

# ***PURULENT MENINGITIS***

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# MENINGITIS

*Acute*

*Subacute and chronic*

*Acute bacterial*

*Bacterial, viral, yeast, mycotic leptospiral, TBC, tumorous, parasitic, chemical, shunt recidive, eosinophilic ...*

*Primary*

*Secondary*

*M. neonates*

*Children*

*Meningitis adults*

*Meningitis elder patients caused by Gram - bacteria*

# MENINGITIS

## Acute bacterial – PRIMARY

Children meningitis

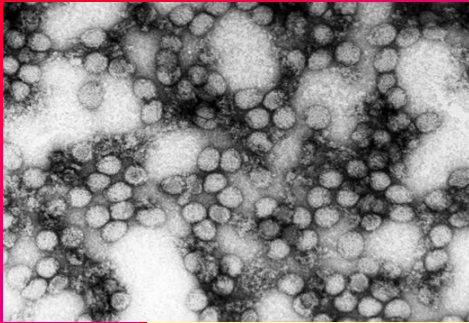
Meningitis  
of adults

*Neisseria meningitidis*  
*Diplococcus pneumoniae*  
(*Haemophilus influenzae*)

*Diplococcus pneumoniae*  
*Neisseria meningitidis*

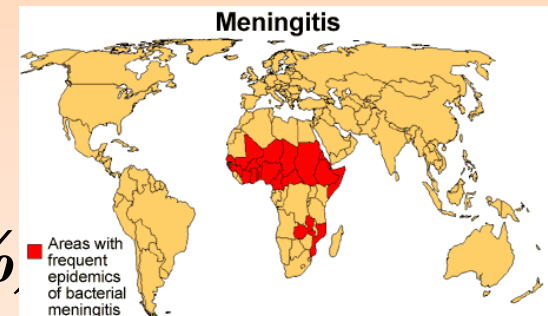
<u>age</u>	<u>Incidence/100 000</u>	<u>Lethality/100 000</u>
neonates	37,2	10,1
1 month -1 year	115,5	11,5
1 – 5 years	28,5	1,0
5 – 16 years	2,8	0,4

# PURULENT MENINGITIS PRIMARY ETIOLOGY



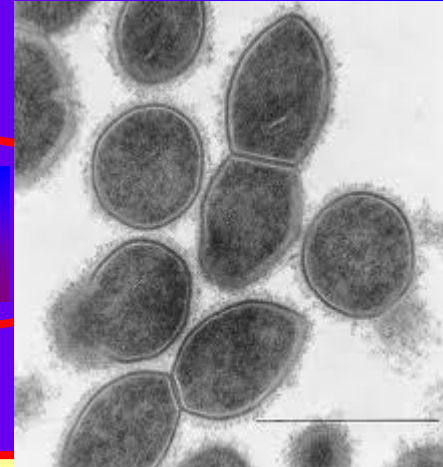
## *Neisseria meningitidis*

- G- diplococcus – intracellular, types A, B, C a Y, W 135; 95% of infections
- Population is infected from early childhood
- Epidemics in:
  - 1) collectives of young people,
  - 2) Mekka,
  - 3) Western Africa,
  - 4) Eastern South America
- Sporadic diseases
- Asymptomatic infection - (5-15%)



# PURULENT MENINGITIS PRIMARY ETIOLOGY

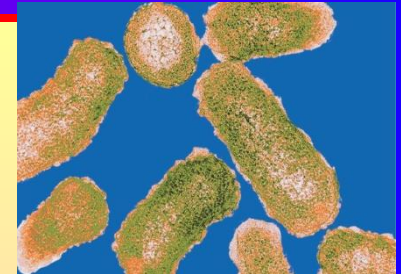
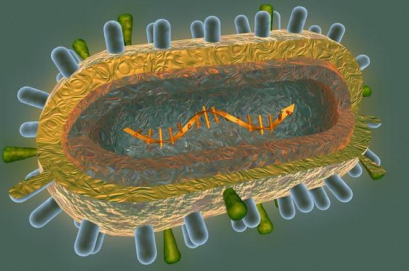
## *Streptococcus pneumoniae*



