



Urogenital Tract Module

2022-2023

Gonorrhea

(Lecture 5)

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Learning Objectives

You should know the:

Epidemiology of gonorrhoea

Pathogenesis of gonorrhoea

Clinical manifestations of gonorrhoea

Diagnosis of gonorrhoea

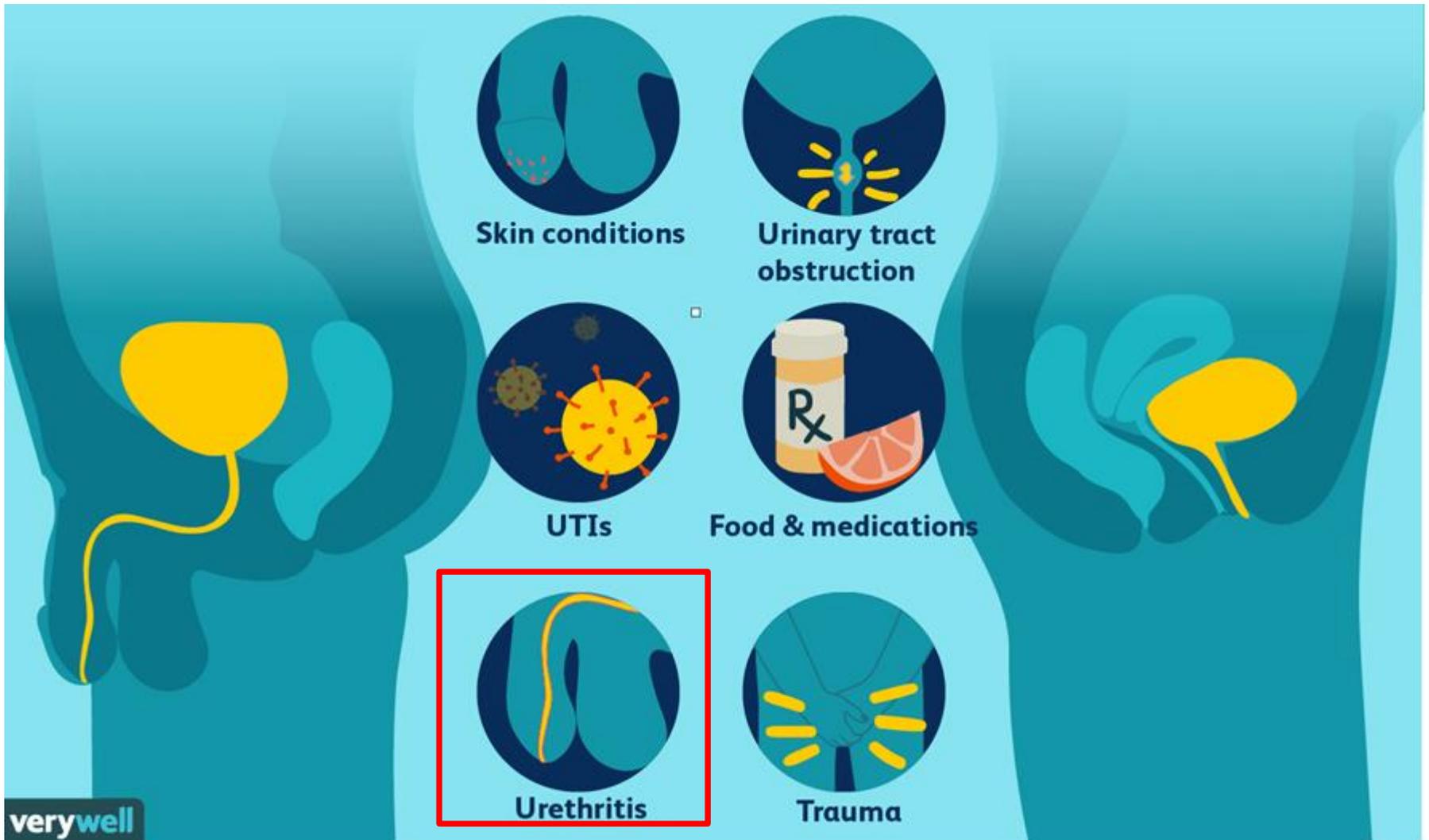
Prevention of gonorrhoea



Top ten Sexually Transmitted Diseases (STDs)

