

# Central Nervous System Infections

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# Questions

- Clinical features of CNS infections
- Aseptic meningitis and encephalitis
- Septic meningitis
- Cerebrospinal fluid examination
- Therapy of septic meningitis
- Differential diagnosis of CNS infections

# Clinical features of CNS infections

- 1) General symptoms and signs of infection
- 2) Meningeal irritation
- 3) Neurological involvement
- 4) Dermatological features
- 5) Signs of raised ICP

# Symptoms and signs of CNS infections

**General:** fever, chills, malaise, nausea, restlessness, photophobia

**Meningeal triad:** fever, headache, vomiting

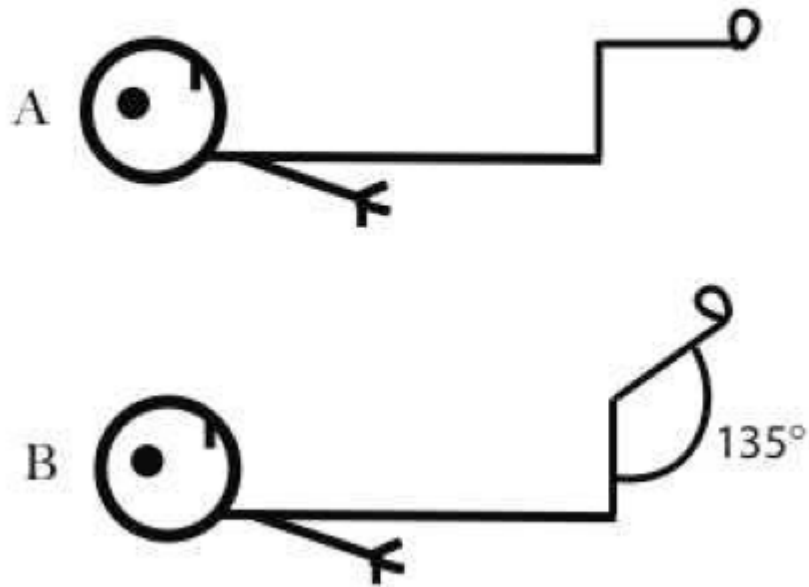
**Neurological features:** neck stiffness, nuchal rigidity, irritability, back pain, stupor, coma, seizures or focal neurological signs

# Neurological signs

- Kernig's sign

*is elicited with the patient in the supine position, in which the thigh is flexed on the abdomen with the knee flexed. The leg is passively extended, and, in the presence of meningeal inflammation, the patient resists leg extension*