- ***G+ diplococcus***
- ***Common in upper respiratory tract and the most frequent pathogen of pur.***
  - ***1/2 of mid ear inflammation, pneumonias,***
- ***On mucosa of URT from neonate period***
- ***80 serotypes (most frequent 3; 19f; 14 ...), capsular polysaccharide is factor pathogenicity***
- ***serotype isolated from mucosa URT has not to be the cause of the meningitis***

# PURULENT MENINGITIS PRIMARY ETIOLOGY

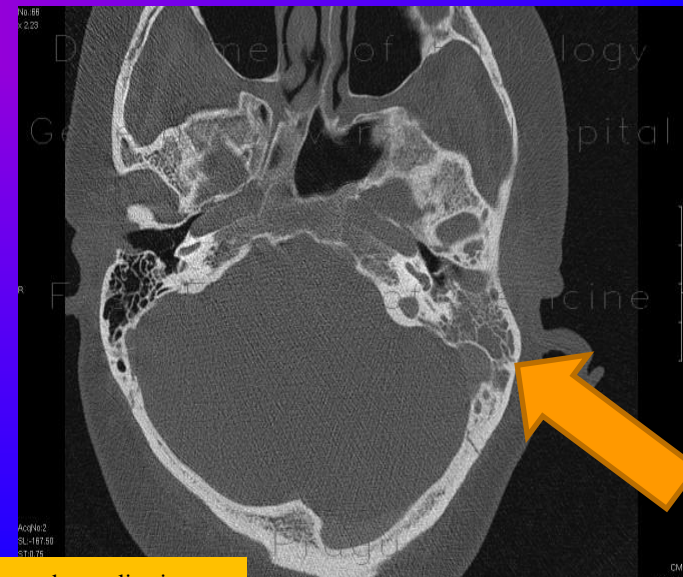
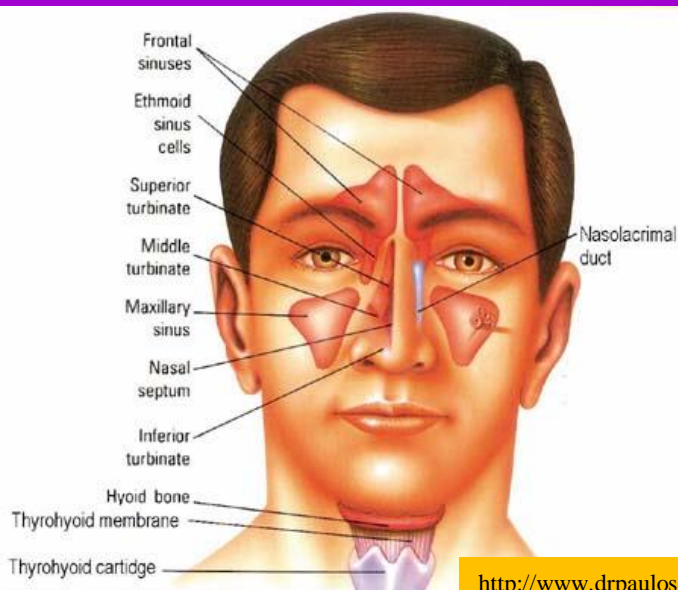
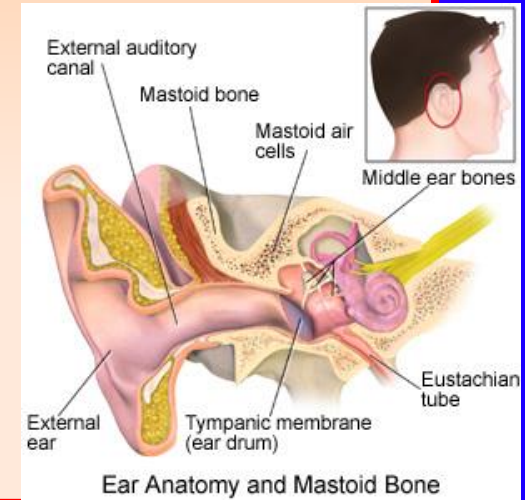
## *Hemophilus influenzae*



- *G - rod*
- *capsula factor pathogenicity - virulence*
- *ubiquitous in URT mucosa*
- *spreading in child collectives*
- *serotype isolated from mucose of URT usually is the pathogen*
- *prevalence in the period 5 moths – 5 years*
- *Vaccination practically elminated the disease*