Organism	Disease
Papillomaviruses (types 6 and 11 associated with visible genital warts)	Genital warts, dysplasias
<i>Chlamydia trachomatis</i> (D-K serotypes)	Non-specific urethritis
<i>C. trachomatis</i> (L1, L2, L3 serotypes)	Lymphogranuloma venereum
<i>Candida albicans</i>	Vaginal thrush, balanitis
<i>Trichomonas vaginalis</i>	Vaginitis, urethritis
Herpes simplex virus types 1 and 2	Genital herpes
<i>Neisseria gonorrhoeae</i>	Gonorrhea
HIV	AIDS
<i>Treponema pallidum</i>	Syphilis
Hepatitis B virus	Hepatitis
<i>Haemophilus ducreyi</i>	Chancroid

What causes urethral pain



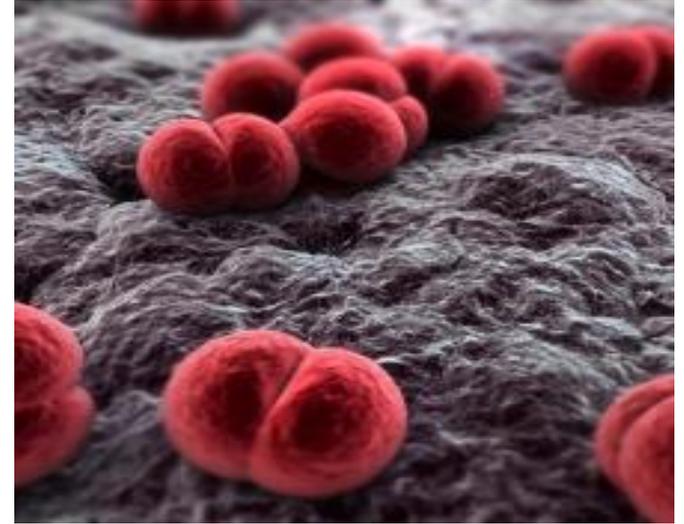
(Urethritis - Causes of urethral discharge)

Physiological	Spermatorrhoea/prostatorrhoea Stimulation
Pathological	<u>Common causes</u> Neisseria gonorrhoeae C. trachomatis Mycoplasma genitalium
	<u>Other causes</u> Trichomonas vaginalis Candida albicans Secondary to intraurethral lesions (Syphilis, herpes, warts) Physical or chemical traumas Foreign body Allergy

General characteristics

Neisseria gonorrhoeae

- Gram negative cocci
- Present in pairs
(the opposing sides are flattened)
- Non-spore forming
- Piliated
- Nonencapsulated
- Nonmotile
- Does not survive in the environment
(must be transmitted through contact)

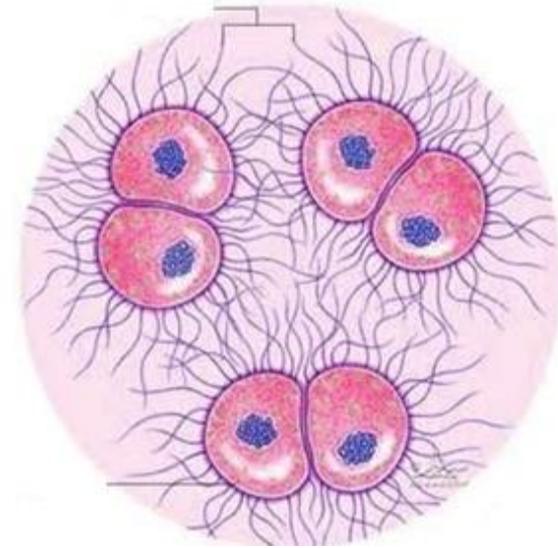


Coffee beans



Virulence factors

1. Pili & Lipooligosaccharides: attachment to and antiphagocytic (nonpiliated strains are a virulent)
3. Outer membrane proteins
 - ✓ Porin A: prevents phagosome lysosome fusion
 - ✓ Opa protein: mediates firm attachment
4. IgA protease: hydrolyzes secretory IgA
(secretory IgA block bacterial attachment to the mucosa)



