TARGOŃSKI, Oskar, TARGOŃSKA, Marta, NIEKURZAK, Rafał, MADEJ, Adrianna, SUŁAWA, Adrian, BUCZEK, Agnieszka, BASIAK, Aneta, PTASIŃSKI, Aleksander, FURGALSKA, Julia and FEDOROWICZ, Sebastian. Overview of Meningitis: Causes, Symptoms, Treatment, and Differential Diagnosis. Quality in Sport. 2024;34:56221 eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.34.56221
https://apcz.umk.pl/QS/article/view/56221

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assig589 ned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 16.11.2024. Revised: 20.11.2024. Accepted: 27.11.2024. Published: 27.11.2024.

Overview of Meningitis: Causes, Symptoms, Treatment, and Differential Diagnosis

Authors:
Marta Targońska
Public University Hospital No. 1 in Lublin Stanisława Staszica 16, 20-400 Lublin, Poland
martatargonska123@gmail.com,
https://orcid.org/0009-0004-9701-6021

Oskar Targoński
Public University Hospital No. 1 in Lublin Stanisława Staszica 16, 20-400 Lublin, Poland
oskartargonski7@gmail.com,
https://orcid.org/0009-0001-8570-0211

Rafał Niekurzak
Public University Hospital No. 1 in Lublin Stanisława Staszica 16, 20-400 Lublin, Poland
niekurzakey@gmail.com
https://orcid.org/0009-0007-3694-0562

Adrianna Madej
Ludwik Rydygier Memorial Specialized Hospital Osiedle Złotej Jesieni 1, 31-826 Kraków, Poland
adrianna.madej.lek@gmail.com
https://orcid.org/0009-0009-1024-8388

Adrian Suława
Lower Silesian Oncology Center, Ludwik Hirszfeld Square 12, 53-413 Wrocław, Poland
sulawa.adrian@gmail.com
https://orcid.org/0009-0005-2451-6321

Agnieszka Buczek
Public University Hospital No. 1 in Lublin Stanisława Staszica 16, 20-400 Lublin, Poland
agnieszka.buczek97@gmail.com
https://orcid.org/0009-0000-6717-2630

Aneta Basiak
Beskid Centre of Oncology - John Paul II City Hospital ul. Wyzwolenia 18, 43-300 Bielsko-Biała, Poland
aneta.basiak.97@gmail.com,
https://orcid.org/0009-0008-4790-8135

Aleksander Ptasiński
Public University Hospital No. 1 in Lublin Stanisława Staszica 16, 20-400 Lublin, Poland
alekpta@gmail.com
https://orcid.org/0009-0004-5326-2028

Julia Furgalska
Lower Silesian Oncology Center Ludwik Hirszfeld Square 12, 53-413 Wrocław, Poland
juliafurgalska@gmail.com
https://orcid.org/0009-0004-1096-6711

Sebastian Fedorowicz
Lower Silesian Specialist Hospital - Emergency Medicine Centre ul. Gen. Augusta Emila Fieldorfa 2, 54-049 Wrocław, Poland
seb.fedorowicz@gmail.com
https://orcid.org/0000-0001-8557-5011

Introduction and purpose:
Meningitis is a serious condition that requires quick diagnosis and rapid implementation of appropriate treatment. Every primary care physician should be particularly alert to symptoms that may suggest meningitis as the cause of a patient's complaints. The purpose of this article

is to present the most common causes of meningitis, symptoms to which special attention should be paid during diagnosis, and the treatment used.

State of knowledge:

Meningitis is an inflammatory process resulting from the penetration of microorganisms into the cerebrospinal fluid - it can be caused by viruses, less commonly by bacteria, fungi, and parasites. Infections usually occur as a result of generalized infections through the transfer of pathogens via the bloodstream, although infections spreading through tissue continuity also occur.

Summary:

Meningitis is an inflammatory process resulting from the penetration of microorganisms into the cerebrospinal fluid - it can be caused by viruses, less commonly by bacteria, fungi, and parasites. Characteristic symptoms suggesting infection of the meninges can aid in diagnosis. Recognition of this clinical condition is a key element of diagnostics, as it requires absolute hospitalization, determination of the cause, and implementation of intensive treatment, as untreated meningitis can be associated with high mortality.

