MICROBIOLOGY OF ACUTE PYOGENEIC MENINGITIS

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Objectives

1. Define acute pyogenic meningitis.
2. Recall the epidemiology of acute pyogenic meningitis.
3. Recall the etiologic agents according to the age and common serotypes of the main causative pathogens
4. Describe the clinical presentation of acute meningitis

Objectives-cont.,

5- Identify microbiology of common causative agents including the morphology, identification ,pathogenesis and complications.

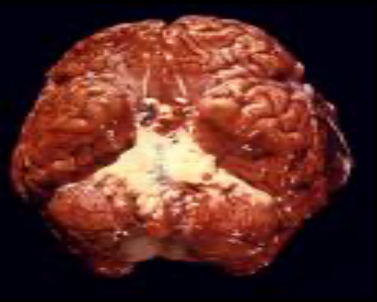
6-Discuss approaches to the clinical diagnosis of acute meningitis case with emphasis on lab diagnosis and comparison between normal and abnormal CSF analysis.

Objectives-cont.,

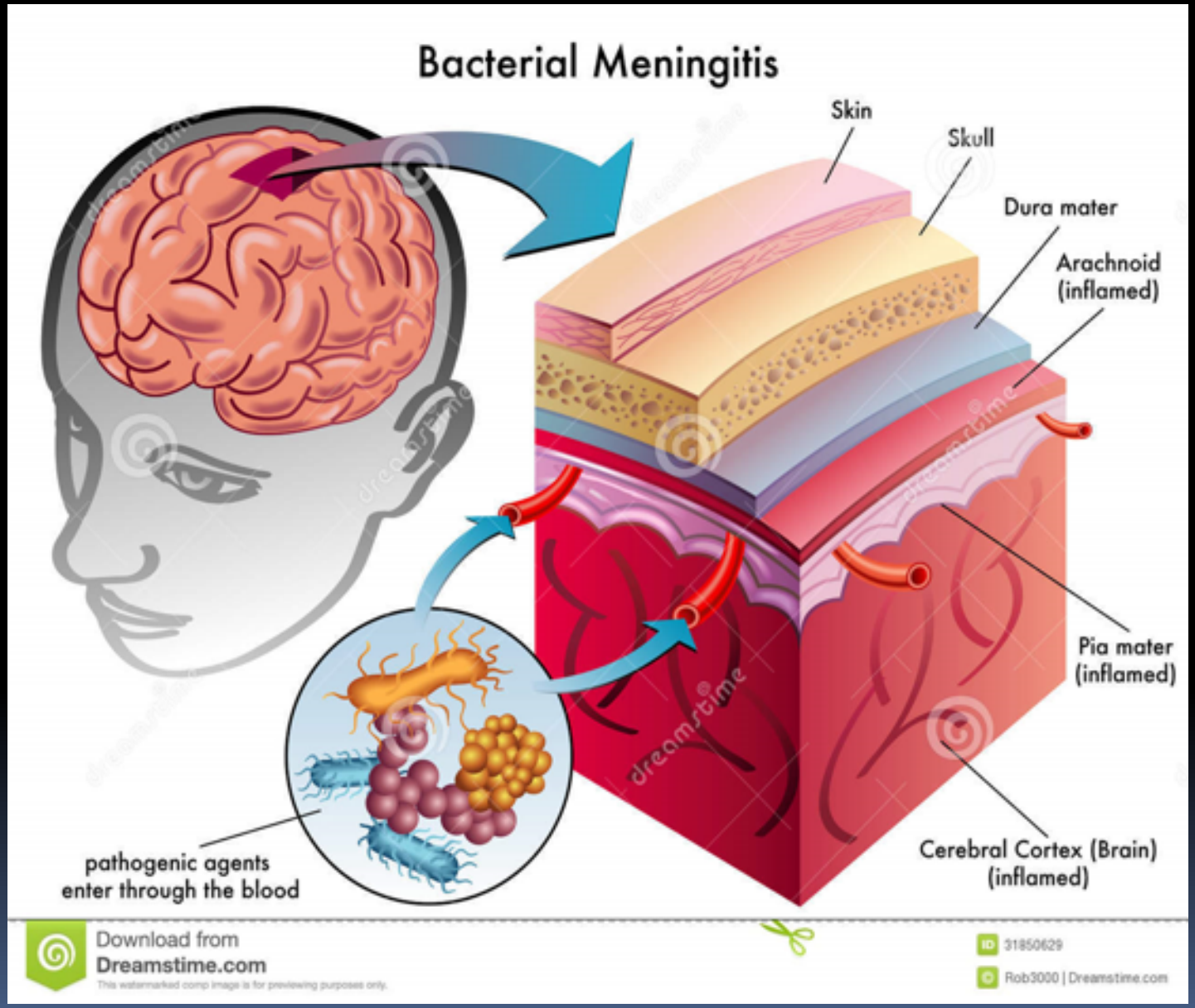
7-Recall the management of acute meningitis with emphasis on rapid diagnosis and selection of empirical antimicrobial therapy for the common pathogens.

