

- A 40 year old patient presented to the ward with severe headache, vomiting and high fever for 5 days duration. On examination he looked ill, and had neck stiffness.
 - Probable Diagnosis?
 - Etiology?
 - Diagnosis?
 - Samples
 - Method
 - CSF profile
 - Management?

Neisseria and Haemophilus

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Objectives

- Aetiological agents of bacterial meningitis
 - *Neisseria meningitidis*
 - *Haemophilus influenzae*
 - *Streptococcus pneumoniae*
 - *Listeria monocytogenes*
- Clinical presentations
- Transmission and epidemiology
- Laboratory diagnosis and
 - culture characteristics
 - identification tests
- Treatment

Bacterial meningitis

- Purulent infection within the subarachnoid space
 - Acute
 - Chronic
- Symptoms and signs
 -
 -
 -
 -

Acute Bacterial meningitis

- Aetiological agents
 - *Streptococcus pneumoniae*
 - *Haemophilus influenzae B*
 - *Neisseria meningitidis*
 - *Streptococcus agalactiae*
 - *Listeria monocytogenes*
 - Coliforms
 - *E. coli*
 - *Klebsiella*

Aetiologies according to age and risk factors

- <1 month
 -
- 1–23 months
 -
- 2–50 years
 -
- >50 years
 -

Basilar skull fracture-

Penetrating trauma-

Postneurosurgery-

CSF shunt-

Reference: IDSA guidelines
for meningitis

Neisseria

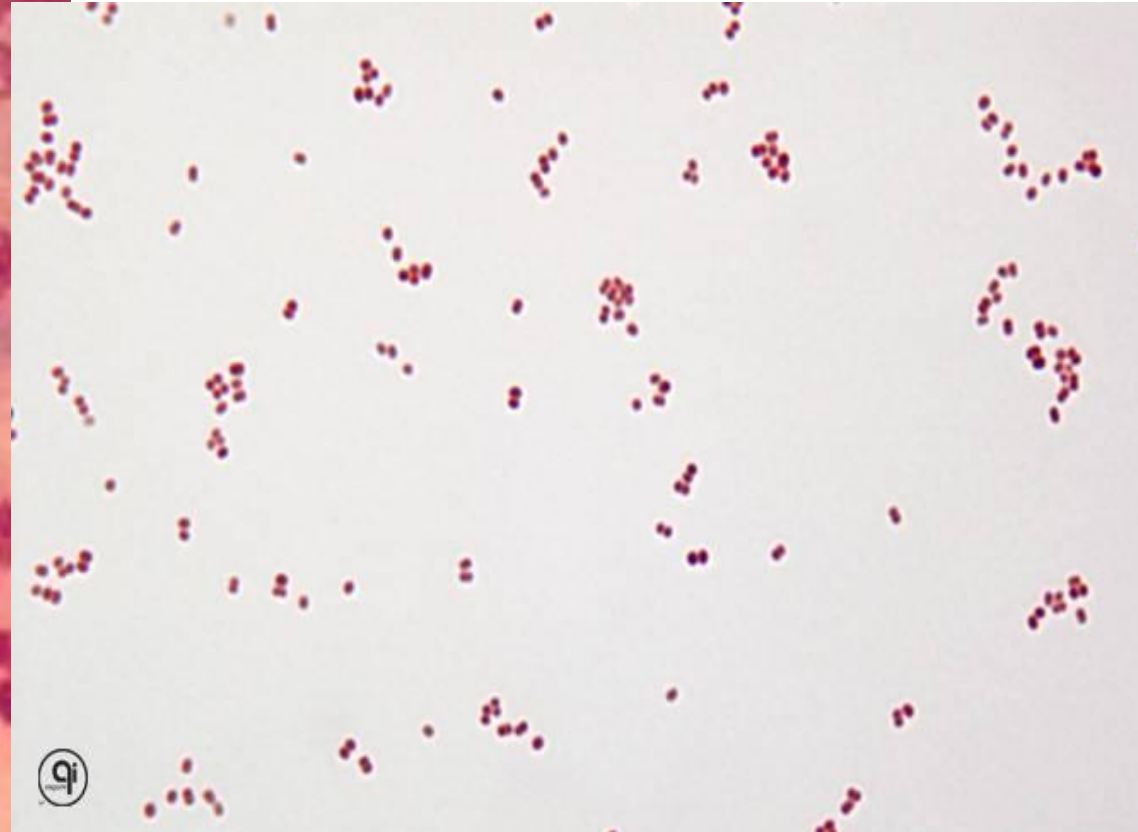
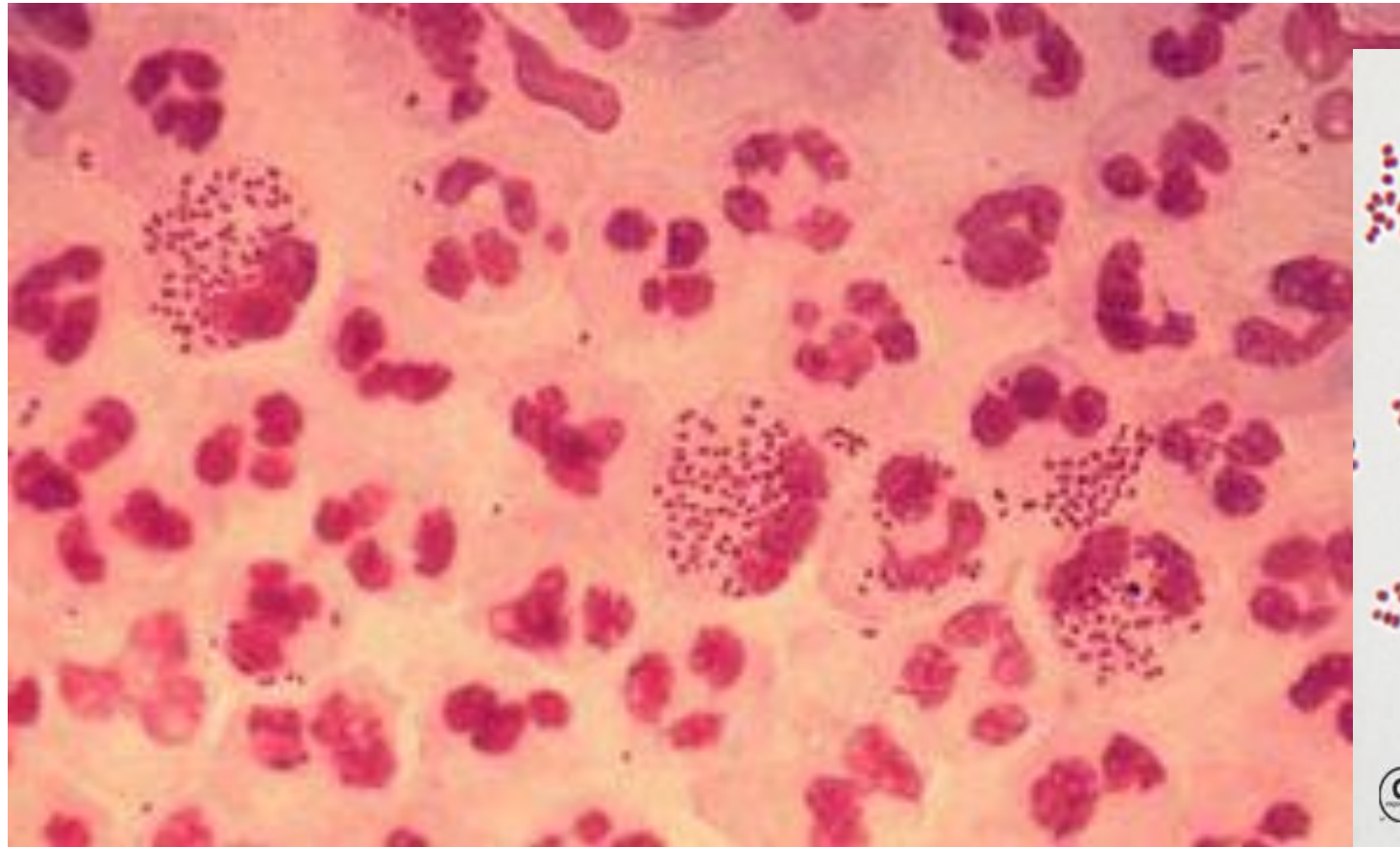
- Two important pathogens
 - *Neisseria meningitidis*
 - Meningitis
 - Meningococemia
 - *Neisseria gonorrhoeae*
 - Gonorrhea
 - Acute pyogenic infection of urethra (urethritis) and cervix (cervicitis)
 - Acute purulent urethral , vaginal discharge , dysuria
 - Asymptomatic in females
 - Rectum & oropharynx may be involved
 - Neonatal conjunctivitis (ophthalmia neonatorum)
 - Pelvic inflammatory disease (PID)
 - Arthritis

