



MEDICAL UNIVERSITY – PLEVEN
FACULTY OF MEDICINE
DEPARTMENT OF INFECTIOUS DISEASES, EPIDEMIOLOGY,
PARASITOLOGY AND TROPICAL MEDICINE

Lecture № 5

**ASEPTIC INFECTIONS OF
THE CENTRAL NERVOUS SYSTEM
(CNS)**

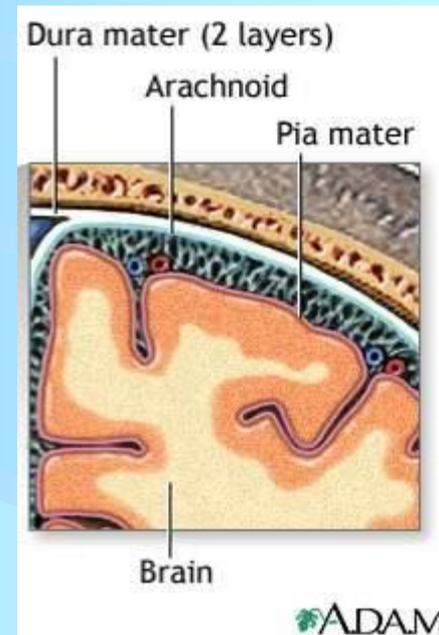
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INFECTIONS OF CNS – introduction

- Acute infections of the CNS – among the most important problems in medicine because are **life-threatening**.
- **Require**
 - ❖ early recognition,
 - ❖ efficient decision-making,
 - ❖ rapid institution of therapy.

INFECTIONS OF CNS – clinical syndromes

- **Meningitis** – inflammation of the meninges → subarachnoid space.
- **Encephalitis** → inflammatory involvement of brain tissue – encephalon (mainly viral).
- **Focal infections** – brain abscess, subdural empyema, infectious thrombophlebitis → focal involvement of brain tissue (bacterial, fungal, parasitic).



INFECTIONS OF CNS – classification

- Causative agents: bacteria, viruses, fungi, parasites.
- **Septic** (bacterial) meningitis – turbid CSF with polymorphonuclear pleocytosis↑, proteinorachia↑↑, glucosa↓↓, **bacteria**
- **Aseptic** meningitis – translucent CSF with mononuclear pleocytosis↑, proteinorachia↑, normal glucosa, **viruses**
Mycobacterium tuberculosis, Listeria monocytogenes

ASEPTIC INFECTIONS OF CNS – introduction

- Historically, aseptic meningitis was the term for an illness with acute onset, clinical signs of meningitis, white blood cells (WBC) but no bacteria in the CSF, and a short and benign course.
- This illness was most likely enteroviral meningitis. Aseptic meningitis is most commonly caused by a viral agent, especially an enterovirus, when the disease occurs in epidemics (summer and autumn). Aseptic meningitis can also result from a wide variety of infectious (*Table 1*) and noninfectious causes.

Table 1. Infectious Causes of Aseptic Meningitis

Bacteria	Mycobacterium tuberculosis, bacteria originated from brain abscess, epidural abscess, acute or subacute bacterial endocarditis; Bartonella henselae (cat scratch disease)
Viruses	Enteroviruses, mumps, lymphocytic choriomeningitis, Epstein-Barr virus, arbovirus, Varicella-zoster virus, Herpes simplex virus, HIV, influenza A and B viruses, adenovirus, measles virus, rubella virus, Cytomegalovirus, and other viruses
Rickettsiae	Rickettsiae rickettsiae (Rocky Mountain spotted fever), Rickettsiae prowazeki (typhus), Coxiella burnetii (Q fever), Ehrlichia chafeensis
Chlamydia	Chlamydia psittaci
Spirochetes	Treponema pallidum, Borrelia burgdorferi, Leptospira interrogans
Mycoplasmas	Mycoplasma pneumoniae, Mycoplasma hominis, and Ureaplasma urealyticum
Fungi	Candida albicans, Cryptococcus neoformans, Coccidioides immitis, Histoplasma capsulatum, Blastomyces dermatidis
Protozoa	Toxoplasma gondii, Plasmodium falciparum, Naegleria fowleri, Acanthamoeba, Trichinella spiralis
Nematodes	Toxocara, Baylisascaris procyonis, Angyostrongylus cantonensis
Cestodes	Taenia solium, Echinococcus granulosus

VIRAL MENINGITIS – etiology

- The **enteroviruses** (coxsackieviruses A and B, echovirus, numbered enteroviruses, and poliovirus) are the most common causes of viral meningitis.
- **Mumps virus** used to be relatively frequent cause of viral meningitis, but the frequency of its involvement has decreased with vaccination.
- **Herpes simplex virus (HSV), rubella, cytomegalovirus (CMV), rabies virus, the arboviruses,** and many other viral agents also may cause meningitis.

