration of anti-CD18 monoclonal antibodies and dexamethasone in experimental *Haemophilus* meningitis. J Clin Invest. 1991;88:2003-11 (https://doi.org/10.1172/JCI115527).

142. Bennett IL, Finland M, Hamburger M, Kass EH, Lepper M, Waisbren BA. The effectiveness of hydrocortisone in the management of severe infections- a double blind study. JAMA. 1963;183:166-9. (https://doi.org/10.1001/jama.1963.63700060029012).

143. Belsey MA, Hoffpauir CW, Smith MHD. Dexamethasone in the treatment of acute bacterial meningitis: the effect of study design on the interpretation of results. Pediatrics. 1969;44:503-13 (https://doi.org/10.1542/peds.44.4.503).

144. DeLemos RA, Haggerty RJ. Corticosteroids as an adjunct to treatment in bacterial meningitis: a controlled clinical trial. Pediatrics. 1969;44(1):30-4. (https://pubmed.ncbi.nlm.nih.gov/4893958/).

145. Bademosi O, Osuntokun BO. Prednisolone in the treatment of pneumococcal meningitis. Trop Geogr Med. 1979;31(1):53-6 (https://pubmed.ncbi.nlm.nih.gov/483371/).

146. Lebel MH, Freij BJ, Syrogiannopoulos GA, Chrane DF, Hoyt MJ, Stewart SM. Dexamethasone therapy for bacterial meningitis. Results of two double-blind, placebo-controlled trials. N Engl J Med. 1988;319:964-71. (https://doi.org/10.1056/NEJM198810133191502).

147. Girgis NI, Farid Z, Mikhail IA, Farrag I, Sultan Y, Kilpatrick ME. Dexamethasone treatment for bacterial meningitis in children and adults. Pediatric Inf Dis J. 1989;8:848-51 (https://doi.org/10.1097/00006454-198912000-00004).

148. Lebel MH, Jean Hoyt M, Waagner DC, Rollins NK, Finitzo T, McCracken GH. Magnetic resonance imaging and dexamethasone therapy for bacterial meningitis. Am J Dis Child. 1989;143:201-306 (https://doi.org/10.1001/archpedi.1989.02150150055017).

149. Odio CM, Faingezicht I, Paris M, Nassar M, Baltodano A, Rogers J et al. The beneficial effects of early dexamethasone administration in infants and children with bacterial meningitis. N Engl J Med. 1991;324:1525-31 (https://doi.org/10.1056/NEJM199105303242201).

150. Schaad UB, Lips U, Gnehm HE, Blumberg A, Heinzer I, Wedgwood J. Dexamethasone therapy for bacterial meningitis in children. Lancet. 1993;342:457-61. (https://doi.org/10.1016/0140-6736(93)91592-a).

151. King SM, Law B, Langley JM, Heurter H, Bremner D, Wang EE et al. Dexamethasone therapy for bacterial meningitis: better never than late? Can J Infect Dis. 1994;5:210-5 (https://doi.org/10.1155/1994/257198).

152. Ciana G, Parmar N, Antonio C, Pivetta S, Tamburlini G, Cuttini M. Effectiveness of adjunctive treatment with steroids in reducing short-term mortality in a high-risk population of children with bacterial meningitis. J Trop Pediatr. 1995;41:164-8 (https://doi.org//10.1093/tropej/41.3.164).

153. Kanra GY, Ozen H, Secmeer G, Ceyhan M, Ecevit Z, Belgin E. Beneficial effects of dexamethasone in children with pneumococcal meningitis. Pediatric Inf Dis J. 1995;14:490-4 (https://doi.org/10.1097/00006454-199506000-00005).

154. Kilpi T, Peltola H, Jauhianen T, Kallio MJT. Oral glycerol and intravenous dexamethasone in preventing neurologic and audiologic sequelae of childhood bacterial meningitis. Pediatric Inf Dis J. 1995;14:270-8 (https://doi.org/10.1097/00006454-199504000-00005).

155. Wald ER, Kaplan SL, Edward OM, Sabo D, Ross L, Arditi M et al. Dexamethasone therapy for children with bacterial meningitis. Pediatrics. 1995;95:21-8 (https://doi.org/10.1542/peds.95.1.21).

156. Qazi SA, Khan MA, Mughal N, Ahmad M, Joomro B, Sakata Y et al. Dexamethasone and bacterial meningitis in Pakistan. Arch Dis Childhood. 1996;75:482-8. (https://doi.org/10.1136/adc.75.6.482).