Epidemiology

- No real estimations for gonorrhoeae in communities
- In Jordan (January 2003 to August 2005)
 - 0.9% (among symptomatic women)
 - 2.2% (among asymptomatic women)

Risk Factors

- Multiple sex partners
- Inconsistent use of barrier methods
- Residence in areas with disease prevalence
- Adolescents (20-25 years)
- Lower socio-economic status

Epidemiology

Transmission

- A symptomatic patients are the major source of infections (infectious for several months)
- Greater efficiency of transmission from male to female
 - Male to female: 50 – 90%
 - Female to male: 20 – 80%
- Rectal oral transmission
- Perinatal transmission (mother to infant)

Pathogenesis

1. Attachment:

Attachment is mediated by Pili, Opa, and LOS

2. Invasion:

Opa & protein 1A mediate the gonococci uptake by the epithelial cells

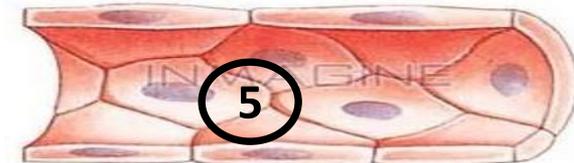
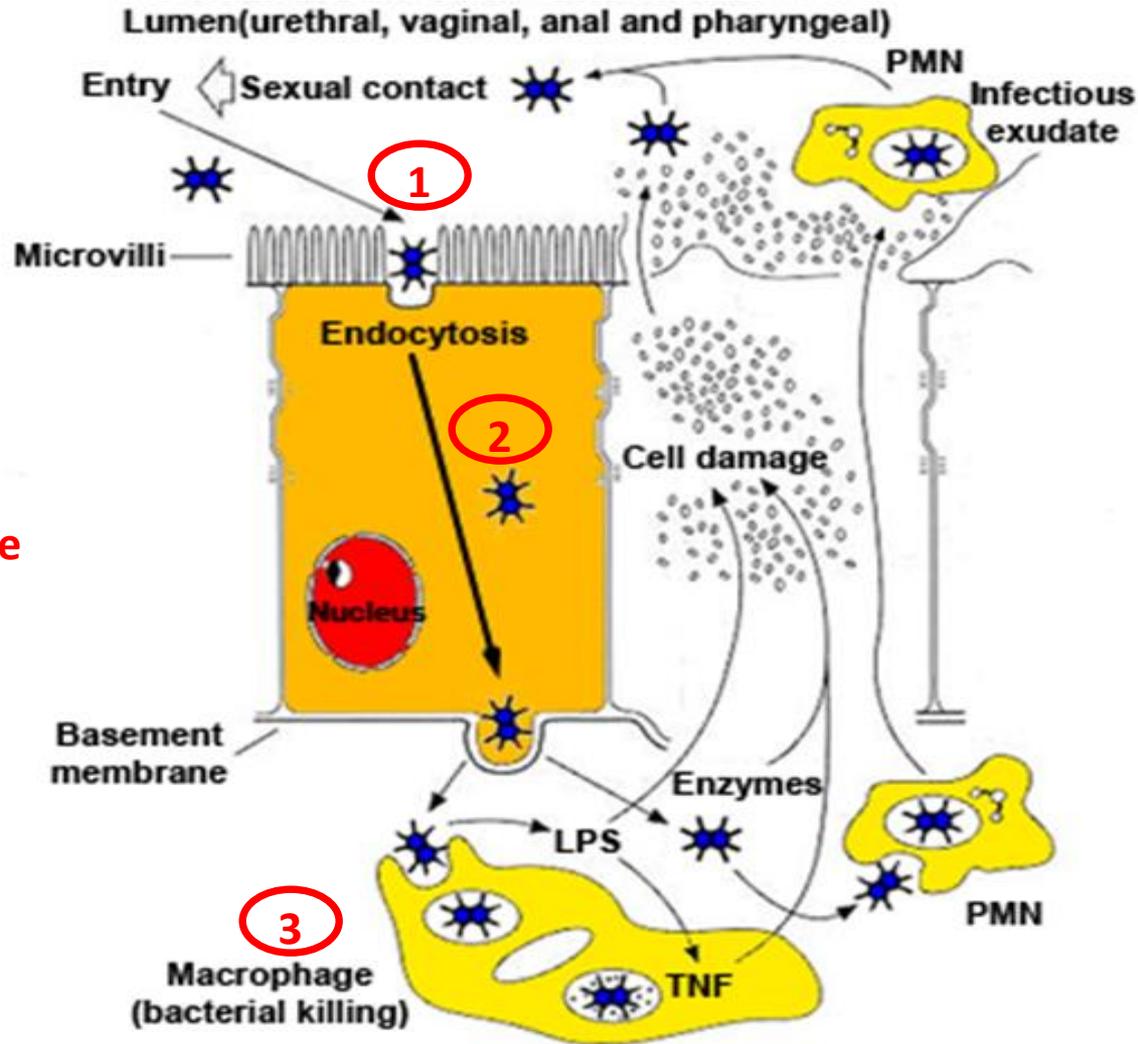
3. Immune response with local tissue injury