Neisseria

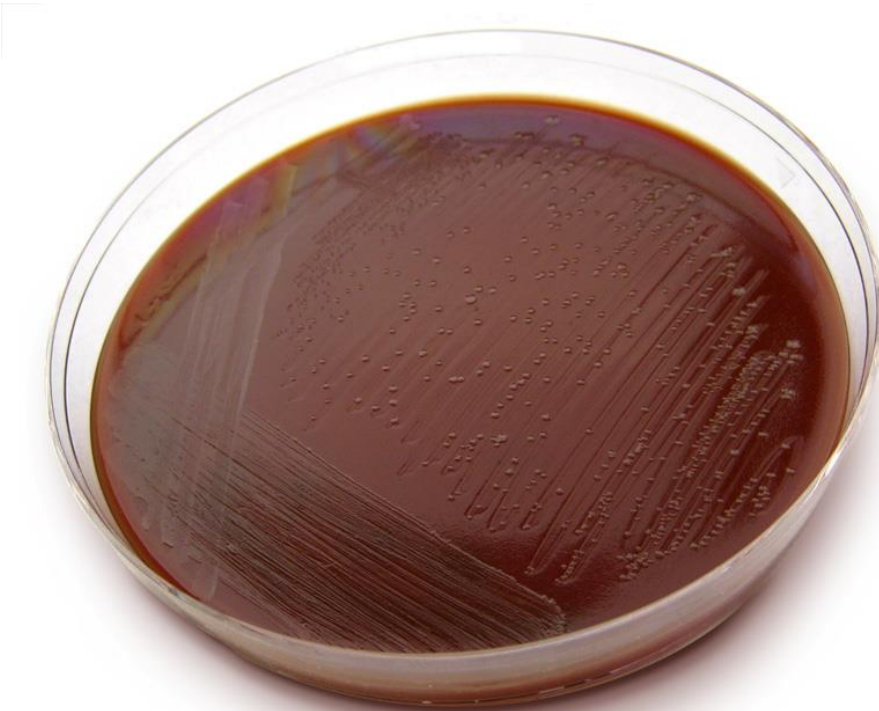
- Gram-negative diplococci (Bean shaped)
- Oxidase-positive
 - possess the enzyme cytochrome c and produce oxidase
- Exacting growth requirements (fastidious)
 - cultured on enriched media for CSF (chocolate agar) and selective media for genital specimens
- Identification by
 - Gram stain and Colony morphology
 - Oxidase test
 - Sugar fermentation
 - N. meningitidis- ferment glucose and maltose
 - N. gonorrhoeae- ferment glucose only

Gram stain

- **Intracellular Gram Negative Diplococci**



Culture and ID tests



	Glucose	Maltose	Sucrose	Lactose
<i>N. gonorrhoeae</i>	Yellow	Red	Red	Red
<i>N. meningitidis</i>	Yellow	Yellow	Red	Red
<i>N. sicca</i>	Yellow	Yellow	Yellow	Red
<i>N. lactamica</i>	Yellow	Yellow	Red	Yellow

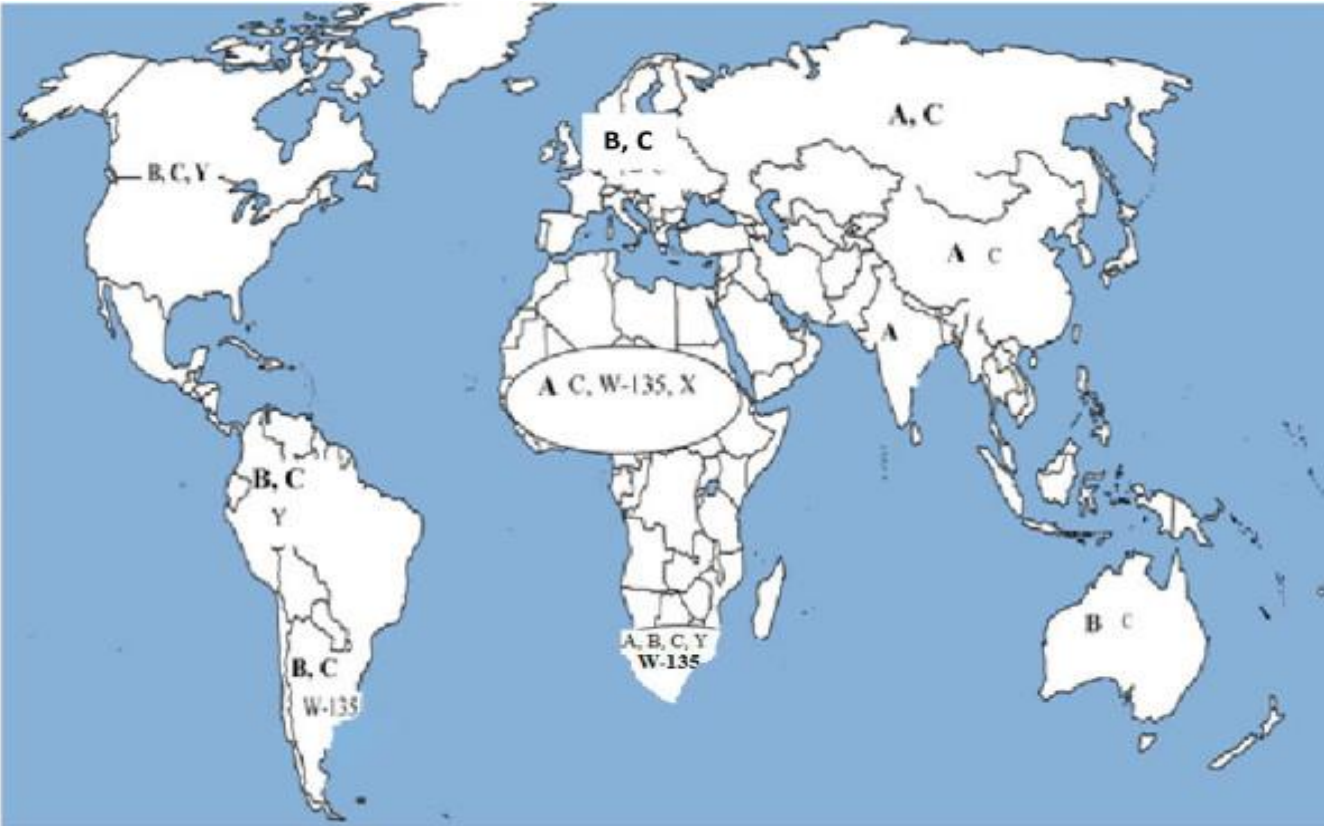
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Neisseria meningitidis