8-Recall preventative strategies (vaccination and prophylaxis) used against common pathogens.

Definition



- Pyogenic meningitis is an inflammation of the meninges affecting Pia , Arachnoid and subarachnoid space.
- A serious infection ,associated with marked inflammatory exudation.
- Acute in onset.
- Usually caused by bacterial infections.
- May be preceded by URTI.
- Can be **fatal** if untreated.


Bacterial Meningitis
Skin
Skull
Dura mater
Arachnoid
(inflamed)
Pia mater
(inflamed)
Cerebral Cortex (Brain)
(inflamed)
pathogenic agents
enter through the blood
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Common Etiologic Agents

Three main bacterial pathogens :

Neisseria meningitidis

Sterptococcus pneumoniae

Hemophilus influenzae

Causes according to the age

Newborns	Group *B Streptococcus*, *E.coli* (and other gram negative bacilli) , *Listeria monocytogenes*,
Infants / Children	*S.pneuomiae*, *N.meningitidis*, *H.influenzae*
Adults	*S.pneumoniae*, *N.meningitidis*
Special circumstances	*S.aureus*, *S.epidermidis*, *S.pneumoniae*, anaerobes, *P.aeruginosa*

Epidemiology of Meningitis

- A worldwide disease, there are 1.2 million cases annually and about 135,000 deaths.
- Bacterial meningitis is one of the top ten infections which cause death worldwide.
- Half of the survivals suffer neurological damage, and /or permanent side effects.

Signs/Symptoms of Acute Meningitis

Most Common

- fever
- Headache
- Stiff neck
- Nausea & vomiting
- Sensitivity to light ,Confusion

Advanced Cases

- bruises under skin , rapidly spread

In infants

- Inactivity
- Irritability
- Vomiting
- Poor feeding

Advanced Disease:

- Brain damage
- Coma
- Death

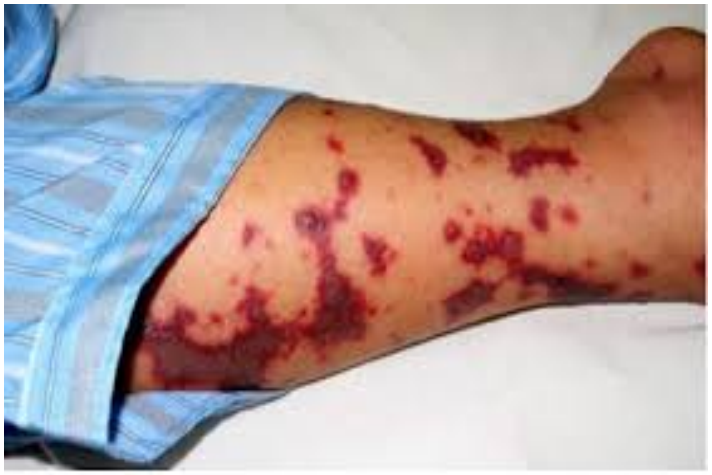
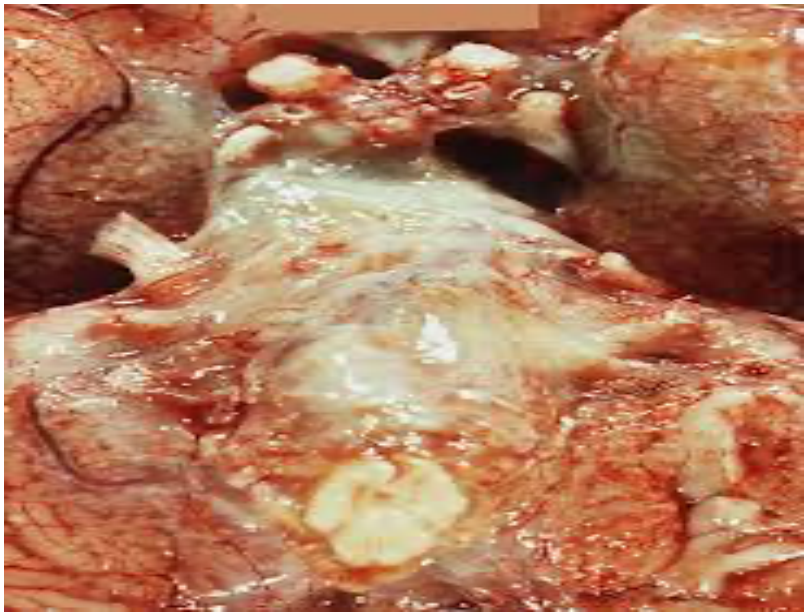


