

Infections of the Central Nervous System

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Infections of the CNS

- **Meningitis**
- **Encephalitis**
- **Myelitis**
- **Abscess**
- **Meningoencephalitis**
- **Encephalomyelitis**
- **Meningoencephalomyelitis**
- and the other combinations

Findings in the Cerebrospinal Fluid

	Purulent infections	Nonpurulent (Aseptic) infections
Typical etiology	Pyogenic bacteria	Viruses and specific bacteria
CSF color change	Milky cloudy	Mostly transparent
Protein level	↑↑ (1.5 – 4.5 g/l)	Normal (< 1 g/l)
Glycorachia	Significantly reduced (up to zero)	Normal (2/3 of glycemia)
Cytology	↑↑ with a predominance of PMN	↑↑ with a predominance of lymphocytes
Microscopy – Gram stain	G+/G- and basic morphology	Absence of bacteria

In the case of **purulent** infection, **ATB** are used.

In the case of **nonpurulent** (an aseptic) infection, **symptomatic treatment** is used.

Purulent Infections of the CNS

- **diffuse** or **localized**
- **Purulent meningitis**
- **Brain abscess, epidural or subdural empyema**

Purulent Meningitis

- inflammation of the soft membranes of the brain due to the penetration of bacteria into the CSF
- serious - fatal infection with acute course and rapid progression
- purulent meningitis = bacterial origin
- **diagnosis:** lumbar puncture with CSF examination + hemoculture
- empirical ATB immediately after collection!
- often permanent consequences despite proper diagnosis and treatment

Clinical manifestations of **Purulent Meningitis**

- **meningeal symptoms**
- **headache, fever, nausea, vomiting**
- **hypersensitivity** to external stimuli (photophobia, phonophobia)
- **disorders of consciousness**
- **neurological symptoms** – various
- **petechiae** – tiny spot-like hemorrhages in the skin
- **septic shock**

Etiology of Purulent Meningitis

bacterial origin

- **Newborns:** *Streptococcus agalactiae*, *Escherichia coli*, *Listeria monocytogenes*
- **Infants:** *Hemophilus influenzae* type b, *Neisseria meningitidis*, *Streptococcus pneumoniae*
- **Children:** *Neisseria meningitidis*, *Streptococcus pneumoniae*, staphylococci, enterobacteria
- **Adults:** *Streptococcus pneumoniae*, *Neisseria meningitidis*, staphylococci, enterobacteria
- **Elderly patients:** *Streptococcus pneumoniae*, *Listeria monocytogenes*, *Hemophilus influenzae* type b, staphylococci, enterobacteria

Etiology of Purulent Meningitis non-bacterial origin

- **Fungal infections:** *Cryptococcus neoformans*, *Candida spp.*, *Aspergillus spp.*
- **Amoebae:** *Naegleria fowleri*

Pathogenesis of Purulent Meningitis

1. Hematogenous dissemination from another site of infection

- **colonization of the nasopharynx** - *N. meningitidis*, *H. influenzae*
- **infectious endocarditis** – viridans streptococci, *S. aureus*, enterobacteria, enterococci
- **pulmonary infection** (pneumonia) – *S. pneumoniae*, *Nocardia sp.*, *Actinomyces sp.*
- **immune disorder** – *Toxoplasma gondii*, fungal infections, enterobacteria, *L. monocytogenes*

Pathogenesis of Purulent Meningitis

2. *Per continuitatem* from another nearby source of infection

- **otitis, mastoiditis** – *S. pneumoniae*, *Bacteroides sp.*, enterobacteria
- **sinusitis** – *S. pneumoniae*, *Bacteroides sp.*, enterobacteria, *S. aureus*
- **dental abscess** – viridans streptococci, *Fusobacterium sp.*, *Bacteroides sp.*

Pathogenesis of Purulent Meningitis

3. Direct inoculation of infection into the CNS

- **neurosurgery** – *S. aureus*, pseudomonads, enterobacteria
- **skull trauma** – coagulase negative staphylococci, enterobacteria, pseudomonads
- **shunt meningitis** – in patients with cerebrospinal fluid drainage from the ventricular system

Risk factors

- individual susceptibility to infection (mainly *N. meningitidis*)
- state of the individual
- age
- head injury
- neurosurgical procedure
- colonization of the birth canal (*S. agalactiae*)
- absence of vaccination

Laboratory Diagnostics of Purulent Meningitis

Clinical material

- CSF
- blood - hemoculture

Laboratory Diagnostics of **Purulent Meningitis**

CSF collection by lumbar puncture

- appearance of CSF
- the pressure under which it flows

Laboratory examination

- **Biochemically**
- **Cytologically**
- **Microbiologically**

Microbiological Diagnostics of Purulent Meningitis

Microbiological diagnostics of CSF

- **Microscopy** – Gram stain
- **Antigen detection** (latex agglutination)
- **PCR**
- **Cultivation**

Microbiological diagnostics of blood

- **hemoculture**

Treatment of Purulent Meningitis

- Immediate application of ATB after lumbar puncture and blood culture collection!