- Habitat: human nasopharynx (10-25%)
- Transmitted by **airborne droplets**
- At least 13 serogroups on the basis of capsular polysaccharides
- Important ones are A,B,C,Y and W-135

Epidemiology



- **African meningitis belt**
 - Highest incidence
 - 25 countries with high incidence

- Eastern Mediterranean region
 - Sudan and Saudi Arabia
 - outbreaks in recent years during the hajj season with serogroup W-135
- European region
- Region of the Americas
 - Uruguay , Brazil , Cuba, Argentina, Canada, Chile, US
- South-East Asia Region
 - Under-recognized
 - India has experienced repeated serogroup A epidemics, the most recent in 2005
- Western Pacific
 - New Zealand and Mongolia
 - Australia

Pathogenesis and virulent factors

nasopharynx → multiply → penetrates the mucosal
cells (1%) → blood stream → crosses the blood–brain
barrier into the cerebrospinal fluid → meningitis

Virulent factors

1. Polysaccharide capsule- Resist phagocytosis and complement-mediated lysis
2. Endotoxin- It induces septic shock by causing release of cytokines
3. IgA protease - It cleaves the IgA antibodies present in respiratory mucosa

Clinical presentation

- Meningitis - most common presentation
 - sudden onset of fever, headache, and stiff neck, often accompanied by other symptoms, such as nausea, vomiting, photophobia (eye sensitivity to light), and altered mental status
- Meningococcal sepsis (bloodstream infection or meningococemia)
 - occurs without meningitis in 5% to 20% of invasive meningococcal infections
 - characterized by abrupt onset of fever and a petechial or purpuric rash, often associated with hypotension, shock, acute adrenal hemorrhage, and multiorgan failure
 - Severe form - Waterhouse-Friderichsen syndrome

Meningitis Symptoms in Adults

These symptoms may not all occur at the same time



Vomiting



Headache



Drowsiness



Seizures



High Temperature



Joint Aching
Joint Pain



Stiff Neck



Dislike of Light

Meningitis Symptoms in Children

These symptoms may not all occur at the same time



A high-pitch
Moaning Cry
Whimpering



Dislike Of
Being Handled,
Fretful



Arching Back,
Neck
Retraction



Blank, Staring
Expression



Difficult to
wake up or
very lethargic



Fever & may
have cold
hands & feet



Refusing feeds
or vomiting



Pale, Blotchy
Skin Color



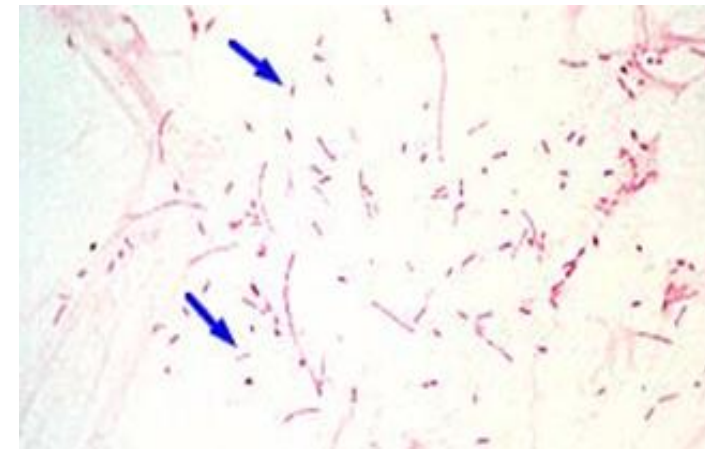
Fig. 110 Haemorrhagic rash (adult with meningitis).

Neisseria meningitidis

Risk Factors for Invasive Disease

- Host factors
 - terminal complement pathway deficiency
 - asplenia
 - genetic risk factors
- Exposure factors
 - household exposure
 - concurrent upper respiratory tract infection
 - socioeconomic factors and crowding
 - active and passive smoking