Photo: VietNamNet

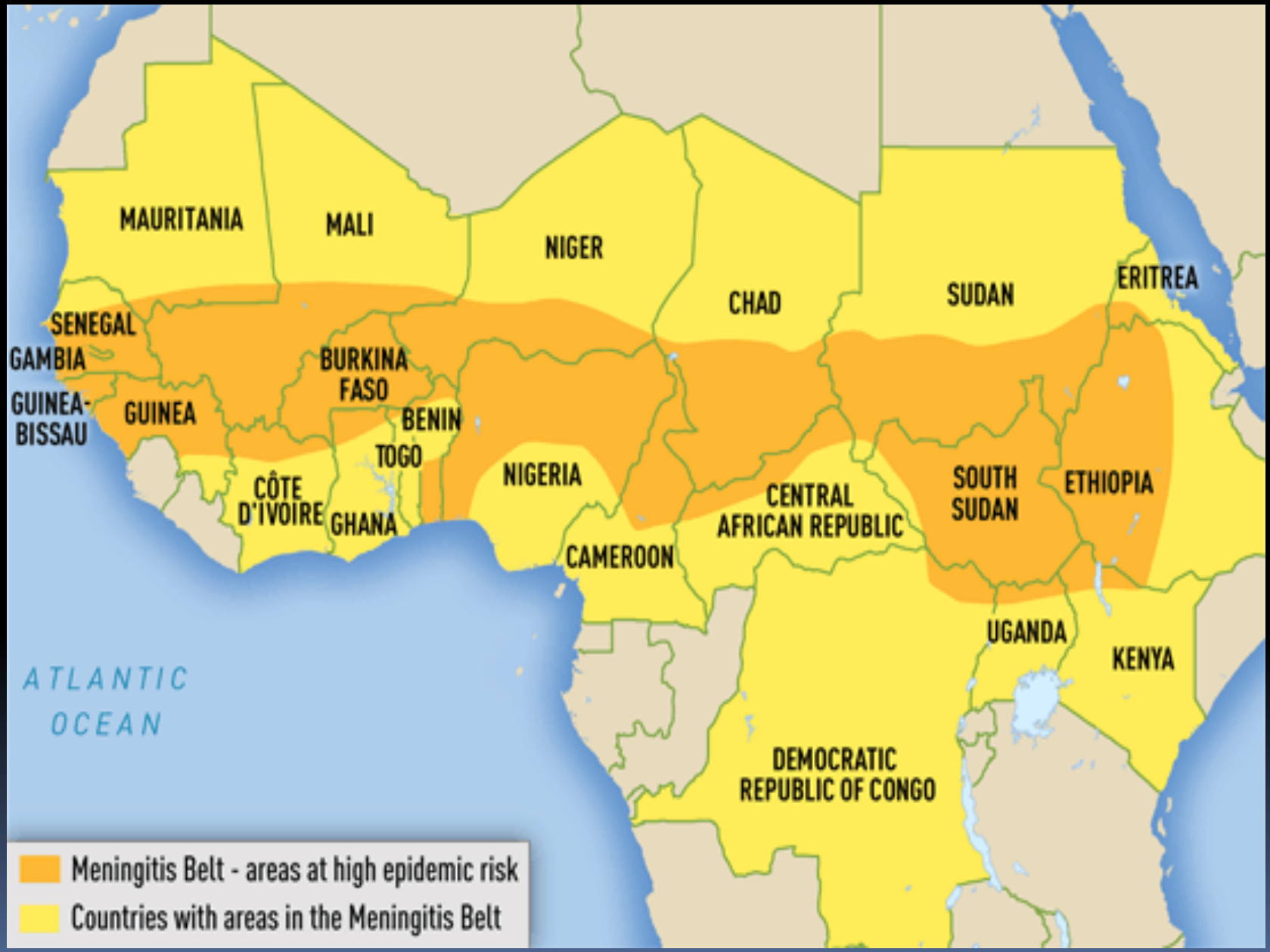


One of the physically demonstrable symptoms of meningitis is Brudzinski's sign. Severe neck stiffness causes a patient's hips and knees to flex when the neck is flexed.

Another of the physically demonstrable symptoms of meningitis is Kernig's sign. Severe stiffness of the hamstrings causes an inability to straighten the leg when the hip is flexed to 90 degrees.

N.meningitidis

- A Gram negative diplococci present in the nasopharynx of 10 % of people.
- Transmitted by inhalation of aerosolized droplets & close contact.
- Common in children < 6 years
- **Risk factor**: susceptible individuals.
- **Serotypes**: **B,C,Y,W135** cause isolated ,sporadic small epidemics in close population.
