Neuroinfections

Department of Pediatric Neurology

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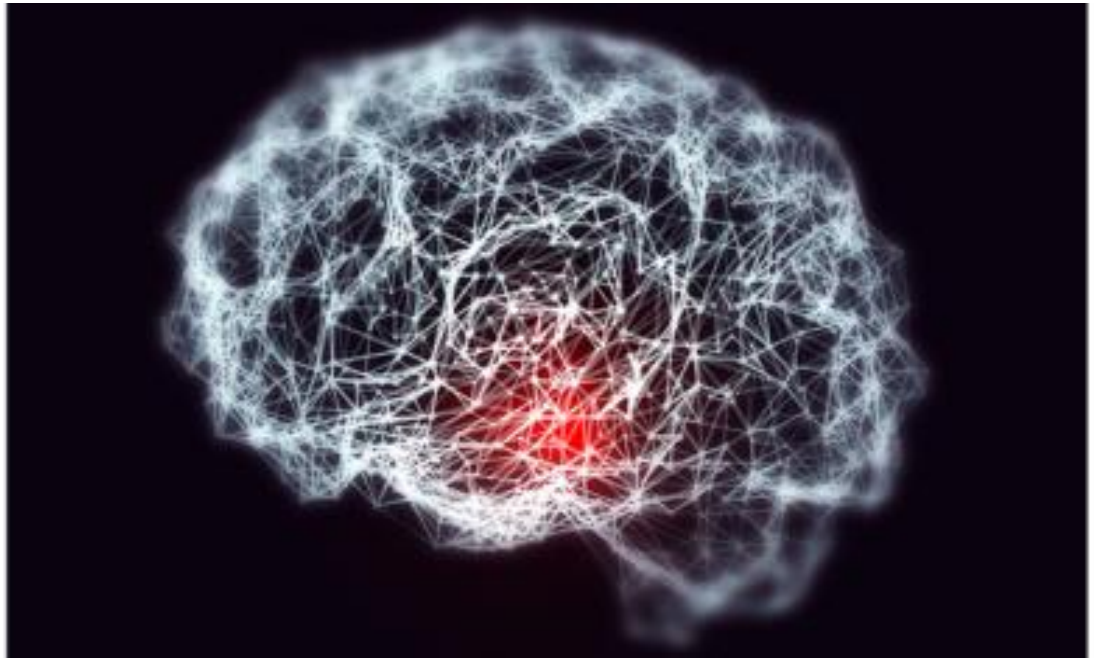
DEFINITION

Infectious diseases of various etiology that involve the nervous system



CLASSIFICATION

Localization

1. **diffused**
- Meningitis- inflammation of meninges
- Encephalitis - brain inflammation
- Myelitis- spinal cord inflammation

2. **Limited**
- Brain abscess
- Epidural abscess
- Subdural abscess

Etiology

- Bacterial
- Viral
- Fungal
- Parasitic
- Prion diseases

Depending on the clinical course

1. Acute (hours, days)
2. Chronic (days, weeks)

Depending on cerebrospinal fluid results

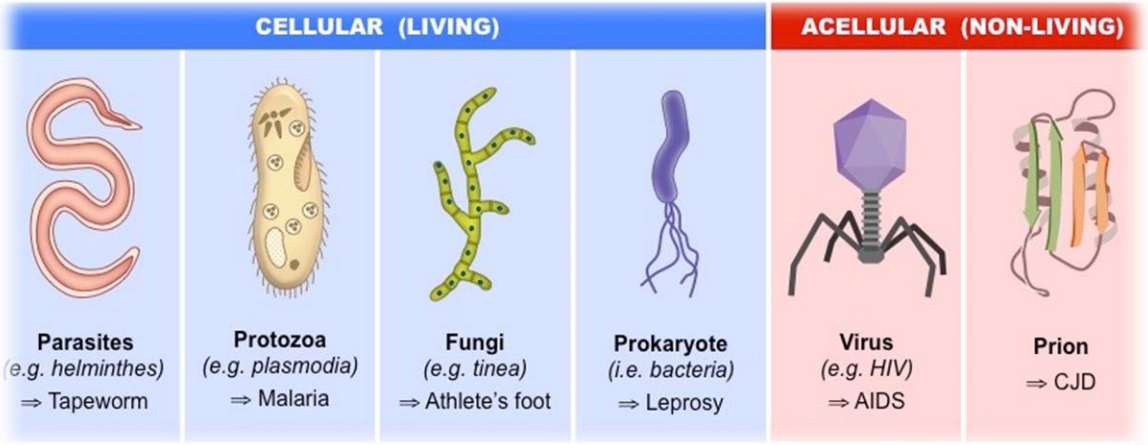
1. Purulent
2. Non-purulent (aseptic)

EPIDEMIOLOGY

- Morbidity: 6 – 8/100 thou./year
- Mostly among children up to 4 years of age:– 40/100 thou./year

ETIOLOGY

- Bacterial – etiology is age dependent
  - Borrelia burgdorferi – it is a bacteria but the clinical presentation is more similar to viral infection (aseptic infection)
- Viral – mostly enteroviruses, tick-borne encephalitis virus, mumps virus, measles, herpes viruses, flu viruses
- Fungal – i.a. Candida spp., Cryptococcus, Aspergillus
- Parasitic – i.a. Toxoplasma gondi
- Prion diseases



Bacterial meningitis – etiology depending on age

Age	Pathogen
Newborns	S.agalactiae, E.coli, Klebsiella spp., gram-negative intestinal bacteria, L.monocytogenes
Newborns (hospital-aquired infection)	Staphylococci, gram-negative intestinal bacteria, P.aerusinosa
Infants up to 3 months of age	N.meningitidis, H.influenzae, S.pneumoniae
Older infants, children, adults	N.Meningitidis (in Poland type B and **C**), S.pneumoniae, H.influenzae (mostly type b (Hib)), L.monocytogenes

Okarska-Napierała M., Kuchar E., Zapalenie opon mózgowo-rdzeniowych u dzieci – postępowanie praktyczne. Standardy Medyczne/Pediatria. 2017;14;373-382.

