LUMBAR PUNCTURE, NEUROINFECTION

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CLINICAL MANIFESTATION OF CNS INFECTIONS

Classification by predominant symptoms - but impact is often combined

Acute purulent meningitis – inflammatory impact on the meninges (purulent discharge), *predominance of polymorphonuclear cells in the cerebrospinal fluid*

Acute serous meningitis – inflammatory impact on the meninges resulting in exudative serous inflammation, *predominance of mononuclear cells in the cerebrospinal fluid*

Chronic meningitis – long history (weeks / months), *abnormal findings in the CSF lasting at least 4 weeks*

Acute encephalitis – impaired consciousness prevails, possibly focal symptoms; meningeal symptoms minimal (purulent rare – secondary with sepsis; non-purulent – perivascul. lymphoplasmacytic infiltrates)

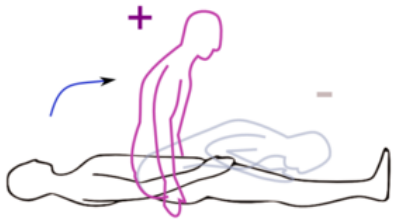
Myelitis – Rarely a standalone condition / encephalomyelitis – fever, paraparesis weak … spastic

Lesions processes (subdural empyema, epidural abscess, brain abscess) - per continuatem, hematogenous spread

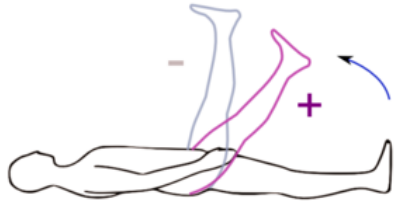
Examining meningeal signs

Příznak opozice šíje

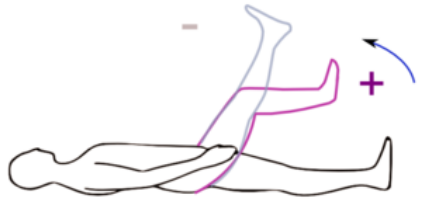
Příznak Brudzinského



Příznak spinální



Lasegueův příznak



Kernigův příznak

Příznak trojnožky

Etiology of purulent meningitis

- **Newborns / infants (< 3 months)**

Streptococcus agalactiae	***E-Coli (+ G⁻ agens)***
Listeria monocytogenes	

- **Childern**

Streptococcus pneumoniae	***Neisseria meningitidis***
Haemophilus influenzae	

- **Adults**

Streptococcus pneumoniae	***Neisseria meningitidis***
Staphylococcus aureus	

- **Adults > 50 years**

Streptococcus pneumoniae	***Neisseria meningitidis***
Listeria monocytogenes	*G⁻ agens, Staphyl. aureus*

Etiology of aseptic meningitis

Enteroviruses	**Arboviruses**
Herpetic viruses	Respiratory viruses
Spirochetes	Rickettsiae, Legionella

Aspergillosis	**Candidiasis**
Cryptococosis	Echinococosis
Cysticerkosis	Amebiasis

Bacterial pathogens in aseptic meningitis

- spirochetes – *B. burgdorferi s. l., T. pallidum, L. interrogans*)
- Rickettsiae, legionella, anaplasma
- *Mycoplasma pneumoniae*

WHEN TO PERFORM

A LUMBAR PUNCTURE (LP)

Positive meningeal signs, fever, photophobia, cephalea, vomiting, phonophobia

Focal neurological findings, impaired consciousness, convulsions, hemorrhagic symptoms

CAUTION - newborn (non-specific signs, thermoregulation disorder, muscle tone, encephalic crying, does not feed properly.)

HISTORY OF HEALTH RISKS

(perinatal history, a tick latched on, epidemiological history, travel history, etc.)