- **Serotype A** has an epidemic potential in sub-Saharan Africa (meningitis belt).


MAURITANIA
MALI
NIGER
CHAD
SUDAN
ERITREA
SENEGAL
GAMBIA
GUINEA-BISSAU
GUINEA
BURKINA FASO
BENIN
TOGO
GHANA
CÔTE D'IVOIRE
NIGERIA
CAMEROON
CENTRAL AFRICAN REPUBLIC
SOUTH SUDAN
ETHIOPIA
UGANDA
KENYA
DEMOCRATIC REPUBLIC OF CONGO
ATLANTIC OCEAN
Meningitis Belt - areas at high epidemic risk
Countries with areas in the Meningitis Belt

Pathogenesis- *N.meningitidis*

Colonization of nasopharynx

Septicemia → blood brain barrier

Wide spread endothelia damage

Activation of coagulation

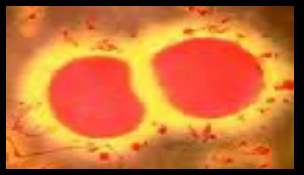
Thrombosis and platelets aggregation

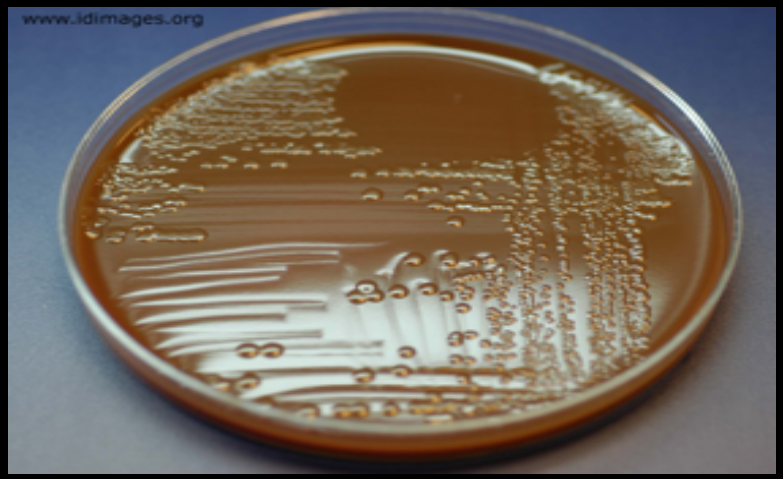
Bleeding : skin rash, adrenal hemorrhage