157. Shembesh NM, Elbargathy SM, Kashbur IM, Rao BN, Mahmoud S. Dexamethasone as an adjunctive treatment of bacterial meningitis. Indian J Pediatr. 1997;64:517-22. (https://doi.org/10.1007/BF02737759).

158. Thomas R, Le Tulzo Y, Bouget J, Camus C, Michelet C, Rennes C et al. Trial of dexamethasone treatment for severe bacterial meningitis in adults. Intensive Care Med. 1999;25:475-80 (https://doi.org/10.1007/s001340050883).

159. Gans JD, Van de Beek D. Dexamethasone in adults with bacterial meningitis. N Engl J Med. 2002;347:1549-56 (https://doi.org/10.1056/NEJMoa021334).

160. Gijwani D, Kumhar MR, Singh VB, Chadda VS, Soni PK, Nayak KC et al. Dexamethasone therapy for bacterial meningitis in adults: a double blind placebo control study. Neurol India. 2002;50:63-7 (https://pubmed.ncbi.nlm.nih.gov/11960154/).

161. Molyneux EM, Walsh AL, Forsyth H, Mwenechanya J, Kayira K, Njobvu LB et al. Dexamethasone treatment in childhood bacterial meningitis in Malawi: a randomised controlled trial. Lancet. 2002;360:211-8 (https://doi.org/10.1016/s0140-6736(02)09458-8).

162. Weisfelt M, Hoogman M, Van De Beek D, De Gans J, Dreschler WA, Schmand BA. Dexamethasone and long-term outcome in adults with bacterial meningitis. Annals of Neurology. 2006;60:456-68 (https://doi.org/10.1002/ana.20944).

163. Thi Hoang Mai N, Thi Hong Chau T, Thwaites G, Van Chuong L, Xuan Sinh D, Dang Trung Nghia H et al. Dexamethasone in Vietnamese adolescents and adults with bacterial meningitis. N Engl J Med. 2007;24:2431-71. (https://doi.org/10.1056/NEJMoa070852).

164. Peltola H, Roine I, Fernández J, Zavala I, Ayala SG, Mata AG et al. Adjuvant glycerol and/or dexamethasone to improve the outcomes of childhood bacterial meningitis: a prospective, randomized, double-blind, placebo-controlled trial. Clin Infect Dis. 2007;45:1277-86 (https://doi.org/10.1086/522534).

165. Sankar J, Singhi P, Bansal A, Ray P, Singhi S. Role of dexamethasone and oral glycerol in reducing hearing and neurological sequelae in children with bacterial meningitis. Indian Pediatrics. 2007;44:649-56 (https://pubmed.ncbi.nlm.nih.gov/17921553/).

166. Muhammad Khan D, Adnan Ahmed Ather CH, Mahfooz Khan I. Comparison of dexamethasone versus placebo for management of bacterial meningitis. Pak J Med Health Sci. 2016;10(4):1296-9 (https://pjmhsonline.com/2016/oct_dec/pdf/1297.pdf).

167. Scarborough M, Gordon SB, Whitty CJ, French N, Njalale Y, Chitani A et al. Corticosteroids for bacterial meningitis in adults in sub-Saharan Africa. N Engl J Med. 2007;357:2441-50 (https://doi.org/10.1056/NEJMoa065711).

168. Brouwer MC, McIntyre P, Prasad K, van de Beek D. Corticosteroids for acute bacterial meningitis. Cochrane Database Syst Rev. 2015;9:CD004405 (https://doi.org/10.1002/14651858.CD004405.pub5).

169. WHO consolidated guidelines on tuberculosis: module 4: treatment: drug-susceptible tuberculosis treatment. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/353829).

170. Durward QJ, Amacher AL, Del Maestro RF, Sibbald WJ. Cerebral and cardiovascular responses to changes in head elevation in patients with intracranial hypertension. J Neurosurg. 1983;59:938-44 (https://doi.org/10.3171/jns.1983.59.6.0938).

171. Stevens RD, Shoykhet M, Cadena R. Emergency neurological life support: intracranial hypertension and herniation. Neurocrit Care. 2015;23(Suppl 2):S76-82. (https://doi.org/10.1007/s12028-015-0168-z).