Keywords: meningitis, inflammatory disease, meningeal signs, lumbar puncture, cerebrospinal fluid examination, TBEV, HSV

Historical Background

There are sources suggesting that even ancient physicians such as Hippocrates might have been aware of the existence of meningitis. Tuberculous meningitis (once known as brain dropsy) was first described by the English physician Robert Whytt in 1768 (unfortunately, he did not demonstrate the link between the pathogen responsible for meningitis and tuberculosis). It seems that the 18th century saw a significant increase in meningitis cases. The first recorded serious outbreaks occurred in Geneva in 1805. Shortly thereafter, several other epidemics were described in Europe and the United States, with the first report of an epidemic in Africa appearing in 1840. Epidemics in Africa became widespread in the twentieth century, starting with major outbreaks affecting Nigeria and Ghana between 1905 and 1908. In 1887, Austrian bacteriologist Albert Weischelbaum first described bacterial infections underlying meningitis. Early reports indicated that the mortality rate due to meningitis exceeded 90%. In 1906, horse-derived immune serum was produced and later refined by American scientist Simon Flexner, significantly reducing the mortality rate from meningococcal diseases. The effectiveness of penicillin in treating meningitis was noted in 1944. By the late 20th century, the introduction of the Haemophilus vaccine led to a marked decrease in meningitis cases associated with this pathogen. It was not until 2002 that evidence emerged showing that steroid treatment could improve the prognosis of bacterial meningitis [1,2].

General Symptoms

Symptoms accompanying central nervous system infections can include fever, photophobia, weakness, severe throbbing headache, psychomotor agitation, altered consciousness, seizures, paralysis, cold sores, vomiting and nausea, petechiae and skin hemorrhages (most commonly

on the limbs but can also occur on the torso and conjunctivae, suggesting meningococcal meningitis).
As the disease progresses, signs of shock may appear (pale, cold, and sweaty skin, weakness, balance disturbances, initial agitation followed by calmness and drowsiness, impaired consciousness, and loss of consciousness) and multiple organ failure [3,4].

Meningeal Symptoms
The primary symptoms present in meningitis are meningeal signs. These are reflex reactions that can be elicited in cases of meningeal irritation. The meningeal signs include the following.

1) **Neck stiffness** (nuchal rigidity) – Attempting to bring the chin to the chest in a patient lying on their back results in a reflex contraction of the neck muscles, preventing the head from bending forward and causing resistance and pain. The severity of neck stiffness is measured by the distance between the chin and the patient's sternum. In extreme cases, the tension of the long spinal muscles is so great that it causes spontaneous backward bending of the head and forward arching of the torso (opisthotonus). This sign should be differentiated from other causes of limited neck flexion (such as cervical spine degeneration, Parkinson's disease, cervical lymphadenitis, severe pharyngitis). Before performing the test, ensure that the patient does not have cervical spine instability (e.g., post-trauma or in the course of rheumatoid arthritis) or is at risk of herniation [4,5].

2) **Brudziński's sign**:
– Upper – Bringing the chin to the chest during the examination of neck stiffness triggers a reflexive flexion of the lower limbs at the hip and knee joints.
– Lower – Pressing on the pubic symphysis triggers a reflexive flexion of the lower limbs at the hip and knee joints.

3) **Kernig's sign** – The patient lies flat on their back; bend the patient's lower limb at the hip joint to a 90° angle, then attempt to straighten it at the knee joint. If the sign is positive, a reflex muscle contraction prevents the knee from extending, causing resistance and pain. Kernig's sign is bilateral (unlike Lasègue's sign in sciatica).

Examinations
After stabilizing the patient's condition, it is necessary to draw blood for culture (before administering the first dose of antibiotics) and to collect cerebrospinal fluid to determine the etiological factor. It is important to first rule out increased intracranial pressure, as performing a lumbar puncture in such a state can cause herniation.

Lumbar Puncture
A lumbar puncture is a fundamental procedure for identifying the etiological agent causing meningitis.

– **Contraindications for lumbar puncture:**

Absolute: Increased intracranial pressure (most commonly due to brain edema or a tumor).
Relative: Skin and tissue infection at the puncture site, spinal cord and spine developmental abnormalities, coagulation disorders, suspected subarachnoid hemorrhage.

– **Preparation for lumbar puncture:**

Obtain patient consent for the medical procedure.
Assess coagulation status, discontinue anticoagulant medications.
Rule out increased intracranial pressure (based on fundoscopic examination - assessment of optic disc edema - or CT scan - enlargement of fluid spaces, presence of tumors, inflammatory changes, areas of brain edema).

