

# Bacterial infections of central nervous system

Microbiology lec. #4 (bacteriology 1)  
Dr. Asem Shehabi

This sheet includes only extra information not mentioned in the slides.  
So you should refer to the slides.

The causative agents of meningitis are classified into acute, subacute and chronic . This difference in the type of the caused meningitis is due to virulence factors and growth pattern of the organism.

Growth pattern : how easily the organism increase in number in blood and later reach the CSF.

The bacteria that Mainly cause <b>acute</b> meningitis, but may rarely cause subacute or chronic type	N.meningitidis S.pneumoniae H.influenzae Group B strept. <i>Listeria monocytogenes</i>
Cause <b>subacute and chronic</b> meningitis	Brucella Salmonella typhae and para typhae Mycobacteria tuberculosis

When mycobacteria reaches the blood stream esp. of infants it increase in number in seconds, where as in Meningococcal septicemia within a short period sepsis reaches a high level and later the organism reaches the CSF.

Concerning the clinical picture meningitis; it is almost similar in all types , with some differences between acute and subacute cases , but it still difficult to distinguish between them in relation to some organisms.

It's difficult to recognize the causative agent of chronic meningitis and brain abscess, in these cases the doctor's experience and basic knowledge help to pinpoint the probability of one organism and not the others.

Acute meningitis constitutes 90% of bacterial infections of the CSF.

Encephalitis may be a complication of viral infection, and rarely directly associated with a bacterial agent so it's rarely a complication of meningitis.

## Slide 2

There are 100 agents that can cause meningitis; 5-7 of them are associated with the majority of cases.

In Africa meningitis is more commonly caused by bacteria (meningocele and meningococcal meningitis), whereas worldwide the major causative agents are viruses (95% of cases); so it depends on the geographic location.

Fungi cause meningitis only patients with severe underlying disease esp. immunodeficiency or in case of contamination during a surgical procedure on the brain or spinal cord.

**This is a table of the most common community acquired causative agents of bacterial meningitis: (THIS TABLE IS VERY IMPORTANT)**

Age group	Health state	The causative bacteria
Children up to 3 months	immunocompetent	Group B strept. E.coli <i>Listeria monocytogenes</i>
3 months - 5 years	immunocompetent	H.influenzae Strept.pneumoniae N.meningitidis
5 years - 20 years	immunocompetent	N.meningitidis
	Have underlying disease esp. immunodeficiency	Strept.pneumoniae H.influenzae

Group B strept. , E.coli and Listeria monocytogenes rarely cause meningitis in children older than 3 months unless in case of surgical operations or presence of underlying disease. In section #2 the doctor said that they cause Neonatal Sepsis and Meningitis.

Hospitalized patients who have surgical procedures might be infected with Gram-ve enteric bacteria such as klebsiella or nonfermental bacteria like acidobacter and pseudomonas aeruginosa.

**Slide 3 ( pneumococcal meningitis):**

pneumococcal meningitis is very common among young and immunodeficient individuals.

S.pneumoniae is associated with young children and adults, its invasiveness contributes for that in addition to the fact that it's common in RT of healthy carriers.

Infection with S.pneumoniae is mainly endogenous , and might be exogenous infection in case of close contact with a healthy carrier.

**Slide 4**

Treatment:

In our community up to 80% of *S.pneumoniae* is penicillin-resistant , so penicillin can't be used in treatment of it. Third generation cephalosporines are used for that and sometimes in association with vancomycin to control the acute type of meningitis.

#### Prevention:

In adults and elderly infection with *S.pneumoniae* is often associated with immunodeficiency , so this category of patients should be protected by vaccine which is of two types : pneumovax and prevenar.

Pneumovax for adults is protective only for a short period , usually for one year.

Prevenar vaccine is composed of less serotypes because children don't easily develop bactericidal antibodies against the capsular antigens, where as adults do. It's best given at age less than 2 years to be protective for 2-3 years, giving the vaccine at an older age won't be protective for a long period.

#### Slide 5

You should distinguish between  $\alpha$  and  $\beta$  hemolytic strept. By using **optochin test** and other tests.

Based on the clinical features infected children should directly be sent to the hospital (not to be treated outside hospital). Diagnosis of the causative agent mustn't delay. The doctor must collect CSF sample and send it to the lab without delay ,because these organisms is die fast outside the body, esp. if it is *N.meningitidis* or *H.influenzae*, a delay of one hour at room temp. causes loss of the organism in the CSF.

#### Slide 6

Neisseria includes 2 types : pathogenic and non-pathogenic .

**N.meningitidis** is the pathogenic type of Neisseria because of its virulence factors such as the 1)capsule(made of polysaccharides) .

2)cell wall components (lipopolysaccharides)

3) presence of extracellular enzymes , such as IgA proteases

\_It is a Gram -Ve diplococccic with many serotypes.