172. Molyneux EM, Kawaza K, Phiri A, Chimalizeni Y, Mankhambo L, Schwalbe E et al. Glycerol and acetaminophen as adjuvant therapy did not affect the outcome of bacterial meningitis in Malawian children. Pediatr Infect Dis J. 2014;33:214-6 (https://doi.org/10.1097/INF.0000000000000122).

173. Ajdukiewicz KMB, Cartwright KE, Scarborough M, Mwambene JB, Goodson P, Molyneux ME et al. Glycerol adjuvant therapy in adults with bacterial meningitis in a high HIV seroprevalence setting in Malawi: a double-blind, randomised controlled trial. Lancet Infect Dis. 2011;11:293-300 (https://doi.org/10.1016/S1473-3099(10)70317-0).

174. Wall EC, Cartwright K, Scarborough M, Ajdukiewicz KM, Goodson P, Mwambene J et al. High mortality amongst adolescents and adults with bacterial meningitis in sub-Saharan Africa: an analysis of 715 cases from Malawi. PLoS ONE. 2013;8 (https://doi.org/10.1371/journal.pone.0069783).

175. Singhi SC, Singhi PD, Srinivas B, Narakesri HP, Ganguli NK, Sialy R et al. Fluid restriction does not improve the outcome of acute meningitis. Pediatr Infect Dis J. 1995;14:495-503 (https://doi.org/10.1097/00006454-199506000-00006).

176. Duke T, Mokela D, Frank D, Michael A, Paulo T, Mgone J et al. Management of meningitis in children with oral fluid restriction or intravenous fluid at maintenance volumes: a randomised trial. Ann Trop Paediatr. 2002;22:145-57 (https://doi.org/10.1179/027249302125000878).

177. Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders, third edition. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/374250).

178. mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings: mental health Gap Action Programme (mhGAP). version 2.0 ed. Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/250239).

179. Dhawan SR, Sahu JK, Singhi P, Sankhyan N, Jayashree M. Comparison of 4 weeks versus 12 weeks antiseizure medication for acute symptomatic seizures in children with acute encephalitis syndrome: an open-label, randomized controlled trial. Seizure. 2021;92:182-8 (https://doi.org/10.1016/j.seizure.2021.09.005).

180. Herzig-Nichtweiß J, Salih F, Berning S, Malter MP, Pelz JO, Lochner P et al. Prognosis and management of acute symptomatic seizures: a prospective, multicenter, observational study. Ann Intensive Care. 2023;13:85 (https://doi.org/10.1186/s13613-023-01183-0).

181. Schiess N, Groce NE, Dua T. The impact and burden of neurological sequelae following bacterial meningitis: a narrative review. Microorganisms. 2021;9 (https://doi.org/10.3390/microorganisms9050900).

182. Jit M. The risk of sequelae due to pneumococcal meningitis in high-income countries: a systematic review and meta-analysis. J Infect. 2010;61:114-24 (https://doi.org/10.1016/j.jinf.2010.04.008).

183. Edmond K, Clark A, Korczak VS, Sanderson C, Griffiths UK, Rudan I. Global and regional risk of disabling sequelae from bacterial meningitis: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10:317-28 (https://doi.org/10.1016/S1473-3099(10)70048-7).

184. Global report on health equity for persons with disabilities. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/364834).

185. Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/371495).

186. World Health Organization (WHO), USAID International Disability Alliance. Priority assistive products list: improving access to assistive technology for everyone, everywhere. Geneva: WHO; 2016 (https://iris.who.int/handle/10665/207694).

187. Convention on the Rights of Persons with Disabilities (CRPD) [website]. New York: United Nations; 2006 (https://social.desa.un.org/issues/disability/crpd/convention-on-the-rights-of-persons-with-disabilities-crpd).

188. Package of interventions for rehabilitation [website]. Geneva: World Health Organization; 2025 (https://www.who.int/teams/noncommunicable-diseases/sensory-functions-disability-and-rehabilitation/rehabilitation/service-delivery/package-of-interventions-for-rehabilitation, accessed 8 January 2025).

189. Package of interventions for rehabilitation: module 2: musculoskeletal conditions. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/370503).

190. Package of interventions for rehabilitation: module 3: neurological conditions. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/370504).

191. Package of interventions for rehabilitation: module 5: neurodevelopmental disorders. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/370507).

192. Package of interventions for rehabilitation: module 6: sensory conditions. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/370508).