# Kernig's sign

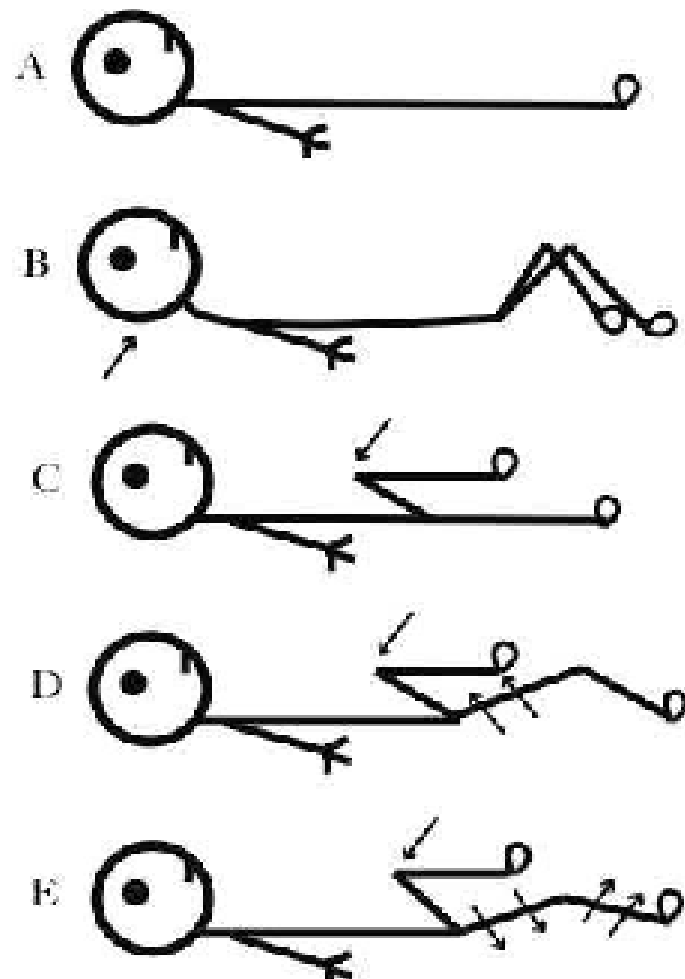


# Neurological signs

- Brudzinski's sign

*the best known is the nape-of-the-neck sign, in which passive flexion of the neck results in flexion of the hips and knees*

# Brudzinski's sign





# Amoss' sign

- *In painful flexion of the spine, inability to sit without supporting the arms behind the torso = („tripod position“)*
- Meningeal patients (children !!!)  
spontaneously assume the tripod-like position

# Dermatological features

- Dermographism
- Maculopapular rash
- Petechial rash
- Purpura fulminans (= multiple bleeding → skin, mucous membranes and organs)

# Dermographism



Maculopapular rash in adenoviral meningitis



Petechiae and ecchymoses in invasive meningococcal infection (IMI)



# Invasive meningococcal infection





Purpura fulminans in IMI

Purpura fulminans







Purpura fulminans

# Clinical syndromes in meningococcal infection

- Sepsis (meningococemia) without meningitis
- Meningitis without sepsis
- Meningitis with sepsis (meningococemia)
- Bacteremia without sepsis
- Respiratory infections (otitis, epiglottitis, fulminant supraglottitis, pneumonia)
- Localized infections (conjunctivitis, urethritis, arthritis, pericarditis)

Erythema migrans in initial phase of neuroborreliosis



EM, the same patient



# Signs in newborns and infants

- Bulging fontanelle
- Opisthotonus = *powerfull contraction of the back and neck mucsles causing the body to arch backwards so that the heels approximate to the head*

# Signs in newborns and neonates

- Lethargy
- Refusal to feed
- Weak suck
- Vomiting
- Irritability
- High-pitched crying
- Temperature instability
- Jaundice

# Signs of raised intracranial pressure

- Bulging fontanelle
- Papilloedema
- Bradycardia
- Hypertension
- Altered state of consciousness

# Neurological involvement

- Meningitis
  - Encephalitis
  - Myelitis
- 
- Acute
  - Peracute
  - Subacute
  - Chronic



# Meningitis x Encephalitis

- Fever
  - Headache
  - Vomiting
  - Meningeal signs
  - **Less frequent:**
  - Somnolence to coma
  - Focal neurologic signs
  - Seizures
- Fever
  - Headache
  - Depressed mental status
  - Focal neurologic signs
  - Seizures (focal or generalized)

# Clinical features (encephalitis)

- Frontotemporal signs: memory impairment, aphasia, personality changes (HSV, HHV6, limbic autoimmune encephalitis)
- Rigidity, rest tremor (flaviviral)
- Seizures (involvement of cortex): HSV
- Brain stem involvement (HSV, ENT 71, WNV)
- Cerebellitis (VZV, EBV, mumps)

# Neurological involvement

- **Diffuse:**
  - Meningitis
  - Encephalitis
  - Myelitis
- **Localized:**
  - Brain absces
  - Subdural, epidural absces
  - Intracranial thrombophlebitis

# Focal CNS syndromes

- **Clinical presentation depends on:**
- the route of spread of the infection  
*hematogenous x direct (trauma)*
- location of the lesion  
*focal neurologic finding: stroke syndrome,  
pareses to complete paralysis*
- severity of increased intracranial pressure

# Etiology

- Aseptic viral meningitis (primary, secondary, post-infectious, post-vaccination)
- Aseptic bacterial meningitis
- Septic (purulent) meningitis (primary, secondary)
- Fungal meningitis
- Tuberculous meningitis