– **Patient position during lumbar puncture:**

The patient lies on their side, close to the edge of the procedure table, with their back facing the practitioner; the lower limbs are bent at the knee and hip joints, knees drawn to the abdomen; the head is bent maximally toward the knees, the back, and shoulder line in a plane perpendicular to the surface. Due to discomfort and the frequent lack of patient cooperation in maintaining the correct position, assistance from additional medical personnel may be necessary.

– **Puncture site:**

The intervertebral space between the spinous processes of L4 and L5 or L3 and L4, not higher than between L2 and L3, in the midline running through the peaks of the spinous processes of the vertebrae or slightly lateral to it [6,7].

Interpretation of Cerebrospinal Fluid (CSF) Examination

Parameter	Normal CSF	Bacterial Meningitis	Viral Meningitis	Tuberculous Meningitis
Color and Clarity	Clear and transparent	Yellow and cloudy	Clear and transparent	Clear and transparent
Cytosis	<5/µL, mostly lymphocytes	Several, predominantly neutrophils	Several to hundreds, predominantly lymphocytes	Dozens to thousands, predominantly lymphocytes
Protein	0,15–0,45 g/L	>2 g/L	<2 g/L	1 g/L
Glucose	60–75 mg/dL	Significantly decreased	No change or slightly decreased	Significantly decreased
Chlorides	>117 mmol/L	Significantly decreased	No change or slightly decreased	Significantly decreased
Lactic Acid	<2,1 mmol/L	Significant increase	No change or slight increase	Significant increase

– Color and Clarity: Bacterial meningitis typically causes the CSF to become yellow and cloudy, whereas in viral and tuberculous meningitis, the CSF remains clear and transparent.
– Cytosis: The presence and type of cells vary; bacterial meningitis shows an increase in neutrophils, viral meningitis shows an increase in lymphocytes, and tuberculous meningitis shows a significant increase in lymphocytes.
– Protein Levels: Elevated protein levels are a marker for bacterial and tuberculous meningitis, with bacterial meningitis showing the highest increase.
– Glucose Levels: A significant decrease in glucose is a hallmark of bacterial meningitis, while viral meningitis may show little to no change, and tuberculous meningitis shows a slight decrease.
– Chlorides: Significant reduction in chloride levels is seen in bacterial and tuberculous meningitis, with viral meningitis showing no or slight changes.
– Lactic Acid: A significant increase in lactic acid is indicative of bacterial and tuberculous meningitis, whereas viral meningitis shows little to no change [8,9].

Etiological Factors

1. Viruses

The most common cause of meningitis is viruses, including enteroviruses, mumps virus, arboviruses (such as the tick-borne encephalitis virus), HSV (Herpes Simplex Virus), VZV (Varicella Zoster Virus), EBV (Epstein-Barr Virus), CMV (Cytomegalovirus), HHV-6 (Human Herpesvirus 6), and adenoviruses. Meningeal infection typically occurs via the hematogenous route during secondary viremia. Less commonly, viruses enter the central nervous system through peripheral nerves. After infection, viruses replicate in the lymphoid tissue of the upper respiratory tract or gastrointestinal tract, causing viremia—where they are present in the blood and reach the central nervous system. The incubation period is usually from a few to several days. Viral meningitis usually follows a biphasic course. In the first phase, symptoms of upper respiratory tract infection or gastrointestinal tract infection (acute diarrhea) appear. After a few days of apparent improvement, fever, chills, and symptoms characteristic of meningeal involvement reappear: vomiting, headache, and neck stiffness. These symptoms are accompanied by various neurological signs: irritability and hypersensitivity to stimuli. Acute symptoms usually last for 3–4 days, then subside. The course of viral meningitis is much milder compared to purulent meningitis. Below are the specific viral strains that cause characteristic forms of meningitis [10,11].

a) HSV (Herpes Simplex Virus)

Infection of the central nervous system (CNS) by the herpes simplex virus (HSV) predominantly affects young individuals. HSV is widespread in the human population, with infections ranging from asymptomatic to keratitis, herpes simplex, and encephalitis or myelitis. In 1960, two types of HSV were identified based on antigenic differences. Both types exhibit latency (typically in sensory ganglia) and reactivation and have a short replication time.
– HSV-1 primarily causes lesions on the oral mucosa, conjunctivae, cornea, and face. It is the most common cause of encephalitis in adults.