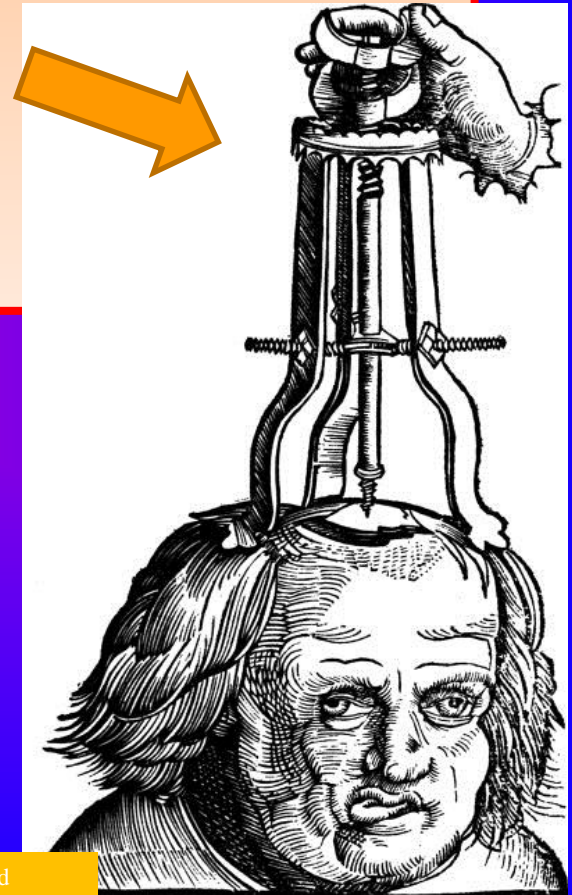
# PURULENT MENINGITIS SECONDARY

- 1) purulent focus in skull
  - *Paranasal sinuses*
  - *Ear*
  - *Mastoiditis*
  - *Most frequently pneumococcus*
  - *Spreading per continuitatem;*



# PURULENT MENINGITIS SECONDARY

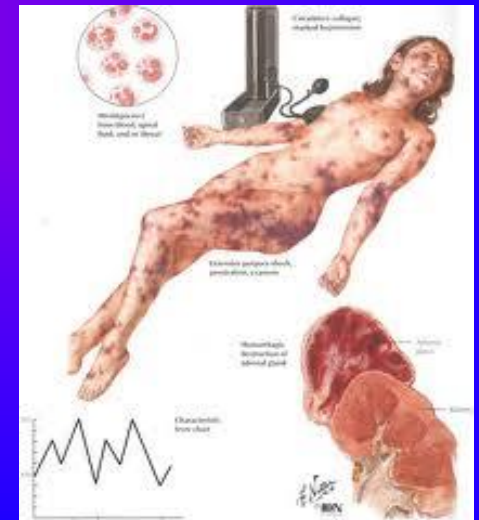
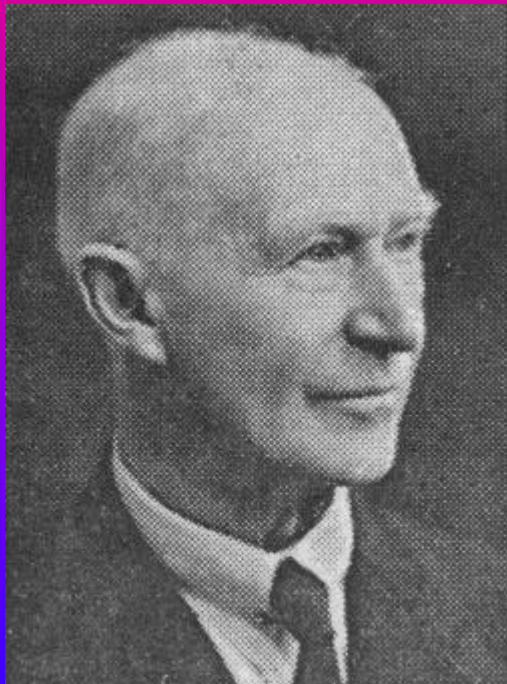
- 2) traumatic
  - microbes entered the tissue by injury
  - most frequent pathogens *S. aureus*, anaerobes, any others ...
- 3) post-operative and posttraumatic
  - Connected with treatment on intensive care unit – patients colonized by many microbes
  - especially G-





# CLINICAL MANIFESTATION

- *Peracute Sepsis – Waterhouse - Friderichsen syndrome; Most acute meningococcus inf. without meningitis*



It was first reported as an entity by [Rupert Waterhouse \(photo\)](#) in 1911, and the subject was comprehensively reviewed in 1918 by the Danish paediatrician Carl Friderichsen.