SUSPECTING A NEUROINFECTION – WE ALWAYS perform LP

DIFFERENTIAL DIAGNOSTICS OF NEUROINFECTION

Brain tumors, post-med reactions, convulsions, migraines, intracranial hemorrhaging, insolation, trauma, intoxication, thrombosis

Meningism – signs of meningeal irritation without the inflammatory correlation in CSF - e.g. at high fevers - when the fever subsides, the meningeal symptoms also subside.

CONTRAINDICATION – LP

- Intracranial HT – risk of spinal cord conus
- Severe coagulation disorders, skin lesions at the LP site, malformations of the L spine
- Circulatory and ventilatory instability of the patient

PRIORITIZING IMAGING METHODS

- Interdisciplinary cooperation - neurologist
  (subacute conditions, or EEG)
- Risk of delay in drug therapy
  (ATB < 1 hour!)

- INDICATION – meets 1 criterion
  - Focal neurological findings
    (X paresis of the cranial nerves)
  - Newly occurring convulsions (max. 7 days)
  - Impaired consciousness (GCS < 10)
  - Significant immunodeficiency
  - CZ – papilledema on OP (with focal neurological findings)
- Consider also: brain ultrasound (enlarged fontanelle)

LP PREP

TEST TUBES - CSF:

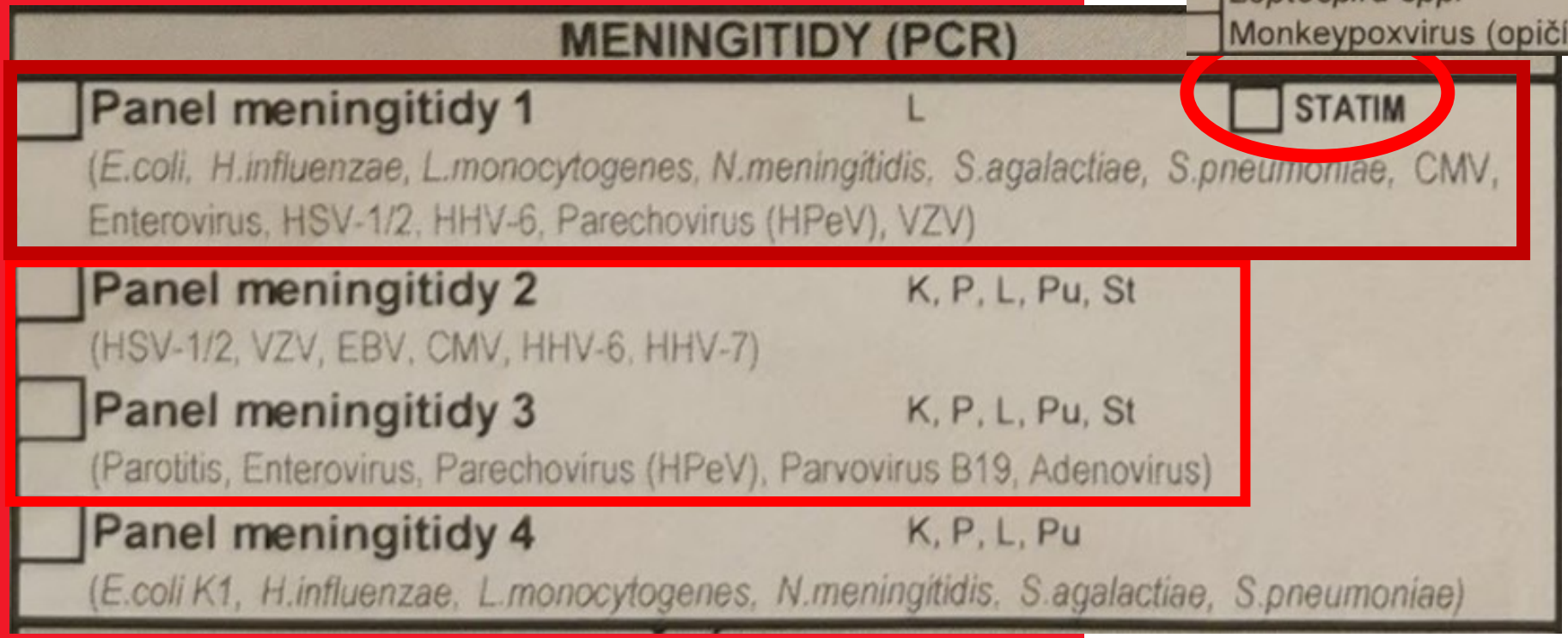
1. Cytology + biochemistry
2. PCR
3. Antibodies
4. H-L barrier …
5. Culture B + C (possible pneumococcal antigen)
6. ….

