

THE GENUS

NEISSERIA

Neisseriae are gramnegative cocci arranged in pairs, so they are diplococci.

- This genus includes two species pathogenic for humans:
 - *N. gonorrhoeae* (s.c. gonococci)
 - *N. meningitidis* (s.c. meningococci)
- Other species (*N. lactamica*, *N. sicca*, *N. subflava*, *N. flavescens*) are normal inhabitants of the human upper respiratory tract (oropharyngeal area) as commensals. They are of importance only for the differential diagnosis.

Neisseria meningitidis

morphology

- Meningococci are typical diplococci.
- They have a coffee berry appearance.
- Meningococci are nonmotile and non-sporeforming.
- They have polysaccharide capsules and fimbriae on their surfaces.

Neisseria meningitidis

physiology

- Meningococci require aerobic atmosphere with 5-10% of carbon dioxide, sufficiently moist agar medium with blood (chocolate agar).
- Colonies are grey, semitransparent, slightly convex, 1 mm in diameter and they remain drops of dew. They are nonpigmented and nonhemolytic.
- Meningococci produce catalase and oxidase. They ferment glucose and maltose (but not lactose and saccharose) without gas production.
- Meningococci can produce two special proteases which split the heavy chains of secretory IgA molecules on mucous membranes.

Neisseria meningitidis

antigenic structure

- Meningococci are divided into nine antigenic groups according to capsule polysaccharides (A,B,C,D,X,Y,Z, 29A and 135 W). H, I, J, K and L groups have been described, but they do not cause a disease.
- Some meningococcal strains remain untypeable.
- Sporadic cases of a disease have been caused by group B meningococci, mainly in children under the age of 4 years. Outbreaks of epidemic diseases are due mainly to group A and C meningococci.
- Endotoxin is also present in the outer membrane.

Neisseria meningitidis pathogenity

- The meningococci are exclusively human pathogens.
- They can either exist as an apparently harmless member of normal microflora or can cause acute disease.

Meningococci can cause:

- Inflammations of nasopharyngeal mucous membranes (from nasopharyngitis to purulent rhinitis).
- Septicemia without meningitis (meningococci penetrate into the blood stream in a relatively small number of patients).
- Meningococcal pneumonia, myocarditis, arthritis.
- Meningitis.

Meningococcal disease pathogenesis

- Microorganism colonizes nasopharynx.
- In some persons microorganism invades bloodstream and causes infection at distant site.

Meningococcal disease clinical features

- Incubation period 3-4 days (range 2-10 days).
- Abrupt onset of fever, meningeal symptoms, hypotension, and rash.
- Fatality rate 9%-12%; up to 40% in meningococemia.

Meningococcal meningitis

- Most common pathologic presentation.
- Result of hematogenous dissemination.
- Clinical findings:
 - fever,
 - headache,
 - stiff neck.

Meningococccemia

- Bloodstream infection.
- May occur with or without meningitis.
- Clinical findings:
 - fever,
 - petechial/purpuric rash,
 - hypotension,
 - multiorgan failure.

Neisseria meningitidis epidemiology

- Source:
 - only a human (healthy or sick)
- Spreading:
 - transmission of meningococci is facilitated by respiratory droplets and requires closed and prolonged contact with carriers
- Site of entrance:
 - upper respiratory tract
 - the frequency of meningococcal carriage in healthy population is varying about 10% during nonepidemic period
- Meningococcal meningitis is a worldwide problem.