# Viruses causing CNS infections

- Nonpolio enteroviruses
- Herpesviruses
- Arboviruses (TBE, WNVE)
- Adenoviruses
- HIV
- Influenza virus, parainfluenza typ 3
- Mumps virus
- Measles virus
- Lymphocytic choriomeningitis virus

# Bacteriae causing aseptic meningitis

- Spirochetes (Treponema, **Borrelia**, Leptospira)
- Rickettsiae (including Ehrlichiae, Anaplasmatacea)
- Mycoplasmataceae, Chlamydiae

# Etiology of septic meningitis in newborns

- *Streptococcus agalactiae*
- *Listeria monocytogenes*
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Salmonella spp.*
- *Proteus spp.*



# Bacterial etiology in infants and children

- *Streptococcus agalactiae* 4 to 12 weeks
  - *Escherichia coli*
  - *Listeria monocytogenes*
  - *Haemophilus influenzae*
  - *Streptococcus pneumoniae*
  - *Neisseria meningitidis*
- 
- *Haemophilus influenzae* 3 months to 18 years
  - *Streptococcus pneumoniae*
  - *Neisseria meningitidis*

# Bacterial etiology in adults

- *Streptococcus pneumoniae* 18 - 50 years
- *Neisseria meningitidis*
  
- *Streptococcus pneumoniae* > 50 years
- *Neisseria meningitidis*
- *Listeria monocytogenes*
- *Aerobic gram-negative bacilli*

# Diagnosis

- Anamnestic and epidemiologic data
- Clinical features
- Examination of CSF (cytology, biochemistry)
- Bacterial etiology:
- Gram-stain smear of CSF, culture, PCR
- Rapid diagnostic tests (antigen detection):  
LA, CIE

# Diagnosis

- Viral etiology
- Direct: viral DNA (RNA) by PCR
- Indirect:
  - Antibodies in CSF (IgM)
  - Intrathecal synthesis of antibodies

# Lumbar puncture

- = passage of a needle between two vertebrae of the spine into the fluid-filled space lying below the termination of the spinal cord
- Risks: headache, neck or back pain, vomiting (postpuncture syndrome)
- Problems with hearing, blurred or double vision, dizziness
- Spinal fluid leakage, bleeding, disk injury
- Nerves or spinal cord damage

# Lumbar puncture technique

- Usually at the L4-L5 level
- (in unusual circumstances, a tap can be done at higher levels, the probability of injuring the spinal cord is small)
- The spinal cord ends at the L1 level in adults (lower in children)

# Preparation

- Spinal needle – disposable
- Inspect the needle for any defects
- A 20-gauge needle for adults
- A 22-gauge needle for children

# Preparation of the patients

- Fetal position (head/neck, arms, legs flexed as much as possible)
- The apex of pelvic bone should be identified and
- A direct line should be visualized to the spine
- Two spinous processes in this area (L4-L5 levels) should be identified by palpation



# Procedure

- Local anesthetic (if necessary)
- Introduction into the skin with the bevel of the needle facing up
- The needle should be advanced slowly at a slightly upward angle (toward the patient's head)

# CSF supernatant colors

- Yellow (blood breakdown products, hyperbilirubinemia, increased proteins or RBC)
- Orange or pink (blood breakdown products)
- Green (hyperbilirubinemia, purulent CSF)
- Brown (meningeal melanomatosis)

# Cell count

- Elevated WBC (seizure, intracerebral hemorrhage, inflammatory conditions)
- Elevated RBC (intracranial hemorrhage, traumatic tap)
- Elevated eosinophils (parasitic, viral, fungal or rickettsial meningitis)

# Protein level

- Elevated CSF protein (infection, intracranial hemorrhage, multiple sclerosis, Guillain-Barré syndrome, malignancies, certain medication use)
- Decreased CSF protein (repeated LP, chronic leak, children 6m-2y, idiopathic intracranial hypertension)

# Glucose level

- Hypoglycorrhachia (bacterial meningitis, chemical meningitis, inflammatory conditions, subarachnoid hemorrhage, hypoglycemia)
- Hyperglycorrhachia (hyperglycemia)