<http://thebackgrounddoc.blogspot.cz/2010/08/purpura-fulminans.html>

# ***CLINICAL MANIFESTATION***

- *Acute*      *Typically 1-2 days*
  - *Fever,*
  - *headaches*
  - *irritability*
  - *meningeal sy*

# ***CLINICAL MANIFESTATION***

- ***Subacute*** *Days – similar symptoms*
- ***Chronic*** *Nonspecific symptoms at the beginning –  
fatigue, headaches, fever  
Sometimes symptoms of focus  
Facultative pathogens*

# COMPLICATIONS

- Inflammatory focus

- Subdural effusion : non-purulent collection of fluid; usually small, potential pressure changes, treatment conservative
- subdural empyema: collections of pus, persistence of purulent inflammation, fevers, pressure changes, antibiotic treatment - surgery
- ventriculitis: most frequent in newborns, life-threatening
- Brain abscessus: cause or result of meningitis; treatment first of all conservative, large focus - surgery

- Vessel involvement

- Ictus - arterial thrombosis, arteriitis
- Trombosis or tromboflebitis - venous sinus occlusion, inflammatory focus; vessel occlusion; treatment anticoagulants, antibiotics

# COMPLICATIONS

- **Hormonal disturbances**
  - **Syndrome of inappropriate ADH secretion :**
  - **Cerebral salt-wasting syndrome**
  - **Diabetes insipidus**
- **Convulsions – EPI parox**
  - **TH - common antiepileptics**
- **CSF circulation disturbances - hydrocephalus**
  - **Non-communicating**
    - **Obstruction – inner x outer hydrocephalus**
  - **Communicating – more frequent**
    - **Hypersecretion CSF**
    - **Hyporesorption CSF**

# COMPLICATIONS

- Neurological involvement
  - Any topic involvement
  - More – relative specific
    - *Hearing loss – cochlear*
    - *Polyneuropathy, cerebellar sy, vestibular sy ...*

# ***COMPLICATIONS of MENINGOCOCCAL MENINGITIS***

- ***Sepsis – shock***
  - ***Disseminated intravascular coagulopathy - DIC***
  - *casue of shock and cause of vessel occlusions –*
  - *necrosis , organ involvement*
  - ***More – relative specific***
    - *Hearing loss – cochlear*
    - *Polyneurpathy, cereballar sy, vestibular sy ...*
- ***Arthritis***
- ***Peri-myocarditis***
- ***Pneumonia – subacute***
- ***Chronic meningococemia***
  - *long-lasting excretion of meningococci*

# PURULENT MENINGITIS - DIAGNOSTIC

- **CLINICAL:**

- \* *fever, meningeal syndrome headache, disturbances of consciousness*

- \* *skin petechia in meningococcus men.*

- \* *focal neurolog. findings*

Table 2. Most frequent symptoms in patients with acute communitarian bacterial meningitis and AIDS.

Symptom	N	%
Headache	24	77.4
Fever	20	64.5
Neck stiffness	16	51.6
Vomiting	12	38.7
Seizures	8	25.8
Kernig sign	2	6.4
Petechias*	1	3.2
Coma*	1	3.2

\*Same patient.



