

# Genito-Urinary System

## *GONORRHEA*

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## *NEISSERIA GONORRHOEAE*

- *N. gonorrhoeae* are Gram-negative cocci that typically appear in pairs (diplococci) with the opposing sides flattened, imparting a “kidney bean” appearance. They are nonmotile, non-spore forming, and non- acid fast.
- *N. gonorrhoeae* grow well only on chocolate agar and on specialized medium enriched to ensure its growth. It requires carbon dioxide supplementation.
- Small, smooth, non-pigmented colonies appear after 18 to 24 hours and are well developed (2 to 4 mm) after 48 hours. They are oxidase positive.
- Gonococci possess numerous pili that extend through and beyond the outer membrane. In general, only fresh virulent isolates have pili.

## GONORRHEA

- It is primarily localized to mucosal surfaces with relatively infrequent spread to the blood stream or deep tissues. Infection is sexually acquired, the primary manifestation is pain and purulent discharge at the infected site.
- In men, this is typically the urethra, and in women, the uterine cervix. Direct extension up the fallopian tubes produces fever and lower abdominal pain, a syndrome called **pelvic inflammatory disease** (PID). For women, sterility or ectopic pregnancy can be long-term consequences of gonorrhoea.

## EPIDEMIOLOGY

- The overall incidence is now 130 cases per 100,000 population, but the rates for adolescents are alarmingly high and increasing by 10% a year. The highest rates are in women between the ages of 15 and 19 years and men between the ages of 20 and 24 years.
- The major reservoir for continued spread of gonorrhea is the asymptomatic patient.
- Almost 50% of infected women are asymptomatic and most men (95%) have acute symptoms with infection.

# PATHOGENESIS

## Attachment and Invasion

- Gonococci are not normal inhabitants of the respiratory or genital flora. When introduced onto a mucosal surface, adherence ligands such as pili and Opa (Opacity) proteins, allow initial attachment of the bacteria to receptors (CD46, CD66) on non-ciliated epithelial cells (urethral and vaginal epithelium). Following attachment, gonococci invade epithelial cells.
- Once inside, the bacteria transcytose the cell and exit through the basal membrane to enter the submucosa.

## Survival in the Submucosa

- Once in the submucosa, the bacteria must survive and resist innate host defenses as well as defenses that may have been acquired from previous infection.
- Receptors on the gonococcal surface enable the organisms to scavenge iron needed for growth from the human iron transport proteins transferrin and lactoferrin.
- Some antibodies to OMPs have blocking effect on bactericidal activity.
- Phagocytosed gonococci resist killing.

## Spread and Dissemination

- *N. gonorrhoeae* bacteria tend to remain localized to genital structures, causing inflammation and local injury.
- Local spread is to epididymis and fallopian tubes. Peptidoglycan shedding causes local injury.
- Reflux during menses may facilitate spread (disseminated gonococcal infection and salpingitis).

## IMMUNITY

- The apparent lack of immunity to gonococcal infection has long been a mystery.
- Both serum and secretory antibodies are generated during natural infection but the levels are generally low, even after repeated infections.
- Gonococcus varies multiple structures to avoid immune surveillance.

## CLINICAL ASPECTS

### MANIFESTATIONS

- **Genital Gonorrhoea**
- In men, the primary site of infection is the **urethra**. Symptoms begin 2 to 7 days after infection and consist primarily of purulent urethral discharge and dysuria. Although uncommon, local extension can lead to epididymitis or prostatitis.
- The **endocervix** is the primary site in women. Symptoms include increased vaginal discharge, urinary frequency, dysuria, abdominal pain, and menstrual abnormalities.

## Other Local Infections

- Rectal and pharyngeal infections relate to sexual practices. These conditions are generally asymptomatic.
- Infection of other structures near primary infection sites, such as Bartholin's glands in women, may lead to abscess formation.
- Severe, acute, purulent conjunctivitis. It may occur at any age, the most serious form is **gonococcal ophthalmia neonatorum**, acquired by a newborn from an infected mother. It can be prevented by the use of prophylactic topical (silver nitrate, erythromycin., tetracycline) at birth.

## Pelvic Inflammatory Disease (PID)

- The clinical syndrome develops in 10% to 20% of women with gonorrhea. The findings include fever, lower abdominal pain, adnexal tenderness, and leukocytosis with or without signs of local infection.
- Organisms causing PID include **anaerobes** and *Chlamydia trachomatis*, which may appear alone or mixed with **gonococci**.
- **Salpingitis** and **pelvic peritonitis** cause scarring and infertility.
- The most serious complications of PID are **infertility** and **ectopic pregnancy**.

## Disseminated Gonococcal Infection (DGI)

- Any of the local forms of gonorrhoea or PID may lead to bacteremia.
- In the bacteremic phase, primary features are **fever**; **migratory polyarthralgia**; and a petechial, maculopapular, or pustular **rash**.
- The bacteremia may lead to metastatic infections such as endocarditis and meningitis, but the most common is **purulent arthritis** which involves large joints such as elbows and knees.
- Gonococci are readily cultured from the pus.

## DIAGNOSIS

### Gram Smear

- The presence of **multiple pairs of bean-shaped, Gram-negative diplococci** within a **neutrophil** is highly characteristic of gonorrhea when the smear is from a genital site.
- The direct Gram smear is more than 95% sensitive and specific in symptomatic men. It is only 50 to 70% sensitive in women.
- Gram smear should not be used as the sole source for diagnosis when the findings are unexpected or have **social** (divorce) or **legal** (rape, child abuse) implications.



## Culture

- In men, the best specimen is urethral exudate or urethral scrapings (obtained with a loop or special swab).
- In women, cervical swabs are preferred over urethral or vaginal specimens.
- Transport media required unless plating is immediate.
- The most common medium is **Martin–Lewis agar**, an enriched selective chocolate agar.
- Isolates are identified by fermentation or immunoassay.

## Direct Detection

- Immunoassay and nucleic acid hybridization methods that detect gonococci in clinical specimens without culture. Such methods could have particular importance for screening populations where culture is impractical. Of these only the DNA amplification methods have the sensitivity to substitute for culture.

## Serology

- Attempts to develop a serologic test for gonorrhoea have not yet achieved the needed sensitivity and specificity.

## TREATMENT

- Penicillin is no longer used, because of the development of resistance.
- Because of their resistance to  $\beta$ -lactamases, shift in treatment of genital gonorrhoea to third-generation cephalosporins has been used as single dose treatment either intramuscularly (**ceftriaxone**) or orally (**cefixime**).
- Other agents recommended for primary treatment include fluoroquinolones (**ciprofloxacin** or **ofloxacin**) and **azithromycin**. **Doxycycline** is also effective but must be given orally for 7 days.

## PREVENTION

- Methods to block direct mucosal contact (**condoms**) or inhibit the gonococcus (**vaginal foams, douches**) provide protection.
- The classic public health methods of case –contact tracing and treatment are important but difficult due to the size of the infected population.
- The availability of a good serologic test would greatly aid control, as it has for syphilis.
- The development of a gonococcal vaccine awaits further understanding of immunity and its relationship to the shifting target.