Viral and other aseptic (non-purulent)* infections

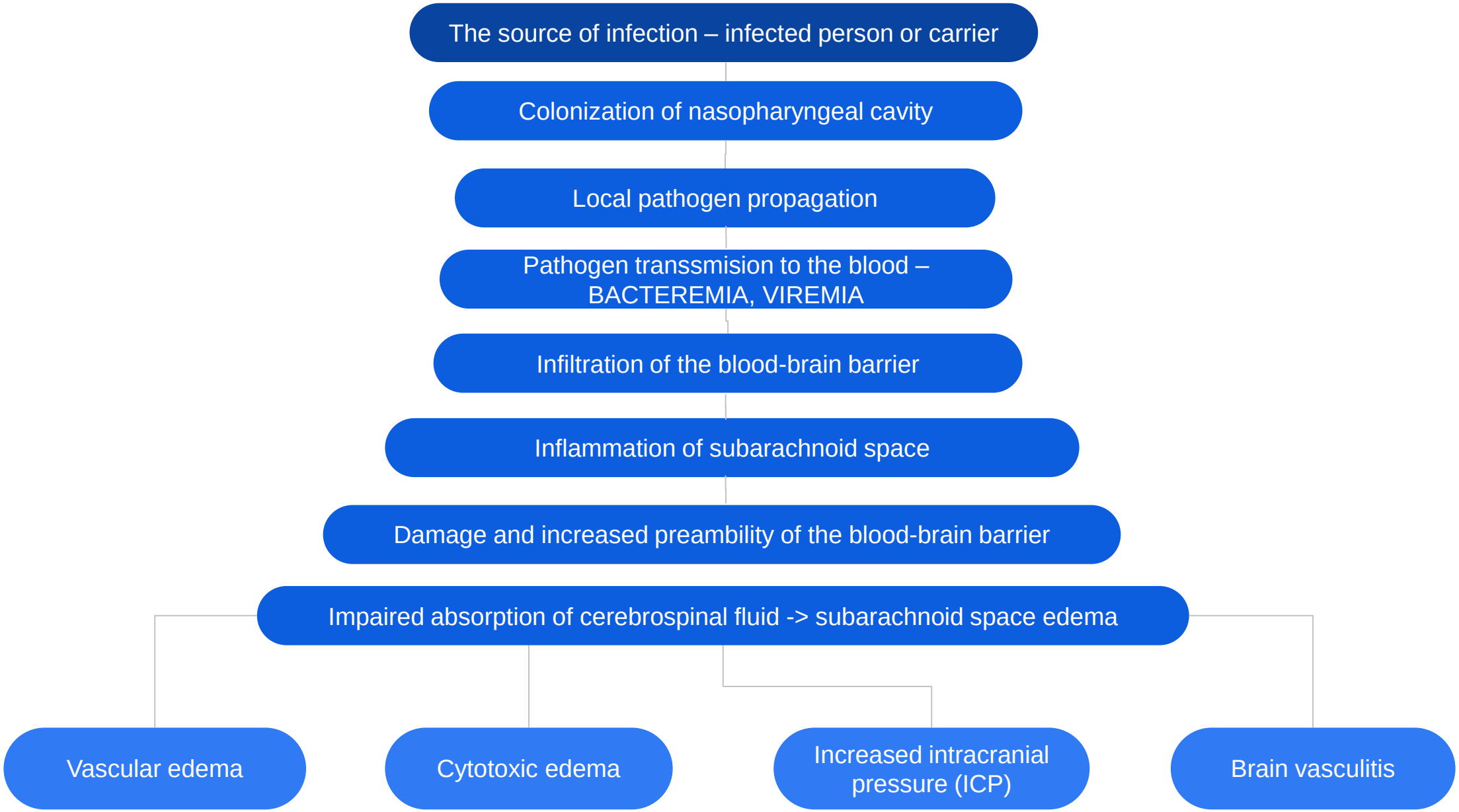
Viruses	Bacteria	Fungus	Other
• enteroviruses (echo, coxsackie, polio) • tick-borne encephalitis virus • Mumps virus • HSV-2 • EBV • Influenza viruses • CMV	• Borrelia burgdorferi sensu stricto • Bartonella henselae (cat-scratch disease) • Mycoplasma pneumoniae • Chlamydia psitacci	• Candida albicans • Cryptococcus neoformans • Histoplasma capsulatum • Blastomyces dermatitidis	• Toxoplasma gondii

*Aseptic (non-purulent) infection – infections in which the cerebrospinal fluid results are similar to viral infection rather than typical bacterial

Pathogenesis – how pathogens are transmitted to the nervous system

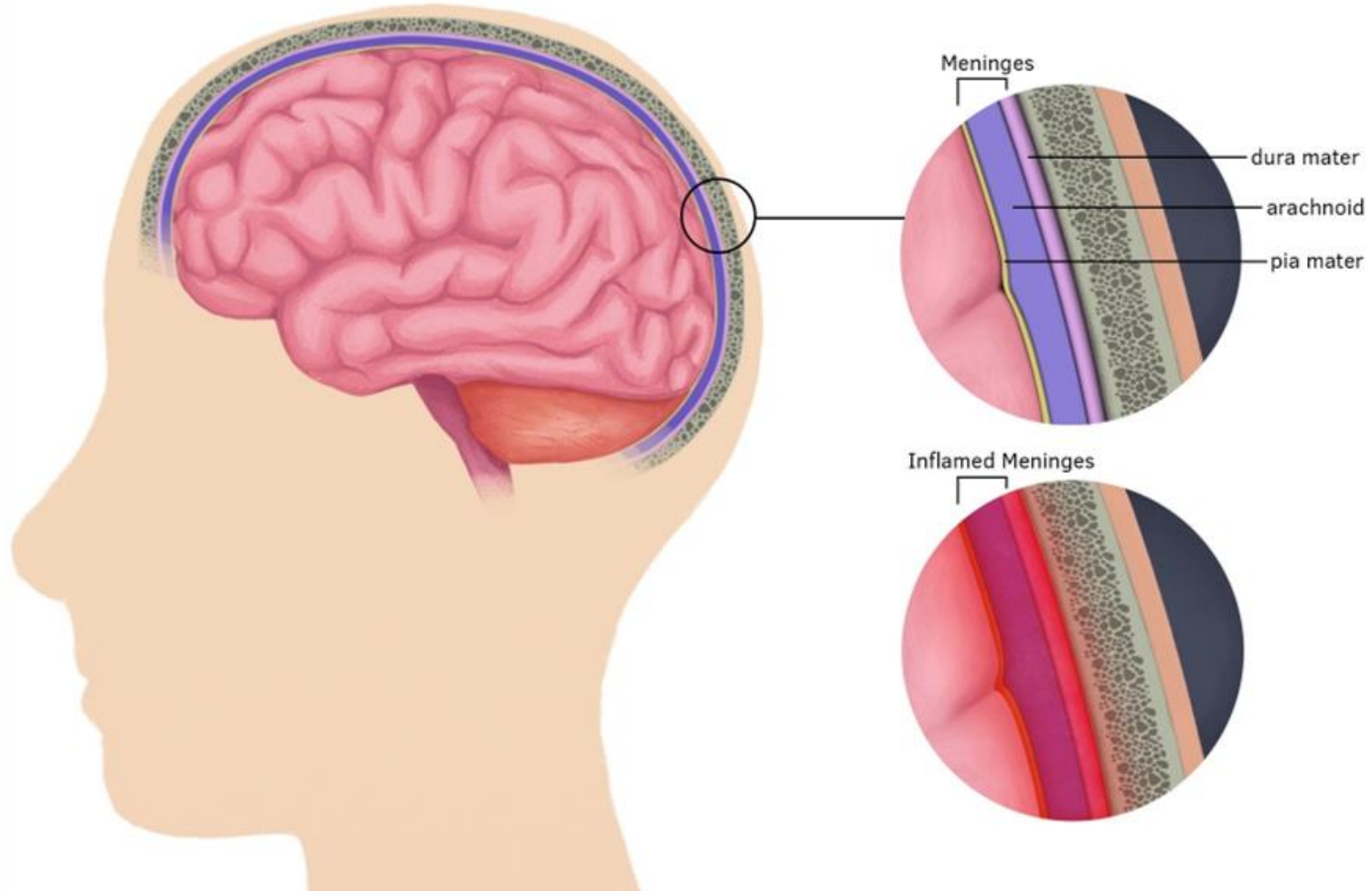
- **Blood-borne transmission**
- From neighbouring organs through continuity i.a. sinusitis, middle ear infection, skull trauma
    - Neuronal transmission – some viruses may infect the central nervous system (CNS) by migration through the axons (herpes viruses, polio, coronaviruses, rabies)

The stages of infection – blood-borne transmission



MENINGITIS

Inflammation caused by the infiltration of the pathogen into the cerebrospinal fluid. It involves pia mater, arachnoid, and subarachnoid space. If untreated, it may extend to neuronal tissue (encephalitis or encephalomeningitis)