193. Christie S, Chan V, Mollayeva T, Colantonio A. Systematic review of rehabilitation intervention outcomes of adult and paediatric patients with infectious encephalitis. BMJ Open. 2018;8:e015928 (https://doi.org/10.1136/bmjopen-2017-015928).

194. Package of interventions for rehabilitation: module 1: introduction. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/370502).

195. Nurturing care for early childhood development: a framework for helping children survive and thrive to transform health and human potential. Geneva: World Health Organization; 2018 (https://iris.who.int/handle/10665/272603).

196. Hearing screening: considerations for implementation. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/344797).

197. The selection and use of essential in vitro diagnostics: report of the fourth meeting of the WHO Strategic Advisory Group of Experts on In Vitro Diagnostics, 2022 (including the fourth WHO model list of essential in vitro diagnostics). Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/373322).

Annex 1. Guideline development teams

WHO Steering Group	
WHO headquarters	
Virginia Benassi	Division of Universal Health Coverage/Life Course Department of Immunization, Vaccines and Biologicals
Silvia Bertagnolio	Division of Antimicrobial Resistance Department of Surveillance, Prevention and Control
Nicolò Binello	Health Emergencies Programme Department of Epidemic and Pandemic Threat Management
Elaine Brohan	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Department of Mental Health, Brain Health and Substance Use
Emilie Calvello Hynes	Division of Universal Health Coverage/Life Course Department of Integrated Health Services
Shelly Chadha	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Department of Noncommunicable Diseases
Janet Diaz	Health Emergencies Programme Department of Country Readiness Strengthening
Tarun Dua	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Department of Mental Health, Brain Health and Substance Use
Antoine Durupt	Division of Universal Health Coverage/Life Course Department of Immunization, Vaccines and Biologicals
Antony Dutine	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Department of Noncommunicable Diseases
Katya Fernandez	Health Emergencies Programme Department of Epidemic and Pandemic Threat Management
Medea Gegia	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Global Tuberculosis Programme
Benedikt Huttner	Division of Antimicrobial Resistance Department of Surveillance, Prevention and Control

Lorenzo Pezzoli	Health Emergencies Programme Department of Epidemics and Pandemic Threat Management
Marie-Pierre Preziosi	Division of Universal Health Coverage/Life Course Department of Immunization, Vaccines and Biologicals
Ajay Rangaraj	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Global HIV, Hepatitis and Sexually Transmitted Infections Programmes
Nicoline Schiess	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Department of Mental Health, Brain Health and Substance Use
Heidi Soeters	Division of Universal Health Coverage/Life Course Department of Immunization, Vaccines and Biologicals
Shamsuzzoha Syed	Division of Universal Health Coverage/Life Course Special Programme on Primary Health Care
Carole Tevi Benissan	Division of Universal Health Coverage/Life Course Department of Immunization, Vaccines and Biologicals
Francesco Venuti	Division of Universal Health Coverage/Communicable and Noncommunicable Diseases Department of Mental Health, Brain Health and Substance Use
Wilson Were	Division of Universal Health Coverage/Life Course Department of Maternal, Newborn, Child and Adolescent Health and Ageing
WHO regional offices	
Florence Baingana	Regional Office for Africa Department of Mental Health and Substance Use
Chido Rwafa Madzvamutse	Regional Office for Africa Department of Mental Health and Substance Use
André Bita Fouda	Regional Office for Africa Department of Vaccine-Preventable Diseases
Andrea Bruni	Regional Office for South-East Asia Department of Mental Health and Substance Use
Jose Hagan	Regional Office for Europe Department of Vaccine-Preventable Diseases and Immunization

Quamrul Hasan	Regional Office for the Eastern Mediterranean Department of Immunization, Vaccine-Preventable Diseases and Polio Transition
Manish Kakkar	Regional Office for South-East Asia Health Emergencies Programme
Chiori Kodama	Regional Office for the Eastern Mediterranean Health Emergencies Programme
Anderson Latt	Regional Office for Africa Department of Epidemic Preparedness and Response
Ledia Lazeri	Regional Office for Europe Department of Mental Health and Substance Use
Tondo Njambe Emmanuel	Regional Office for South-East Asia Department of Immunization and Vaccine Development
Renato Oliveira e Souza	Regional Office for the Americas Department of Mental Health and Substance Use
Pilar Ramon-Pardo	Regional Office for the Americas Department of Communicable Diseases Prevention, Control and Elimination
Angel Rodriguez	Regional Office for the Americas Health Emergencies Programme
Khalid Saeed	Regional Office for the Eastern Mediterranean Department of Mental Health and Substance Use
Gina Samaan	Regional Office for the Western Pacific Health Emergencies Programme
Martin Vandendyck	Regional Office for the Western Pacific Department of Mental Health and Substance Use
Xiaojun Wang	Regional Office for the Western Pacific Department of Vaccine-Preventable Diseases and Immunization
Marc-Allain Widdowson	Regional Office for Europe Health Emergencies Programme