**It is the major causative agent of meningitis, it may cause myelitis and encephalitis.**

*Staph. aureus* can't cause acute meningitis under normal conditions ( normal conditions here means no previous surgical manipulation or catheters introduction )

*H.influenzae* and *N.meningitidis* infect upper respiratory tract (URT) of all ages , but they are associated with more cases of meningitis in children than adults because adults develop immunity against them , this immunity is not necessarily due to colonization by the organism , but might originate from other non-pathogenic Neisseria . in other words; antigenic structure

of other non-pathogenic Neisseria contribute for developing immunity in mucosa of RT and this prevents easy dissemination of the organism to blood stream.

They (H.influenzae and N.meningitidis) can't cause acute meningitis directly from respiratory tract, **first** the organism has to reach the blood , **then** if there isn't sufficient specific antibodies it might reach CSF and meningies causing acute infection .

N.meningitidis and H.influenzae are not easily distinguished.

after collecting the CSF sample, the doctor prepares Gram stain without delay and performs culture, and in the same time begins the treatment since delay means fetal outcome or later complications. part of the sample can be sent for hematology and biochemistry departments to detect any change in proteins, glucose and number of inflammatory cells like lymphocytes and neutrophils.

In acute bacterial meningitis always there is increased number of neutrophils, where as mycobacterial and fungal meningitis increase the number of lymphocytes which is normally few.

It's rare to have increased lymphocytes alone in acute bacterial meningitis, and if happens it may be caused by partial antibiotic treatment.

Organisms that cause meningitis are categorized into highly contagious and not highly contagious. N.meningitidis is the only highly contagious one, this means that If one case is diagnosed, 100 case should be expected to be present, these cases are a source of infection of any susceptible person.

In Jordan and in any community, when a case is detected close contacted people(like family members and school mates) should also be treated to prevent spread of the infection in the community.

### Slide 8

N.meningitidis is a G-ve diplococcic that is usually nonpathogenic , the pathogenic type of it usually carries large number of pili.

Some labs can't distinguish between N.meningitidis and H.influenzae in CSF, so the doctor should detect whether it's intracellular or extracellular.

N.meningitidis always exist in intracellular form in addition to the extracellular one, where as H.influenzae and S.pneumoniae and other always exist in the extracellular form and this is easily detected in a direct Gram stain.

### Slide 9 ( Haemophilus influenza)

Hib vaccine appeared early in the 80s , introduced to Jordan later in 1990, before that (1990-1990) a case was detected each weak, after that it was rare to detect any case.

Hib vaccine is highly protective (up to 90% or more) , one dose of the the vaccine is not enough, 2 doses give 30% protection while 3 doses give 95%.

The vaccine should be given at age younger than 3 years, after that age it might be complicated. Adults shouldn't be vaccinated, it's not beneficial and may cause complications for them.

**Treatment** of H.influenzae is by 3<sup>rd</sup> generation cephalosporins (Ceftriaxone, Cefotaxime )

### **Slide 10**

Presence of capsule is the most imp. Virulent factor in S.pneumoniae, in the other two organisms there are capsules but are thinner and less imp.

IgA protease is imp. To overcome the bactericidal effect of the mucosa, it's present in all of the three contributing to colonization and invasion of the blood.

**Pili** are not present in S.pneumoniae but found in N.meningitidis and H.influenzae.

Endotoxins are mostly associated with N.meningitidis and H.influenzae since they are Gram - ve (not found in G+ve)

Please Refer to the Table in the slides .

### **Slide 11**

H.influenzae is found as small bacilli or large filaments in CSF, the large filament form is special for H.influenzae, easily demonstrated and not found in N.meningitidis ,E.coli and other G-ve bacteria.

### **Slide 12**

**Source** of Group B Strept.(GBS) meningitis is women vagina (for example, S.Agalactiae colonize 10-30% of Adult Women Vagina) , where as the source of it in case of H.influenzae, strept.pneumoniae and N.meningitidis is upper respiratory tract infection that causes invasion of the blood and then acute meningitis

Early-onset meningitis is recognized within the first week, often is acute and fatal if not rapidly treated with antibiotics. It's associated with severe sepsis and meningitis.

Late-onset meningitis results in subacute infection, it starts as sepsis and later progresses to meningitis.

**Prevention** is by screening all pregnant women 1-2 weeks before delivery for the presence of group B strept., if it's present antibiotic like amoxicillin is given for the mother and to neonate in case of sepsis and meningitis.

### **Slide 13 (Listeria monocytogenes)**

It's a gram +Ve intracellular small bacilli

It's not a common causative agent of meningitis in **Jordan**, it's more common in western countries.

It manages to escape the intestine of human and reach female vagina (similar to group B strept.), so the source is the intestine.

It might reside in the vagina without any clinical features (group B is associated with burning sensation), its presence is dangerous since it can cause sepsis (like group B strept.) and can infect newborn with a fatal meningitis, more commonly it cause abortion (it's one of the most imp. Organisms as a causative agent of abortion).

**Listeria cause abortions in both animals and humans, whereas Brucella (an imp. Causative agent of abortion in animals) can't induce abortion in humans.**

Lab diagnosis of Listeria is difficult, it's often not detected without history information from the physician because it's found in few numbers, so it might be considered as diphtheria ( between G-ve and G+ve )and so considered as contamination.