– HSV-2 has a particular affinity for the mucous membranes of the genitourinary tract and anus and is the etiological agent responsible for mildly symptomatic lymphocytic meningitis.
Following primary infection, HSV can remain latent within sensory ganglia and nerves. Reactivated virus or its genetic material migrates peripherally along sensory nerves.
Most CNS infections manifesting as encephalitis are thought to result from reactivation of the latent virus. A peculiar and unexplained tendency is the more frequent localization of changes in the left hemisphere. Herpes simplex encephalitis, although relatively rare, is considered the most common cause of sporadic fatal encephalitis (200–500 deaths annually in the United States).
Acyclovir is an additional drug used in treating herpes infections. It should be administered via slow intravenous infusion at a dose of 10 mg/kg every 8 hours for 10–21 days. In mild cases, oral administration is possible [12,13].

b) TBEV (Tick-Borne Encephalitis Virus)
The tick-borne encephalitis virus (TBEV) belongs to the group of RNA viruses. Its main vector is the common tick (Ixodes ricinus), in which the virus resides in the salivary glands and enters the host's body upon tick bite. Initially, it localizes and replicates in lymph nodes, then crosses the blood-brain barrier and affects regions of the central nervous system such as the brainstem, cerebellum, basal ganglia, thalamus, and anterior horns of the spinal cord.
The diagnosis of tick-borne encephalitis should be considered in any patient presenting symptoms such as altered consciousness, nausea and vomiting, headache, seizures, photophobia, phonophobia, or tactile hypersensitivity, and who may have been exposed to tick bites (or, less commonly, consumption of unpasteurized dairy products from infected animals). The diagnostic method of choice is the quantitative determination of specific IgM and IgG antibodies using enzyme-linked immunosorbent assay (ELISA) in the patient's cerebrospinal fluid or serum. Imaging studies do not allow for a definitive diagnosis.
Patients who have had tick-borne encephalitis should be referred to neurological clinics (for periodic neurological assessments, particularly sensitive to the occurrence of chronic headache or memory disturbances), otolaryngological clinics (for early detection of possible hearing loss), and should receive psychological care (due to the potential occurrence of chronic fatigue and depressive thoughts).
Primary prevention of tick-borne encephalitis involves the use of personal protective measures to prevent tick bites. The TBE vaccine is characterized by very high safety and efficacy (in Austria, where vaccination coverage exceeds 80%, there are 1-2 cases of TBE per 100,000 persons per year). Adverse reactions following vaccination are rare.
Tick-borne encephalitis vaccination is recommended for all children after their first year of life, especially for those who spend a lot of time outdoors, live in rural areas, have contact with farm and domestic animals, are scouts, or participate in outdoor sports. Vaccination for tick-borne encephalitis in children over 1 year of age involves administering three doses of the vaccine. The second dose is given 1-3 months after the first, and the third dose 5-12 months after the second. Booster doses for children up to 15 years of age are given every 5 years [14,15].

2. Bacteria

The etiology of bacterial meningitis depends on the age of the patient, local epidemiology, and underlying factors predisposing to the disease, such as immunosuppression, diabetes, or malnutrition. Bacterial meningitis can be classified into septic and aseptic forms. In newborns, the most common etiological agents of bacterial meningitis are group B streptococci and gram-negative rods (Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa).

In children older than 3 months, the most common bacteria responsible for bacterial meningitis are Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae, and less frequently, Listeria monocytogenes. Aseptic meningitis can be caused by Borrelia burgdorferi, Leptospira, Treponema pallidum, Francisella tularensis, Brucella, and Mycobacterium tuberculosis. Infections often occur via the bloodstream.

Symptoms of bacterial meningitis appear suddenly, without preceding prodromal symptoms. In rare cases, after a few days of illness, the patient may develop herpes labialis due to immune deficiencies. Severe forms of bacterial meningitis may be accompanied by sepsis or Waterhouse-Friderichsen syndrome (a shock-like state of severe sepsis characterized by fever, disseminated intravascular coagulation (DIC), and skin petechiae) [16,17].