TEST TUBES - BLOOD:

1. Basic blood work (blood count, biochemistry)
2. H-L barrier
3. Antibodies
4. Hemoculture, coagulation / septic patient, exanthema
5. Toxicology (history of health risks, impaired consciousness, age)

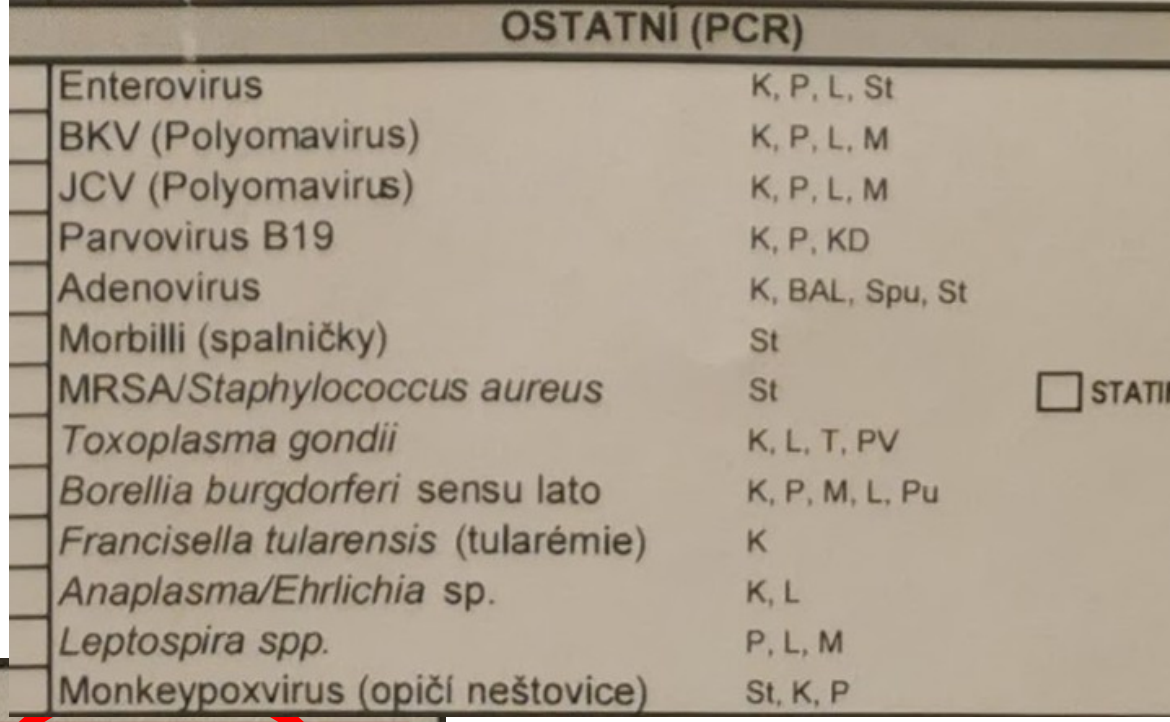
LP interval / blood draw - 30 min., max. 4 hrs

PCR tests from CSF - Test forms examples



MENINGITIDY (PCR)

