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***Neisseria***

The genus *Neisseria* contains two important human pathogens, *N. gonorrhoeae* and *N. meningitidis. N. gonorrhoeae*causes gonorrhea, and *N. meningitidis* is the cause of meningococcal meningitis.

*Neisseria gonorrhoeae*infections are acquired by sexual contact and usually affect the mucous membranes of the urethra in males and the endocervix and urethra in females, although the infection may disseminate to a variety of tissues. The pathogenic mechanism involves the attachment of the bacterium to non-ciliated epithelial cells via pili and the production of lipopolysaccharide endotoxin. Similarly, the lipopolysaccharide of *Neisseria meningitidis* is highly toxic, and it has an additional virulence factor in the form of its antiphagocytic capsule. Both pathogens produce IgA proteases which promote virulence. Many normal individuals may harbor *Neisseria meningitidis* in the upper respiratory tract, but *Neisseria gonorrhoeae*is never part of the normal flora and is only found after sexual contact with an infected person (or direct contact, in the case of infections in the newborn).

***Neisseria gonorrhoeae***

*Neisseria gonorrhoeae* is a Gram-negative coccus, 0.6 to 1.0 µm in diameter, usually seen in pairs with adjacent flattened sides and the organism is frequently found intracellularly in polymorphonuclear leukocytes (neutrophils) of the gonorrhea pustular exudate.

*Neisseria gonorrhoeae* possesses a typical Gram-negative outer membrane composed of proteins, phospholipids, and lipopolysaccharide (LPS). However, neisserial LPS is distinguished from enteric LPS by its highly-branched basal oligosaccharide structure and the absence of repeating O-antigen subunits. For these reasons, neisserial LPS is referred to as **lipooligosaccharide** (**LOS**).

**Clinical features**:

In women, the major genitourinary symptoms of gonorrhea include the following:

* Vaginal discharge: The most common presenting symptom of gonorrhea, vaginal discharge from endocervicitis is usually described as thin, purulent, and mildly odorous; however, many patients have minimal or no symptoms from gonococcal cervicitis
* Dysuria
* Intermenstrual bleeding
* Dyspareunia (painful intercourse)
* Mild lower abdominal pain

If the infection progresses to pelvic inflammatory disease (PID), symptoms may include the following:

* Lower abdominal pain: Most consistent symptom of PID
* Increased vaginal discharge or mucopurulent urethral discharge
* Dysuria: Usually without urgency or frequency
* Cervical motion tenderness
* Adnexal tenderness (usually bilateral) or adnexal mass
* Intermenstrual bleeding
* Fever, chills, nausea, and vomiting (less common)

In males, the major genitourinary symptoms of gonorrhea include the following:

* Urethritis: The major manifestation of gonococcal infection in men; initial characteristics include burning upon urination and a serous discharge; a few days later, the discharge usually becomes more profuse, purulent, and, at times, tinged with blood
* Acute epididymitis: Usually unilateral and often occurs in conjunction with a urethral exudate
* Urethral strictures: Have become uncommon in the antibiotic era, but they can present with a decreased and abnormal urine stream, as well as with the secondary complications of prostatitis and cystitis
* Rectal infection: May present with pain, pruritus, discharge, or tenesmus

In males and females, the classic presentation of disseminated gonococcal infection (DGI) is an arthritis-dermatitis syndrome. Joint or tendon pain is the most common presenting complaint in the early stage of infection. The second stage of DGI is characterized by septic arthritis. The knee is the most common site of purulent gonococcal arthritis.

In neonates, in whom bilateral conjunctivitis (ophthalmia neonatorum) often follows vaginal delivery from an untreated mother with a gonococcal infection, symptoms of gonococcal conjunctivitis include the following:

* Eye pain
* Redness
* Purulent discharge

**Pathogenesis:**  
Gonorrhea in adults is almost invariably transmitted by sexual intercourse. The bacteria adhere to columnar epithelial cells, penetrate them, and multiply on the basement membrane. Many factors influence the manner in which gonococci mediate their virulence and pathogenicity. Pili help in attachment of gonococci to mucosal surfaces and contribute to resistance by preventing ingestion and destruction by neutrophils. Opacity-associated (Opa) proteins increase adherence between gonococci and phagocytes, promote invasion into host cells, and possibly down-regulate the immune response. So adherence is mediated through **pili** and **opa** (**P.II**) proteins, then bacteria enter the epithelial cells by a process called **parasite-directed endocytosis**. During endocytosis the membrane of the mucosal cell retracts and pinches off a membrane-bound vacuole (phagosome) that contains the bacteria. The vacuole is transported to the base of the cell, where the bacteria are released by exocytosis into the sub epithelial tissue. The neisseriae are not destroyed within the endocytic vacuole, but it is not clear whether they actually replicate in the vacuoles as intracellular parasites.