Bacterial central nervous system (CNS) infections - symptoms

Symptoms are usually acute

OLDER CHILDREN AND ADULTS

- **headache**
- **fever**
- **vomits and nausea**
- **photophobia**
- **meningeal signs** (not all required)
- reluctance to eating and drinking
- sleepness
- irritability
- consciousness disturbances, emotional lability
- seizures
- focal neurological signs – i.a. cranial nerves paralysis, paresthesis, paralysis

These signs suggest the involvement of neuronal tissue (encephalitis)

NEWBORNS AND INFANTS

- sleepness
- irritability
- reluctance to eating, vomits
- fever or hypothermia!!!
- opisthotonus
- elevated, tense, pulsing fontanelle
- seizures
- General hipo/hipertonia (change of muscle tone)
- Focal neurological signs – i.a. hemiplegia, cranial nerves paralysis

IMPORTANT: typical meningeal signs may be not observed!!!
(due to fontanelle -> „safety vent” for increased intracranial pressure (ICP)

Meningeal signs

Sign	Description
Neck stiffness (nuchal rigidity)	It is an inability to flex the neck forward due to **rigidity** of the neck muscles.
Brudzinski's neck sign (upper)	This is an involuntary flexion of the lower extremities when the neck is passively flexed.
Brudzinski's sympheseal sign (lower)	Pressure on the pubic symphysis elicits a reflex flexion and abduction of the lower extremities
Brudzinski's cheek sign	Applying the pressure on both cheeks inferior to the zygomatic arch leads to spontaneous flexion of the forearm and arm
Kernig's sign	The patient is kept in a supine position, hip and knee are flexed to a right angle, and then the knee is slowly extended by the examiner. The sign is positive when there is resistance during the knee extension +/- pain
Herman's sign	Big toe extension in response to neck flexion
Flatau sign	mydriasis (pupillary constriction) in response to neck flexion (assisted if neccesery)
Amoss' sign	the patient sits up from a supine position by supporting himself with his arms placed behind him

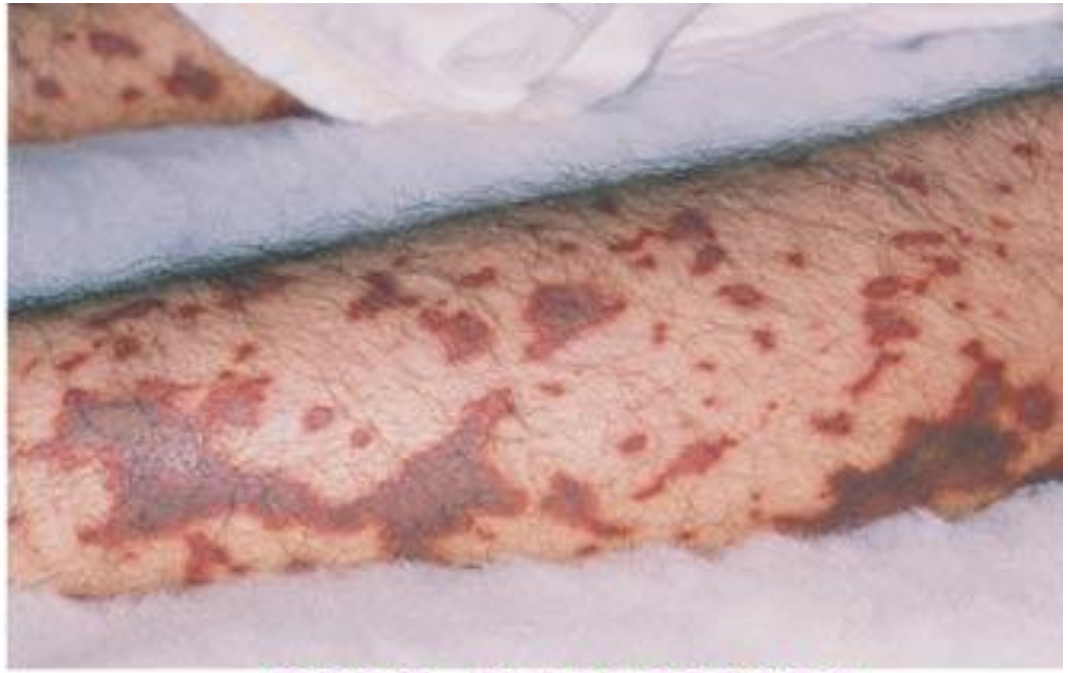
Bacterial meningitis – characteristic depending on the etiology

	N. meningitidis	*S. pneumoniae*	*H. influenzae*
Additional characteristic features	Hemorrhagic rash (10-50%)	Middle ear infection, pneumonia Neuroinfection may recur	Middle ear infection
Predisposed age groups	Children < 4yrs, teenagers, young adults	Children < 2 yrs, adults > 65 yrs	Children < 2 yrs
Risk factors	Immunosuppression, asplenia or post-splenectomy, autoimmunological diseases, bad socioeconomic conditions	Immunosuppression, pre-term children with bronchopulmonary dysplasia, CNS abnormalities, CSF leak	Immunosupression
Disease dynamics	**Very** fast (a few hours)	Fast (dozen of hours)	Fast (dozen of hours) or moderate (12-48h)
Neurological consequences	20%	20-50%	25%
Mortality	10-12%, in septic shock even 50%	10-25%	5%

Pediatria, tom 2. *Neuroinfekcje.* Pod red. Kawalec W., et al. 2015, PZWL, Warszawa.

Hemorrhagic rash in meningococcal sepsis

RASH- EARLY STAGES



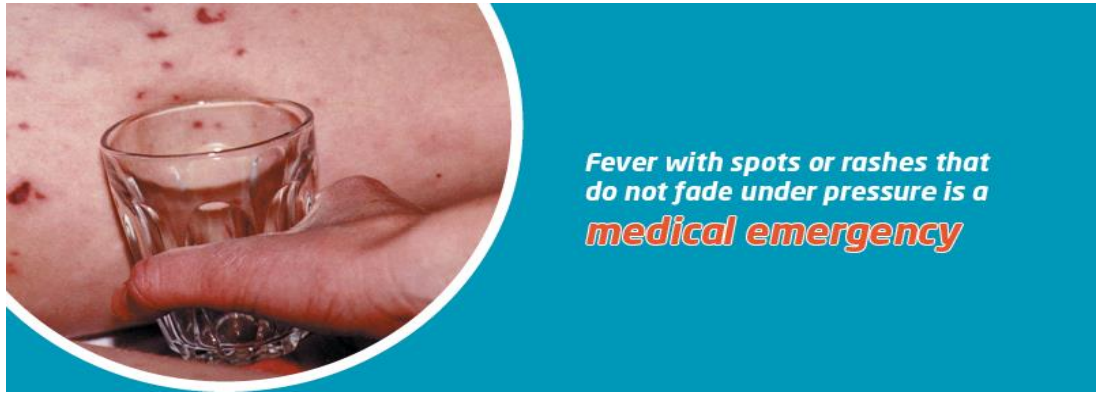
RASH - FINAL STAGES

Viral and aseptic neuroinfections – symptoms

- Variable:
  - From asymptomatic or mild
  - To acute and severe infections with consciousness disturbances, seizures, and focal neurological signs
- Signs of neuroinfections may occur after a few days of unspecified flu-like or gastrointestinal symptoms (two-stage course)
- Symptoms may be unspecified e.g. headache and facial nerve palsy – they may indicate on neuroborreliosis

Natural course

- Depending on pathogen and localization of the infection (meningitis vs encephalitis and myelitis)
- Bacterial infections, especially typical (septic/purulent), are usually severer than viral and aseptic infections
- Very severe infection may rapidly progres to shock and death
  - Remember about haemorrhagic rash -> glass test-> meningococcal sepsis!!!