☐ Panel meningitidy 1 (*E.coli*, *H.influenzae*, *L.monocytogenes*, *N.meningitidis*, *S.agalactiae*, *S.pneumoniae*, CMV, Enterovirus, HSV-1/2, HHV-6, Parechovirus (HPeV), VZV)	L	☐ STATIM
☐ Panel meningitidy 2 (HSV-1/2, VZV, EBV, CMV, HHV-6, HHV-7)	K, P, L, Pu, St	
☐ Panel meningitidy 3 (Parotitis, Enterovirus, Parechovirus (HPeV), Parvovirus B19, Adenovirus)	K, P, L, Pu, St	
☐ Panel meningitidy 4 (*E.coli* K1, *H.influenzae*, *L.monocytogenes*, *N.meningitidis*, *S.agalactiae*, *S.pneumoniae*)	K, P, L, Pu	



OSTATNÍ (PCR)

☐ Enterovirus	K, P, L, St	
☐ BKV (Polyomavirus)	K, P, L, M	
☐ JCV (Polyomavirus)	K, P, L, M	
☐ Parvovirus B19	K, P, KD	
☐ Adenovirus	K, BAL, Spu, St	
☐ Morbilli (spalničky)	St	
☐ MRSA/*Staphylococcus aureus*	St	☐ STATI
☐ *Toxoplasma gondii*	K, L, T, PV	
☐ *Borellia burgdorferi* sensu lato	K, P, M, L, Pu	
☐ *Francisella tularensis* (tularémie)	K	
☐ *Anaplasma/Ehrlichia* sp.	K, L	
☐ *Leptospira spp.*	P, L, M	
☐ Monkeypoxvirus (opičí neštovice)	St, K, P	

Panels or individual pathogens

Bacteria

Viruses (enteroviruses, herpetic, respiratory)

Testing antibodies in blood + CSF – example

Test forms

NOT PCR in these cases

TBE, borrelia - IT syntesis of antibodies, cytokine CXCL13)

FAKULTNÍ NEMOCNICE BRNO

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Pracoviště nemocnice Bohunice a Porodnice
Ústav laboratorní medicíny
Oddělení klinické mikrobiologie a imunologie
Imunologie a molekulární mikrobiologie

JIHLAVSKÁ 20, 625 00 BRNO
TEL.: 532 233 389

Oddělení klinické mikrobiologie a imunologie - INFEKČNÍ IMUNOLOGIE (serologie)

Nákladové středisko: *Telefon:* *Razítko (IČP), jmenovka a podpis lékaře, odbornost:*

Číslo pojištěnce:

Jméno a příjmení:

Datum narození: *Pohlaví: muž žena*

Dg.: *Další dg.:* *Pojišťovna:*

Odebral: *Datum a čas odběru:*

Vyšetřovaný materiál: ☐ **STATIM**[1] ☐ **Dodělávka / materiál již v laboratoři**

- ☐ periferní krev - srážlivá
- ☐ periferní krev - EDTA
- ☐ sérum
- ☐ likvor
- ☐ synoviální tekutina
- ☐ pupečníková krev
- ☐ plazma
- ☐ stěr / výtěr z:
- ☐ jiné:

HEPATITID, HIV

- ☐ hepatitidy dif. dg. S
- ☐ HAV IgG, IgM S
- ☐ HBc Ig celkové S
- ☐ HBc IgM S
- ☐ HBe Ig celkové
- ☐ HBs Ig celkové
- ☐ HBeAg
- ☐ HBsAg S
- ☐ HCV Ig celkové S
- ☐ HCV Ag
- ☐ HDV Ig
- ☐ HEV IgG, IgM
- ☐ HIV 1,2 (Ag + Ab) S

KLÍŠŤATY PŘENÁŠENÁ ONEMOCNĚNÍ

- ☐ Borrelia burgdorferi sensu lato IgG, IgM
- ☐ Borrelia burgdorferi sensu lato IgG, IgM - **WB**[2]
- ☐ **WB vyšetřit při pozitivitě ELISA**
- ☐ Borrelia burgdorferi sensu lato IgG, IgM - **ITS**[3]
- ☐ CXCL-13 z likvoru
- ☐ Klíšťová encefalitida IgG, IgM
- ☐ Klíšťová encefalitida IgG, IgM v likvoru
- ☐ Anaplasma phagocytophilum IgG, IgM