At time the organism is detected in case of neonatal meningitis it's too late to cure the patient since he rapidly suffers from complications.

according to the slides the treatment is : Co-trimoxazole, Floroquinlones, and Aminoglycosides.

### **Slide 14**

Any G-ve bacteria can reach the CSF following manipulation of brain and spinal cord causing meningitis and other complications like sepsis.

**Brucella** mainly cause meningitis, it's chronic or sub acute meningitis but never acute .

### **Slide 15**

**mycobacteria** are expected to cause chronic meningitis if they manage to reach the kidney or blood stream, so lung infection is not enough to cause mycobacterial meningitis in children.

Exactly like mycobacteria, N.asteroides have to reach blood stream in order to be able to cause meningitis. It cause subacute form of meningitis.

To **distinguish** between **mycobacteria and narcoidosis** doing acid fast stain and culture is the only possible way.

M.tuberculosis cause chronic meningitis because it's generation time is long ( while in acute its shorter), and also it's cell wall composition and its ability to produce granuloma.

## Slide 16

**Syphilis** causes chronic meningitis that may cause neurosyphilis, it's not easily detected.

**Lyme disease** : few percentage of it causes chronic meningitis, it's not found in Jordan.

## Fungal Meningitis

### Slides 17+18

Two fungi are important as causative agents of chronic and sub acute meningitis in case of immunodeficiency, and rare to cause it in immunocompetents. Both might reside in lungs producing abscess and later might disseminate to the meninges, reach the brain and cause meningitis and brain abscess.

These two fungi are *C.neoformans* and *C.albicans*

*C.albicans* is less associated with brain abscess than *C.neoformans*.

*H.capsulatum* and *B.dermatitidis* are both not found in Jordan but in USA. Infection by these two is first manifested as lung infection and oral cavity abscesses, in immunosuppressed patients these two may reach the meninges causing chronic meningitis (like crypt.)

Blast. , Hist. and crypt. Have similar clinical picture, the only way of distinguish between them is detection by culture mainly or other means.  
In laboratory diagnose we can find little change in glucose and protein levels, and an increase in lymphocytes levels. We usually culture it on Sabouraud Dextrose Agar + blood agar.  
Remember that serological methods are not useful here.  
Treatment : Amphotericin B + flucytosine/fluconazole  
There are no vaccines.

## Laboratory Diagnosis for bacterial meningitis

### Slides 19+20

The classical test is to perform a Gram stain by a direct wet preparation, it's used for crypt. And candida.

Serological agglutination test is done following the growth of the organism to know exactly the serotype.

For group B; following the culture and hemolytic activity we test for the group whether it's B, C or D.

Rapid tests which allow recognition of the organism within a short period, are based on detection of antigen by latex test.

**Latex test** is composed of a disc with particles associated with AB which agglutinate in the presence of specific Ag.

Recently molecular techniques are used especially PCR, it's found in research labs and some advance labs, it detects all the aforementioned organisms by detecting the DNA of each.

Problems associated with PCR include :

- It's difficult to distinguish between typical and atypical mycobacteria, and between strept.pneumoniae and other viridian strept.
- It's not possible to detect the susceptibility of the organism, so you must rely on your experience and on the available data about susceptibility of the various organisms which still not well established in Jordan.

Problems related to usage of antibiotics :

- More than needed is used.
- Toxicity
- Use of antibiotics in Jordan is often based on experiences of other countries which cause problems.

The doctor hopes from our generation to look for the best antibiotic for each case by studying the susceptibility of each organism before treatment of the patient and before the lab results are available.

Done by : Ward Thneebat

**MENINGITIS**  
INFLAMMATION OF BRAIN LINING

**SYMPTOMS CAN APPEAR IN ANY ORDER AND MAY NOT APPEAR AT ALL**

<b>EARLY SYMPTOMS</b> Develop within 8 hours of infection <b>Cold hands/feet</b> <b>Leg pain</b> <b>Unusually pale/mottled skin</b>	<b>SYMPTOMS IN BABIES</b> Also may include <b>Blotchy skin/pale/turning blue</b> <b>Poor feeding</b> <b>Tense or bulging soft spot on baby's head</b> <b>High-pitched cry/irritable (especially when touched)</b>
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**CLASSIC SIGNS**  
Take 13-22 hours to develop  
**Purple rash (see test at right)**  
**Sensitive to light/sound**  
**Severe headache**  
**Fever/vomiting/diarrhea**  
**Stiff neck/joints**  
**Confused/delirious**  
**Severe lethargy/coma**  
**Severe joint/muscle pain**

**CLEAR GLASS TEST**  
Press the side of a clear glass against the rash

If the rash does **NOT** change color or appearance, call a doctor immediately

**DO NOT WAIT FOR A RASH**  
The rash is often a **late** symptom and may not appear at all.

**Meningitis can KILL in less than 4 hours**