Parameter	Normal	Purulent meningitis	Aseptic meningitis	Fungal meningitis	Tuberculous meningitis
Volume	40 – 120 ml				
Appearance	clear	Turbid	clear to opalescent	turbid	slightly turbid
Pressure	< 180-200 mm H <sub>2</sub> O	Raised	normal or slightly raised	raised	usually raised
Leukocytes	PMNs 0 MNs 0-5x10 <sup>6</sup> /l	PMNs in thousands	MNs in hundreds, lymphocytes predominate	early PMNs, later MNs predominate	early PMNs lymphocytes predominate through most of course
Protein	0,4-0,5 g/l	elevated 1-5 g/l	normal or slightly elevated to 0,5 g/l	elevated 2,5-5 g/l	elevated 1-5 g/l
Glucose	2,2-3,3 mmol/l	decreased 0-2,2 mmol/l	normal or slightly decreased (mumps)	decreased	decreased
Lactate	1,2-2,4 mmol/l	elevated	normal	elevated	elevated
Culture	negative	positive (40-80%)	negative (with the exception of spirochetes, rickettsiae, mycoplasma)	positive	positive

# Aseptic meningitis

- CSF-mono 240.0 /ul (0 - 3) VH
  - CSF-poly 5.0 /ul (0 - 0.3) H
  - CSF-proteins 1.54 g/l (0.15 - 0.45) VH
  - CSF-gl 3,2 mmol/l
  - CSF-la 2,7 mmol/l
- 
- 70 % lymphocytes
  - Dg neuroborreliosis

# Septic meningitis

- CSF-mono 507 /ul (0 - 3) VH
- CSF-poly 14 000 /ul (0 - 0.3) VH
- CSF-proteins 2.65 g/l (0.15 - 0.45) VH
- CSF-gl 0 mmol/l
- CSF-la 7.2 mmol/l

- Dg septic meningitis (*S. agalactiae*)



# Microscopic examination

- Gram stain is positive in 60-80 % (untreated cases of bacterial meningitis):
- G- diplococcus intracellular (*N.m.*)
- G+ diplococcus extracellular (*S.p.*)
- G- rods (*H.i.*, *E.coli*)
- G+ rods (*L. monocytogenes*)
- G+ cocci (*Streptococci*, *Staphylococci*)

# Latex-agglutination

- LA = rapid detection of bacterial antigens
- Useful in partially treated meningitis
- Sensitivity 60-100 %
  
- CSF, blood, urine
- False positive findings

# PCR

- Small volume of CSF
- Sensitivity 95-100 %
- Viral meningitis or encephalitis (HSV1, 2, VZV, EBV, CMV, HHV6, ENT, HIV)
- TBC meningitis
- Bacterial meningitis

# Antibody detection

- Estimation of intrathecal synthesis of specific antibodies in CSF
  - $AI = \text{antibody ratio/IgG (IgM) ratio}$
  - Positive greater than 1.5
  - (AR= antibody-concentration in CSF to serum)
  - (IgG/IgM = IgG – concentration in CSF to serum)

# Differential diagnosis

- **Other infectious syndromes:**
- Parameningeal foci or infection (brain abscess, sinusitis, otitis, mastoiditis, subdural or epidural abscess, venous sinus thrombophlebitis, cranial osteomyelitis)
- Infective endocarditis
- Viral postinfectious syndrome
- Postvaccination (mumps, measles, polio, pertussis, rabies, vaccinia)

# Differential diagnosis

- **Meningism** = triad of nuchal rigidity, headache and vomiting → irritation of meninges
- „**Meningismus**“ = symptoms are present without actual inflammation of CNS
- (other acute illnesses in paediatric population: viral or bacterial, febrile status)

# Diff dg



1. Viral petechial rash
2. Petechiae in CMV infection due to thrombocytopenia

# Diff dg



1. Atypical form of chickenpox with thrombocytopenia x
2. Petechiae, ecchymoses due to DIC in IMI





Petechiae in ALL

# Postinfectious meningitis

- Neurologic involvement develops one to three weeks after the illness (measles, rubella)
- Destructive CNS inflammation is caused by autoimmune mechanism similar to postvaccination involvement.