**Porin channels (porA, porB)** in the outer membrane play key roles in virulence and they act as invasin that mediates penetration of a host cell. Gonococcal strains with porA may have inherent resistance to normal human serum and an increased ability to invade epithelial cells, explaining their association with bacteremia

**Rmp** (**P.III**) **reduction-modifiable protein** is an outer membrane protein found in all strains of *N. gonorrhoeae.* It does not undergo antigenic variation and is found in a complex with Por and LOS.

During infection, bacterial lipooligosaccharide (LOS) and peptidoglycan are released by autolysis of cells. Both LOS and peptidoglycan activate the host alternative complement pathway, while LOS also stimulates the production of tumor necrosis factor (TNF) that causes cell damage.

Strains of *N. gonorrhoeae* produce two distinct extracellular **IgA1 proteases** which cleave the heavy chain of the human immunoglobulin at different points within the hinge region.

**Diagnosis:**

1. Microscopy of a direct smear of the discharge stained with Gram stain reveals Gram-negative diplococci within polymorphonuclear leucocytes. The sensitivity of the microscopy is highest in urethral samples in men, reaching 90–95%, whereas for endocervical smears sensitivity drops to 30–50%. In asymptomatic patients sensitivity is extremely low (20%).
2. Culture of *N. gonorrhoeae* requires the use of agar enriched with blood or hemoglobin and several agents such as glucose, amino acids and antibiotics (colistin, vancomycin, nystatin, etc.), to suppress the growth of commensal neisseriae, and Gram-positive and Gram-negative bacteria and fungi. These selective media are **modified Thayer Martin medium**. Plates should be incubated at 35-37°C with 3-7% CO2 (capnophilic) in a moist atmosphere for 24–48 hours. Identification of the growing colonies is based on the oxidase test and carbohydrate utilization assays.
3. Oxidase test: Positive
4. Enzyme immunoassays (EIAs) can be used for quick identification of gonococcal urethritis with good sensitivity and specificity. These tests lack sensitivity and specificity when used for cervical, pharyngeal and rectal samples.
5. Nucleic acid detection methods

**Treatment**  
  
currently recommended antimicrobial agents are ceftriaxone, cefixime, ciprofloxacin. Cephalosporins remained the foundation of gonorrhea treatment in the combination therapy treats frequently co-occurring pathogens (e.g., *Chlamydia trachomatis*) and might hinder the spread of cephalosporin antimicrobial resistance. Sex partners should be referred and treated.

***Neisseria meningitides***

***Neisseria meningitidis***, often referred to as **meningococcus**, is a [gram negative bacterium](https://en.wikipedia.org/wiki/Gram-negative_bacteria) that can cause [meningitis](https://en.wikipedia.org/wiki/Meningitis) and other forms of [meningococcal disease](https://en.wikipedia.org/wiki/Meningococcal_disease) such as [meningococcemia](https://en.wikipedia.org/wiki/Meningococcal_disease#Meningococcemia), a life-threatening [sepsis](https://en.wikipedia.org/wiki/Sepsis). About 10% of adults are carriers of the bacteria in their [nasopharynx](https://en.wikipedia.org/wiki/Nasopharynx).

As an exclusively human pathogen it is the main cause of bacterial meningitis in children and young adults, causing developmental impairment and death in about 10% of cases. Disease-causing strains are classified according to the [antigenic](https://en.wikipedia.org/wiki/Antigen) structure of their [polysaccharide](https://en.wikipedia.org/wiki/Polysaccharide) capsule into 12 serogroups, Among the 12 identified capsular types of *N. meningitidis*, six (A, B, C, W135, X, and Y) account for most disease cases. some of which are subdivided according to the presence of outer membrane protein and lipopolysaccharide antigens.