Neuroinfections – Diagnostic workup

- Clinical presentation – the suspicion of neuroinfection is an indication for the lumbar puncture. Assess the basic parameters (heart and respiratory rate, blood pressure, saturation, temperaturę) and general patient's state.
  Medical interview and physical examination are the most important - you do not need additional tests to suspect neuroinfection!
- Lumbar puncture
- Laboratory tests
- Fundoscopic examination
- Neuroimaging studies
- Electroencephalography (EEG)

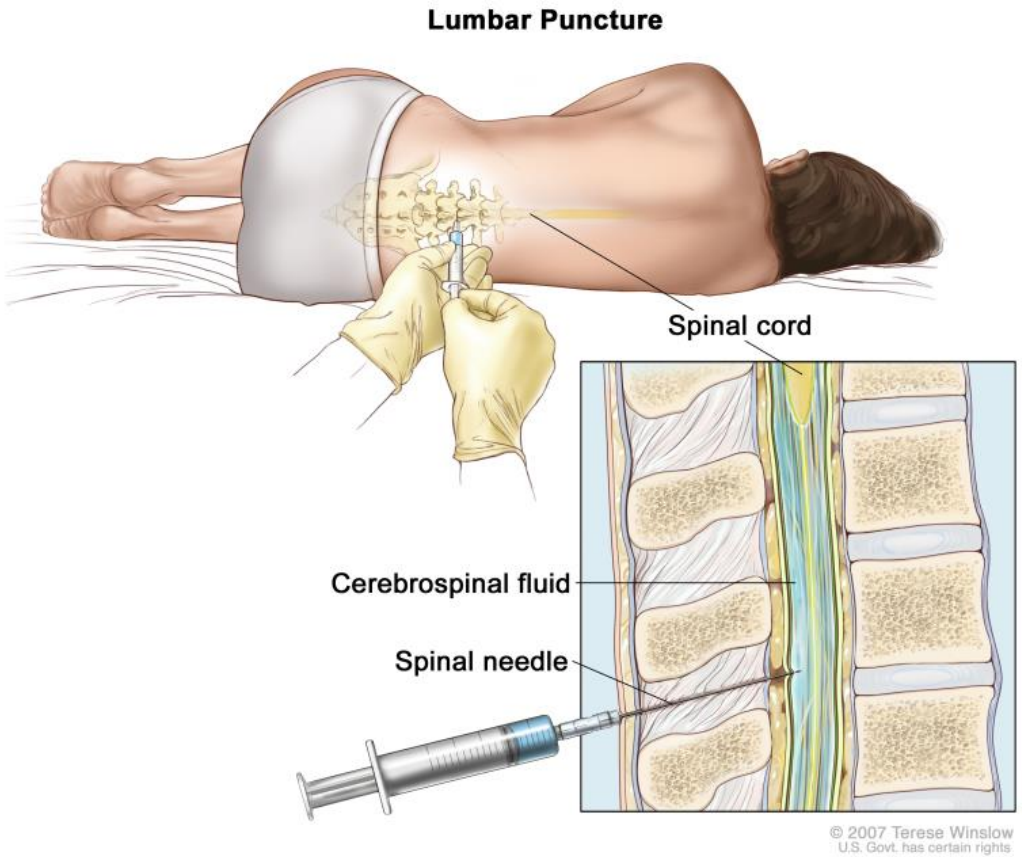
Stabilization of the patient's condition and quick antibiotics introduction are the priority!
If there are contraindications for the lumbar puncture -> begin the treatment with antibiotics before diagnostic workup!

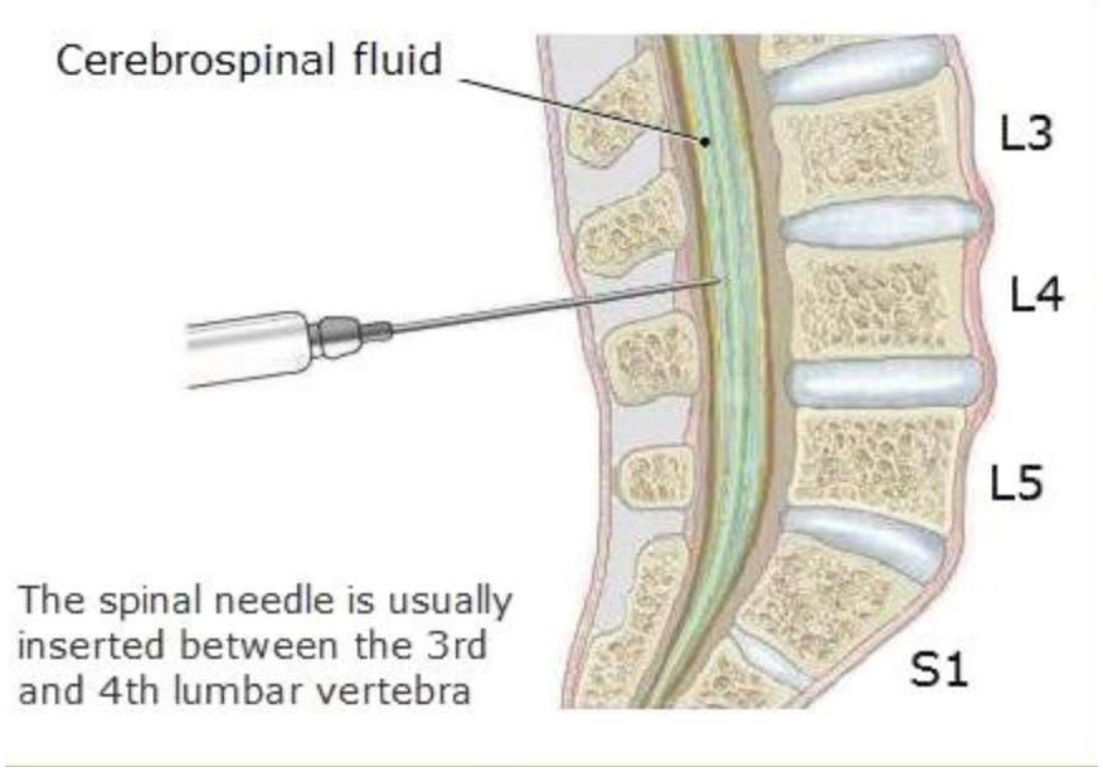
Diagnostic standarts – Time!

- Time from the first contact with a doctor to the beginning of empiric treatment should not exceed 3 hours
- If you suspect meningococcal infection it should be up to 30 minutes!!!

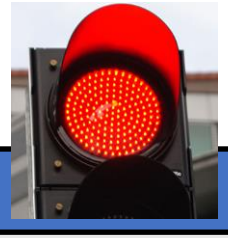
Albrecht P, Hryniewicz W, Kuch A i wsp. *Rekomendacje postępowania w zakażeniach bakteryjnych ośrodkowego układu nerwowego. Rekomendacje diagnostyczno-terapeutyczno-profilaktyczne.* Warszawa, Narodowy Instytut Leków 2011.