HERPESVIRY

- ☐ CMV IgG, IgM
- ☐ CMV IgG - avidita[2]
- ☐ EBV (VCA IgM, VCA IgG, EBNA IgG)
- ☐ HSV 1,2 IgG, IgM
- ☐ HSV 1,2 IgG
- ☐ VZV IgG, IgM
- ☐ HHV 6 IgG

STD

- ☐ RPR (screen.)
- ☐ Treponema pallidum Ig celk. (screen.)
- ☐ Treponema pallidum IgG, IgM (konfirm.)
- ☐ Treponema pallidum - **WB**[2] (konfirm.)
- ☐ **konfirmace při pozitivitě screeningu**
- ☐ Treponema pallidum IgG - **ITS**[3]
- ☐ Chlamydia trachomatis IgG, IgM, IgA

RESPIRAČNÍ VIRY

- ☐ Influenzavirus A IgM, Influenz. B IgM
- ☐ RS virus IgM
- ☐ Adenovirus IgG, IgM

SARS-CoV-2

- ☐ SARS-CoV-2 Ig celkové anti-S
- ☐ SARS-CoV-2 Ig celkové anti-N
- ☐ SARS-CoV-2 antigen - stěr[4] S
- ☐ N antigen (krev) - diagnosticky
- ☐ N antigen (krev) - prognosticky

RESPIRAČNÍ BAKTERIE

- ☐ Chlamydophila pneumoniae IgG,IgM,IgA
- ☐ Mycoplasma pneumoniae IgG, IgM
- ☐ Bordetella pertussis toxin IgG, IgA
- ☐ Bordetella pertussis toxin IgG
- ☐ Bordetella parapertussis IgG, IgA, IgM
- ☐ TBC / QuantiFERON-TB[5]

Doplňkové informace:

ostatní - VIRY

- ☐ Parvovirus B19 IgG, IgM
- ☐ Enterovirus sp. IgG, IgM, IgA
- ☐ Parotitis (příušnice) IgG, IgM
- ☐ Rubeola (zarděnky) IgG, IgM
- ☐ Morbilli (spalničky) IgG, IgM S
- ☐ MRZ reakce - **ITS**[3]

ostatní - BAKTERIE

- ☐ Salmonella Ig celkové - Widalova r.
- ☐ Campylobacter jejuni IgG, IgA
- ☐ Yersinia IgG, IgA
- ☐ Francisella tularensis Ig celkové
- ☐ Listeria monocytogenes Ig celkové
- ☐ Bartonella IgG, IgM
- ☐ Helicobacter pylori IgG, IgA

postvakcinační protilátky

- ☐ Klíšťová encefalitida IgG
- ☐ Rubeola (zarděnky) IgG
- ☐ Morbilly (spalničky) IgG
- ☐ Parotitis (příušnice) IgG - postvakcin.
- ☐ Haemophilus influenzae IgG
- ☐ Corynebacterium diphteriae IgG
- ☐ Streptococcus pneumoniae IgG
- ☐ Clostridium tetani IgG

HODNOCENÍ NÁLEZU

- ☐ specifikujte:

1 Vyšetření dostupná v režimu STATIM jsou označená příznakem S.

2 Nelze objednat samostatně.

3 ITS = intratekální syntéza protilátek. Pro vyšetření je nutné odebrat vzorek srážlivé krve a likvoru s časovým rozestupem odběru max. 4 h. (optimum

LP – PREP

Information

- Inform the parent fully, signed Informed Consent
- Age-appropriate information for the child