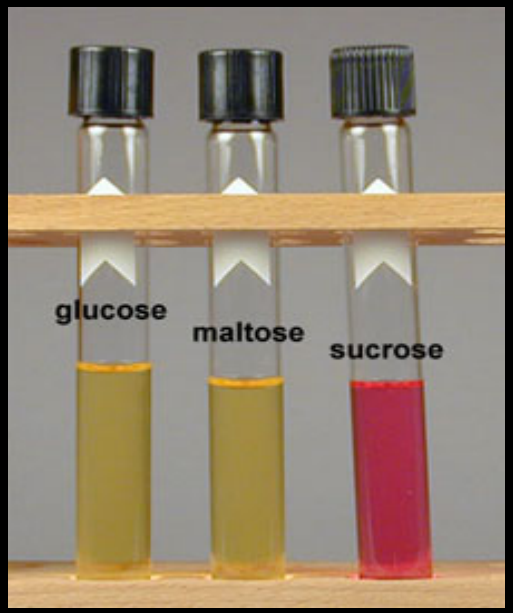
Pathogenesis- *N.meningitidis*

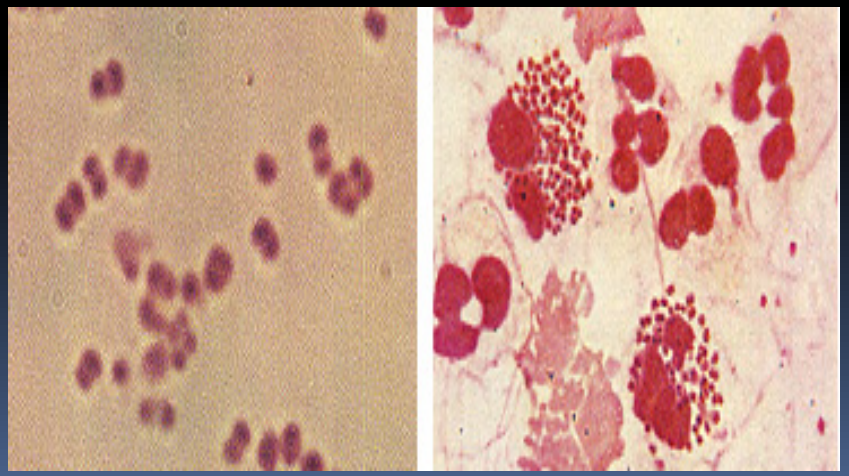
- In carriers ; it stimulates antibody production
- Pili attach to microvilli of nasopharynx , invasion ,then bacteremia, endotoxin (LPS) produced which spreads to the meninges.
- Capsule resists phagocytosis.
- 11-20 % of recovered patients suffer permanent hearing loss, mental retardation.
- 10-14 % of cases are fatal.

N.meningitidis









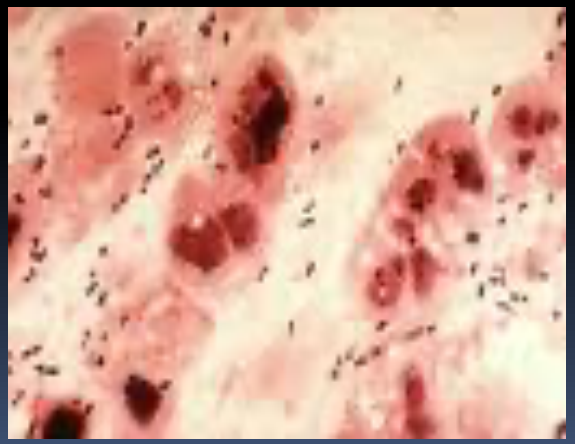
S.pneumoniae

- A Gram positive diplococci. Meningitis may follow pneumococcal pneumonia, or other infections with the bacteria.
- May develop after trauma to the skull.
- **High mortality rate >30% due to invasive disease.**
- Capsule is a polysaccharide polymer
- **Pneumolysin** toxin decreases inflammatory immune response and leads to severe infection.

S.pneumoniae ,cont.,

- Infection rate decreased due to vaccination .
- Recovered cases develop sustained learning disabilities .