4. Spread

Local spread is to epididymis and fallopian tubes

5. Dissemination

In a small proportion of infections, organisms reach the bloodstream to produce disseminated Gonococcal infection (DGI).



Clinical manifestations

Levels of Gonococcal infection

Systemic infections

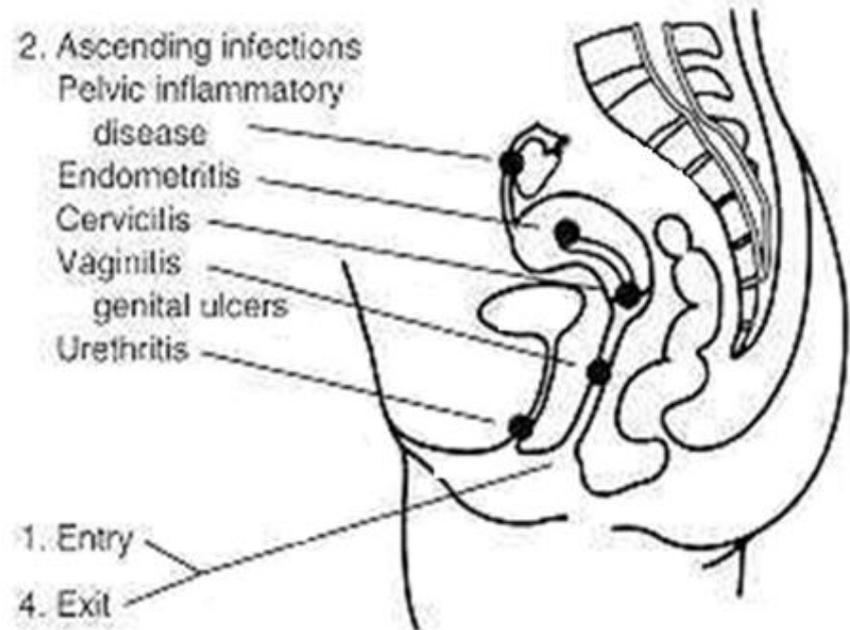
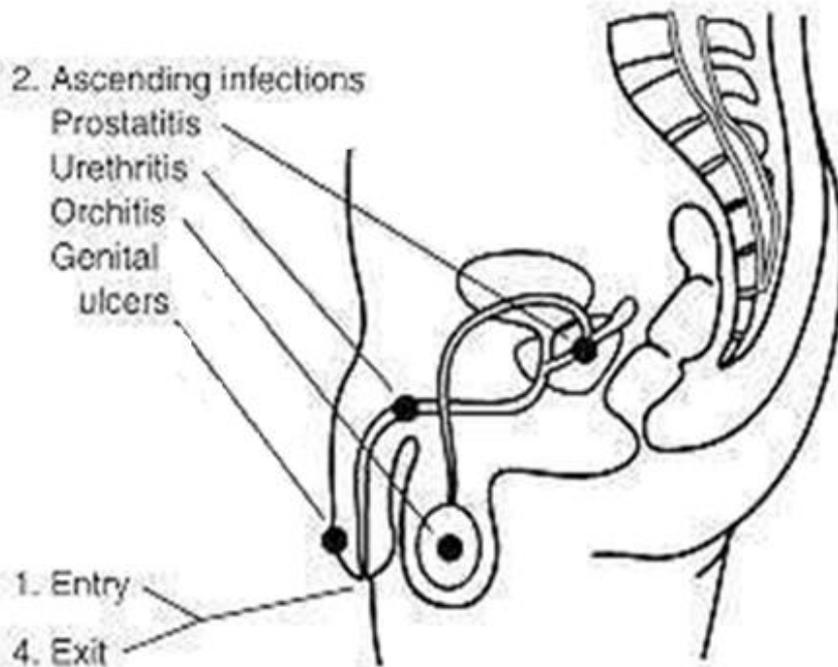
Pelvic inflammatory disease