**Pathogenesis:**

The disease **meningitis** is caused by a number of different bacteria and viruses. Bacterial causes include *Haemophilus influenzae , E. coli, Streptococcus pneumonia, Streptococcus pyogenes, Staphylococcus aureus,* and *Neisseria meningitidis.* Although a variety of cocci cause meningitis, the term ***meningococcus*** is reserved for the Gram-negative, bean-shaped diplococcus, *Neisseria meningitidis.* Like its relative *N. gonorrhoeae,* the organism tends to occur intracellularly in the cytoplasm of neutrophils which are attracted to the site of inflammation in the mininges, so this type of infection is called pyogenic (pus-forming).

[**Lipopolysaccharide**](https://en.wikipedia.org/wiki/Lipopolysaccharide) (LPS) is a component of the [outer membrane](https://en.wikipedia.org/wiki/Bacterial_outer_membrane) of *N. meningitidis*. This acts as an [endotoxin](https://en.wikipedia.org/wiki/Endotoxin) and is responsible for [septic shock](https://en.wikipedia.org/wiki/Septic_shock) and hemorrhage due to the destruction of red blood cells. Other virulence factors include a polysaccharide [**capsule**](https://en.wikipedia.org/wiki/Capsule_(microbiology)) which prevents host [phagocytosis](https://en.wikipedia.org/wiki/Phagocytosis) and aids in evasion of the host immune response; [**fimbriae**](https://en.wikipedia.org/wiki/Fimbria_(bacteriology)) mediate attachment of the bacterium to the [epithelial cells](https://en.wikipedia.org/wiki/Epithelial_cells) of the nasopharynx. It infects the cell by sticking to it mainly with long thin extensions called [pili](https://en.wikipedia.org/wiki/Pilus) and the surface-exposed proteins **Opa** and Opc. Meningococci produce an **IgA protease**, an enzyme that cleaves IgA class antibodies and thus allows the bacteria to evade a subclass of the humoral immune system.

Infection occur by aspiration of infective bacteria, which attach to epithelial cells of the nasopharyngeal and oropharyngeal mucosa, cross the mucosal barrier, and enter the bloodstream. If it is not cleared bacteria may enter the central nervous system and cause meningitis.

## Clinical features :

A common outcome of meningococcal infection is meningitis. When caused by Neisseria meningitidis bacteria it is known as meningococcal meningitis. As the meninges, become infected and swell. The symptoms include sudden onset of fever, headache, and stiff neck. There are often additional symptoms, such as

* Nausea
* Vomiting
* Photophobia (increased sensitivity to light)
* Altered mental status (confusion)

The symptoms of meningococcal meningitis can appear quickly or over several days. Typically they develop within 3-7 days after exposure.

In newborns and infants, the classic symptoms of fever, headache, and neck stiffness may be absent or difficult to notice. The infant may appear to be slow or inactive, irritable, vomiting or feeding poorly. In young children, doctors may also look at the child’s reflexes, which can also be a sign of meningitis.

## Meningococcal Septicemia

Another common outcome of meningococcal infection is bloodstream infection, either septicemia or bacteremia. The more serious of the two is septicemia. When caused by Neisseria meningitidis bacteria it is known as meningococcal septicemia or meningococcemia. This is the more dangerous and deadly illness caused by Neisseria meningitidis bacteria. When someone has meningococcal septicemia, the bacteria enter the bloodstream and multiply, damaging the walls of the blood vessels and causing bleeding into the skin and organs.

Symptoms may include:

* Fever
* Fatigue
* Vomiting
* Cold hands and feet
* Chills
* Severe aches or pain in the muscles, joints, chest or abdomen
* Rapid breathing
* Diarrhea
* In the later stages, a dark purple rash

**Diagnosis**

A. Specimens include:

1. Blood for culture and smears

2. Spinal fluid for smear, culture, chemical analysis.

B. Blood smears show gram negative bean shaped diplococci.

C. Culture. The organism grows best on chocolate agar incubated at 37°C in a 5% CO2, colonies are transparent or opaque.

**Treatment**  
  
Penicillin G is the drug of choice to treat meningococcemia and meningococcal meningitis. Either chloramphenicol or a third-generation cephalosporin such as cefotaxime or ceftriaxone is used in persons allergic to penicillins.

Nowadays, rifampin is the chemoprophylactic agent of choice