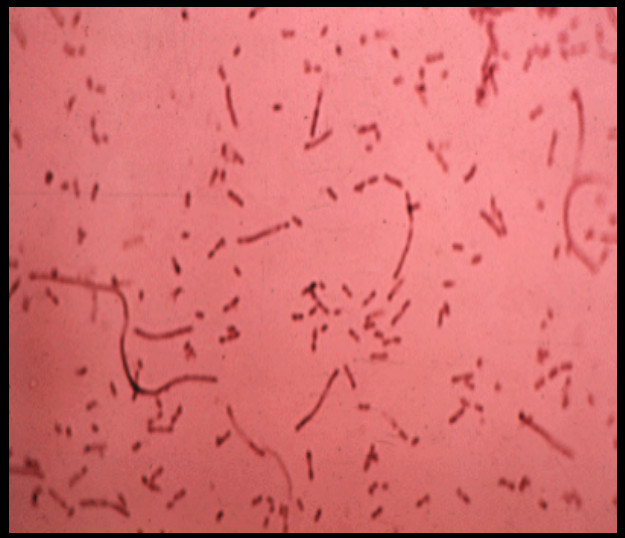
S. pneumoniae



H. influenzae

- A small Gram negative coccobacilli
- Has polysaccharide capsule , other species has no capsule.
- Need blood for optimal growth, **Hematin** (factor **X**) and NAD (factor **V**)
- Many serotypes a-f , *H.influenzae* type *b* has a capsule made of a polymer of PRP (*Polyribosyl Ribitol Phosphate*) causes acute life threatening invasive infections .

H.influenzae, cont,



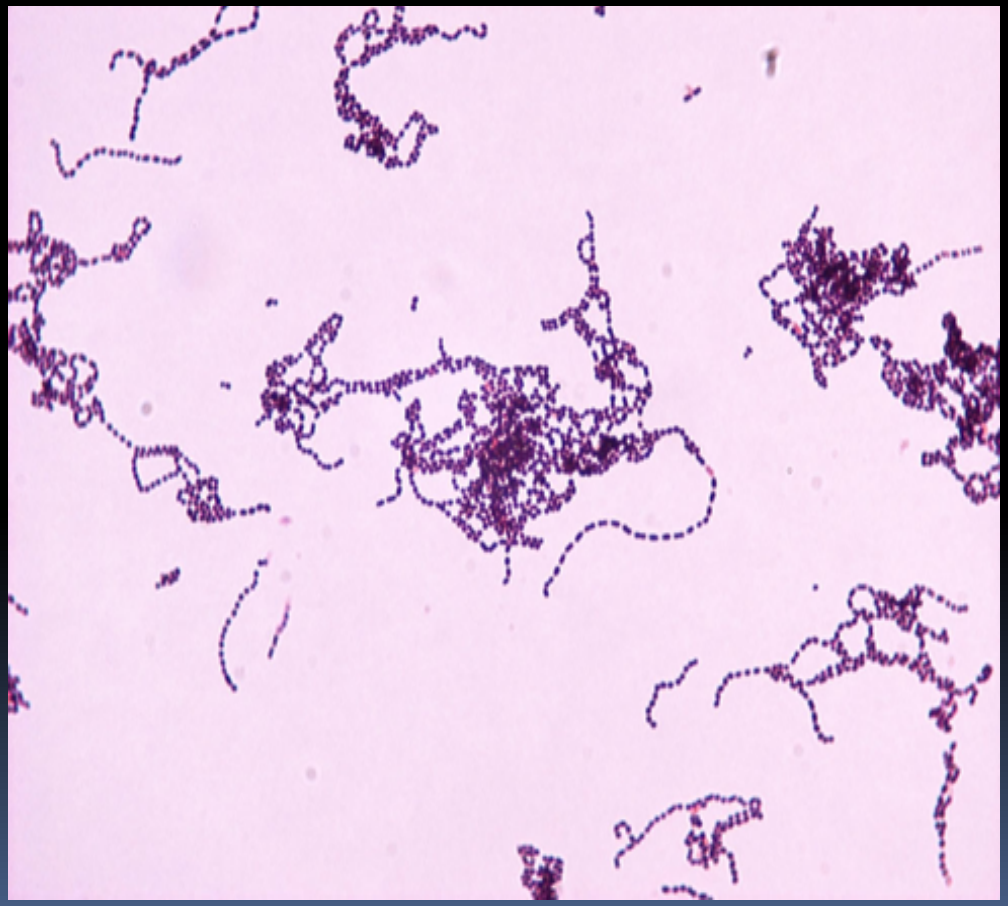
H.influenzae –cont,

- Found in the nasopharynx normal flora
- Major cause of lower RTI , occasionally invade deeper tissues and cause bacteremia.
- **Bacteremia** : bacteria spread to the CNS ,bones or other organs.
- 3-6% mortality rate
- 1/3 of survivals have significant neurological sequelae
- Infection rate decreased since the routine use of *Hib* vaccine .