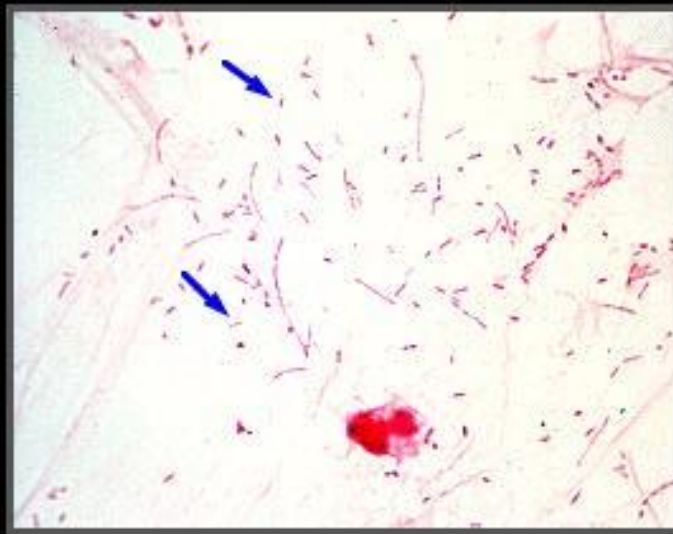
Haemophilus



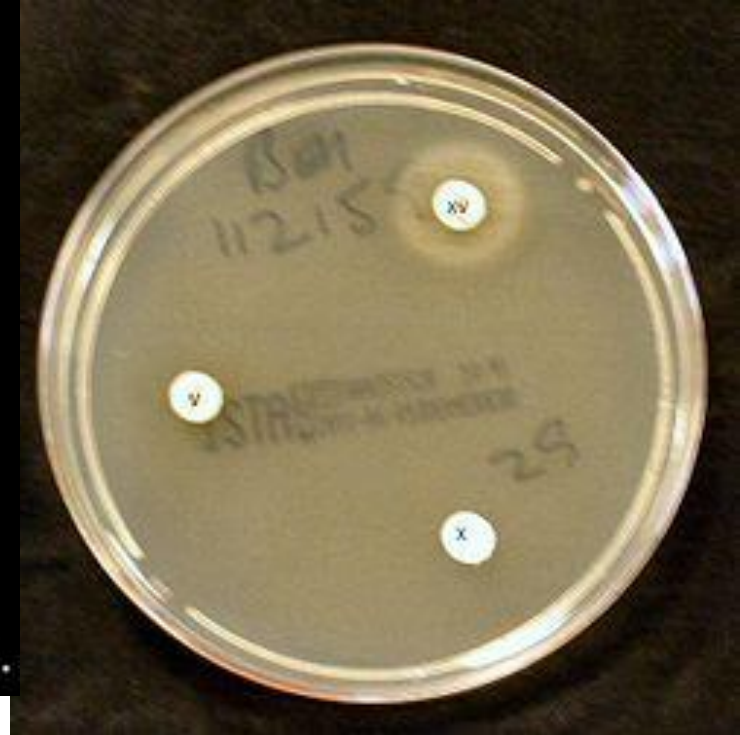
- Small gram negative cocco-bacilli + long filamentous forms
- Most common pathogenic spp.- *H. influenzae*
- Other spp.
 - *H. ducreyi*- causes genital ulcers (Chancroid)
 - *H. parainfluenzae*- rarely cause pneumonia and endocarditis
- Some *H. influenzae* are capsulated (cause invasive infections)
 - 7 serotypes of *H. influenzae* (a-f) - based on type of capsule
 - Commonest pathogenic serotype is b (*H. influenzae b*/ Hib)
- Non capsulated
 - Causes sinusitis, otitis media, bronchitis and pneumonia in young children and adults

Growth requirement

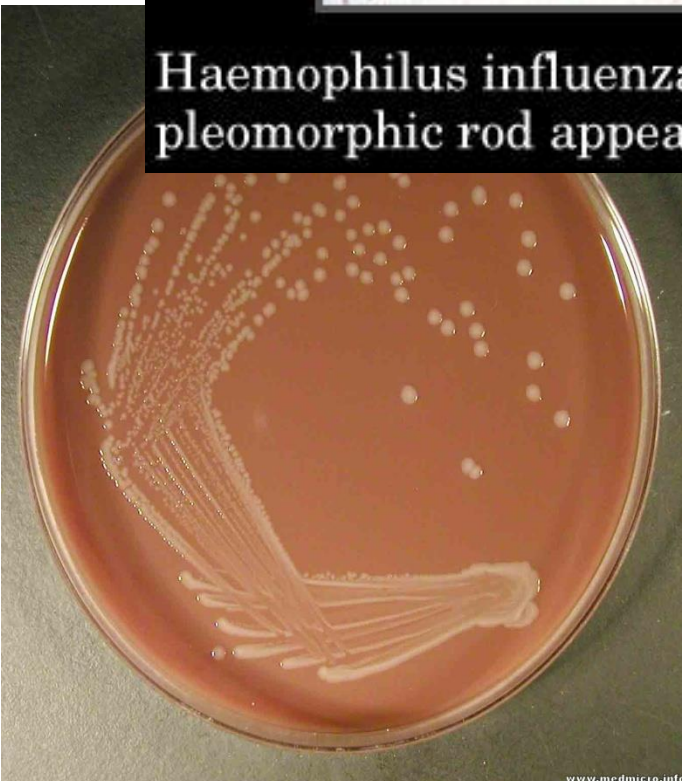
- Fastidious- needs additional growth factors
 - *H. Influenzae*- needs **X factor (Haemin)**, and **V factor (NAD)**
 - No growth on BA which lacks NAD
 - Grow on chocolate agar (both X +V present)
 - Grow around colonies of Staphylococci in Blood agar (Staph provides NAD) – Satellitism
 - *H. parainfluezae* – needs V only
 - *H. ducreyi* – needs X only



Haemophilus influenzae a gram negative pleomorphic rod appears pink of gram stain.