Genital infections

Clinical manifestations

Male

Female



Clinical manifestations

1. Genital Infection

In men:

a- Urethritis

- 2-7 days incubation period
- Symptoms
 - frequency, urgency, dysuria
 - purulent urethral discharge
 - blood in the semen or urine
- Asymptomatic in 10% of cases
- Male seeks treatment early preventing serious complications, but not soon enough to prevent transmission to other sex partners

b. Epididymitis

- Signs and symptoms
 - abdominal or lower back pain
 - fever, nausea
 - testicular pain and swelling
 - discharge from the urethra
 - pain on urination, occasionally blood in the urine

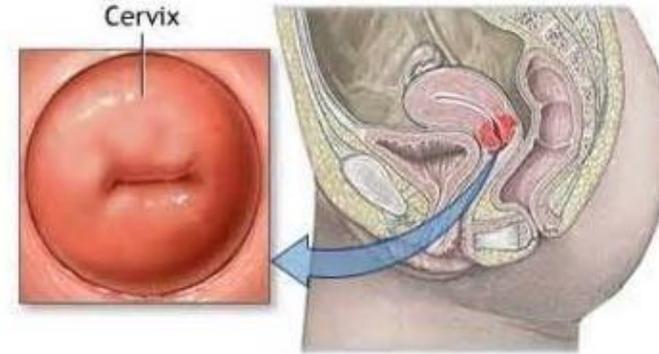
Clinical manifestations

1. Genital Infections

In women → Most infections are asymptomatic

a. Cervicitis

- Endocervix is the primary infection site
- Symptoms:
 - mucopurulent abnormal vaginal discharge
 - intermenstrual bleeding
 - dysuria
 - lower abdominal pain
- 50% of women are asymptomatic
- Incubation period unclear, but symptoms may occur within **10 days of infection**
- 40%-60% of women with cervical gonococcal infection may have urethral infection