# Noninfectious diseases

- Intracranial tumors and cysts
- Medications (ATB, cytosine, azathioprine, phenazopyridin, immune globulin)
- Systemic illnesses (lupus erythematosus)
- Procedure-related (postneurosurgery, intrathecal injections, spinal anesthesia)
- Miscellaneous (seizures, migraine or migraine-like syndromes)

# Therapy in bacterial meningitis

- All patients with presumed bacterial meningitis must be isolated for the first 24 hours of therapy.
- The CSF should be reexamined (48 to 72 hours after starting antibiotics) for sterility and conversion to lymphocytic predominance

# ATB

- Ampicillin plus cefotaxime; ampicillin plus an aminoglycoside (*neonates*)
- Ampicillin plus a third-generation cephalosporin (*children*)
- Third-generation cephalosporin; ampicillin plus chloramphenicol (*adults*)
- Third-generation cephalosporin ± vancomycin or ampicillin + rifampicin (*> 50 years*)

# Additional therapy

- 1) treatment of cerebral oedema
- 2) supportive therapy: fever, dehydration and electrolyte disorders require correction
- 3) anticonvulsive therapy (in seizures)
- 4) vascular collapse
- 5) for infants with subdural effusion, repeated daily subdural taps
- 6) intravenous immunoglobulins
- 7) therapy of DIC in the case of meningococemia