<http://www.google.cz/imgres?q=meningococcal+meningitis+pictures&um>

<http://www.answers.com/topic/meningitis>



# PURULENT MENINGITIS - DIAGNOSTIC

## LABORATORY:

- CSF examination:
  - Antigen
  - Cytologic examination
  - Biochemical
  - Cultivation +
  - PCR

Table 1. Typical CSF Findings in Patients With and Without Meningitis

Parameter	Normal	Bacterial Meningitis	Viral Meningitis	Fungal Meningitis	Tuberculous Meningitis
Opening pressure (mm H <sub>2</sub> O)	<180	200-500	NA	>250 ( <i>Cryptococcus</i> sp)	NA
WBC count (mm <sup>3</sup> )	0-5	100-20,000 (mean 800)	5-500 (mean 80)	20-2,000 (mean 100)	5-2,000 (mean 200)
WBC differential	No predominance	>80% PMN	>50% L, <20% PMN	>50% L	>80% L
Protein (mg/dL)	15-50	100-500	30-150	40-150	>50
Glucose (mg/dL)	45-100 (2/3 of serum)	≤40 (<40% of serum)	30-70	30-70	<40
Gram stain (% +)	NA	60-90	–	–	37-87 (AFB smear)

+: positive; -: negative; AFB: acid-fast bacilli; CSF: cerebrospinal fluid; L: lymphocytes; NA: not applicable; PMN: polymorphonuclear cells; WBC: white blood cells. Source: References 9, 10.

# ***PURULENT MENIGITIS - DIAGNOSTIC***

- ***Searching for foci***  
*ORL, spondylitis, parapharyngeal abscess, other clinical foci*
- ***CT – MRI:***
  - *focus: sinusitis, mastoiditis, air - injury, abscessus, subdural empyema*
- ***biochemical parameters – intensive care***
  - *hemocultivation*
- \* ***MRI angiography (trombosis)***

# ***PURULENT MENINGITIS SUMMARY of THERAPY***

- ***1) Antimicrobial***
- ***2) Anti-shock***
  - *Corticosteroids (dexamethason 0,8 mg/kg/D; methylprednisolon, hydrocortison)*
- ***3) Antiedematic***
  - *manitol 1,5-2 g/kg/G*
- ***4) Analgetics, sedation***
- ***5) Anticonvulsants***
  - *Diazepam, valproat acid, phenytoin ...*

# ***PURULENT MENINGITIS ANTIBIOTIC THERAPY***

- **EMPIRICAL:**

- *Ceftriaxon*
- *Cefotaxim*
- *Ampicillin*
  - (CHLM)

- **TARGETED:**

- **hemophilus:**

- *CTX,CTR, after ATB sensitivitypo AMP; cefepim*

- **meningococcus:**

*penicilin G (possible rezistence), ampicilin,  
Ceftriaxon, cefotaxim*

- **pneumococcus:**

*penicilin G (ATB sensitivity !!), ceftriaxon  
Cefotaxim, cefepim*

# **PURULENT MENINGITIS**

## **ANTIBIOTIC TREATMENT**

- **Shunt:**
  - ATB sensitivity*
  - S. epidermidis: vankomycin, linezolid*
- **Gramnegatives:**
  - \* cefalosporin 3 rd gen. + aminoglykosid*
  - \* Meropenem, cefepim*
- **Mycotic:**
  - amfotericin B (liposoluble);*
  - flucytosin;*
  - ((flukonasol –only cryptococcus; intrakonazol aspergillus))*

# ***PURULENT MENINGITIS ANTIBIOTIC TREATMENT 1***

**TABLE 1-4** Recommended Doses for the Antibiotics Commonly Used in the Treatment of Bacterial Meningitis

<b>Antibiotic Agent</b>	<b>Total Daily Dosage (Dosing Interval in Hours)</b>
Ampicillin	Neonate: 150 mg/kg/d (every 8 hours) Infants and children: 300 mg/kg/d (every 6 hours) Adult: 12 g/d (every 4 to 6 hours)
Cefepime	Infants and children: 150 mg/kg/d (every 8 hours) Adult: 6 g/d (every 8 hours)
Cefotaxime	Neonate: 100 mg/kg/d to 150 mg/kg/d (every 8 to 12 hours) Infants and children: 225 mg/kg/d to 300 mg/kg/d (every 6 to 8 hours) Adult: 8 g/d to 12 g/d (every 4 to 6 hours)
Ceftriaxone	Infants and children: 80 mg/kg/d to 100 mg/kg/d (every 12 hours) Adult: 4 g/d (every 12 hours)
Gentamicin	Neonate: 5 mg/kg/d (every 12 hours) Infants and children: 7.5 mg/kg/d (every 8 hours) Adult: 5 mg/kg/d (every 8 hours)