Lumbar puncture





Contraindication to the lumbar puncture



Absolute

- **Signs of increased intracranial pressure (ICP)** (bradycardia, increased blood pressure, breathing disturbances, optic disc edema)
- Coagulopathy – platelet level <50 thou/mm3 or INR > 1.6, or DIC
- Cardiorespiratory failure, shock
- Regional skin infection in the lumbar region

Conditional

- Coagulopathy – platelet level 50 – 100 thou/mm3, INR 1,4 – 1,6
- Deformation of the lumbar spine
- Significant dehydration
- If performing of the lumbar puncture will significantly delay the introduction of antibiotics

Increased intracranial pressure is the most important contraindication for the lumbar puncture! -> the risk of brainstem herniation -> pressure on the brainstem -> cardiorespiratory failure and sudden death

Before the lumbar puncture

- Exclude the contraindications:
  - Increased ICP (fundoscopic examination, neuroimaging studies (computer tomography))
  - Laboratory tests: blood count, coagulogram, blood culture
  - Assess the anatomical structures and skin condition in the lumbar region
  - The glucose level in the blood (for the proper interpretation of CSF results)
- Obtain the written consent for the procedure

Computer tomography (CT) before the lumbar puncture

CT may exclude increased ICP or indicate other abnormalities: brain edema, anatomical abnormalities, brain tumor.

However, there are no recommendations for routine CT scan before the lumbar puncture.
Indications for CT in patients suspected of neuroinfection:

- Consciousness disturbances
- CSF leak
- Hydrocephalus or ventriculoperitoneal shunt
- Focal neurologic deficit (eg, dilated nonreactive pupil, gaze palsy, or arm or leg drift)
- Recent head trauma or neurosurgical intervention
- Papilledema
- Immunocompromised state
- History of CNS disease (eg, mass lesion, stroke, or focal infection)
- Seizure within 1 week of presentation

However, postpone the CT if it significantly delays the performance of the lumbar puncture or antibiotics treatment.
Although remember to exclude the increased ICP before the lumbar puncture by other methods e.g. fundoscopic exam

Albrecht P, Hryniewicz W, Kuch A i wsp. *Rekomendacje postępowania w zakażeniach bakteryjnych ośrodkowego układu nerwowego. Rekomendacje diagnostyczno-terapeutyczno-profilaktyczne.* Warszawa, Narodowy Instytut Leków 2011.

Cerebrospinal fluid tests

- Basic test
- Smear
- Bacterial culture
- Serological and molecular tests (specific antibodies, PCR)

CSF findings depending on etiology

	Normal results > 12 months of age	Bacterial	Viral	Tuberculosis	Borreliosis/syphilis
Color and clarity	**Clear**	Yeallow or green, cloudy	Clear	Clear	Clear
Cytosis (in ul)	**≤ 5**	> 1000	Dozen to hundreds	Dozen to hundreds	Dozen to hundreds
CSF smear	**Lymphocytic**	Neutrophilic	Lymphocytic	Lymphocytic	Lymphocytic
Protein concentration [mg/dl]	**15 - 45**	↑↑ (>100)	N lub ↑ (50-200)	↑↑ (>100)	N lub ↑ (50-200)
Glucose level: CSF/serum	**≥ 0,6**	< 0,4	> 0,6 or rarely decreased	< 0,4	0,6 or rarely decreased

Okarska-Napierała M., Kuchar E., Zapalenie opon mózgowo-rdzeniowych u dzieci – postępowanie praktyczne. Standardy Medyczne/Pediatria. 2017;14;373-382.

Differential diagnosis

- Irritation of meninges (meningismus) – meningeal signs without abnormalities in CSF
- Increased ICP due to other causes e.g. brain tumor
- Subarachnoid haemorrhage, stroke
- Drug poisoning
- Severe dehydration or metabolic imbalance (including diabetes)

Treatment – empiric antibiotic therapy

At least 2 intravenous (i.v) antibiotics in maximal doses

- Newborns:
  - Ampicylin + cefotaxime
  - Ampicylin + aminoglycoside

Hospital-aquired infections: ceftazidime + vancomycin

- Infants, older children, adults:
  - Cefalosporin III generation (ceftriaxone, cefotaxime) + vancomycin

  (in infants 1-3 months: consider addition of ampicylin)

Empiric treatment depending on the risk factors

Risk factor	Antibiotics
Fracture of the skull base bones	Cefotaxime OR ceftriaxone + vancomycin
Injury penetrating to the CNS	Ceftazidime OR cefepime OR meropenem + vancomycin
After neurosurgery	Ceftazidime OR cefepime OR meropenem + vancomycin
CNS infections transmitted through ventriculoperitoneal shunts	Ceftazidime OR cefepime or meropenem + vancomycin

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Antibiotic treatment – Dosage

Antibiotic	Newborns		Infants and children	Adults
	0-7 days	8-28 days		
Amikacin	15-20 mg/kg/day in 2 divided doses	30 mg/kg/day in 3 divided doses	20-30 mg/kg/day in 3 divided doses	15 mg/kg/day in 3 divided doses
Ampicylin	150-300 mg/kg/day in 3 divided doses	300-400 mg/kg/day in 3-4 divided doses	300-400 mg/kg/day in 4-6 divided doses	12 g/day in 6 divided doses
Cefotaxime	100-150 mg/kg/day in 2-3 divided doses	150-200 mg/kg/day in 3-4 divided doses	225-300 mg/kg/day in 3-4 divided doses	8-12 g/day in 4-6 divided doses
Ceftazidime	100-150 mg/kg/day in 2-3 divided doses	150 mg/kg/day in 3 divided doses	150 mg/kg/day in 3 divided doses	6 g/day in 3 divided doses
Ceftriaxone	-		80-100 mg/kg/day in 1-2 divided doses	4 g/day in 2 divided doses
Meropenem	-		120 mg/kg/day in 3 divided doses	6 g/day in 3 divided doses
Vancomycin	20-30 mg/kg in 2-3 doses	30-45 mg/kg in 3-4 doses	60 mg/kg/day in 4 divided doses	30-60 mg/kg/day in 2-3 doses

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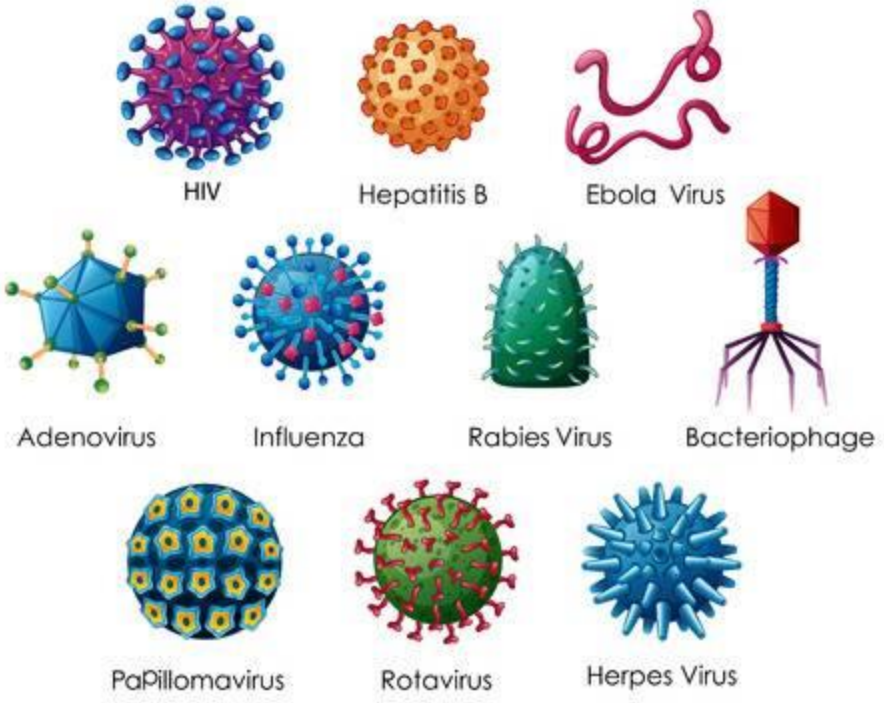
Treatment of viral neuroinfections