Group *B Streptococcus (GBS)*

- Gram positive cocci in chains
- Resident bacteria in GIT & vagina (10-30%)
- Gain access to amniotic fluid during delivery or colonize newborn during passage through birth canal.
- Risk factors: premature rupture of membrane, prematurity, low infant innate immunity .
- Causes sepsis and meningitis in the first few days of life and after 4 weeks.

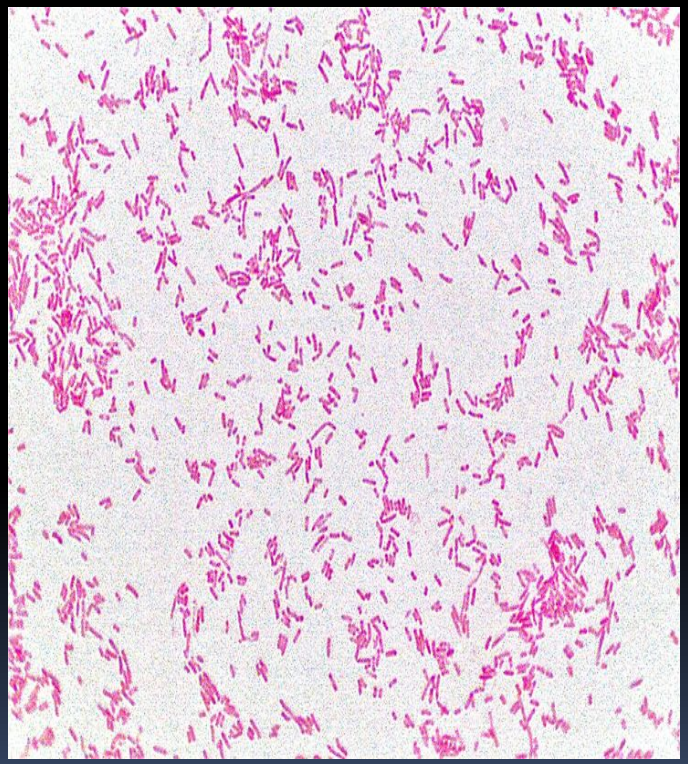
Group B *Streptococcus*



E.coli

- A Gram negative bacilli
- Most common cause of neonatal meningitis
- Many features similar to GBS .
- Vaginal *E.coli* colonize infant via rupture of amniotic membrane or during birth.
- Failure of preterm maternal IgM to cross placenta & special susceptibility of newborn.
- K1 sialic acid capsule of some strains invade brain microvascular endothelial cells.

E.coli




2A
Escherichia coli (BA)

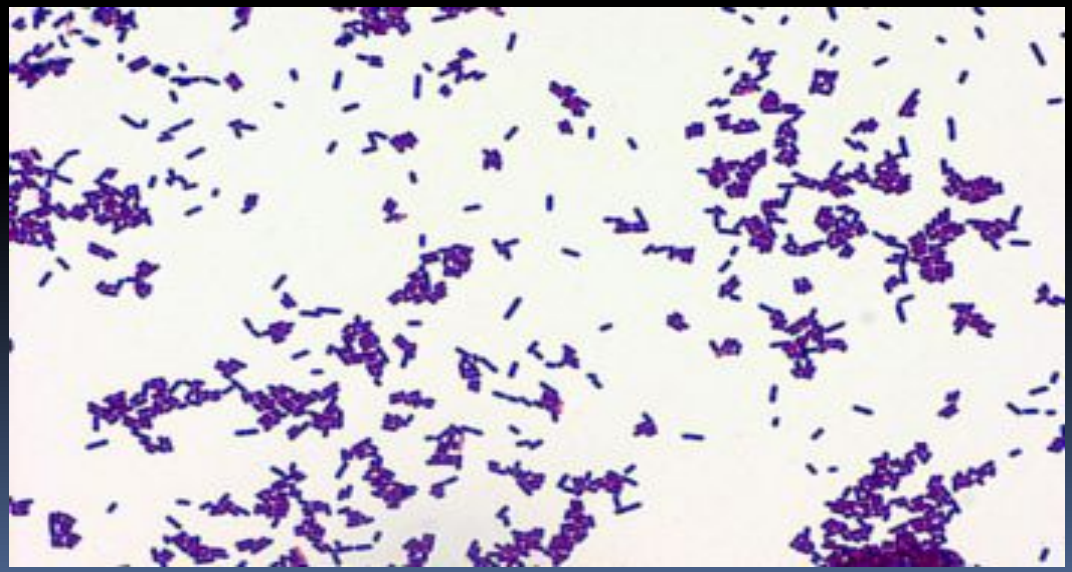

Lactose fermenting colonies
Non-lactose fermenting colonies

Listeria monocytogenes

- Gram positive rods (*diphtheroids like*)
- Wide spread among animals in nature including those associated with certain foods (cheese and meat).
- Human intestinal colonization (2-12%)
- Spread to fetus following hematogenous spread in mother or from birth canal.

