Chapter 16

Gram negative cocci

Neisseria

Diseases

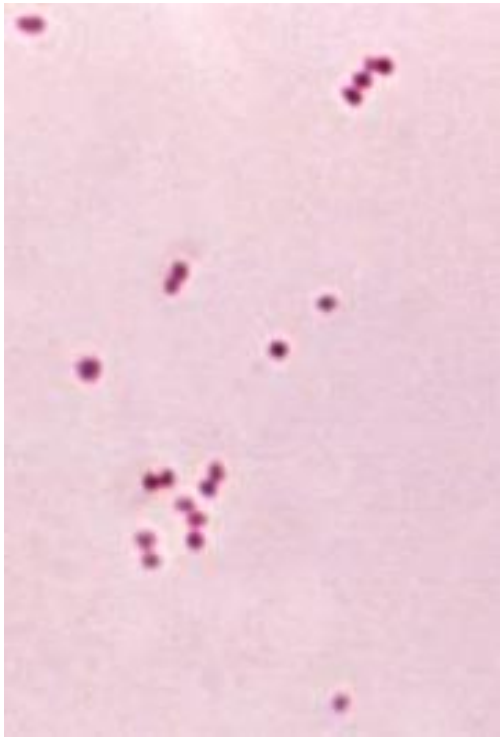
-- There are **two important human pathogens**: ***Neisseria meningitidis*** **(meningococcus)** and ***Neisseria gonorrhoeae*** **(gonococcus)**.

-- ***Neisseria meningitidis*** causes **meningitis** and **meningococcemia**.

-- ***Neisseria gonorrhoeae*** causes **gonorrhea**, **neonatal conjunctivitis** and **pelvic inflammatory disease**.

Important properties

These are **Gram negative diplococci** that resemble paired kidney beans



-- **Meningococcus** has a prominent **polysaccharide capsule** *not seen in the gonococcus*.

-- The capsule is **antiphagocytic** and is an important virulence factor in meningococcal disease.

-- ***N. meningitidis*** strains are grouped into **13 serogroups** on the basis of their capsular polysaccharides.

-- **Five serotypes** are more important, **A, B, C, Y, and W-135**. **Serotype A** is most prevalent globally.

-- **Gonococcus** has **no capsule** but has multiple **serotypes** based on the antigenicity of **pilus protein**.

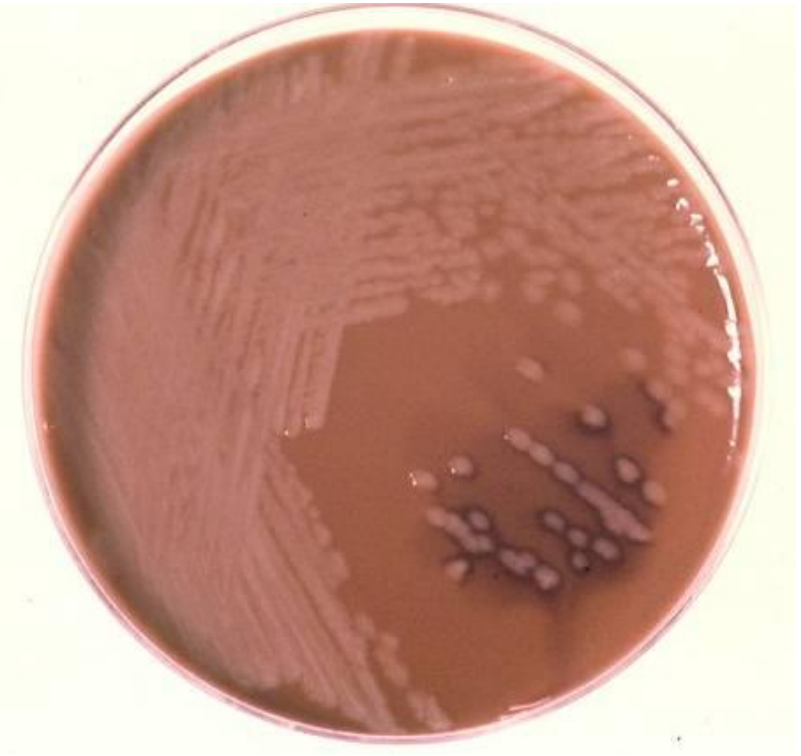
-- There is **marked antigenic variation** due to chromosomal rearrangement and there are **more than 100 serotypes**.

