CHAPTER IV
PATHOGENIC GRAM NEGATIVE COCCI

Learning objectives

At the end of this chapter, the student will be able to:

1. Discuss the general characteristics of the genus Neisseria.
2. List the virulence factors of *N. gonorrhoea.*
3. Discuss the pathogenesis and clinical manifestation of *N. meningitidis.*
4. Differentiate *N. gonorrhoea* from *N. meningitidis* using biochemical tests..

Genus Neisseria

General characteristics

- They are non-motile, gram-negative intracellular diplococci
- Rapidly killed by drying, sunlight, heat, and disinfectants
- Ferment carbohydrate producing acid but not gas
- Are kidney-shaped with adjacent concave sides.
- Grow best on complex media under aerobic conditions containing

5%co_2

- Are oxidase positive.
- .The main species of medical importance are:

  - *N. meningitidis*

  - *N.gonorrhoea.*

- Neisseria species grow best on media containing: Heated blood, hemin, animal protein, 3- 10% Co_2 and other supplements.
- The organisms are sensitive to: drying, sunlight, moist heat and disinfectants.

4.1 *Neisseria gonorrhoeae*

The name ‘gonorrhoea’ derives from the Greek words gonos (seed) and rhoia (flow), and described a condition in which Semen fluid from the male organ without erection.

General characteristics

- An obligate parasite of the human urogenital tract.
- Has no polysaccharide capsule but has multiple serotypes based on the antigencity of its pilus protein.
- There is a marked antigenic variation in the gonococcal pili as a result of chromosomal rearrangement.
- More than 100 serotypes are known.

Virulence factors

1. Pili

- Hair like appendages that mediate initial attachment to non –

ciliated human cells (e.g. epithelium of vagina , fallopian tube

and buccal cavity.

- Made from pilin proteins.
- Resistance to phagocytosis (interferes with neutrophil killing)

2. Por protein (Protein I)

- Pores on the surface of bacteria through which nutrients enter the cell.
- Promotes intracellular survival by preventing phago-lysosome fusion in neutrophils.

3. Opa (Protein II)

Important for firm attachment and invasion of bacteria to host

cells.

4. RMP (protein III)

- Outer membrane protein found in all strains of *N. gonorrhoeae*
- It is associated with por in the formation of pores in the cell.
- Protects other surface antigens (por proteins and lipo oligosaccaride) from bacterial antibodies.

5. Lipooligosaccharide (LOS)

- Is responsible for most of the symptoms / toxicity of gonorrhea

due to endo-toxin effect of LOS.

- Gonococcal LOS triggers an intense inflammatory response.
- Subsequent activation of complement, attraction and feeding

by phagocytes, and the lysis of the phagocytes themselves, contributes to the purulent discharge.

6. Transferrin and lactoferrin binding proteins

Mediate acquisition of iron for bacterial metabolism.

7. Beta- lactamase

Hydrolyzes beta -lactam ring in penicillin.

Pathogenesis and clinical manifestations

- Gonorrhea in adults is almost invariably transmitted by sexual

Intercourse

- Gonococci attack mucous membrane of genito urinary tract,

eye, rectum and throat.

- In males there is urethritis, with yellow, creamy pus and painful urination.
- In females , primary infection is in the endo-cervix and extends to the cervix and vagina giving rise to muco-purulent discharge.
- Gonococcal ophthalmia neonatorum is iinfection of the eye of the new born during passage via infected birth canal.

Laboratory diagnosis

Specimen: Urethral swab, cervical swab, eye swab.

Smear: Gram-negative intracellular and/or extra diplococci

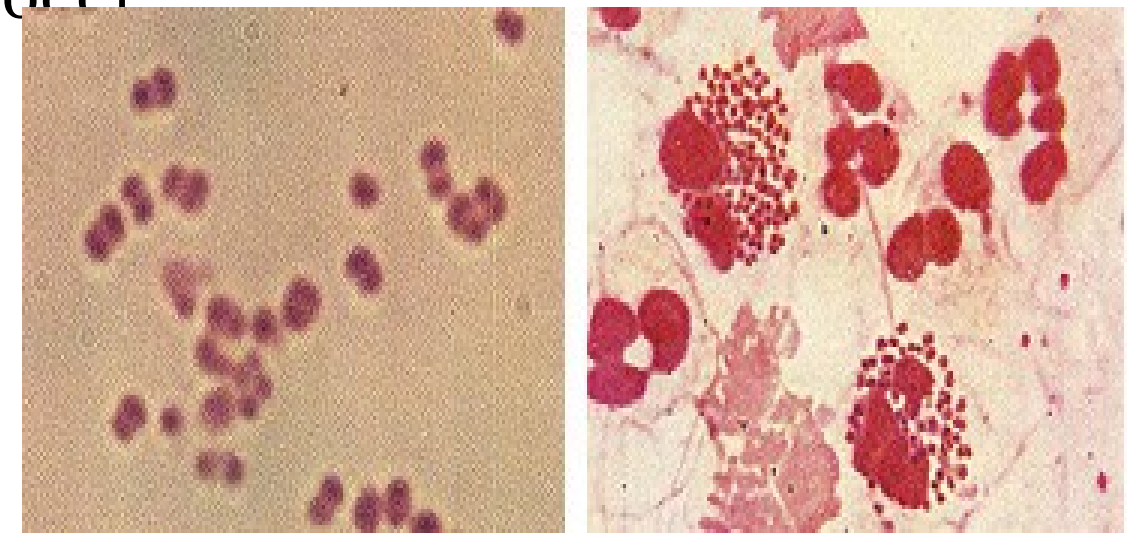


Figure . ….. Left: *N. gonorrhoeae* Gram stain of pure culture
Right: *N. gonorrhoeae* Gram stain of a pustular exudates

Culture: Requires an enriched media like chocolate agar, Thayer-Martin agar and/or Modified New York City medium..