Listeria monocytogenes

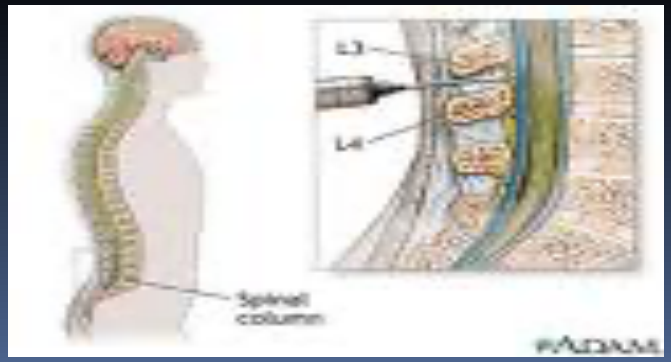
- Has tropism to the CNS.
- Causes meningitis in newborns and immunosuppressed patients.



Diagnosis of Meningitis

- Clinically: signs & symptoms
- Specimens : **CSF** acquired through lumbar puncture and **blood** specimen for culture.

CSF :analysis of cells, protein, glucose and chloride in addition to culture and antimicrobial susceptibility testing.



CNS parameters

Normal CSF

Adults

WBC =0-5 /cmm3,

PMN= 0 %, glucose= > 60 % of blood,

protein =< 30 mg/dl, chloride = 115-130 mmol/l

Neonates

term : WBC =0-32 /cmm3,

PMN=>60 %, glucose = >60 % of blood,

protein= 20-170 mg/dl

Preterm: WBC=0-29/cmm3,

PMN= <60 %, glucose = >60 % of blood,

protein= 60-150 mg/dl

Pyogenic meningitis

WBC= 5 - 5000/cmm3

PMN= > 60%

Glucose = < 45 % of blood

Protein= >60 mg/dl

Chloride= 110 mmol/l

NORMAL & TURBID CSF

Figure 2 – Grossly cloudy cerebrospinal fluid obtained from lumbar puncture is shown.

CSF evaluation

Condition	WBC	Protein (mg/dL)	Glucose (mg/dL)
Normal	<5, ≥75% lymphos	**20–45**	**>50 (or 75% serum glucose)**
Bacterial, acute	100–10,000 or more; usually 300–2,000; Neutros predominate	usually 100–500	Decreased, usually <40 (or <50% serum glucose)
Bacterial, part rx'd	5 – 10,000	usually 100-500	Low to normal
TB	10 – 500	100-3000	<50
Viral or Meningoencephalitis	rarely >1000	Usually 50-200	Generally normal; may be decreased

Abnormal findings of CSF in some pathological conditions

Parameter	Condition			
	Bacterial Meningitis	Tuberculous Meningitis	Viral Meningitis	Brain Tumor
Protein	↑↑	↑↑	Normal	↑
Glucose	↓↓	↓↓	Normal or slightly ⋮↓	↓
Chlorides	↓↓	↓↓	Normal or ⋮↓	Normal or ⋮↓

Management

- **A MEDICAL EMERGENCY**
- Antibiotics given after taking specimens for lab diagnosis. Parenteral administration.
- Children & Adults:

Ceftriaxone (or Cefotaxime) + Vancomycin (*cover the main 3 pathogens*).

If the patient is > 50 or at risk for Listeria add ampicillin

- Neonates :

Ampicillin + Gentamicin + Cefotaxime

- Modify treatment after lab results (as needed).

Management

- Duration : 10-14 days (or more) according to the medical condition.
- Prevention:

. Vaccination

. Prophylactic antimicrobial agent for contacts (*Hib & N. meningitidis*)

Reference book

***Sherris* Medical Microbiology, an Introduction to Infectious Diseases.**

Latest edition, Kenneth Ryan and George Ray. Publisher : McGraw Hill .