VIRAL MENINGITIS – epidemiology

- Enterovirus infections commonly occur in late summer and early autumn; mumps viral infections typically occur in late winter and early spring.
- Viral meningitis is principally a disease of the young; it rarely occurs after age 40.

VIRAL MENINGITIS – clinical manifestations

Signs and symptoms of viral meningitis develop gradually over a few days to a week.

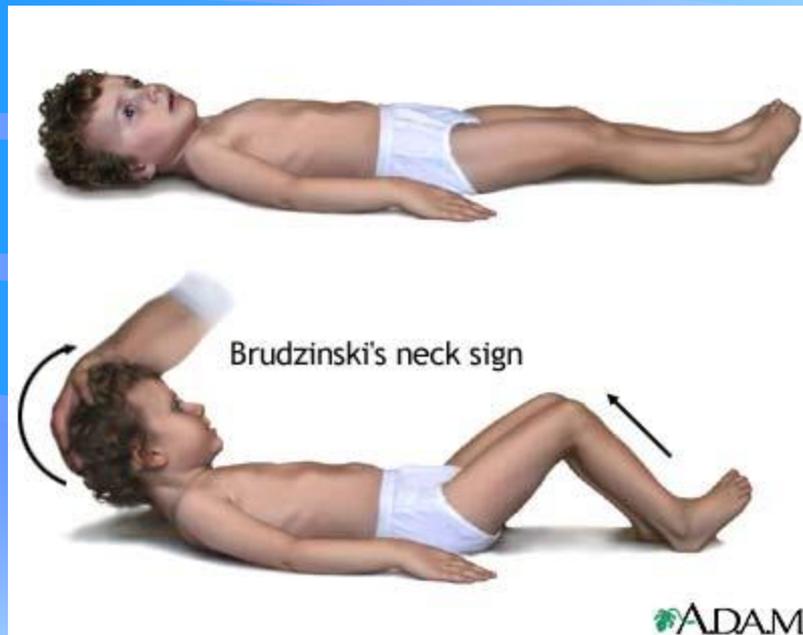
- Patients usually complain of a sore throat, fever, anorexia, malaise, and myalgia.
- More indicative symptoms develop with time, including lethargy, vomiting, severe headache and stiff neck.
- Physical findings include fever and nuchal rigidity, with or without Brudzinski's sign and Kernig's sign.

In older children and adults, the severity of symptoms varies.

Nearly all patients have fever, headache, and nuchal rigidity.

The most common finding is a stiff neck characterized by pain and resistance on flexion.

Neurological findings include Brudzinski's sign, and Kernig's sign



Tripod sign of spinal rigidity



VIRAL MENINGITIS – clinical presentation

- **Symptoms in infants:**
 - ❖ fever – temperature instability;
 - ❖ lethargy and/or change in level of alertness;
 - ❖ poor feeding and/or vomiting;
 - ❖ screaming cry;
 - ❖ respiratory distress, apnea, cyanosis;
 - ❖ neurological examination – may be false negative (looking for symptom of Lesage);
 - ❖ bulging fontanel late;
 - ❖ Paradoxical irritability (i.e., quiet when stationary, cries when held).
- **Key to early diagnosis** → high index of suspicion – lumbar puncture (LP)!!!

CLINICAL MANIFESTATIONS:
vary considerably depending on the
virulence of the organism and the
age of patient.

In neonates the signs of meningeal
irritations (nuchal rigidity, Brudzinski's
sign, and Kernig's sign) are
infrequent and are often minimal when
found. Early signs include:

temperature instability

irritability

poor feeding

vomiting.

In children 1-18 months of age

signs and symptoms are often
non specific:

fever

irritability

drowsiness

vomiting

poor feeding

crying when handled

bulging fontanels (due to increased
intravascular pressure)

seizures.