Hib grows around XV disc only

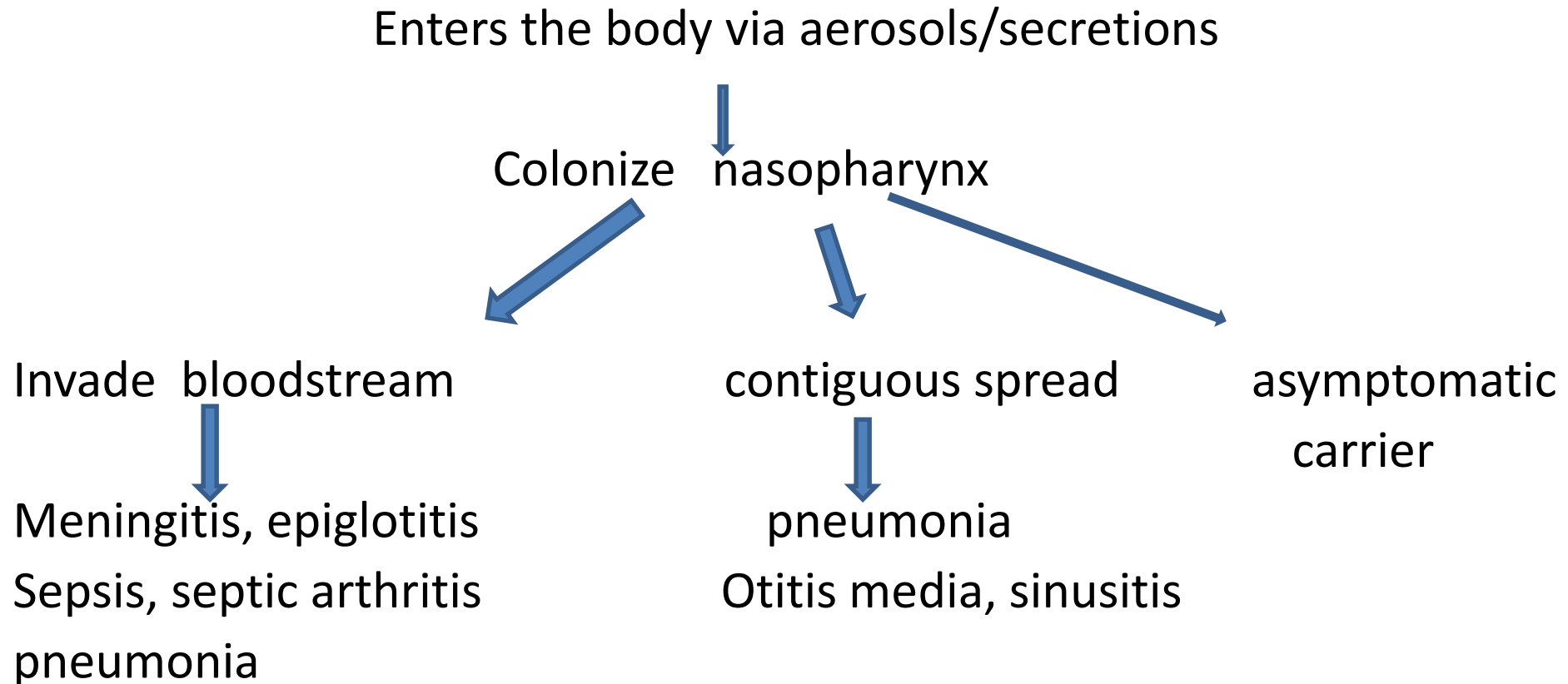


grayish-white, small and mucoid, smell of semen



Satellitism of Hib around Staphylococcus streak

Pathogenesis of H. influenzae b (Hib)



- Age dependant susceptibility – 6 months to 5-6 years

Contiguous spread
(often involving
unencapsulated
strains) from site of
colonization in the
respiratory tract

Disseminated spread
(often involving
capsular type b
strains) via blood
stream

Otitis media

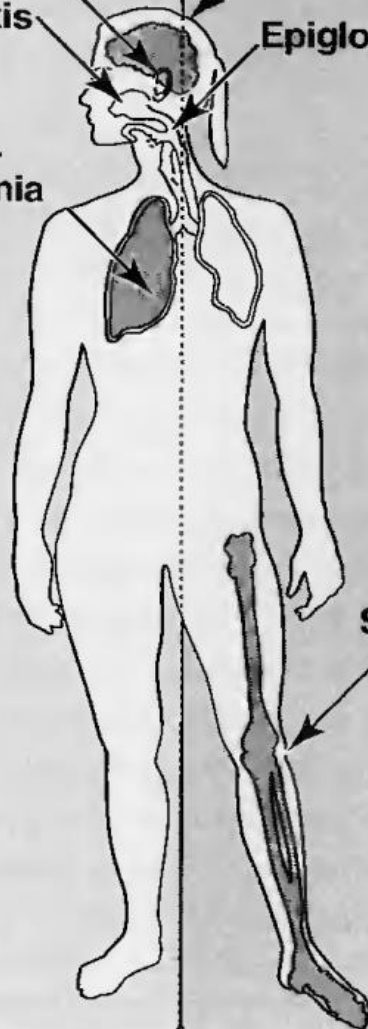
Sinusitis

Broncho-
pneumonia

Meningitis

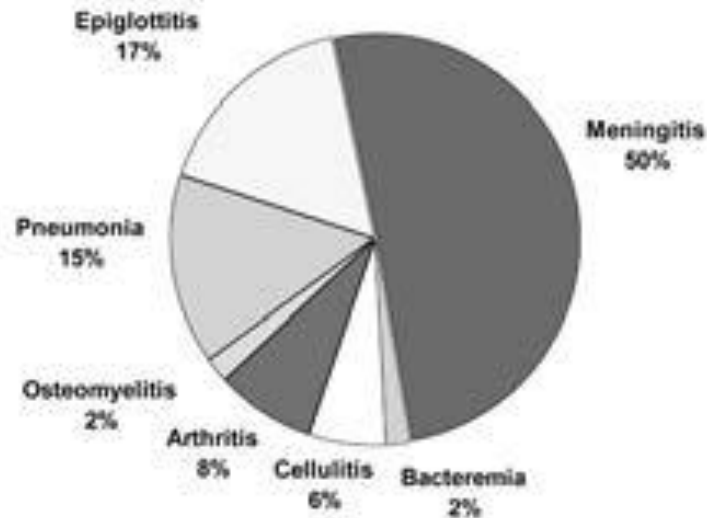
Epiglottitis

Septic
arthritis



Clinical presentations of Hib

Haemophilus influenzae* type b Clinical Features



*prevaccination era

The frequency of *H. influenzae* type b infections in children has declined dramatically since the introduction of the Hib conjugate vaccine

***Haemophilus influenzae* type b Meningitis**

- Accounted for approximately 50%-65% of cases in the prevaccine era
- Hearing impairment or neurologic sequelae in 15%-30%
- Case-fatality rate 2%-5% despite appropriate antimicrobial therapy

Hib epiglottitis

- Infection and swelling of the epiglottis
- Epiglottitis may cause life-threatening airway obstruction.

Laboratory diagnosis of meningitis

- Specimens- CSF, Blood
 - Methods
 - Direct smear and gram stain of CSF and blood
 - ICGND – Neisseria
 - GPC in chains – Pneumococci
 - GNCB – *H. influenzae*
 - GNB- Coliforms
 - Blood culture
 - CSF culture
- on blood agar, chocolate agar, MacConkey agar
incubated in CO₂

Laboratory diagnosis of meningitis ctd...

- ID tests
 - Gram stain
 - Oxidase, sugar fermentation- *N. meningitidis*- oxidase+, ferment glu and mal
 - X and V requiremen, satellitism around staph colonies on BA – *H. influenzae*
 - optochi test, bile solubility- *S. pneumoniae*
 - Catalase positive, CAMP test positive- *Listeria*
- CSF full report
- CSF antigen detection – Latex agglutination
 - For Hib, *N. meningitidis* A, B, C, Y W135, *S. pneumoniae*, E.coli, Group B strep

CSF Ag detection kit



Negative reaction

Positive reaction

Antibiotic treatment

- *S. pneumoniae*- IV penicillin
 - 3rd gen ceph +/- Vancomycin
 - x 10-14 days
- *Neisseria meningitidis* – IV Penicillin or
 - 3rd gen ceph
 - x 7 days
- *H. influenzae* – 3rd gen ceph
 - x 7 days
- *Listeria monocytogenes* - Ampicillin or IV penicillin
 - x>21 days
- Group B strep - Ampicillin or IV penicillin
 - x 14-21 days
- Coliform - 3rd gen ceph
 - x 21 days

Meningitis Prophylaxis

- **Meningococcal Infection**

- only for close contacts in the preceding seven days:
 - shared living/sleeping accommodation with case
 - were mouth kissing contacts
 - nursery
 - were boarding school dormitory contacts
- 1st line: Rifampicin 600mg every 12 hours for 4 doses
2nd line: Ciprofloxacin 500mg po stat (if on OCP)
- Pregnant - Ceftriaxone