Neisseria meningitidis diagnosis

- clinical symptoms
- examination of liquor after lumbar puncture or examination of other specimens (Gram staining, cultivation)
- serological examination (e.g. latex agglutination)

Neisseria meningitidis

treatment

- **Prophylaxis:**

- it is given to groups at risk of infection (oral penicillins)
- treatment with penicillin does not eradicate carrier state in all patients, a single 500 mg dose of ciprofloxacin can be effective

- **Therapy:**

- penicillin G is the drug of choice
300 000 IU/kg/day q4h, usually 4x4-5 ml IU
- 3rd generation cephalosporins:
 - ceftriaxone 100 mg/kg/day in 1-2 doses
 - cefotaxime 200-300 mg/kg/day in 3 doses
 - ceftazidime 150 mg/kg/day in 3 doses
- chloramphenicol 100 mg/kg/day in 3 doses

Prevention of meningococcal disease

Polyvalent vaccine containing serogroups A, C, Y, and W135 is effective in people older than 2 years of age for immunoprophylaxis.

Neisseria gonorrhoeae

- *Neisseria gonorrhoeae* has same morphological and cultural characters as *N. meningitidis*.
- Gramnegative oval cocci occurring in pairs with the apposed surfaces flat or even slightly concave (bean shaped).

- *N. gonorrhoeae* is the cause of the sexually transmitted disease gonorrhoea.
- This commonly presents as a purulent infection of the mucous membrane of the urethra and also the cervix uteri in the female.
- There may be rectal or pharyngeal infection and secondary local and metastatic complications, e.g. epididymitis, salpingitis and arthritis, may occur if the primary infection is not promptly treated.

- In the newborn children the gonococci may give rise to a purulent conjunctivitis (ophthalmia neonatorum) and in young girls a vulvovaginitis.
- Disseminated gonococcal infection, which is recognized by a rash and evidence of blood spread, may also occur, more commonly in women.

- *N. gonorrhoeae* is exclusively a human pathogen.
- It is never found as a normal commensal although a proportion of those infected, particularly women, may remain asymptomatic. These individuals, may develop systemic or ascending infection at a later stage.

- The commonest clinical presentation of the disease is acute urethritis a few days after unprotected vaginal or anal sexual intercourse.
- Asymptomatic infection is rare in the active man.
- In women with vaginal infection, only half may have symptoms of discharge and dysuria. Asymptomatic carriage in women is common, especially in the endocervical canal.
- *N. gonorrhoeae* can also cause tonsillopharyngitis (but very rare).

Gonorrhoea

<u>Females</u>	<u>Males</u>
50% risk of infection after single exposure	20% risk of infection after single exposure
Asymptomatic infections frequently not diagnosed	Most initially symptomatic (95% acute)
Major reservoir is asymptomatic carriage in females	Major reservoir is asymptomatic carriage in females
Genital infection primary site is cervix (cervicitis), but vagina, urethra, rectum can be colonized	Genital infection generally restricted to urethra (urethritis) with purulent discharge and dysuria
Ascending infections in 10-20% including salpingitis, tubo-ovarian abscesses, pelvic inflammatory disease (PID), chronic infections can lead to sterility	Rare complications may include epididymitis, prostatitis, and periurethral abscesses
Disseminated infections more common, including septicemia, infection of skin and joints (1-3%)	Disseminated infections are very rare
Can infect infant at delivery (conjunctivitis, ophthalmia neonatorum)	More common in homosexual/bisexual men than in heterosexual population

Neisseria gonorrhoeae diagnosis

- clinical symptoms
- Gram staining
- cultivation and biochemical tests

Neisseria gonorrhoeae treatment

- tetracyclines (doxycycline)
- fluoroquinolones (ciprofloxacin, ofloxacin, levofloxacin)
- spectinomycin
- 3rd generation cephalosporins
 - e.g. ceftriaxone, cefotaxime
- others

Neisseria gonorrhoeae treatment

- Uncomplicated infections of urethra, cervix and rectum
 - cefixime 400 mg p.os
 - ciprofloxacin 500 mg p.os
 - ofloxacin 400 mg p.os
 - levofloxacin 250 mg p.os
 - if chlamydia not ruled out – add azithromycin 1g p.os, clarithromycin 2x250-500 mg p.os 7 days or doxycyclin 2x100 mg p.os 7 days
 - fluoroquinolone resistance is increasing