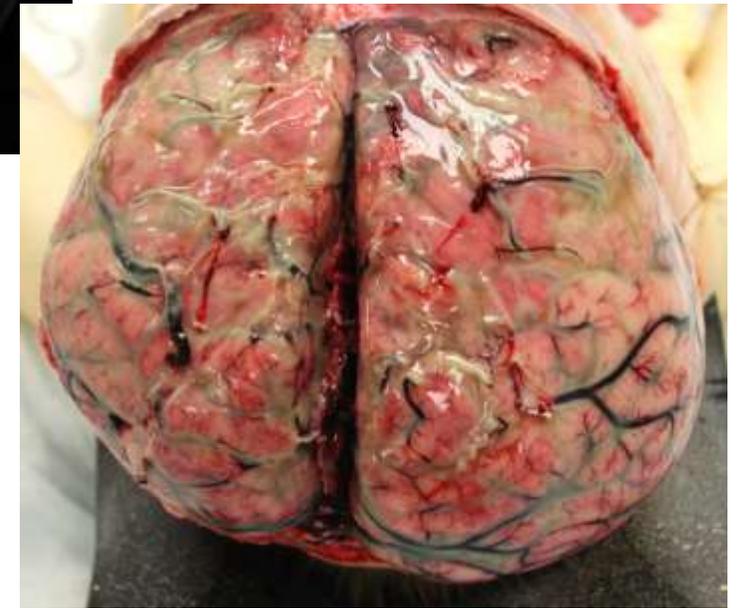
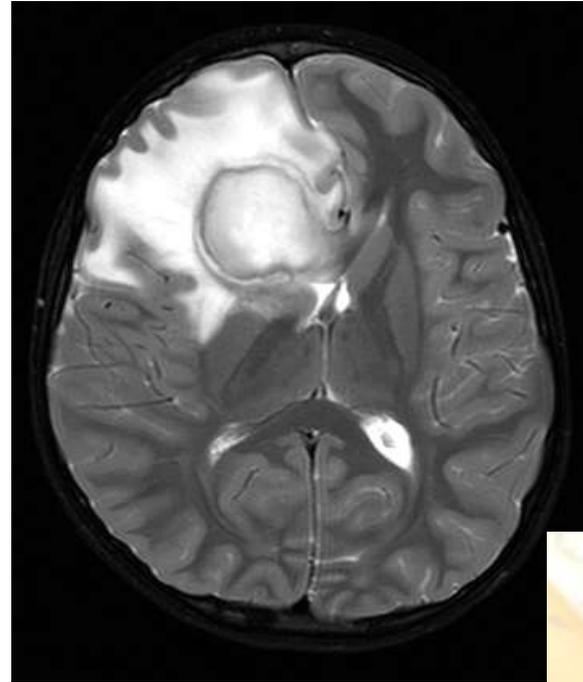


Microbiology of the central nervous system



Anas Abu-Humaidan
M.D. Ph.D.

Additional meningitis guidelines

ESCMID guideline: diagnosis and treatment of acute bacterial meningitis

D. van de Beek¹, C. Cabellos², O. Dzunpova³, S. Esposito⁴, M. Klein⁵, A. T. Kloek¹, S. L. Leib⁶, B. Mourvillier⁷, C. Ostergaard⁸, P. Pagliano⁹, H. W. Pfister⁵, R. C. Read¹⁰, O. Resat Sipahi¹¹ and M. C. Brouwer¹, for the ESCMID Study Group for Infections of the Brain (ESGIB)

1) Department of Neurology, Academic Medical Center, Amsterdam, The Netherlands, 2) Department of Infectious Diseases, Hospital Universitari de Bellvitge, Barcelona, Spain, 3) Department of Infectious Diseases, Charles University, Third Faculty of Medicine, Prague, Czech Republic, 4) Pediatric Highly Intensive Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano, Milan, Italy, 5) Department of Neurology, Klinikum Großhadern, Munich, Germany, 6) Institute for Infectious Diseases, University of Bern, Bern, Switzerland, 7) Department of Intensive Care Medicine, Groupe Hospitalier Bichat-Claude Bernard, Paris, France, 8) Department of Clinical Microbiology, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark, 9) Department of Infectious Diseases, "D. Cotugno" Hospital, Naples, Italy, 10) Department of Infectious Diseases, Southampton General Hospital, Southampton, United Kingdom and 11) Department of Infectious Diseases and Clinical Microbiology, Ege University, Izmir, Turkey

TABLE I.1. Quality of evidence

Class	Conclusions based on:
1	Evidence from at least one properly designed randomized controlled trial.
2	Evidence from at least one well-designed clinical trial, without randomization; from cohort or case-control analytic studies (preferably from >1 centre); from multiple time series; or from dramatic results of uncontrolled experiments.
3	Evidence from opinions of respected authorities, based on clinical experience, descriptive case studies.

European Society for Clinical Microbiology and Infectious Diseases (ESCMID)

[https://www.clinicalmicrobiologyandinfection.org/article/S1198-743X\(16\)00020-3/fulltext](https://www.clinicalmicrobiologyandinfection.org/article/S1198-743X(16)00020-3/fulltext)

Key Question 1. What are the causative microorganisms of community-acquired bacterial meningitis in specific groups (neonates, children, adults and immunocompromised patients)?

Level 2 Most common causative pathogens in neonatal meningitis are *Streptococcus agalactiae* and *Escherichia coli*.

Level 2 Most common causative pathogens in children beyond the neonatal age are *Neisseria meningitidis* and *Streptococcus pneumoniae*.