Meningitis Prophylaxis

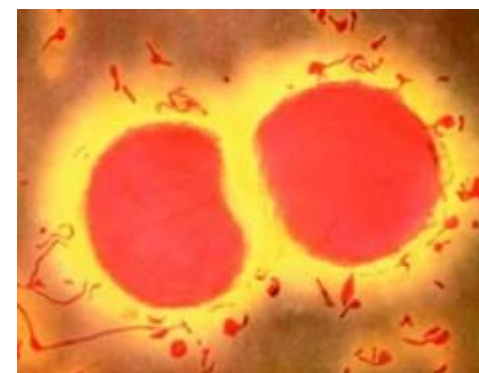
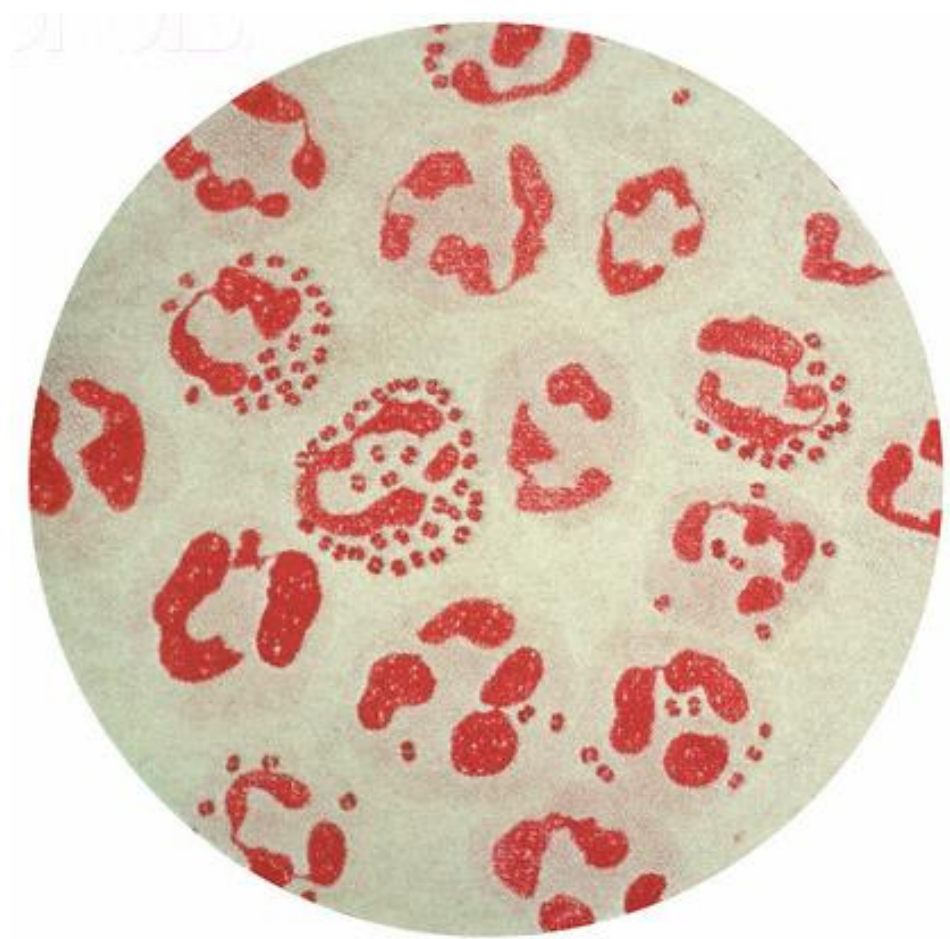
- Hib meningitis
 - Unvaccinated or incompletely vaccinated children or persons at increased risk (e.g. asplenia or complement deficiency) in the household
 - Also patients who were not given 3rd gen ceph
 - Rifampicin 20mg/kg once daily for 4 days up to max of 600mg/day

Summary

- *Neisseria meningitides and Haemophilus*
 - Habitat
 - Epidemiology
 - Characteristics and identification
 - Pathogenesis
 - Lab diagnosis
 - Treatment and prevention

Neisseria gonorrhoeae (Gonococcus)

- *N. gonorrhoeae* causes the sexually transmitted disease **gonorrhoea**.
- Gram negative diplococci with adjacent sides concave, being typically kidney shaped.
- They are usually found with in the polymorphs



CULTURE & CULTURAL CHARACTERISTICS:

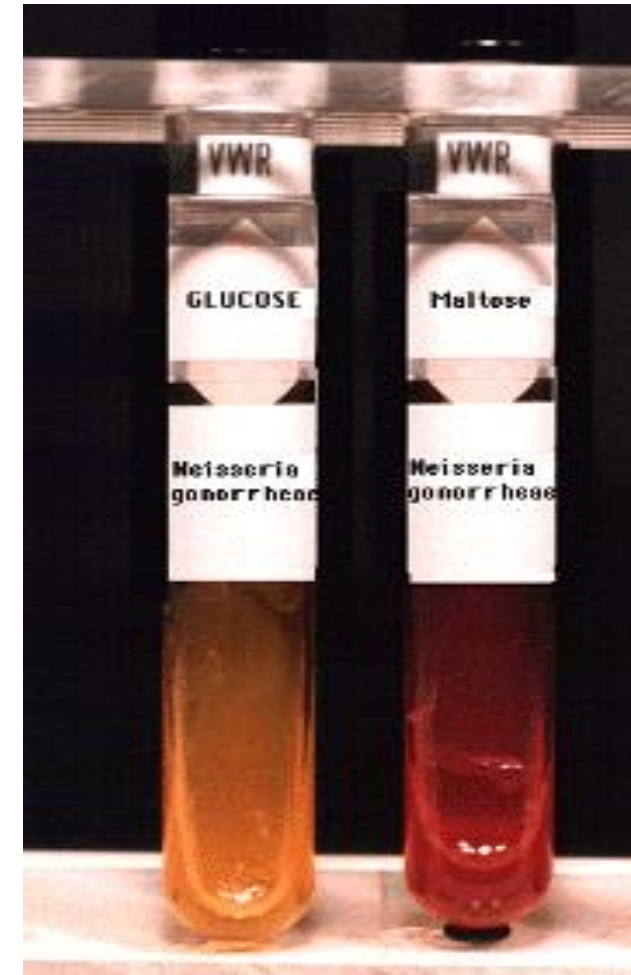
- Gonococci are fastidious organisms and do not grow on ordinary culture media.
- It is essential to provide 5-10% CO₂

Media used

- Selective media
 - Thayer Martin medium with antibiotics (Vancomycin, Colistin & Nystatin).
 - NYC medium

Biochemical reactions:

- 1) Oxidase test: Positive
- 2) Ferments only glucose but not maltose.



PATHOGENICITY:

Source of infection:

1. Asymptomatic carriers
2. Patients

Mode of infection:

1. Venereal infection (sexual contact)
2. Nonvenereal infection

Antigenic structure & virulence factors:

- 1. Pili:** They help in adherence of bacteria to host epithelial cells & they are antiphagocytic.
- 2. Lipooligosaccharide:** Endotoxic.
- 3. Outer membrane proteins:** 3 types
 - a) Protein I (por)- it is a porin & helps in adherence.
 - b) Protein II (opa)- helps in adherence.
 - c) Protein III (rmp)- it is associated with protein I.
- 4. IgA1 protease:** Splits & inactivates IgA.