Guideline Development Group		
Name and affiliation	**WHO Region**	**Area of expertise**
Taoufik Alsaadi American Center of Psychiatry and Neurology Abu Dhabi, United Arab Emirates	Eastern Mediterranean	Neurology Epilepsy
Action Amos International Bureau of Epilepsy Blantyre, Malawi	Africa	Person with lived experience Epilepsy and disability
Satinder Aneja (co-chair) Lady Hardinge Medical College New Delhi, India	South-East Asia	Paediatric neurology
Matthijs Brouwer Amsterdam University Medical Centers Amsterdam, Netherlands (Kingdom of the)	Europe	Neurological infectious diseases
Chahnez Charfi Triki University of Sfax Sfax, Tunisia	Eastern Mediterranean	Paediatric neurology
Adam Cohen Centers for Disease Control and Prevention Atlanta, United States of America	Americas	Epidemiology of infectious diseases Infectious disease control and prevention
Matt Coldiron (co-chair) Médecins Sans Frontières, Epicentre New York City, USA	Americas	Epidemiology of infectious diseases
Isabel Elicer Hospital Dr. Sótero del Río Santiago, Chile	Americas	Neurological infectious diseases
Nora Groce University College London London, United Kingdom of Great Britain and Northern Ireland	Europe	Medical anthropology Disability Public health
Mariam Hassan Shaukat Khanum Memorial Cancer Hospital and Research Centre Lahore, Pakistan	Eastern Mediterranean	Clinical infectious diseases Clinical trials

Robert Heyderman University College London London, United Kingdom	Europe	Clinical infectious diseases Epidemiology of infectious diseases
Angelina Kakooza Makerere University Kampala, Uganda	Africa	Paediatric neurology Paediatric infectious diseases
Hanan Khalil Qatar University Doha, Qatar	Eastern Mediterranean	Neurological rehabilitation Disability
Andy Marso American Academy of Family Physicians Kansas, USA	Americas	Person with lived experience
Kate Milner University of Melbourne Melbourne, Australia	Western Pacific	Paediatric neurology Neurodevelopmental disorders Disability
Charles Newton University of Oxford Oxford, United Kingdom	Europe	Paediatric neurology Neurological infectious diseases Epidemiology of infectious diseases
Njideka Okubadejo African Academy of Neurology Lagos, Nigeria	Africa	Neurological infectious diseases
Pierre Ongolo Zogo University of Yaounde Yaounde, Cameroon	Africa	Epidemiology Public health Radiology
Armel Poda University Nazi Boni Bobo-Dioulasso, Burkina Faso	Africa	Clinical infectious diseases Epidemiology of infectious diseases
Kameshwar Prasad All India Institute of Medical Sciences New Delhi, India	South-East Asia	Neurology Epidemiology Clinical trials
Paula Reges Oswaldo Cruz Foundation/Fiocruz Rio de Janeiro, Brazil	Americas	Clinical infectious diseases Epidemiology of infectious diseases Public health

James Sejvar Centers for Disease Control and Prevention Atlanta, USA	Americas	Neuroepidemiology Infectious disease control and prevention
Pratibha Singhi Amrita Hospital Faridabad, India	South-East Asia	Paediatric neurology Paediatric infectious diseases
Tom Solomon University of Liverpool Liverpool, United Kingdom	Europe	Neurological infectious diseases
Kevin Tan Duke–NUS Medical School Singapore, Singapore	Western Pacific	Neurology Neuroimmunology Neurological infectious diseases
Mekonnen Teferi Armauer Hansen Research Institute Addis Ababa, Ethiopia	Africa	Clinical infectious diseases Clinical trials