Level 2 Most common causative pathogens in adults are *Streptococcus pneumoniae* and *Neisseria meningitidis*. Another important causative microorganism in adults is *Listeria monocytogenes*.

Key Question 2. What are the clinical characteristics of community-acquired bacterial meningitis, and what is their diagnostic accuracy?

Level 2 Neonates with bacterial meningitis often present with nonspecific symptoms.

Level 2 In children beyond the neonatal age the most common clinical characteristics of bacterial meningitis are fever, headache, neck stiffness and vomiting. There is no clinical sign of bacterial meningitis that is present in all patients.

Level 2 In adults the most common clinical characteristics of bacterial meningitis are fever, headache, neck stiffness and altered mental status. Characteristic clinical signs and symptoms such as fever, neck stiffness, headache and altered mental status can be absent.

Diagnostic accuracy of laboratory techniques in bacterial meningitis

Level 2 It has been shown that in both children and adults, classic characteristics (elevated protein levels, lowered glucose levels, CSF pleocytosis) of bacterial meningitis are present in $\geq 90\%$ of patients. A completely normal CSF occurs but is very rare.

Level 2 In neonatal meningitis, CSF leukocyte count, glucose and total protein levels are frequently within normal range or only slightly elevated.

Level 2 CSF culture is positive in 60–90% of bacterial meningitis patients depending on the definition of bacterial meningitis. Pretreatment with antibiotics decreases the yield of CSF culture by 10–20%.

Diagnostic accuracy of laboratory techniques in bacterial meningitis

Level 2 CSF Gram stain has an excellent specificity and varying sensitivity, depending on the microorganism. The yield decreases slightly if the patient has been treated with antibiotics before lumbar puncture is performed.

Level 2 In patients with a negative CSF culture and CSF Gram stain, PCR has additive value in the identification of the pathogen.

Level 2 In adults and children with bacterial meningitis, blood cultures are useful to isolate the causative microorganism. The yield of blood cultures decreases if the patient is pretreated with antibiotics.

Subquestion 4.1. If lumbar puncture is delayed, should we start treatment?

Recommendation

Grade A It is strongly recommended to perform cranial imaging before lumbar puncture in patients with:

- Focal neurologic deficits (excluding cranial nerve palsies).
- New-onset seizures.
- Severely altered mental status (Glasgow Coma Scale score <10).
- Severely immunocompromised state.

In patients lacking these characteristics, cranial imaging before lumbar puncture is not recommended.

Grade A It is strongly recommended to start antibiotic therapy as soon as possible in acute bacterial meningitis patients. The time period until antibiotics are administered should not exceed 1 hour. Whenever lumbar puncture is delayed, e.g. due to cranial CT, empiric treatment must be started immediately on clinical suspicion, even if the diagnosis has not been established.

Key Question 5. What is the optimal type, duration and method of administration of antibiotic treatment when started empirically, after the pathogen has been identified or in culture-negative patients?

Level 2 A delay in antibiotic treatment administration is associated with poor outcome and should therefore be avoided.

Level 3 The empiric antibiotic treatment in bacterial meningitis patients is based on expert opinion and differentiated for demographic/epidemiologic factors (age and rate of reduced antibiotic susceptibility).

Level 3 The specific antibiotic treatment in bacterial meningitis patients is based on antimicrobial susceptibility testing.

Key Question 6. Does dexamethasone have a beneficial effect on death, functional outcome and hearing loss in adults and children with bacterial meningitis?

Level 1

Corticosteroids significantly reduced hearing loss and neurologic sequelae but did not reduce overall mortality. Data support the use of corticosteroids in patients with bacterial meningitis beyond the neonatal age in countries with a high level of medical care. No beneficial effects of adjunctive corticosteroids have been identified in studies performed in low-income countries. The use of dexamethasone for neonates is currently not recommended.

Level 3

In the absence of scientific evidence, the committee has reached consensus that when antibiotic treatment has already been started, adjunctive dexamethasone treatment can still be started up to 4 hours after initiation of antibiotic treatment.

Key Question 8. Does the use of prophylactic treatment of household contacts decrease carriage or secondary cases?

Level 1 Prophylactic antibiotic treatment of household contacts of meningococcal meningitis patients prevents secondary cases and eradicates meningococcal carriage.

Level 3

- Based on the recurrence risk of 1–5% of pneumococcal meningitis, the committee sees substantial benefits in vaccination with pneumococcal vaccines after an episode of pneumococcal meningitis.
- Vaccination with pneumococcal vaccines is deemed beneficial in bacterial meningitis patients with CSF leakage to reduce recurrences.

Key Question 9. What complications occur during community-acquired bacterial meningitis, what ancillary investigations are warranted when complications occur and how should they be treated?

Level 2 Neurologic and systemic complications occur in a large proportion of children and adults with bacterial meningitis. In patients with neurologic deterioration, cranial imaging (MRI or CT) is often indicated, and repeated lumbar puncture and EEG may be indicated in selected cases.

Level 3 Bacterial meningitis complicated by hydrocephalus, subdural empyema and brain abscess may require neurosurgical intervention.

Key Question 10. What follow-up of community-acquired bacterial meningitis patients should be provided (e.g. testing for hearing loss, neuropsychological evaluation)?

Level 2 Sequelae occur in a substantial proportion of children and adults with bacterial meningitis and most frequently consist of hearing loss, neuropsychologic defects and focal neurologic deficits.

Level 2 Hearing loss needs to be detected early during the disease course to facilitate effective cochlear implantation in the case of severe hearing loss.