Herpes viruses (effective in HSV and VZV infections and implemented as empiric treatment of aseptic infection):

- Acyclovir i.v. 10 mg/kg every 8 hours

CMV (not in empiric treatment):

- Gancyclowir i.v. 5 mg/kg every 12 hours



Supportive treatment – etiology independent

Anti-edema therapy (20% mannitol, Dexamethasone, Furosemide, elevation of the head up to 20-30 degree), treatment of the metabolic abnormalities, anti-seizure (antiepileptic) treatment

Antipyretic treatment e.g.:

- Paracetamol every 4-6 h
  - i.v. 7,5 mg/kg/dose in child < 10 kg OR 15 mg/kg/dose in child > 10 kg
  - p.o. 15 mg/kg/dose p.r 25 mg/kg/dose
  - Older children (> 12 years) and adults i.v. lub p.o 500-1000 mg/dose
- Ibuprofen every 6 – 8 h
  - p.o., p.r. 5-10 mg/kg/dose
  - Older children (> 12 years) and adults p.o 200-400 mg/dose

Dexamethasone: 0,4 mg/kg every 12 hours for 2 days
Dehydration: 0,9% NaCl 20 ml/kg i.v bolus or within 1-2 hours depending on the clinical condition
Hypoglycemia: with consciousness disturbances: 10% glucose 2-2,5 ml/kg V=2-3 ml/min
Coagulopathy: FFP 10-15 ml/kg
Seizures: Diazepam p.r 0,5 mg/kg or i.v 0,2 mg/kg
Brain edema: 20% mannitol 2-2,5 ml/kg infusion within 20-30 min

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Empiric treatment should be replaced with pathogen-specific treatment as soon as possible

Pathogen	Treatment duration
Neisseria meningitidis	7 days
Haemophilus influenzae typ b	7-10 days
Streptococcus pneumoniae	10-14 days
Streptococcus agalactiae	14-21 days
Staphylococcus aureus	14 days
Listeria monocytogenes, Pseudomonas aeruginosa, Gram-negative gastrointestinal bacteria	> 21 days
Unknown etiology	10-14 days
HSV virus	21 days

The supervision of the diagnosis and treatment of bacterial neuroinfections

- KORUN - National Reference Centre for Bacterial Infections of the Central Nervous System
- KORLD- National Reference Centre for Antimicrobial Susceptibility Testing

Particular neuroinfections

Tick-borne encephalitis

- Virus transmitted by ticks (Ixodes)
- Two subtypes of the disease: European – milder and far-eastern – severer
- Seasonality: spring and summer
- Time of incubation: 7 – 14 days
- 35 – 59% of patients present focal neurological deficits. A long time of convalescence
- Bi-phasic clinical course

Phase 1 - preliminary	Phase 2 – symptomatic (about 50% of patients)
• Flu-like symptoms: ▪ Malaise, ▪ Weakness, ▪ Headache and neck pain, ▪ Muscle pain, ▪ Eyeballs pain, ▪ Nausea, vomit, stomach ache, diarrhoea, ▪ Subfebrile state Symptoms last for about a week	❖ **Meningitis:** fever, headache, dizziness, vomit, meningeal signs ❖ **Encephalitis:** consciousness disturbances, ataxia, aphasia, seizures, cerebral nerves palsy, hemiplegia, etc. ❖ **Encephalomeningitis** ❖ **Myelitis:** limb paresis (upper>lower), paresthesia, sphincter disturbances

Tick-borne encephalitis

Among all infected patients about:

- 30% do not develop any symptoms
- 30%–50% develop only phase-1 symptoms
- up to 30% develop full, bi-phasic clinical course with CNS involvement

Incidence rate is higher among men than women

- Severer clinical course in old people
- Up to 46% patients develop long-term neurological complications during phase-2

Tick-borne encephalitis in children

Milder clinical course in children. However:

- about 20%−30% of pediatric patients develop meningitis and encephalitis
- about 25% of children develop long-term neurological complications
- about 2% of children develop persistent neurological consequences

Tick-borne encephalitis – laboratory tests

1. SERUM:
    a. Leucocytosis
    b. Elevated CRP level
    c. Elevated erythrocyte sedimentation rate (ESR)
    d. Detection of specific antibodies (IgG and IgM subtype)

2. CSF
    a. Cytosis, usually lymphocytes
    b. Protein of 50-200 mg/dl
    c. Detection of specific antibodies (IgG and IgM subtype) – it confirms the diagnosis

Tick-borne encephalitis - treatment

1. No specific treatment
2. Only a symptomatic treatment: anti-edema, anti-pain, antipyretic, fluids, immunoglobulins

Tick-borne encephalitis – long-term consequences

- Ataxia,
- consciousness disturbances,
- diplopia,
- urine incontinence or retention,
- paresis or paralysis (sometimes involving respiratory muscles),
- dysphagia,
- dysarthria

NEUROBORRELIOSIS

http://www.bristoluniversitytickid.uk/

- Etiology: Borrelia burgdorferii (bacteria)
- Transmitter – Tick (*Ixodes)*
- Time of incubation: 7-30 dni
- The nervous system is involved in about 15% of cases (both peripheral and central nervous system)
  - Lymphocytic meningitis (aseptic)
  - Cranial nerve palsy (mostly facial nerve, also bilaterally)
  - Radiculopathy
  - Unspecified symptoms e.g. headaches
- Diagnosis: detection of specific antibodies in serum and CSF (ELISA – screening test, Western Blot – confirming test)
- Treatment: depending on age and localization of the infection (peripheral vs central nervous system)
- Treatment duration: 21 days

Treatment of neuroborreliosis

Symptoms/localization	Age group	First-choice drugs	Second-choice drugs
Involvement of cranial or peripheral nerves	Adults and children > 12 yrs	**Doxycyclinum p.o** 2x100 mg or 1x200 mg for 21 days	Amoksycylina p.o 3x1g przez 21 dni
	Children 9 – 12 yrs	**Doxycyclinum p.o** children < 45 kg: 1 day - 5 mg/kg in 2 divided doses, since 2nd day - 2,5 mg/kg/day in 1-2 didived doses for 21 day If the symptoms are severe, continue the dose of 5 mg/kg/day	Amoksycylina p.o <33 kg: 3x 30 mg/kg/dawkę przez 21 dni
	Children < 9 yrs	**Amoxicillin p.o** children <33 kg: 3x 30 mg/kg/dose for 21 days	
Involvement of the central nervous system	Adults and children > 12 yrs	**Ceftriaxone i.v**. 2x 2g lub 1x 4g for 21 days	**Doxycyclinum p.o** 2x 200 mg or 1x 400 mg for 21 days
	Children 9 – 12 yrs	**Ceftriaxone i.v** < 50 kg: 1x 80 mg/kg (max. 4 g) for 21 days	**Doxycyclinum p.o** children < 45 kg: 1 day - 5 mg/kg in 2 divided doses, since 2nd day - 2,5 mg/kg/day in 1-2 didived doses for 21 day If the symptoms are severe, continue the dose of 5 mg/kg/day
	Children < 9 yrs	**Ceftriaxone i.v** < 50 kg: 1x 80 mg/kg (max. 4 g) for 21 days	