VIRAL MENINGITIS – laboratory investigations

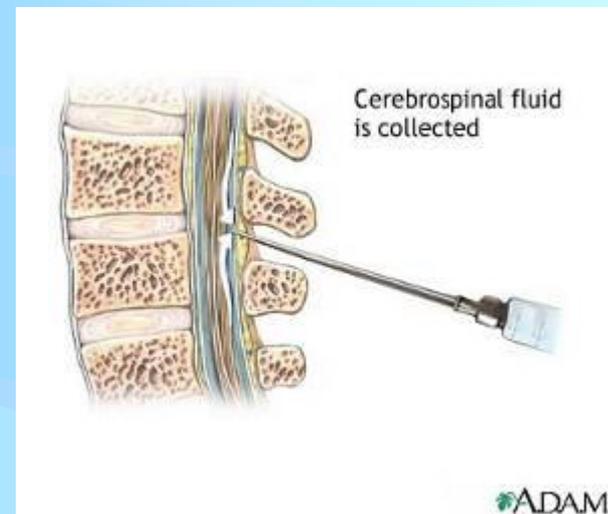
As in bacterial meningitis, the diagnosis is usually confirmed by the examination of CSF obtained by lumbar puncture (see *Table 2*).

- The opening pressure may be elevated.
- The **number of leucocytes** is moderately increased, typically to 100-500 to $10^6/L$; counts over 1000 to $10^6/L$ are rarely observed.
- The CSF **protein concentration** may be normal or moderately elevated.
- The CSF **glucose concentration** is usually normal.

CSF findings in meningitis with different etiology

Type of meningitis	Leucocytes x 10 ⁶ /l (range)	Predominant cell type	Glucose level (mmol/l)	Protein level (g/l)	Micro biological tests
Bacterial	0 – 60 000	Neutrophils	Low (0.5 – 2.0)	Elevated	Positive*
Viral	0 – 1 000	Mononuclear cells**	Normal (2.2 – 4.4)	Normal to slightly elevated	Negative
Tuberculous	25 – 500	Mononuclear cells	Very low (0.2 – 0.4)	Elevated	Negative
Fungal	0 – 1 000	Mononuclear cells	Low	Elevated	Negative

Lumbar puncture



VIRIAL MENINGITIS – supportive treatment

- **Corticoids:** dexamethazone – 0,15 mg/kg every 6 hours 2-4 days.
- **Dehydration:**
 - ❖ mannitol 10% 1-2 g/kg/24 h i.v. for 30 min – 2x daily – 3-5 days
 - ❖ furosemid – 1mg/kg
- Sedation – sedative, analgesics
- controlling aggravating factors
 - ❖ fever, seizures- anticonvulsant
- Fluids – restrict only in SAH (Na<130)

Primary aseptic viral meningitis and meningoencephalitis

1. Enteroviral meningitis and meningoencephalitis:

- Etiology – enteroviruses (Coxsackie A and B viruses, ECHO viruses, Polioviruses).
- Fecal-oral or respiratory route of transmission.

2. Choriomeningitis:

- Etiology – Lymphocytic choriomeningitis virus (Arenaviridae family).
- Zoonosis: reservoirs – rodents, hamsters, dogs, swine etc.).
- Fecal-oral route (consumption of contaminated food), respiratory route of transmission (less common), or by animal biting.

Enteroviral rash



Primary aseptic viral meningitis and meningoencephalitis

3. Russian spring-summer encephalitis:

- Etiology – Russian spring-summer virus (Flaviviridae family).
- Reservoirs and hosts – >130 wild and domestic animal species, >100 avian species, ticks.
- Transmissive mechanism – by the bite of arthropod vectors (ticks).
- Sporadic and epidemic.
- Peak – late summer, early fall.
- Natural cycle: vertebrates-arthropods.
- Man accidentally “dead end” host
- Most common – flaccid paralysis of the neck, shoulders, proximal muscles of the arms, encephalitis, cranial palsies.

Primary aseptic viral meningitis and meningoencephalitis

4. Central European meningoencephalitis:

- Etiology – Central European born encephalitis virus (Flaviviridae family).
- Reservoirs and hosts – rodents, goats, Ixodes-ticks.
- Alimentary route of transmission – by consumption of non-boiled milk of goats (rare cows). Rare – after tick biting.