-- There are **three outer membrane proteins**, I, II, and III. **Protein II** plays a role in **attachment** of the organism to cells and varies antigenically as well.

-- **Neisseriae** being Gram negative, have **endotoxin** in their outer membrane which is **lipooligosaccharide (LOS)** instead of LPS in enteric pathogens. Both LOS and LPS contain lipid A.

-- Growth of both organisms is inhibited by toxic trace metals and fatty acids found in certain culture media, e.g., blood agar. They are, therefore, cultured on **chocolate agar**.

-- They are **oxidase positive** possessing enzyme cytochrome c. Colonies exposed to **phenylenediamine** turn **purple or black** as result of oxidation.



Meningococcus on chocolate agar

Oxidase test

Meningococcus

Pathogenesis and Epidemiology

-- **Humans are the only natural hosts** and transmission is by airborne droplets.

-- **They colonize the membranes of nasopharynx** and carriers are asymptomatic.

-- From nasopharynx, they can enter the blood stream and spread to specific sites such as **meninges** or **joints** or disseminated throughout the body (**meningococococcemia**).

-- About **5% people become carrier**, but carrier rate can be up to **35%** in people living together in close quarters.

-- Along with ***Strept. pneumoniae***, meningococci are responsible for **80% cases of meningitis** in infants older than 2 months.

-- These are the **most common cause of meningitis** in age group 2-18 years.

-- Although **pneumococci are more common cause of meningitis**, **meningococci**, esp. **Group A are most likely to cause epidemics**.

There are **three important virulence factors**:

1. **Capsule** that resists phagocytosis

2. **Endotoxin**, the cause of fever, shock and other pathophysiological changes.

3. **IgA protease** that help attachment to membranes by cleaving secretory IgA.

-- Most carriers develop protective antibody **within 2 weeks**.

-- **Immunity is group specific**, so it will not work against other groups.

-- **Complement** is also important, and those having deficiencies esp. in **late acting components (C6-C9)** have increased incidence of bacteremia.

Clinical findings

-- Two most important diseases are **meningococcemia** and **meningitis**.

-- The most severe form of meningococcemia is **Waterhouse-Friderischen syndrome** with high fever and shock.

-- Meningitis has symptoms of **fever, headache**, and **stiff neck**.

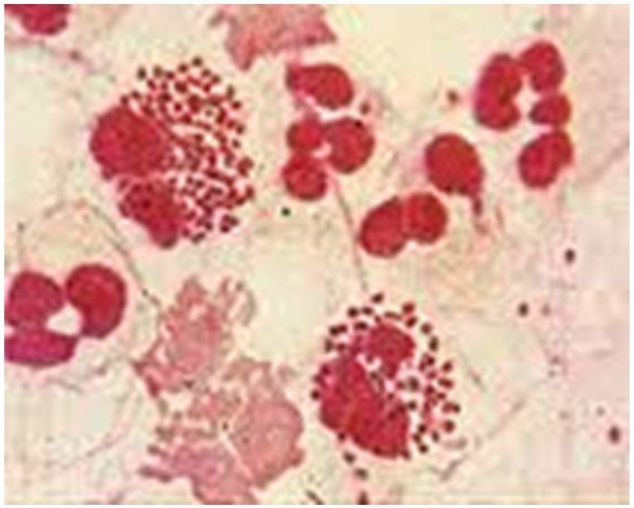
meningococcemia

Laboratory diagnosis

-- **Smear and culture of blood and CSF** are most common procedures.