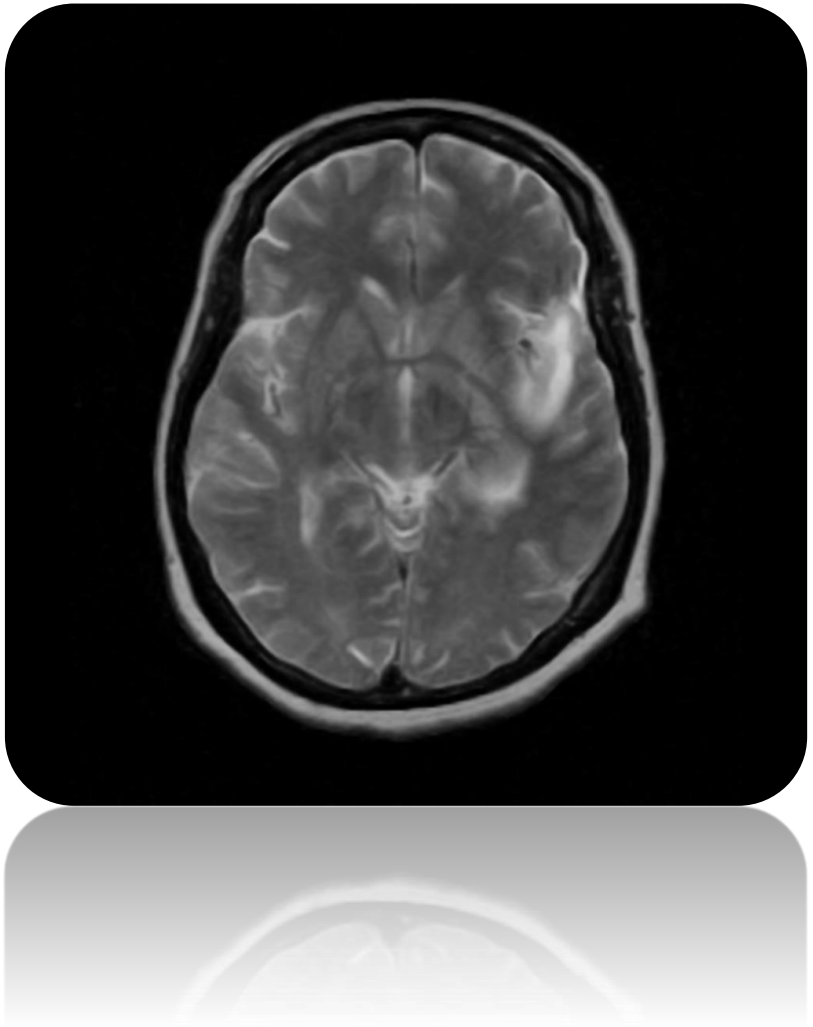
Based on NICE 2018 recommendations

Tick-borne infections – prophylactics

1. Adequate clothes
2. Repellents
3. Anti-tick-borne encephalitis vaccine

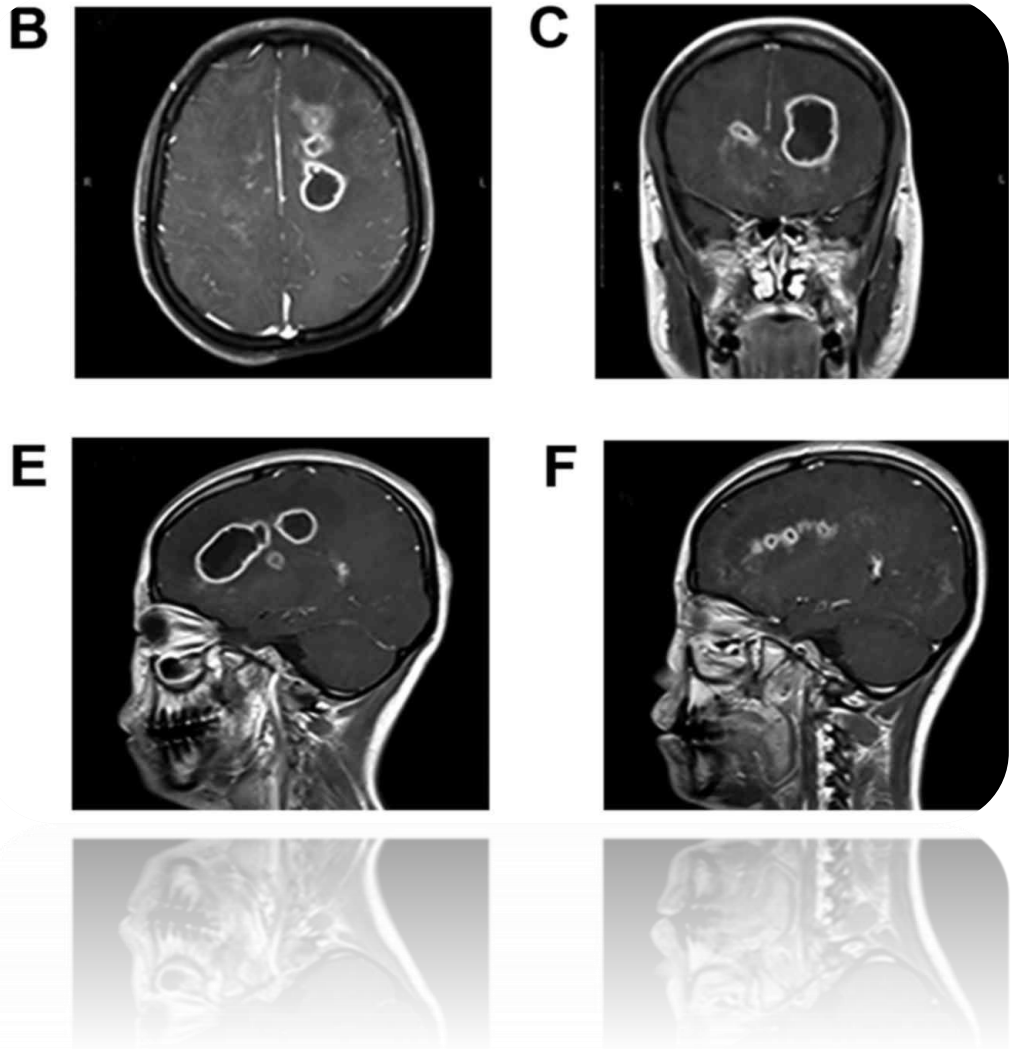
Herpes virus’ encephalitis (HSV)

- HSV virus (>95% HSV-1)
- Mostly due to primary infection -> the virus is transmitted from mouth cavity through axons to the central nervous system
- Mostly newborns, children between 6 months and 4 years of age, and adults
- It constitute for about 10% of all encephalitis
- Symptoms:
  - At the begenning - unspecified (fever, upper respiratory tract infection, hedache, vomit)
  - Subsequently, neurological symptoms (seizures, paresthesia, paresis, memory deficits, aphasia, halucinations, consciousenss disturbances)
- Diagnosis: CSF examination including molecular tests for viral DNA, neuroimaging studies – lesions in the temporal lobes
- Treatment:
  - Acyclovir i.v. 10 mg/kg every 8 h for 21 days
  - Symptomatic treatment