# ***PURULENT MENINGITIS ANTIBIOTIC TREATMENT 2***

Meropenem	Infants and children: 120 mg/kg/d (every 8 hours) Adult: 6 g/d (every 8 hours)
Nafcillin	Neonates: 75 mg/kg/d (every 8 to 12 hours) Infants and children: 200 mg/kg/d (every 6 hours) Adult: 9 g/d to 12 g/d (every 4 hours)
Penicillin G	Neonates: 0.15 mU/kg/d to 0.2 mU/kg/d (every 8 to 12 hours) Infants and children: 0.3 mU/kg/d (every 4 to 6 hours) Adult: 24 mU/d (every 4 to 6 hours)
Rifampin	Infants and children: 10 mg/kg/d to 20 mg/kg/d (every 12 to 24 hours) Adults: 600 mg/d to 1200 mg/d (every 12 hours)
Vancomycin* <sup>†</sup>	Neonates: 20 mg/kg/d to 30 mg/kg/d (every 8 to 12 hours) Infants and children: 60 mg/kg/d (every 6 hours) Adults: 2 g/d to 3 g/d (every 6 to 12 hours)

\*For intravenous vancomycin therapy, maintain serum trough concentrations of 15 µg/mL to 20 µg/mL. Recommended peak levels 1 hour after intravenous administration, vancomycin 25 µg/mL.

<sup>†</sup>Intraventricular vancomycin administration: children 1 mg/d to 2 mg/d, adults 10 mg/d to 20 mg/d.

# ***PURULENT MENINGITIS – OUTCOME***

- *Paresis*
- *Movement disorders*
- *Mental deficiency*
- *EPI*
- *Peripheral neuropathy*
- *Hearing loss*
- *Hydrocephalus*
  
- *Meningococcus:*
  - *Acral necrosis, myocardial lesions, arthropathy*



# ***PURULENT MENINGITIS PREVENTION***

- **VACCINATION:**
- *1) HIB: children, part of polyvaccines*
- *2) Meningococcus: optional, some groups (recruits)*
- *3) Pneumococcus: risk groups (elders, splenectomized ...)*
  
- **Chemoprophylaxis:**
  - *N. meningitis, (H.influenzae) V-PCR; ERY; (rifampicin, ciprofloxacin)*

# ***MENINGITIS - OPPORTUNISTIC PATHOGENS***

- **PATOGENESIS:**

- \* *immunosuppression (HIV, NEO, elder pat.)*

- **CLINICAL SYMPTOMS:**

- *Symptoms of basic disease, slowly increasing problem, subfebrility – fever, headaches*

- **DIAGNOSTIC:**

- *Cultivation of CSF*
  - *hemokultivation,*
  - *„Black ink“, uncertain prognosis – due to basic disease*

- **TREATMENT:**

- *2-3 weeks, toxic reactions*

## ***MENINGITIS - OPPORTUNISTIC PATHOGENS***

- ***TBC***
- ***Listeria monocytogenes***
- ***Mykosis***
- ***Protozoa***
- ***Gram - negative pathogens***
- ***Shunt - S. epidermidis***
- **Neonates – *E. coli*, *Listeria monoc.*, *Str. agalactiae***

# **MENINGITIS - TBC**

- **Slow beginning**
- **TBC infection in history**
- **Carefull examination of CSF**
- **Cultivation of CSF !!!** – high volume (20-40ml of CSF) centrifugation, PCR examination, sometimes Abs in CSF
- **Long – time treatment**
- **4 combination of antituberculous - ATB**

# ***MENINGITIS - LISTERIA MONOCYTOGENES***

- ***G + Rod aerobic – facultative anaerobic***
- ***Nature:***
  - *Ubiquitous; in nature, in intestine; source – food*
  - *Incidence low (0,7/100000)*
  - *Immunocompromized patients – newborns and elderly, HIV, Mortality up to 20%, in CR cca 10 cases per year*
- ***Pathogenesis:***
  - *Intracellular localization – capability of phagosome lysis*
  - *Low pH, penetration to cytolosol and continuing spreading*
- ***Clinical symptoms:***
  - *Congenital and adnate infections – granulomatous inflammation*
  - *Later period – granulatous and septic infections, invasive meningitis slowly progressive*
  - ***Lesion on scull basis and cranial nerves***