Systematic review teams

Name and affiliation	Thematic domain
Nina Groeneveld Amsterdam University Medical Centers Amsterdam, Netherlands (Kingdom of the)	Diagnosis
Daniel Munblit King's College London, United Kingdom	Qualitative evidence across all domains
Netravathi M. National Institute of Mental Health and Neuro-Sciences Bengaluru, India	Adjunctive treatment and supportive care
Manya Prasad Institute of Liver and Biliary Sciences New Delhi, India	Anti-seizure medicines and sequelae
Priscilla Rupali Christian Medical College Vellore Tamil Nadu, India	Antimicrobial treatment and prophylaxis
Kiran Thakur Columbia University New York, USA	Sequelae

Guideline methodologist

Name and affiliation
Ani Movsisyan Ludwig-Maximilians-Universität München Munich, Germany

WHO librarian

Name and affiliation
Kavita Kothari WHO Library and Digital Information Networks Geneva, Switzerland

External Review Group

Name and affiliation	WHO Region
Melody Asukile University Teaching Hospitals Lusaka, Zambia	Africa
Gidu Said Bakhit Juba Teaching Hospital Juba, South Sudan	Africa
Matthew Broom Auckland City Hospital Auckland, New Zealand	Western Pacific
Dominique Andree Yvette Caugant Norwegian Institute of Public Health Oslo, Norway	Europe
Lindsey Enajet ItsME Foundation Amsterdam, Netherlands (Kingdom of the)	Europe
Brian Greenwood London School of Hygiene & Tropical Medicine London, United Kingdom	Europe
Jean Luc Kagayo United Nations Children's Fund (UNICEF) New York, USA	America

Brenda Kwambana Liverpool School of Tropical Medicine Liverpool, United Kingdom	Europe
Bruce Langoulant Meningitis Centre Australia Perth, Australia	Western Pacific
Lucy McNamara Centers for Disease Control and Prevention Atlanta, USA	America
Zomer Sardar Shalamar Medical and Dental College Lahore, Pakistan	Eastern Mediterranean
Miklos Szolics Tawam Hospital Abu Dhabi, United Arab Emirates	Eastern Mediterranean

Annex 2. Declarations of interest

This annex provides a summary of the declared interests of the members of the Guideline Development Group (GDG) and the External Review Group (ERG) and how they were managed.

Guideline Development Group	Declaration of interest	Conflict of interest and management
Taoufik Alsaadi	None	No conflict of interest identified
Action Amos	None	No conflict of interest identified
Satinjar Aneja (co-chair)	None	No conflict of interest identified
Matthijs Brouwer	None	No conflict of interest identified
Chahnez Charfi Triki	None	No conflict of interest identified
Adam Cohen	None	No conflict of interest identified
Matthew Coldiron (co-chair)	None	No conflict of interest identified
Isabel Elicer	None	No conflict of interest identified
Nora Groce	None	No conflict of interest identified
Mariam Hassan	None	No conflict of interest identified
Robert Heyderman	None	No conflict of interest identified
Angelina Kakooza Mwesige	None	No conflict of interest identified
Hanan Khalil	None	No conflict of interest identified
Andy Marso	Paid US$ 500 by the Community Care Network of Kansas (a non-profit group for primary care and safety net clinics) in June 2022 to speak at the training on “Immunizations: It takes all of us”.	No conflict of interest identified
Kate MacKinnon Milner	None	No conflict of interest identified
Charles Newton	None	No conflict of interest identified
Njideka Okubadejo	None	No conflict of interest identified
Pierre Ongolo Zogo	None	No conflict of interest identified
Armel Poda	None	No conflict of interest identified

Kameshwar Prasad	None	No conflict of interest identified
Paula Reges	None	No conflict of interest identified
James Sejvar	None	No conflict of interest identified
Pratibha Singhi	None	No conflict of interest identified
Tom Solomon	Member of the Encephalitis Society (a charity focused on encephalitis awareness, support and research) since 1998 and President of the Encephalitis Society since 2019. Director of The Pandemic Institute (since September 2021), which has received funding from Innova, CSL Seqirus, Aviva and DAM Health (unpaid). Advisor to the GSK Ebola Vaccine programme in 2015 and the Siemens Diagnostic Programme in 2018 and 2019 (paid). Part of the Data Safety Monitoring Committee of the GSK Study to Evaluate the Safety and Immunogenicity of a Candidate Ebola Vaccine in Children GSK3390107A (ChAd3 EBO-Z) vaccine (unpaid). Chaired the Siemens Healthineers Clinical Advisory Board in 2018 and again in 2019 (paid). Co-Chaired the World Health Organization Covid Neuro Coalition task force in 2020 (unpaid) and sat on the United Kingdom of Great Britain and Northern Ireland Government's Advisory Committee on Dangerous Pathogens (ACDP) between 2019 and 2023 (unpaid), and the Medicines and Healthcare products Regulatory Agency (MHRA) Expert Working Group on COVID-19 vaccines between 2020 and 2023 (paid). Advised the United Kingdom COVID-19 Therapeutics Advisory Panel (UK-CTAP) between 2020 and 2021 (unpaid). Member, COVID-19 Vaccines Benefit Risk Expert Working Group, for the Commission on Human Medicines (CHM) committee of the MHRA between 2020 and 2023 (paid). Committee Member of the Wellcome Trust Pathogen Biology and Disease Transmission Discovery Advisory Group (paid).	No conflict of interest identified
Kevin Tan	None	No conflict of interest identified
Mekonnen Teferi	None	No conflict of interest identified