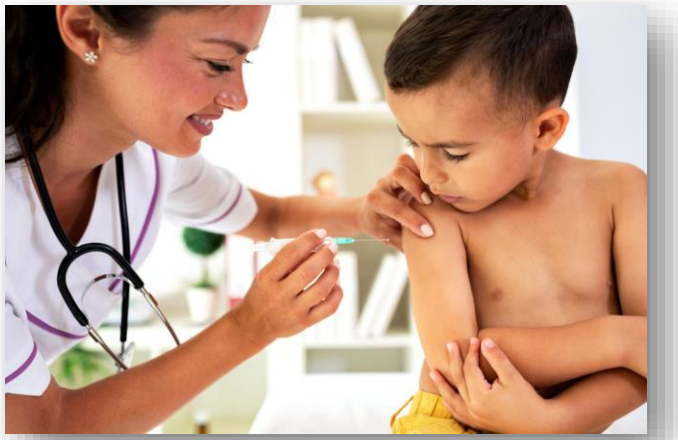


Local CNS infections – brain abscess

- Etiology: bacteria (staphylococci, streptococci, anaerobic bacteria), fungus
- Brain abscess is often secondary to other neighboring infections e.g. sinusitis, middle ear infections, a periodontal abscess
- Higher risk in patients with immunosuppression (be aware of untypical etiology)
- Symptoms: headache, fever, focal neurological deficits
- Diagnosis: neuroimaging studies (CT, MRI)
- Treatment: neurosurgical + antibiotics



Currently, we may prevent some neuroinfections and neurological complications by vaccines



Obligatory vaccines in Poland:

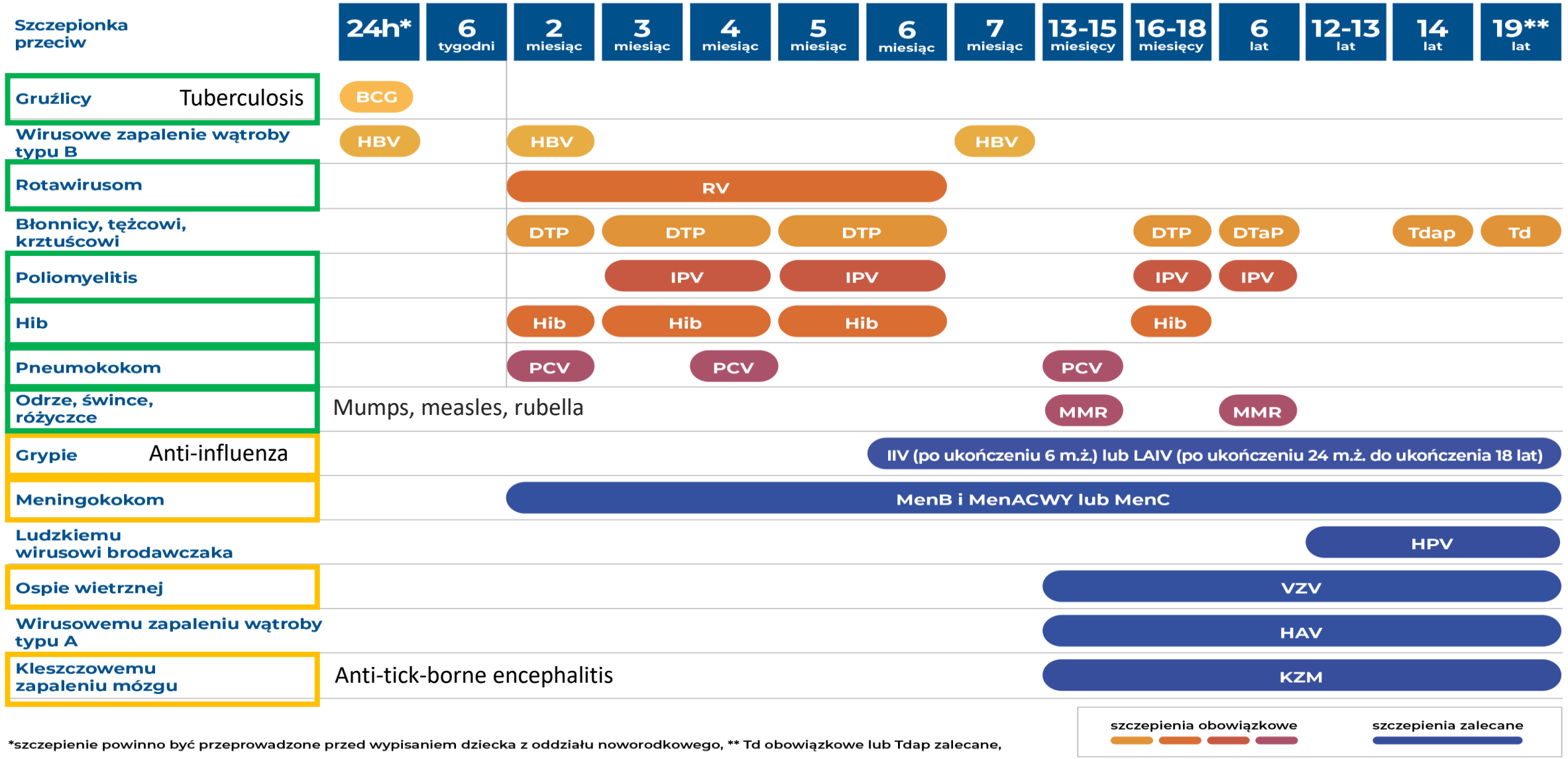
- Anti-Hib (anty ***Haemophilus influenzae*** **typu b)**
- Anti- Streptococcus pneumonie (several serotypes)
- Anti-rotaviruses
- Vaccination for „forgotten" diseases:
  - Tuberculosis
  - Polio
  - Mumps, measles, rubella

Recommended but not obligatory vaccination in Poland:

- Anti– Neisseria meningitidis
- Anti-tick-borne encephalitis
- Anti-influenza vaccine

KALENDARZ SZCZEPIEŃ NA 2021 ROK

szczepienia info



*szczepienie powinno być przeprowadzone przed wypisaniem dziecka z oddziału noworodkowego, ** Td obowiązkowe lub Tdap zalecane,

BCG - szczepionka przeciw gruźlicy, **HBV** (Hepatitis B Vaccine) - szczepionka przeciw wirusowemu zapaleniu wątroby typu B, **DTP** - szczepionka przeciw błonicy, tężcowi i krztuścowi, całokomórkowa, **RV** - szczepionka przeciw rotawirusom, **DTaP** - szczepionka przeciw błonicy, tężcowi i krztuścowi, bezkomórkowa, **Tdap** - szczepionka przeciw błonicy, tężcowi i krztuścowi, bezkomórkowa z obniżoną zawartością antygenów błonicy i krztuśca, **IPV** (Inactivated Polio Vaccine) - szczepionka przeciw poliomyelitis, zabita, **Hib** - szczepionka przeciw Haemophilus influenzae typu b, **MMR** - szczepionka przeciw odrze, śwince i różyczce, **PCV** - skoniugowana szczepionka przeciw pneumokokom, **IIV** (Inactivated Influenza Vaccine) - szczepionka przeciw grypie (inaktywowana), **LAIV** (Live Hepatitis A Vaccine) - szczepionka przeciw grypie (żywa, donosowa), **MenB** - szczepionka przeciw meningokokom grupy B, **MenACWY** - szczepionka przeciw meningokokom grupy A, C, W, Y lub C, **HPV** - szczepionka przeciw ludzkiemu wirusowi brodawczaka, **VZV** - szczepionka przeciw ospie wietrznej, **HAV** (Hepatitis A Vaccine) - szczepionka przeciw wirusowemu zapaleniu wątroby typu A, **KZM** - szczepionka przeciw kleszczowemu zapaleniu mózgu.

Thank you for your attention

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