1. phase – empiric treatment

- cephalosporins III. generation i.v. (meningococcal, pneumococcal or streptococcal infections) in combination with acyclovir (herpetic encephalitis); *in infants*, ampicillin is added i.v. (*Listeria monocytogenes*); in the case of *penetrating skull injury*, a combination of cephalosporins III. generation with vancomycin i.v. (staphylococcal infection)

Treatment of Purulent Meningitis

2. phase – targeted ATB treatment

cephalosporins III. generation, penicillin G (*N. meningitidis*, *S. pneumoniae*); ampicillin (*L. monocytogenes*); antituberculotics (*Mycobacterium tuberculosis*)

Prevention of Purulent Meningitis

- vaccination against *S. pneumoniae*
- vaccination against *H. influenzae* type b
- vaccination against *N. meningitidis*

Brain Abscess

- **rare** but **very serious** CNS infection
- **brain tissue**, but also in the **epidural** or **subdural** space
- most often of **bacterial origin**
- subdural empyema - **anaerobic**
- **cryptogenic abscess** – abscess with no clear pathogenesis

Pathogenesis of **Brain Abscess**

- **a chronic primary site** (chronic sinusitis, otitis, dental abscess),
hematogenously from other sites, **open skull injury, neurosurgery**

Clinical symptoms of **Brain Abscess**

- **headache**
- **fever** (in immunocompromised without fever)
- **focal neurological deficit**
- **vomiting**

Etiology of Brain Abscess

- ***S. aureus*** and other staphylococci
- **streptococci** (*S. anginosus*) and **viridans streptococci**
- **anaerobes** – *Bacteroides*, *Fusobacterium*, *Prevotella spp.*
- **enterobacteriaceae** – *Proteus spp.*, *Escherichia coli*, *Klebsiella spp.*
- *Nocardia spp.*, *Actinomyces spp.*
- **fungal infections** (*Aspergillus spp.* infections)

Diagnostics of **Brain Abscess**

- **Imaging methods**
- **Microbiological diagnostics**
- **Hemoculture**
- Collection of CSF – risk of cerebral conus formation due to possible intracranial hypertension
- **Absces puncture**

Treatment of Brain Abscess

- **Empiric treatment** – vancomycin in combination with metronidazole and cephalosporin III. generation
- **Causal treatment** – neurosurgery

Nonpurulent Infections of CNS

- a wide group of infections characterized by **aseptic inflammation** of the CNS and **diffuse involvement** of nervous system tissue (brain parenchyma, CSF, spinal cord)
- the course is **slower** and **milder** than purulent
- **complication** – **postencephalic syndrome**
- most often **viral etiology** – most often tick-borne encephalitis virus in adults and enterovirus infections in children
- bacterial origin - neuroborreliosis

Classification of **Nonpurulent** Infections of CNS

- **Primary encephalitis** – caused by neurotropic viruses
- **Secondary encephalitis** – a complication of the underlying disease

Nonpurulent Infections - Encephalitis

Classification

- **Polioencephalitis**
- **Leukoencephalitis**
- **Panencephalitis**

Etiology of **Nonpurulent** Infections of CNS

Viral meningoencephalitis

- Picornaviruses – enteroviruses, parechoviruses, echoviruses, Coxsackie viruses, poliovirus
- Herpetic viruses – HSV-1, HSV-2, VZV, CMV, HHV-6, HHV-7, EBV,
- Flaviviruses – tick-borne meningoencephalitis, dengue virus, Japanese encephalitis virus, Zika virus
- Rabies virus
- HIV
- Adenoviruses
- Lymphocytic choriomeningitis virus
- Others – influenza viruses, parainfluenza virus 1-4, RS virus, measles virus, mumps virus, rubella virus

Etiology of **Nonpurulent** Infections of CNS

Bacterial meningoencephalitis

- Spirochetes – *Leptospira interrogans*, *Borrelia burgdorferi*, *Treponema pallidum*
- intracellular bacteria – *Chlamydia pneumoniae*, *Legionella*, *Rickettsia*, *Ehrlichia*
- *Mycoplasma pneumoniae*

Etiology of **Nonpurulent** Infections of CNS

Parasitic meningoencephalitis

- *Toxoplasma gondii*
- *Taenia solium*
- *Plasmodium* spp. (*Plasmodium falciparum*)

Pathogenesis of **Nonpurulent** Infections of CNS

- **Cytopathic effect of virus or effect of bacterial exotoxins and subsequent immunopathological process**
- **Viremia** is followed by virus transfer via HEB (most viruses)
- **Retrograde axonal transport** (alfa-herpesviruses – herpetic encephalitis, rabies virus, newborns passing through the birth canal with active HSV infection – neonatal herpetic encephalitis)
- **Transport within infected cells** (HIV, CMV, enteroviruses, *Toxoplasma gondii*)
- **Multiplication in vascular endothelial cells and their damage** (arboviruses)
- **Hematogenous transmission after infection with a vector** (Lyme disease, tick-borne encephalitis virus)

Risk Factors

- Seasonal occurrence
- Tick in anamnesis
- Travel history

Clinical symptoms

- **Prodromal/nonspecific stage:** headache, fatigue, muscle pain, joint pain due to viremia
- **Latent stage**
- **Specific stage:** symptoms of CNS involvement

Microbiological Diagnostics of **Nonpurulent** Infections of CNS

- **Medical history**
- **Lumbar puncture** - CSF
- **Blood collection** – serological examination, PCR
- **Indirect diagnostics** – methods for the detection of specific antibodies
- **Direct diagnostics** – PCR

Treatment of **Nonpurulent** CNS infections

- mainly – **symptomatic supportive treatment**
- certain cases – **specific treatment** (HSV and VZV, CMV, Lyme disease)
 - HSV and VZV encephalitis – **aciclovir i.v.**
 - CMV encephalitis/retinitis – **ganciklovir** or **foscarnet i.v.**
 - Lyme disease – 1. stage (**doxycycline, amoxicillin, cefuroxime** or **macrolides**), other stages (the same preparations for a long time also parenterally, neuroborreliosis – **crystalline penicillin**)