Primary aseptic viral meningitis and meningoencephalitis

5. Japanese encephalitis:

- Etiology – Japanese encephalitis virus (Flaviviridae family).
- Reservoirs – rodents, wild and domestic animals, birds.
- Transmissive mechanism by vectors (mosquitoes – genders *Culex* and *Anopheles*).
- Geographic distribution – south East Asia, Far East.
- Thalamus involvement.
- Tremor, myoclonus.
- Vaccine preventable.

Primary aseptic viral meningitis and meningoencephalitis

6. West Nile encephalitis (WN) – emerging viral disease

- Etiology – West Nile virus (Flaviviridae family).
- 1999 – first was reported in USA
- Avian reservoir – epizootic disease.
- Transmissive mechanism by vectors (mosquitoes – genders Culex and Aedes).
- sever muscle weakness or flaccid paralysis, suggestive Guillain-Barre syndrome

Secondary aseptic viral meningitis and meningoencephalitis

1. Mumps – meningitis and meningoencephalitis.
2. Influenza – meningitis and meningoencephalitis.
3. Measles – meningitis and meningoencephalitis.
4. Rubella – meningitis and encephalitis.
5. Varicella – encephalitis and cerebellitis.
6. Herpes zoster – encephalitis and meningoencephalitis.
7. Herpes simplex – encephalitis and meningoencephalitis.
8. Infectious mononucleosis (Epstein-Barr virus) – encephalitis and meningoencephalitis.

Viral meningitis and meningoencephalitis – laboratory investigations

- Blood cells – normocytosis or leucopenia with lymphocytosis, monocytosis.
- Normal or slightly elevated erythrocytes' sedimentation rate (ESR)
- Normal c-reactive protein and fibrinogen.
- CSF – transparent CSF with mononuclear pleocytosis \uparrow , protein – normal or proteinorachia \uparrow , normal glucose level; *culture – negative.*

Nonviral aseptic meningitis and meningoencephalitis

1. Leptospiral meningitis and meningoencephalitis.

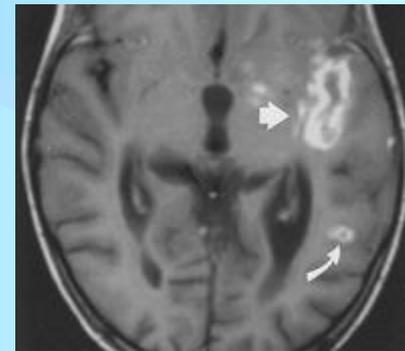
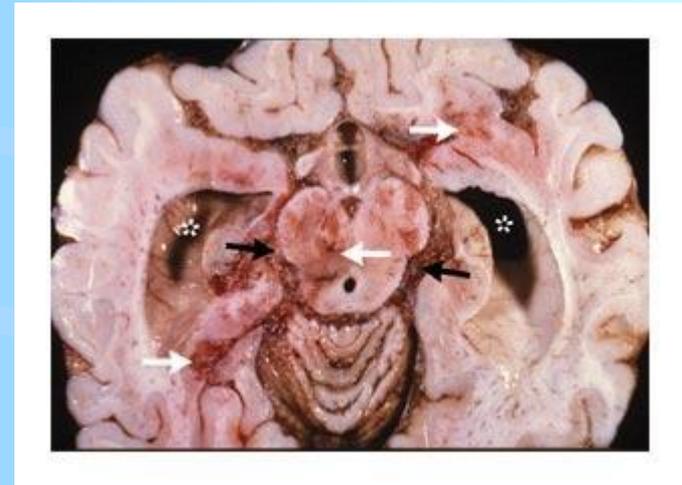
2. Tuberculous meningitis and meningoencephalitis.

CSF – protein is increased in rate more than is increased number of leucocytes – **protein-cells dissociation**;
pleocytosis – tens to hundreds leucocytes (nearly 50:50% polymorphonuclear and mononuclear cells); low glucose level.

3. Listeria monocytogenes-meningitis and meningoencephalitis.

4. Infectious polyneuritis and polyradiculoneuritis.

Tuberculous meningitis



**THANK YOU
FOR YOUR ATTENTION !**