Disease:

A) In men:

The disease starts as an acute urethritis with a mucopurulent discharge



The infection extends to the prostate, seminal vesicles & epididymis



In some it may become chronic urethritis leading to stricture formation



The infection may spread to the periurethral tissues, causing abscesses & multiple discharging sinuses
(Watercan perineum)



B) In women:

The initial infection is urethritis & cervicitis



The infection may extend to Bartholin's glands,
endometrium & fallopian tubes causing
Pelvic Inflammatory Disease (PID)

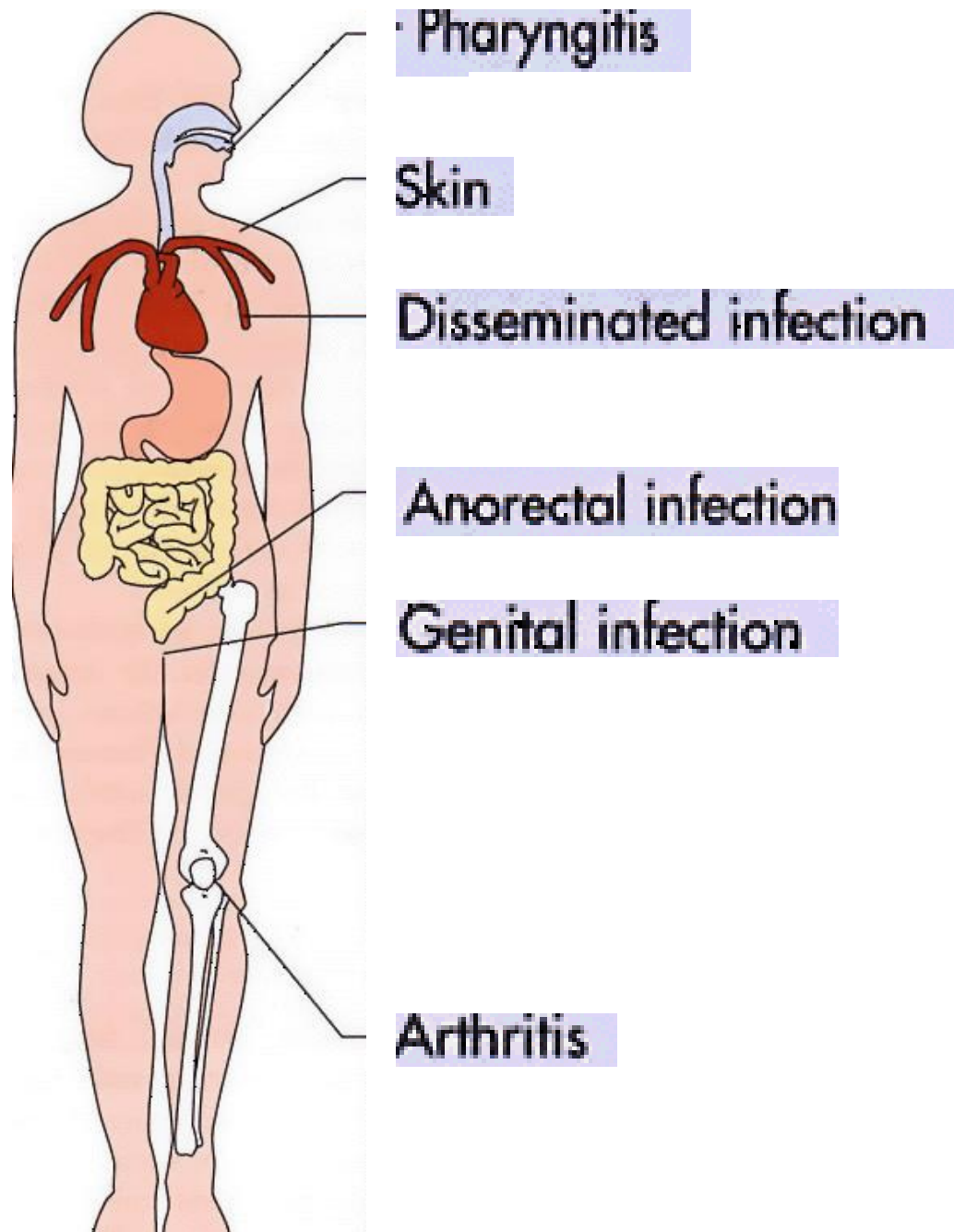


Rarely peritonitis may develop with perihepatic
inflammation (Fitz-Hugh-Curtis syndrome)

C) In both the sexes: Proctitis, pharyngitis, conjunctivitis, bacteraemia which may lead to metastatic infection such as arthritis, endocarditis, meningitis, pyemia & skin rashes.

D) In neonates: **Ophthalmia neonatorum** (nonvenereal gonococcal conjunctivitis in the newborn) results from direct infection during passage through birth canal.





LABORATORY DIAGNOSIS:

Specimens collected:

A) In men:

- a) Acute infection- Urethral discharge
- b) Discharge collected after prostatic massage
- c) Centrifuged deposit of urine

B) In women:

- i) Urethral discharge
- ii) Endo-Cervical swabs

C) In both the sexes: Blood, CSF, synovial fluid, throat swab, rectal swab & material from skin rashes.

Transport: If there is delay in processing than the specimens should be sent in “ Stuart’s medium”.



Methods of examination:

A) Direct microscopy:

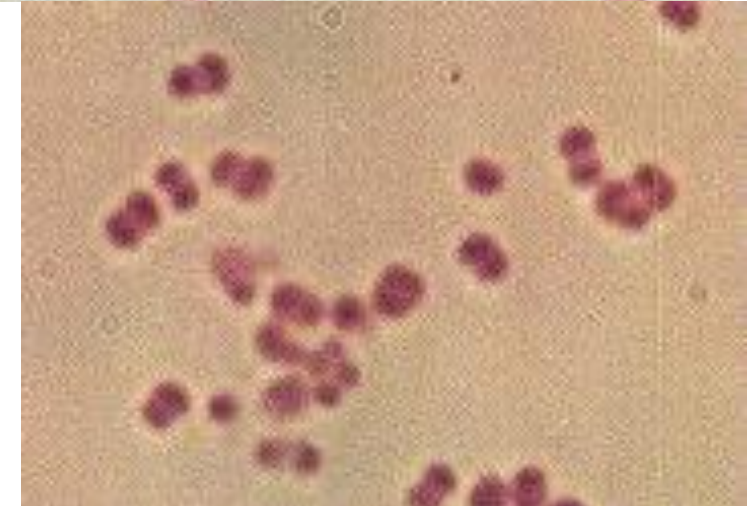
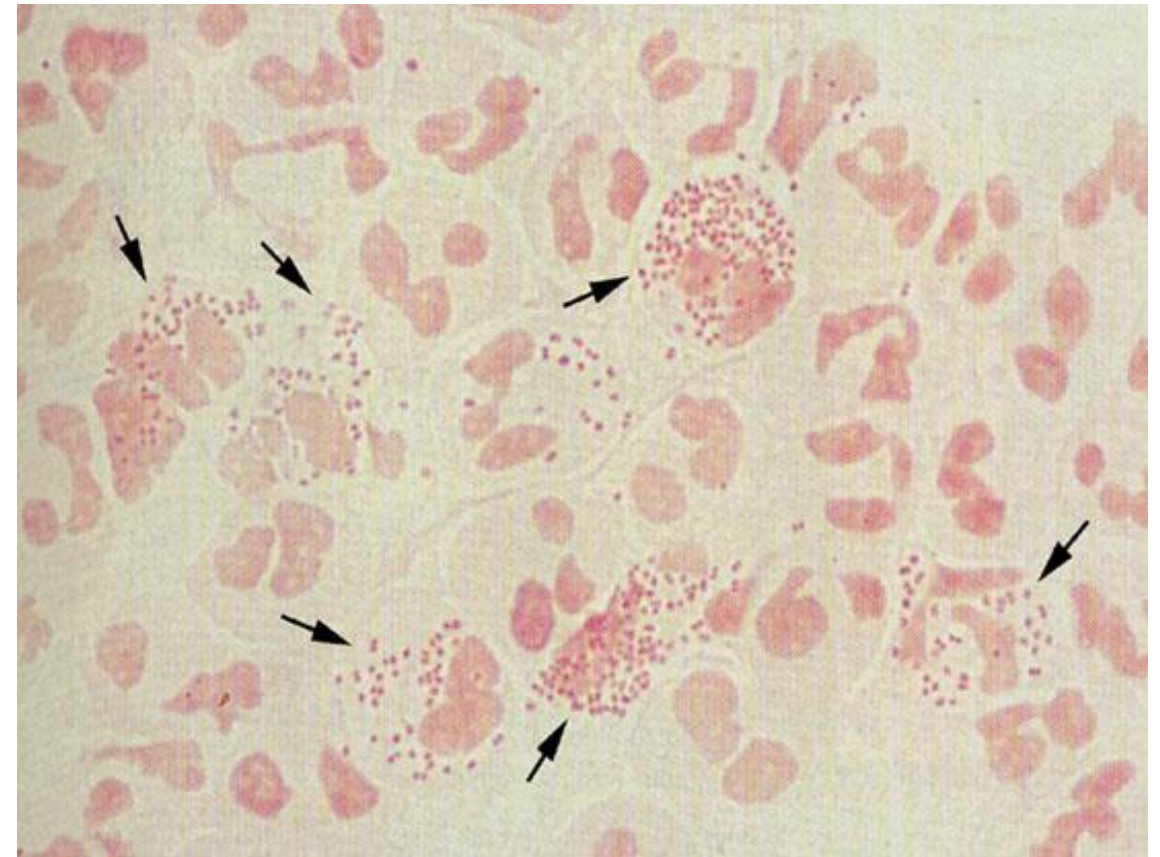
1. Gram staining:

Smear provides a presumptive evidence of gonorrhea in men.

Gram negative intracellular diplococci are found.

But it is unreliable in women.

- In males (urethral swab)- >95% sensitive
- In females (endocervical swab)- 50-70% sensitive



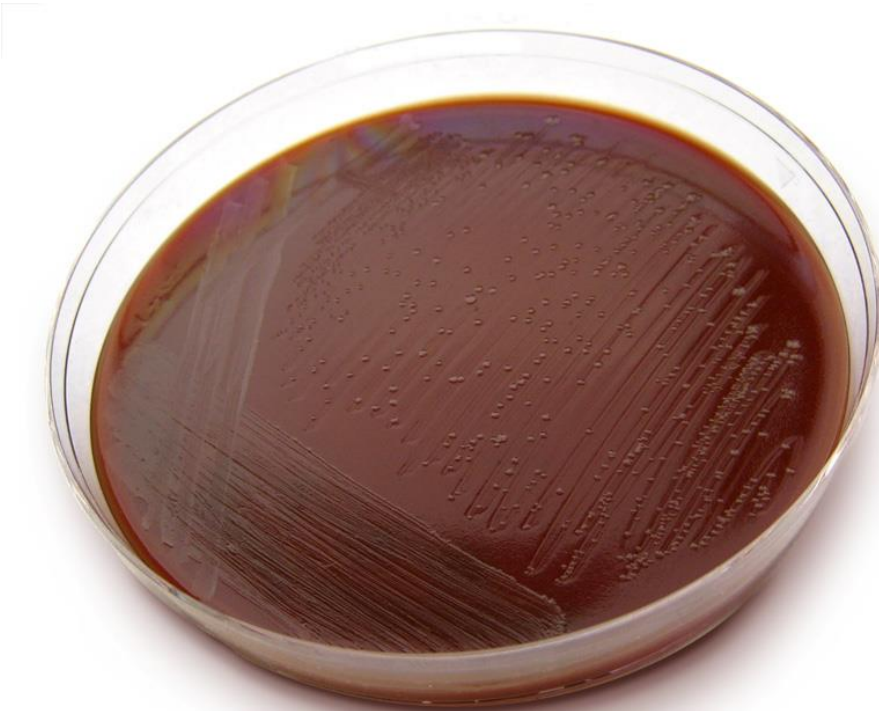
Diagnosis of GU

- Methods

- 2. Culture and ABST

- Gold standard
 - Need nutritive selective medium
 - Modified Thayer-Martin (MTM)
 - Martin-Lewis (ML)
 - New York City (NYC)
 - Inoculated at bed side
 - Incubated in CO₂ for 72 hours
 - Identified by- colony morphology, GS, Oxidase +, catalase +, sugar fermentation (gluc+, mol -, lac-, sucr-)

Culture and ID tests



	Glucose	Maltose	Sucrose	Lactose
<i>N. gonorrhoeae</i>	Yellow	Red	Red	Red
<i>N. meningitidis</i>	Yellow	Yellow	Red	Red
<i>N. sicca</i>	Yellow	Yellow	Yellow	Red
<i>N. lactamica</i>	Yellow	Yellow	Red	Yellow

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Diagnosis of GU

- Rapid Methods
 - PCR/ DNA probes
 - Rapid POC tests- ICT for Ags

TREATMENT:

- Previously Penicillin was drug of choice but resistance developed rapidly.
- Penicillin resistant is due to production of penicillinase enzyme & the strains are called as penicillinase producing *Neisseria gonorrhoeae* (PPNG).
- Now Ceftriaxone or Ciprofloxacin plus Doxycycline or Erythromycin is useful.

SDL

- Clinical presentations of *N. gonorrhoeae*
- *Pathogenesis*

SDL

- CSF full report in different types of meningitis
 - Acute bacterial
 - Chronic meningitis
 - TB
 - Viral
 - Partially treated meningitis
- Vaccinations available for
 - Meningococci
 - Hib

Summary

- Aetiological agents of bacterial meningitis
 - *Neisseria meningitidis*
 - *Haemophilus influenza*
- Gonorrhoea
- Clinical presentations, transmission and epidemiology
- Laboratory diagnosis
- Treatment