# ***MENINGITIS - LISTERIA MONOCYTOGENES***

- **DIAGNOSTIC:**

- *Immunodeficiency*
- *CSF findings: hundreds of lymphs.;*
- *Cave pleomorphism of listeria (2/3 of microscopic examination of CSF are assessed as „negative“ !!!)*
- *Hemocultivation is positive in 1/2 of patients*

- **TREATMENT – basic is length and choice of ATB:**

- *Ampicillin, mega-doses or PNC*
- *PNC + aminoglycosides*
- *Less effective: TMP-SMX; imipenem/cilastatin,; fluoroquinolons*
- *Length of treatment 3-4 weeks; immunosuppressed - longer*

# ***MENINGITIS - UNCOMMON PATHOGENS***

- **ACTINOMYCETES**

*cotrimoxazol*

- **MYCOSES:**

– *Cryptococcus; aspergillus, candida*

- **Pathogenesis** – *influenced by specific sensitivity of organism; Immunocompromized; newborns, AIDS ...*

- **Examination of CSF – volume, cultivation**

- **CSF synthesis of antibodies**

- **PCR**

- **Long-term therapy**

- **Amphotericine + lipide emulsions (AmBisome)**

- **Flukonasol, intraconasol, voriconasol (Vifend)**

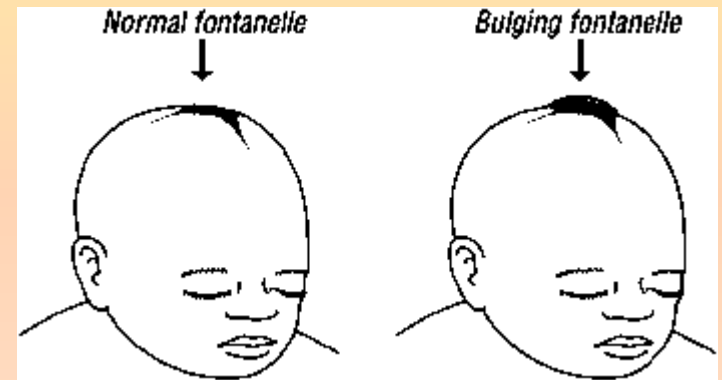
# ***MENINGITIS - NEONATES***

- ***Clinical symptoms:***

*poore clinical picture*

*somnolence, hypotonia, high cry*

*bulging of fontalle – late symptom*



- ***Pathogenes:***

*– Listeria monocytgenes; E.coli, Str. agalctiae ...*

- ***Treatment:***

*– Cefotaxim, ampicillin + according to culture*



# ***MENINGITIS - UNCOMMON PATHOGENS***

- **TOXOPLASMA GONDII**

- **Nature:**

- *Inborne infection*
- *Later infection - meat*
- *Immunocompromized patients – HIV*

- **DIAGNOSIC:**

- *Brain CT, CSF negative or non-specific; cultivation not helpfull*

- **TREATMENT:**

- *Combination ATB: pyrimethamin, sulfadiazin, clindamycin, spiramicin*

# ***MENINGITIS - OPPORTUNISTIC PATHOGENS***

- **AMOEBAE:**
- **Negleria gruberi:**
  - *Bathing*
  - *Clinical sympt: fever or without, men. Sy.*
  - *Diagnostic: microscopy of CSF – laboratory worker must be informed*
  - *CSF finding is nonspecific*
  - *Th: amfotericin B – rifa or TTC*
- **Balamuthia mandrilaris + acathamoebae:**
  - *Meiningitis, encephalitis*
  - *Therapy unknown*

# **MENINGITIS - OPPORTUNISTIC PATHOGENS**

- **GRAM-NEGATIVE PATHOGENS**
- **Pseudomonas, proteus, acinetobacter ...**
- **Immunocompromized – intensive care**
- **Clinical symptoms:**
  - *fever or not*
  - *Meningeal syndrome differently expressed*
- **Diagnostic:**
  - *Cultivation necessary, sensitivity to ATB*
- **Treatment:**
  - *Ceftriaxon, cefotaxim, meropenem, cefepim*
- **Bad prognosis**

***THANKS for ATTENTION***