Premedication

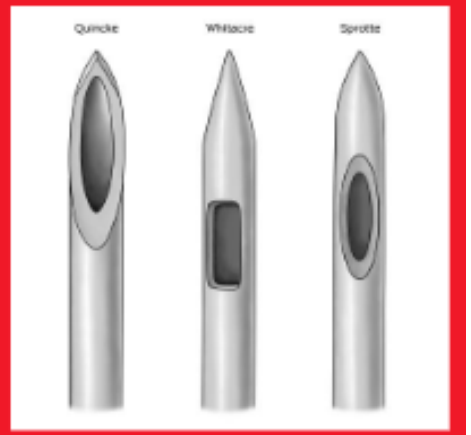
- X, ev. analgosedation, local anesthetic

Positioning the patient

- lying down
- **sitting up - knees bent, head bent forward**

Needle

- Patient habitus



Needle type	Advantages	Disadvantages
Atraumatic (25G, 0.53 mm)	The least damage to the tissue - < PLPH (post-lumbar-puncture syndrome) (2 %)	Longer action, practice, price 2x
Traumatic Quincke (22G, 0.7 mm), černá,	Compared to 20G significantly < PLPH	Longer draw
Traumatic Quincke (20G, 0.9 mm), žlutá	Fast action	> PLPH (40 %)

*** PLPH – post-lumbar-puncture syndrome**

LP – TECHNIQUE

Determining the puncture site

Edges of the hip bone blades - junction - intervertebral space L3/4 - L4/5, upper side of the lower vertebra, marking the puncture site

Preparing the site

Disinfection, sterility, face-masks

Needle direction

Needle going slightly upwards, ca 15 degrees

Conus rotated to the side – minim. tissue trauma

Collecting the sample

We collect the required amount drop by drop

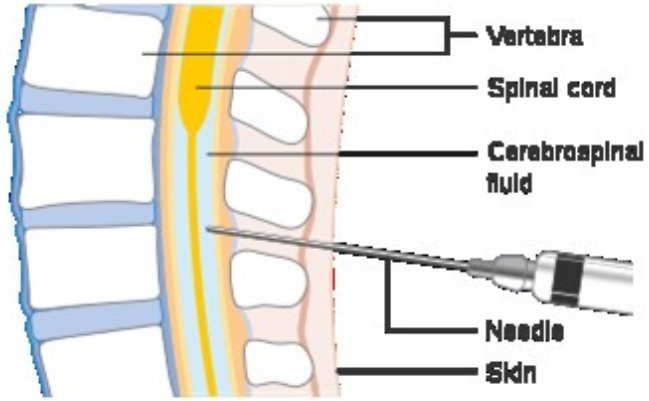
Concluding the LP

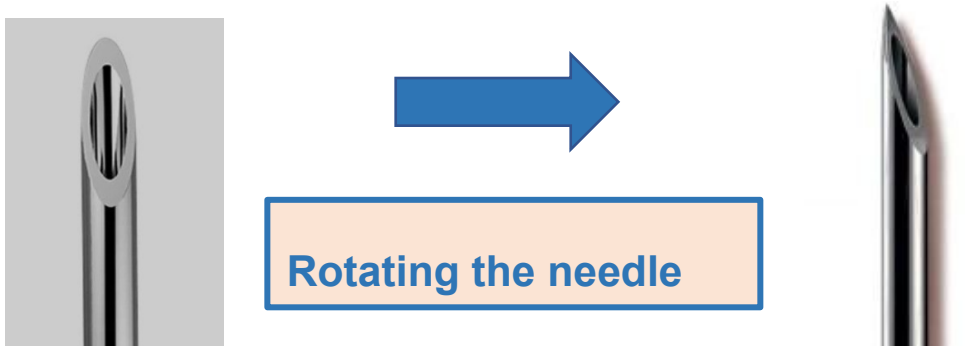
Inserting the mandrin / up to 2/3 of length, removing the needle, compression, coverage

Post-LP regime

Flat pad 8-10 hrs. (1 hour supine position) / min. 6 (PLPH)

Atraumatic needle (2-4 hrs.)