3. Tuberculosis

The etiological factor of tuberculous meningitis is Treponema pallidum. It is the most common form of tuberculosis affecting the nervous system, typically occurring as a secondary infection (3-6 months after primary infection). During the course of this disease, tuberculosis bacilli spread hematogenously to the brain, where they form small inflammatory foci called tubercles. Tuberculous meningitis is characterized by various types of neuropathological changes: limited or diffuse acute caseous inflammation, single caseous foci, disseminated tuberculomas, or limited or diffuse proliferative inflammation. The clinical picture is also characterized by a diverse, atypical presentation consisting of three periods: prodromal, irritative, and paralytic.

The prodromal period lasts from 7 days to even 3 months and is associated with nonspecific prodromal symptoms (low-grade fever, drowsiness, apathy, excessive excitement, pallor, fatigue, nausea, vomiting, headache). Towards the end of this period, neck stiffness or other meningeal signs may be observed. During the irritative period, the meningeal syndrome predominates (neck stiffness, Kernig's and Brudzinski's signs, photophobia, hyperacusis, lying on the side with flexed legs or on the back with the head extended backward (opisthotonus)). Symptoms may be accompanied by disturbances in pulse and breathing, seizures. Brain and cranial nerve damage occurs during the paralytic period. Symptoms of increased intracranial pressure worsen, headaches intensify, consciousness disturbances occur, seizures, limb weakness (usually hemiparesis), and cranial nerve paralysis. In untreated cases, coma, respiratory disturbances, and death can occur within a few weeks [18,19].

4. Fungi

Fungal meningitis is a relatively rare occurrence. In recent years, there has been an increase in fungal meningitis in developed countries, likely due to the aging population. These infections are secondary to primary inflammation occurring in other tissues or organs. Typically, the

cause of fungal infection is the weakening of the patient's immune system. In countries with a high natural incidence, there is an increase in exogenous infections through the respiratory system (Histioplasma capsulatum, Coccidioides immitis). Fungal meningitis is most commonly caused by Cryptococcus neoformans and Coccidioides immitis. It is characteristic that fungal inflammation progresses very slowly, subacutely, and chronically. Unlike bacterial infection, fungal meningitis more often leads to hydrocephalus. Treatment involves hospitalization and the use of antifungal drugs [20,21].

Monitoring

Effective patient monitoring involves frequent assessment and comparison of clinical status, inflammatory changes in the cerebrospinal fluid (CSF), and blood culture. Further monitoring depends on the etiological factor:

– Bacterial meningitis - assessment of glucose concentration increase in the cerebrospinal fluid, decrease in CRP and procalcitonin concentration in serum.

– Fungal meningitis - assessment of fungal antigens in cerebrospinal fluid and blood.

Treatment

The approach to each type of meningitis involves osmotic and anti-inflammatory therapy (intravenous dexamethasone 8-10mg every 6 hours for 2-4 days - with the first dose administered 15 minutes before starting antibiotic therapy or simultaneously with it). Mechanical ventilation should be considered to maintain PaCO2 in the range of 28-30 mm Hg. Recently, there has been an emphasis on using barbiturates for osmotic therapy (e.g., intravenous infusion of thiopental 100/60 mg/h). However, it should be noted that despite their cytoprotective and intracranial pressure-lowering effects, barbiturates also have a depressive effect on the respiratory center.

In caring for patients with meningitis, particular attention should be paid to preventing and treating complications such as cerebral edema, hypogammaglobulinemia, septic shock, and disseminated intravascular coagulation (DIC) [22,23].

Complications

The highest risk and severity of complications occur in cases of bacterial, tuberculous, and fungal meningitis. The most common complications include status epilepticus, epilepsy, hydrocephalus, cerebral edema, syndrome of inappropriate antidiuretic hormone secretion (SIADH), weakness or spastic paralysis, cognitive impairment and speech disorders, intellectual disability, and hearing impairment. Less common complications include brain abscess, mycotic aneurysm, transverse myelitis, and sphincter dysfunction [24,25].

Prognosis

The etiology of meningitis significantly affects the prognosis:

– Viral - prognosis is good, usually with mild course and no lasting effects, mortality <1%.

– Bacterial - prognosis is fair, with permanent neurological sequelae occurring in about 9% of patients, mortality depends on the etiological factor (average 20%).

– Tuberculous - prognosis is fair, with permanent neurological sequelae occurring in about 40% of patients, mortality depends on delayed diagnosis and treatment initiation.
– Fungal - prognosis is poor, with high mortality [26,27].