Grows best in carbon dioxide enriched aerobic atmosphere with optimal temperature of 35-37^{0}c.

- On culture, Neisseriae species form convex, elevated and mucoid. colonies
- On Thayer - Martin and Chocolate agar media, colonies are transparent or opaque and non - pigmented.

Growth characteristics

- Most Neisseriae grow best under aerobic conditions but some grow under anaerobic situations
- Ferment carbohydrate and produce acid without gas

Serology: Antibodies to gonococcal pili & outer membrane proteins using RIA and/or ELISA.

Genetic probes : For detection of nucleic acids.

Treatment

Drug of choice (CDC) : Ceftriaxone, doxycycline, ciprofloxacin,

or oflaxacin. Penicillin resistance due to beta- lactamase enzyme

producing *N. gonorrhoeae* have been identified.

For ophthalmia neonatorum - 1% silver nitrate , 1% tetracycline or 0.5% erythromycine eye ointments.

Prevention and control

- Early detection and treatment of cases.
- Using condom
- Health education
- There is no effective vaccine to prevent gonorrhea

4.2 *Neisseria meningitidis*

- *N. meningitidis* has a prominent antiphagocytic polysaccharide capsule. *N. meningitidis* strains are grouped on the basis of their capsular polysaccharides, into 12 serogroups, some of which are subdivided according to the presence of outer membrane protein and lipopolysaccharide antigens.
- The organism tends to colonize the posterior nasopharynx of humans, and humans are the only known host. Individuals who are colonized are carriers of the pathogen who can transmit disease to nonimmune individuals.

- Medically important sero-groups in humans disease are encapsulated strains belonging to A, B, C, Y and W135.
- Sero -groups C and A are associated with epidemic disease.
- Meningitis is the inflammation of the meninges of the brain or spinal cord.

Virulence factors

- **Meningoccal endotoxin (LOS)** : is responsible for many toxic effects.
- **Capsule** : Protects bacteria from anti body mediated phagocytosis.
- **Pili :** Allow to colonization of nasopharynx.

Pathogenesis and clinical manifestations

Infection with *N. meningitidis* has two presentations:

Meningococcemia, characterized by skin lesions, and acute

bacterial meningitis

- Infection is by inhlation of the bacteria, which attach to epithelial cells of the nasopharyngeal and oropharyngeal mucosa, cross the mucosal barrier, and enter the bloodstream.

- The onset of meningococcal meningitis may be abrupt or insidious.
- Fulimenant meningo cocci (with/without meningitis) characterized by:

  - Fever

  - Petechiae (minute hemorrhagic spots in the skin) or purpura (hemorrhages into the skin). Occurs from first to third day of illness in 30 to 60% of patients with meningococcal disease.

- Pulmonary insufficiency developed within a few hours, and many

patients die within 24 hours of being hospitalized.

- Meningitis begins suddenly with intense headache,vomiting,

photophobia, stiff of the neck or spinal rigidity (meningeal irritation**),** neurologic signs (coma or convulsions) in 1/3 of patients.

- The most severe form of meningococcemia is the life threatening **Water House Friderichsen syndrome**, which is characterized by high fever, shock, widespread purpura, disseminated intravascular coagulation and adrenal insufficiency.

Diseases caused by *Neisseria meningitidis* includes :

- Pyogenic (purulent) meningitis
- Meningococcal bacteremia (Water House Friderichsen syndrome)
- Meningococcal encephalitis
- Pneumonia
- Arthritis and endocardiatis
- Urethritis.

Laboratory diagnosis

- **Specimen**: Cerebrospinal fluid, blood
- **Smear:** Gram-negative
- **Culture:** Transparent or grey, shiny, mucoid colonies in chocolate agar after incubation at 35-37^{O}c in a CO2 enriched atmosphere. intracellular diplococci
- **Serology**: Antibodies to meningo- coccal polysacharides can be measured using: latex agglutination or hemagglutination tests.

Biochemical reactions

Species	Glucose	Lactose	Maltose	Sucrose
Neisseria gonorrhoeae	Positive	Negative	Negative	Negative
Neisseria meningitidis	Positive	Negative	Positive	Negative

- **Drug of choice:** Penicillin, Chloramphenicol, Cefotaxime ceftriaxone
- Vaccination is available for sero groups A, C, Y and W135.
- No effective vaccine for sero group B as it is poorly immunogenic in humans.