Rotating the needle

1 test tube - 15 drops (10 minimum)

CAUTION – PCR sample – prevent contamination

Link to an LP video / Study materials in IS

https://next.simu.med.muni.cz/s/gGCT29WcTEg5HmR

CSF RESULTS ANALYSIS

- **Macroscopic**
  - Color / transparency
    - XANTOCHROMIA – yellow, orange or pink discoloration - waste products of hemoglobin – 90 % patients after 12 hrs of subarachnoid hemorrhaging (newborns with hyperbilirubinemia)
  - Pressure

- **Microscopic**
  - Cytology

    Pleocytosis (polymorphonuclear / mononuclear), Ery up to 20% in traumatic LP

  - Biochemistry
    - Total protein – significantly increased level in purul. inflammation, bleeding, Guillain-Barré syndrome, tumors, etc. (physiol. newborns)
    - Glycorrhachia – 2/3 glycemia, low in purul. inflammation
    - Lactate – purulent meningitis (significantly increased > 3.5 mmol/l)

	Norm	Purulent	Serous	Mycotic	Guillain-Barré syndrome
Appearance	Clear	Cloudy, yellowish	Clear	Cloudy	Clear
Leu (PN/MN / mm³)	< 5 cells / mm³	Hundreds, thousands (PN)	Tens, hundreds (MN)	PN / later MN	Norm / slightly elevated
CB	0,4-0,5 g/l	↑↑↑	Norm / ↑	↑↑↑	↑↑↑
Glycorrhachia	2,2-3,3 mmol/l	↓↓	Norm / ↓	↓↓	Norm
Lactate	1,2-2,4 mmol/l	↑↑↑	Norma	↑↑↑	Norma

Guillain-Barré syndrome – acute demyelinating polyradiculoneuritis – proteinocytological dissociation in the cerebrospinal fluid (severe disorder of the H-L barrier) – acute, subacute course; weak limb paresis - mainly DK, risk of respiratory muscle paralysis; often infections (EBV, CMV, HBV, HIV, VZV, mycoplasma, chlamydia, *Campylobacter jejuni*) in pre-illness 1-3 weeks

CAUSAL THERAPY

- Antibiotics
- Antivirals
- Antimycotics

ACICLOVIR! – antivirals at suspect herpetic encephalitis

HERPETIC ENCEPHALITIS
Impairment of consciousness (**qualitative** / quantitative) – involvement of frontal and temporal lobes; clinical presentation - convulsions, focal neurol. symptoms, aphasia, symptoms of brain edema - ↑ PRIMARY INFECTION (Family history - HSV)

ATB < 1 hour

Empiric therapy by broad-spectrum ATB with penetration into CNS

SYMPTOMATIC THERAPY

- Infusion therapy, antipyretics, analgesics
- Antiedematous treatment, elevated head
- Anticonvulsants, or sedation upon restlessness
- If sepsis – complex approach

Corticoids →

Improve the prognosis, hearing impairment prevention; I. dose shortly before/with ATB.

CAUTION – if suspected herpetic encephalitis, we wait for the aciclovirus to come into effect, depending on the clinical condition, min. 3-4 days (controversial topic; x edema – we have to give to patient)

Mannitol →

Not enough studies of use in children / not recommended for routine use.

In **CZ included** in the entry treatment of purulent meningitis; **at signs of severe intracranial hypertension or brain edema (ev. on CT).**

Across-the-board administration of antiepileptics, paracetamol, activated protein C, heparinization, hypothermia – NOT RECOMMENDED

INTRAVENOUS IMMUNOGLOBULINS - YES

Resources

- http://infektologie.cz/DoporMenPur17t.htm (2017)
- Beck D, Cabellos C, Dzupova O, Sipahi OR, Brouwer MC, ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. *Clinical mikrobiology and infection*. 2016