-- Presumptive diagnosis is made if **typical cocci are seen in CSF**.

Neisseria meningitidis



In smears from specimens, meningococci are found inside pus cells (intracellular)

-- After cultivation on **chocolate agar** in presence of 5% CO_2, **oxidase positive growth is diagnostic**.

Treatment

-- **Penicillin G** is the drug of choice.

-- Penicillin resistance is rarely observed but sulfonamide resistance is common.

Prevention

-- **Chemoprophylaxis** and **immunization** are both used to prevent meningococcal disease.

-- **Rifampin** and **ciprofloxacin** are preferred to penicillin G because they are **efficiently secreted into saliva**.

-- All meningococcal vaccines include groups **A, C, Y, and W-135**.

-- The **conjugate vaccines** are preferred because these induce higher titres of antibodies in **children**.

-- **Unconjugated vaccine** can be useful in preventing **epidemics** and **reducing carrier rate**.

Gonococcus

Pathogenesis and Epidemiology

-- **Gonococci**, like meningococci cause disease **only in humans**.

-- Organism is usually **transmitted sexually** and **newborns can be infected during birth**.

-- They are quite **sensitive to dehydration and cold**.

-- **Gonorrhea** is usually **symptomatic in men** but often **asymptomatic in women.**

-- **Genital tract infections are the most common source** but **anorectal** and **pharyngeal** infections are also important.

-- Only **piliated** gonococci are virulent.

-- There are **two virulence factors** in the cell wall, **endotoxins** and outer membrane proteins (**OMPs)**.

-- **IgA protease** is also important.

-- Main **host defenses** are **antibodies (IgA and IgG)**, **complement**, and **neutrophils**.

-- **Repeated infections** can occur due to **antigenic changes** of pili and OMPs.

-- **Infection is primarily through mucosal surfaces** but dissemination of some strains occurs.

-- These strains have better resistance against antibodies and complement.

-- It is suggested that they have **porin A** in cell wall that inactivates **C3b** component of complement.

-- Persons with **deficiency of C6-C9** and women during **menses and pregnancy** are more at risk of disseminated infection.

Clinical findings

-- **Gonorrhea in men** is characterized primarily by **urethritis** accompanied by dysuria and a purulent discharge. **Epididymitis** can occur.

-- In **women** there is **purulent vaginal discharge** and **cervicitis.** Ascending infection of uterine tubes (**salpingitis**) can result in sterility.

-- **Disseminated infection** commonly manifest as **arthritis**, **tenosynovitis** or **skin pustules**.

-- **Anorectal area**, **throat** and **eyes** may also be infected.

-- In the **throat, pharyngitis** may occur but many cases are asymptomatic.

-- In **newborn infants** purulent conjunctivitis (**ophthalmia neonatorum**) may occur due to infection acquired from mother.

-- **Prophylactic erythromycin ointment** and **silver nitrate** greatly reduce this incidence when applied shortly after birth.