Summary
Meningitis is an inflammatory process resulting from the entry of microorganisms into the cerebrospinal fluid - it can be caused by viruses, less frequently by bacteria, fungi, and parasites. Characteristic symptoms suggesting meningitis infection can aid in diagnosis.
Recognition of this clinical condition is a key element of diagnosis, as it requires immediate hospitalization, determination of the cause, and initiation of intensive treatment, as untreated meningitis can be associated with high mortality.

Author's contribution:
Conceptualization: Oskar Targoński, Marta Targońska, Adrian Suława
Methodology: Julia Furgalska, Agnieszka Buczek, Aleksander Ptasiński
Software & Check: Aneta Basiak, Sebastian Fedorowicz
Formal Analysis & Investigation: Marta Targońska, Sebastian Fedorowicz, Adrianna Madej
Resources & Data Curation: Adrian Suława, Aleksander Ptasiński
Writing-Rough Preparation: Adrianna Madej, Agnieszka Buczek
Writing-Review and Editing: Adrian Suława, Aneta Basiak, Sebastian Fedorowicz
Visualization: Marta Targońska, Agnieszka Buczek, Rafał Niekurzak
Supervision & Project Administration: Aneta Basiak, Rafał Niekurzak, Julia Furgalska

The authors have read and agreed with the published version of the manuscript.

Funding Statement:
The Study Did Not Receive Special Funding.

Institutional Review Board Statement:
Not Applicable.

Informed Consent Statement:
Not Applicable.

Data Availability Statement:
Not Applicable.

Conflict Of Interest:
The authors declare no conflict of interest.

References
1. Walusinski O. History of the Concept of Tuberculous Meningitis. Eur Neurol. 2021;84(1):61-70. doi: 10.1159/000512468. Epub 2020 Dec 16. PMID: 33326957

2. Mercer A. Protection against severe infectious disease in the past. Pathog Glob Health. 2021 May;115(3):151-167. doi: 10.1080/20477724.2021.1878443. Epub 2021 Feb 11. PMID: 33573529
3. Durand M.I., Calderwood S.B., Weber D.J. et al. Acute bacterial meningitis in adults. A review of 493 episodes. N Engl J Med. 1993; 328: 21-28.
4. Fiszer U. Zapalenia opon mózgowo-rdzeniowych i mózgu. Przew Lek 2004; 9: 36-42
5. Davis L.E., Katzman J.G. Chronic daily headache: when to suspect meningitis. Curr Pain Headache Rep 2008; 12:50-55.
6. Sempere AP, Berenguer-Ruiz L, Lezcano-Rodas M, Mira-Berenguer F, Waez M. [Lumbar puncture: its indications, contraindications, complications and technique]. Rev Neurol. 2007 Oct 1-15;45(7):433-6. PMID: 17918111
7. Hudgins PA, Fountain AJ, Chapman PR, Shah LM. Difficult Lumbar Puncture: Pitfalls and Tips from the Trenches. AJNR Am J Neuroradiol. 2017 Jul;38(7):1276-1283. doi: 10.3174/ajnr.A5128. Epub 2017 Mar 16. PMID: 28302612
8. Seehusen DA, Reeves MM, Fomin DA. Cerebrospinal fluid analysis. Am Fam Physician. 2003 Sep 15;68(6):1103-8. PMID: 14524396
9. Wilson MR, Sample HA, Zorn KC, Arevalo S, Yu G, Neuhaus J, Federman S, Stryke D, Briggs B, Langelier C, Berger A, Douglas V, Josephson SA, Chow FC, Fulton BD, DeRisi JL, Gelfand JM, Naccache SN, Bender J, Dien Bard J, Murkey J, Carlson M, Vespa PM, Vijayan T, Allyn PR, Campeau S, Humphries RM, Klausner JD, Ganzon CD, Memar F, Ocampo NA, Zimmermann LL, Cohen SH, Polage CR, DeBiasi RL, Haller B, Dallas R, Maron G, Hayden R, Messacar K, Dominguez SR, Miller S, Chiu CY. Clinical Metagenomic Sequencing for Diagnosis of Meningitis and Encephalitis. N Engl J Med. 2019 Jun 13;380(24):2327-2340. doi: 10.1056/NEJMoa1803396. PMID: 31189036
10. Służewski W. Ostre wirusowe zapalenie mózgu u dzieci. Przew Lek 2002; 5(3): 109-116
11. Solomon T., Hart I.J., Beeching N.J. Viral encephalitis: a clinician's guide. Pract Neurol 2007; 7:288-305
12. Landau Z.,Miller E.B.,Roif M. Recurrent herpes simplex encephalitis. European Journal of Internal Medicine 2005; 16(7): 513-514
13. Steiner I., Kennedy P.G.E. Herpes simplex virus type 1 latent infection in the nervous system. J Neurovirol 1995; 1: 19-29
14. Martello E, Gillingham EL, Phalkey R, Vardavas C, Nikitara K, Bakonyi T, Gossner CM, Leonardi-Bee J. Systematic review on the non-vectorial transmission of Tick-borne encephalitis virus (TBEv). Ticks Tick Borne Dis. 2022 Nov;13(6):102028. doi: 10.1016/j.ttbdis.2022.102028. Epub 2022 Aug 11. PMID: 36030646
15. Yoshii K. Epidemiology and pathological mechanisms of tick-borne encephalitis. J Vet Med Sci. 2019 Mar 14;81(3):343-347. doi: 10.1292/jvms.18-0373. Epub 2019 Jan 23.
PMID: 30674746
16. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. Clin Microbiol Rev. 2010 Jul;23(3):467-92. doi: 10.1128/CMR.00070-09. PMID: 20610819
17. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, Leib SL, Mourvillier B, Ostergaard C, Pagliano P, Pfister HW, Read RC, Sipahi OR, Brouwer MC;