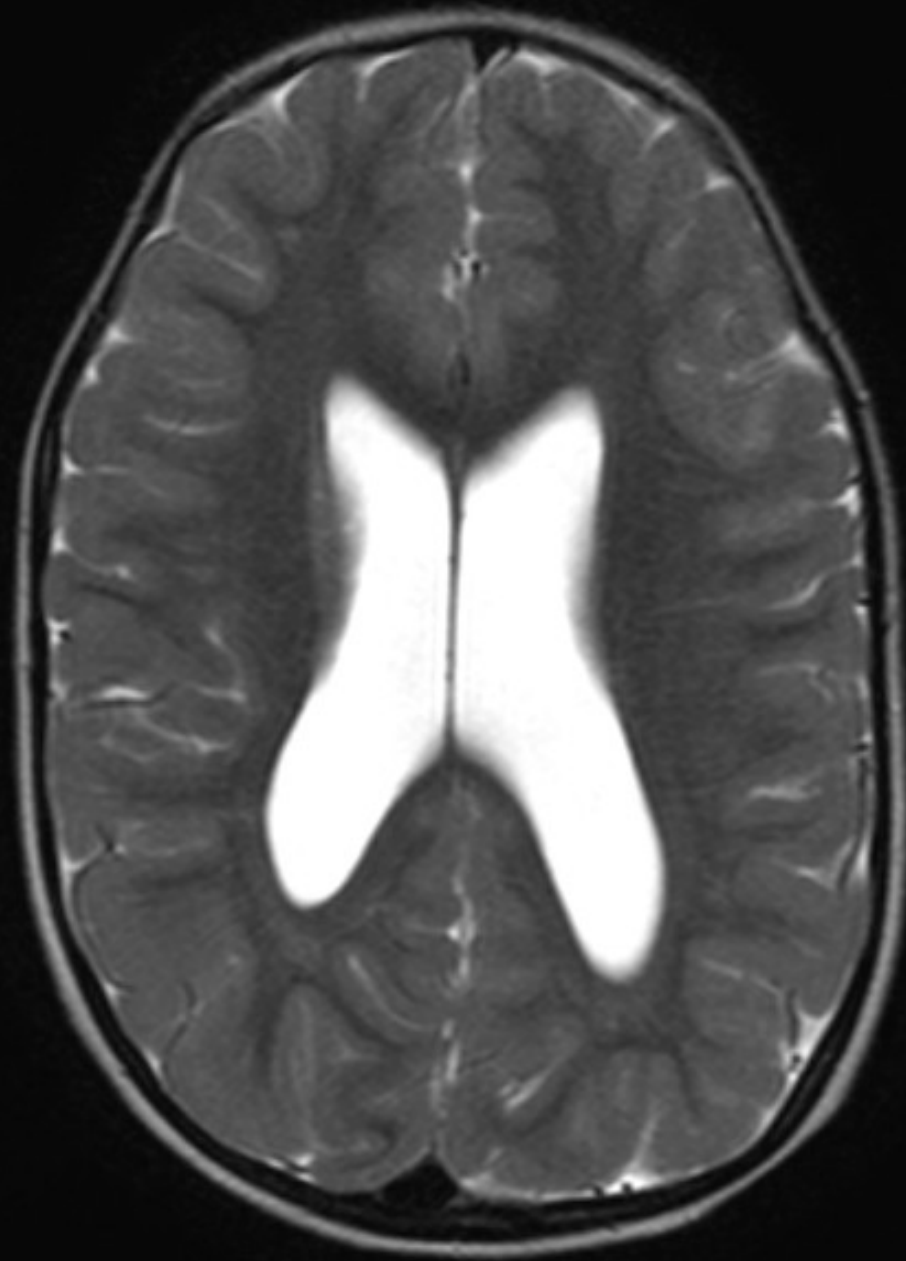
# Prevention: immunoprophylaxis

- **Bacterial:**
- *H. influenzae* typ b conjugate vaccine
- *N. meningitidis* conjugate vaccine  
monovalent to tetravalent against  
serogroups A, C, Y, W135, B!
- *S. pneumoniae* conjugate vaccine  
hepta- to 23-valent
- **Viral:** rabies, TBE, VZV

# Complications after purulent meningitis

- Subdural effusion (hygrom, empyem)
- Epidural empyem
- Suppurative intracranial thrombophlebitis
- Septic venous thrombosis
- Hydrocephalus
- Deafness, blindness
- Neurological deficits (mental retardation, behavior disorder)

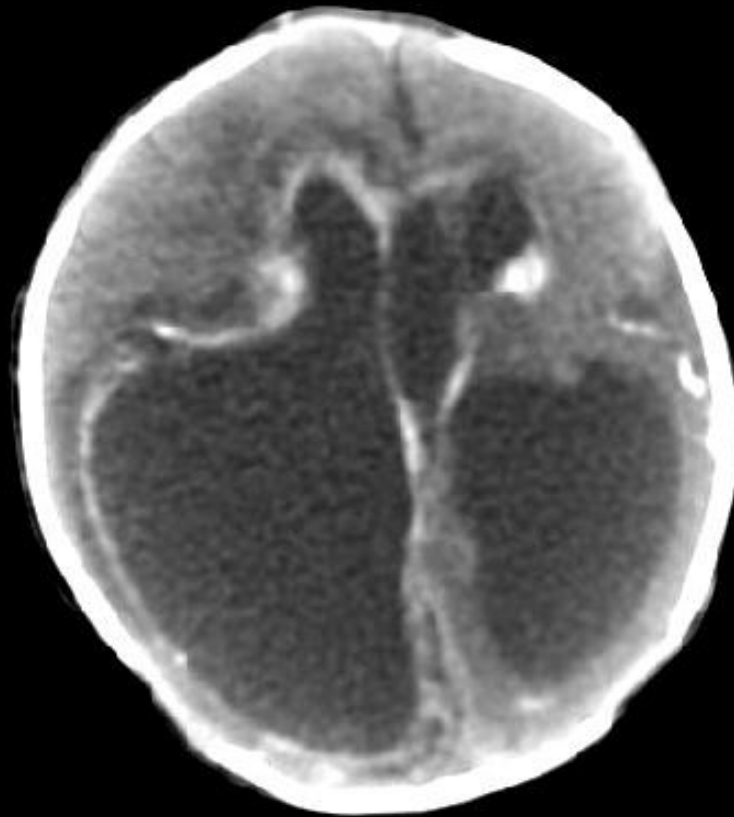




Hydrocephalus

DoB: 2003-01-09  
2003-01-14  
11:46:18  
No.16

Fak. detska n  
SOMAT



R

RM  
GT:-19.5  
SP:233.3  
SL:5  
CM:

PF

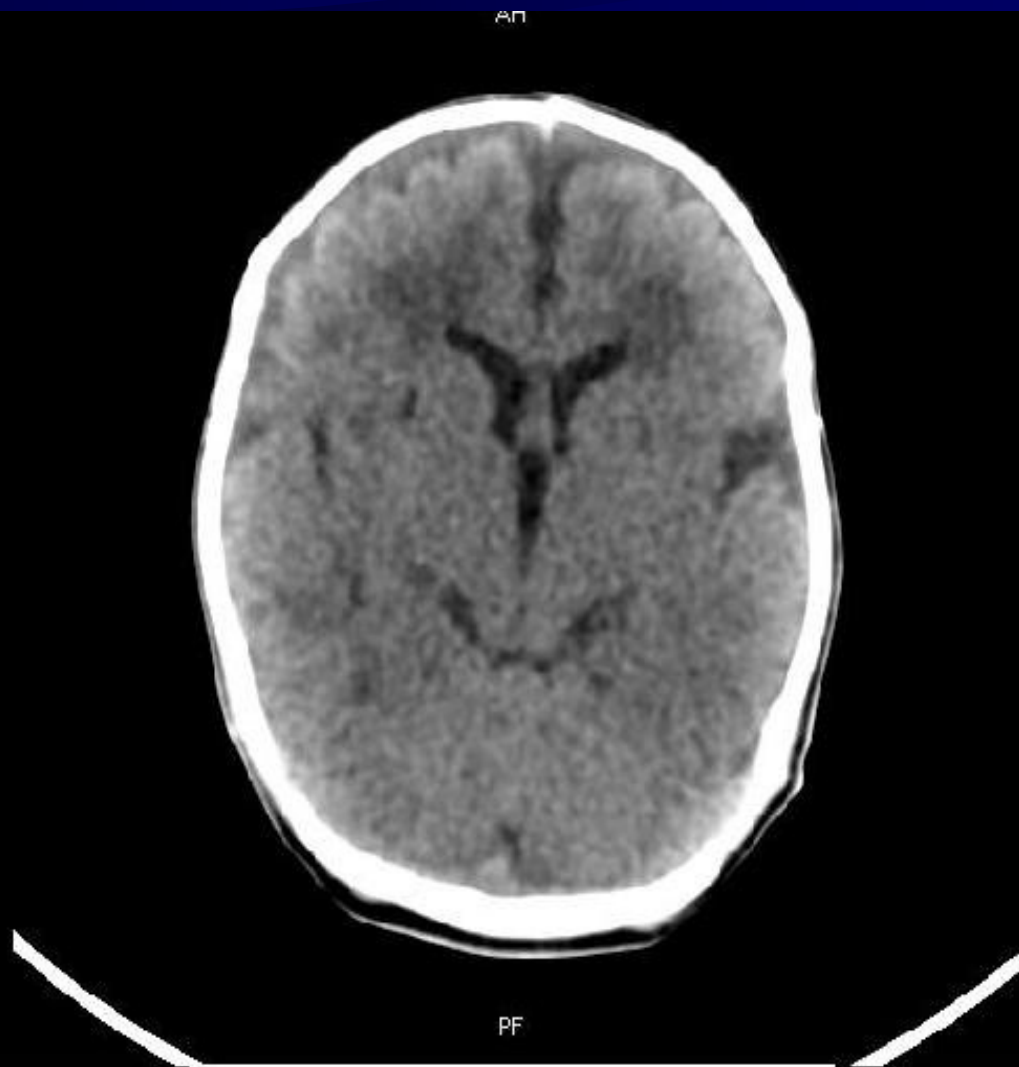
Hydrocephalus with ventriculo-peritoneal shunt

D:061002/8100  
DoB:2006-10-02  
2006-11-28  
08:13:16  
No.13

U: 8  
Fak. detska r  
SOMATO

R

RM  
PT:-12.5  
SP:587  
SL:5  
CM:



Subdural effusion bilateral in fronto-temporal region

# Prevention of CNS infections

## Prevention due to mandatory vaccination:

- Hib vaccine
- Polio vaccine
- MMR (measles-mumps-rubella) vaccine

## Prevention due to facultative vaccination:

- Pneumococcal vaccine
- Meningococcal vaccine
- TBE vaccine
- Vaccination against chickenpox

## Prevention in special situations:

- Vaccination against rabies