External Review Group	Declaration of interest	Conflict of interest and management
Melody Asukile	None	No conflict of interest identified
Gidu Said Bakhit	None	No conflict of interest identified
Matthew Broom	None	No conflict of interest identified
Dominique Andree Yvette Caugant	None	No conflict of interest identified
Lindsey Enajet	None	No conflict of interest identified
Brian Greenwood	None	No conflict of interest identified
Jean Luc Kagayo	None	No conflict of interest identified
Brenda Kwambana	None	No conflict of interest identified
Bruce Langoulant	None	No conflict of interest identified
Lucy McNamara	None	No conflict of interest identified
Zomer Sardar	None	No conflict of interest identified
Miklos Szolics	None	No conflict of interest identified

Annex 3. Rehabilitation interventions for sequelae

Overview of rehabilitation interventions for sequelae following acute meningitis

Functioning domain[a]	Intervention categories	Examples[b]
Vision impairment	Therapeutic techniques and procedures, exercises and training	Vision skills training Orientation and mobility training
	Assistive products	Provision and training in the use of assistive products for vision, reading and writing, and mobility
Speech, language and communication	Therapeutic techniques and procedures, exercises and training	Speech and language therapy Communication skills training
	Assistive products	Provision and training in the use of assistive products for communication
Neurocognitive functions	Therapeutic techniques and procedures, exercises and training	Cognitive stimulation or training, remediation or behavioural therapy Graded sitting and standing training Relaxation training Physical exercise training
	Assistive products	Provision and training in the use of assistive products for cognition
Motor functions and mobility	Therapeutic techniques and procedures, exercises and training	Swallowing therapy Muscle strengthening exercises Range of motion exercises (Functional) positioning (for prevention of spasticity and contractures) Balance, gait and mobility training Functional training for hand and arm use (including bimanual therapy or constraint-induced movement therapy)
	Assistive products	Provision and training in the use of orthoses, lower or upper limb prostheses, adapted seating equipment, assistive products for mobility

Activities of daily living (ADL)	Therapeutic techniques and procedures, exercises and training	Activities of daily living (ADL) training
	Assistive products	Provision and training in the use of assistive products for self-care
	Environmental modification	Modification of the home environment
Interpersonal interactions and relationships	Therapeutic techniques and procedures, exercises and training	Social skills training Psychosocial interventions
Education and vocation	Therapeutic techniques and procedures, exercises and training	Educational or vocational counselling, training and support
Community and social life	Therapeutic techniques and procedures, exercises and training	Participation-focused interventions
Mental health (depression, anxiety, emotional distress, challenging behaviours)	Therapeutic techniques and procedures, exercises and training	Psychological therapies (including cognitive behavioural therapy) Stress management training Physical exercise training Behavioural interventions
Self-management	Self-management interventions	Education, advice and support for self-management of the health condition
Carer and family support	Self-management interventions	Carer and family training and support

[a] Selection of functioning domains relevant to the sequelae and their consequences following acute meningitis.

[b] Selection of interventions extracted from the 2023 WHO *Package of interventions for rehabilitation* (PIR) modules for musculoskeletal conditions, neurological and sensory conditions, and neurodevelopmental disorders (available at: https://www.who.int/teams/noncommunicable-diseases/sensory-functions-disability-and-rehabilitation/rehabilitation/service-delivery/package-of-interventions-for-rehabilitation).

For more information please contact:

Brain Health Unit
Department of Mental Health, Brain Health and Substance Use
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27
Switzerland

Email: brainhealth@who.int

Website: https://www.who.int/health-topics/brain-health