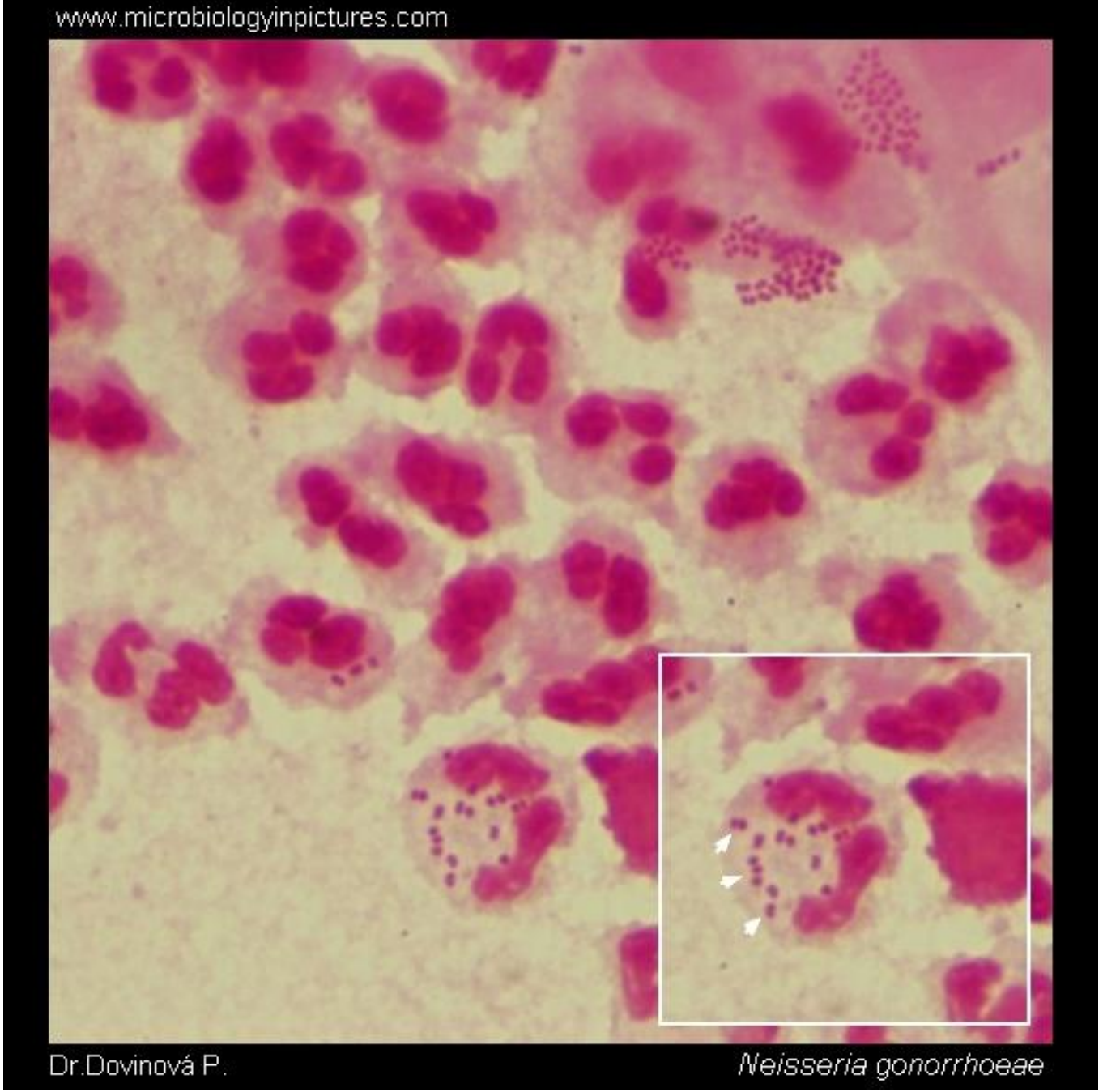
ophthalmia neonatorum

Laboratory diagnosis

-- Diagnosis depends on **Gram staining** and **culture of discharge**.

-- In men, finding of **Gram negative diplococci *within PMNs*** in a urethral discharge is diagnostic.