ESCMID Study Group for Infections of the Brain (ESGIB). ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect. 2016 May;22 Suppl 3:S37-62. doi: 10.1016/j.cmi.2016.01.007. Epub 2016 Apr 7. PMID: 27062097
18. Golden MP, Vikram HR. Extrapulmonary tuberculosis: an overview. Am Fam Physician. 2005 Nov 1;72(9):1761-8. PMID: 16300038
19. Leonard JM. Central Nervous System Tuberculosis. Microbiol Spectr. 2017 Mar;5(2). doi: 10.1128/microbiolspec.TNMI7-0044-2017. PMID: 28281443

20. Mohamed SH, Nyazika TK, Ssebambulidde K, Lionakis MS, Meya DB, Drummond RA. Fungal CNS Infections in Africa: The Neuroimmunology of Cryptococcal Meningitis. Front Immunol. 2022 Apr 1;13:804674. doi: 10.3389/fimmu.2022.804674. eCollection 2022. PMID: 35432326
21. Rajasingham R, Wake RM, Beyene T, Katende A, Letang E, Boulware DR. Cryptococcal Meningitis Diagnostics and Screening in the Era of Point-of-Care Laboratory Testing. J Clin Microbiol. 2019 Jan 2;57(1):e01238-18. doi: 10.1128/JCM.01238-18. Print 2019 Jan. PMID: 30257903
22. Steiner I., Budka H., Chaudhuri A., Koskiniemi M., Sainio K., Salonen O., Kennedy P.G. Viral Meningoencephalitis: a review of diagnostic methods and guidelines for management. Eur J Neurol 2010; 17(8): 999-1009
23. Solomon T., Michael B.D., Smith P.E., Sanderson F., Davies N.W., Hart I.J., Holland M., Easton A.,Buckley C., Kneen R., Beeching N.J. Management of suspected viral encephalitis in adults -Association of British Neurologists and British Infection Association National Guidelines. J Infect 2012;64(4): 347-73
24. Beckham J.D., Tyler K.L. Neuro-Intensive care of patients with acute CNS infections. Neurotherapeutics 2012; 9: 124-38.
25. Kyotani M, Kenzaka T, Akita H, Arakawa S. Campylobacter insulaenigrae bacteremia with meningitis: a case report. BMC Infect Dis. 2021 Jul 1;21(1):633. doi: 10.1186/s12879-021-06353-8. PMID: 34210285
26. Hussein K, Bitterman R, Shofty B, Paul M, Neuberger A. Management of post-neurosurgical meningitis: narrative review. Clin Microbiol Infect. 2017 Sep;23(9):621-628. doi: 10.1016/j.cmi.2017.05.013. Epub 2017 May 18. PMID: 28529027
27. Johnson R.T. Acute encephalitis. Clin Infect Dis 1996; 23: 219-226-129