-- **In women, cultures should be done** as Gram stains can be falsely positive because of normal flora and falsely negative due to very small number of gonococci.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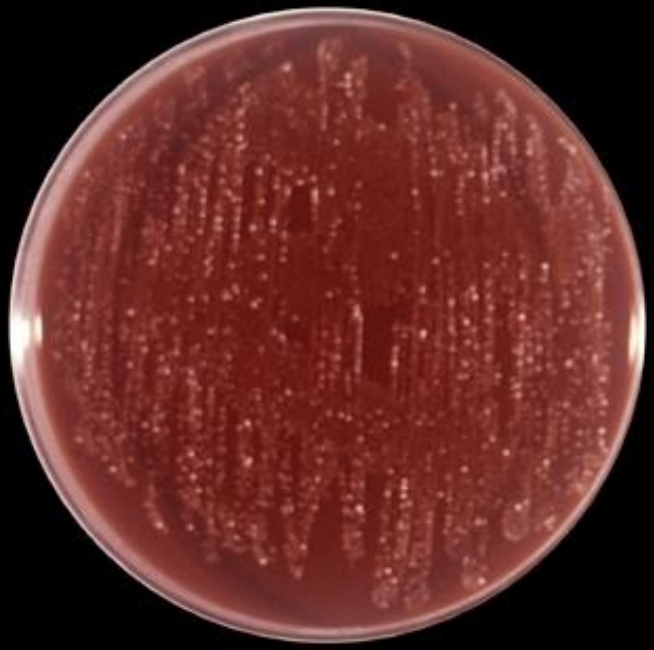
Dr.Dovinová P.
Neisseria gonorrhoeae

-- **Cultures** must also be used in diagnosing suspected **pharyngitis** or **anorectal infections**.

-- Cultures are done on **Thayer-Martin medium** which is **chocolate agar containing antibiotics** (vancomycin, colistin, trimethoprim and nystatin) to suppress normal flora.

Rectal Specimen

(Testing for *Neisseria gonorrhoeae*)

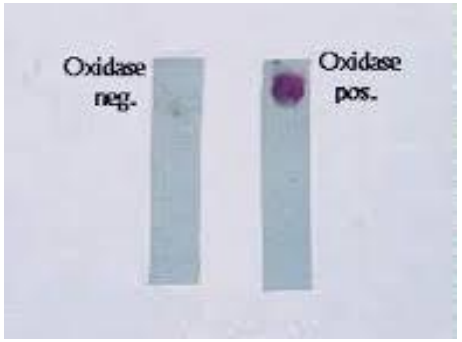


Chocolate Medium
Overgrowth

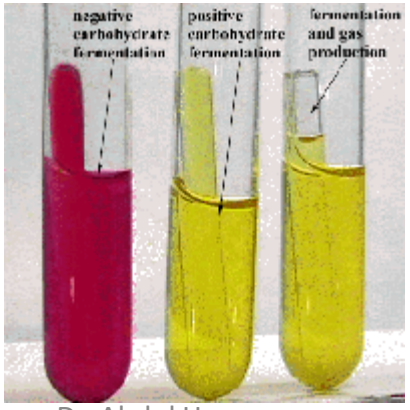
Thayer-Martin Medium
***Neisseria* Only**

CDC/ Renelle Woodall

-- Detection of **oxidase positive colonies** of **Gram negative diplococci** is sufficient for initial identification.



-- Specific identification can be made by **fermentation of glucose but not maltose** or by **fluorescent antibody staining**.



-- Specimens from sterile sites can be cultured on **chocolate agar**.

-- **Nucleic acid based screening tests such as PCR** are widely used. These are highly sensitive and specific.

Treatment

-- **Ceftriaxone** is treatment of choice in uncomplicated cases.

-- Oral **cefixime, spectinomycin** or **ciprofloxacin** may also be used.

-- In mixed infections with ***C. trachomatis***, **azithromycin** is preferable. A follow up culture should be performed after one week.

-- **Low level resistance** to penicillins, tetracycline and chloramphenicol is due to **altered binding sites**.

-- Penicillinase producing strains (**PPNG**) now constitute nearly 10% of all isolates.

-- **Ciprofloxacin resistance** is also emerging rapidly.

Prevention

-- It is based on **prophylaxis** and **prompt treatment** of patients and contacts.

-- A major problem is how to detect **asymptomatic carriers**.

-- **Gonococcal conjunctivitis** is prevented by use of **erythromycin ointment** or less frequently **silver nitrate drops**.

-- **No vaccine** is available.


Thank You!