Clinical manifestations

1. Genital Infections

In women

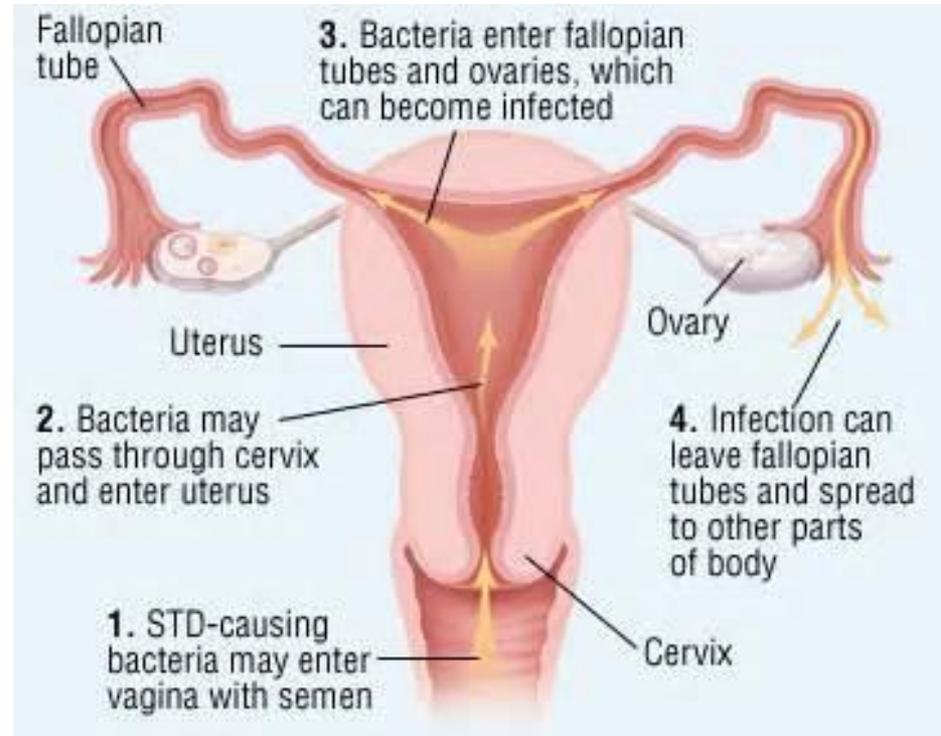
b. Urethritis

- Inflammation of the urethra
- Symptoms
 - frequency, urgency, dysuria
 - Pain during sex
 - Discharge from the urethral opening or vagina

Clinical manifestations

2. Pelvic Inflammatory Disease (PID)

- Is a term for inflammation of the uterus, fallopian tubes, and/or ovaries
- causes severe lower abdominal pain, especially during intercourse.
- PID infection **itself may be cured** but effects of the infection may be **permanent** (due to scarring inside the reproductive organs, which can later cause serious complications, including chronic pelvic pain, infertility, ectopic pregnancy)
- infection can **spread to the peritoneal cavity** causing inflammation
- Infection in the abdomen may **concentrate around the liver** (perihepatitis)



Clinical manifestations

Syndromes in Men and Women

- Anorectal infection
- Pharyngeal infection
- Conjunctivitis
- Disseminated gonococcal infection (DGI)

Clinical manifestations

Conjunctivitis

- Babies born to infected women may suffer conjunctival infection called **ophthalmia neonatorum (neonatal conjunctivitis)**
- A severe purulent eye discharge with peri-orbital oedema occurs within a few days of birth.
- If untreated, ophthalmia leads rapidly to blindness.
- It may be prevented in areas of high prevalence by the instillation of 1% aqueous silver nitrate in the eyes of newborn babies.
- Alternatively, topical erythromycin can be used; this has the advantage of being active against chlamydia and less toxic
- May occur at any age



Clinical manifestations

Disseminated gonococcal infection (DGI)

Manifestations :

- Occurs in < 5% of GC-infected patients
- More common in females
- Patients with congenital deficiency of C7, C8, C9 are at high risk

Clinically

- Dermatitis-arthritis syndrome
 - Arthritis 90% (Characterized by fever, chills, skin lesions, arthralgias, tenosynovitis)
 - Skin rash characterized as macular or papular, pustular, hemorrhagic or necrotic, mostly on distal extremities
- **Rarely**, disseminated gonococcal infection may present as **endocarditis** or **meningitis**.

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

Diagnosis

Type of specimens

- ✓ Discharge swab tests
- ✓ Urine tests
- ✓ Cervix swab test
- ✓ Throat swab

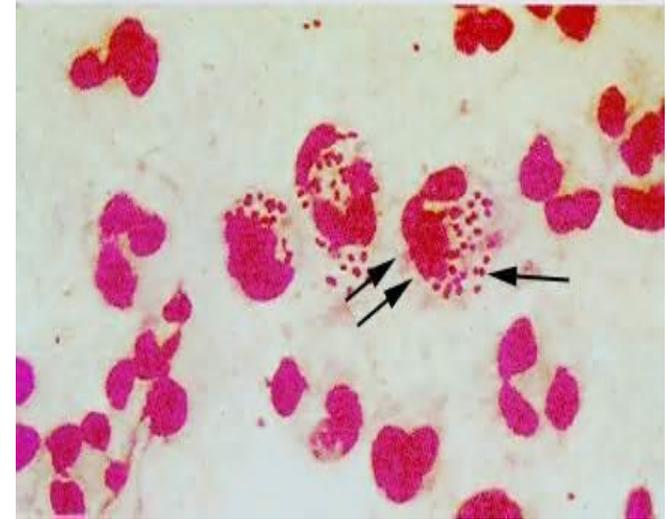
Methods of diagnosis

1. Staining
2. Culture
3. Direct detection

Diagnosis

1. Staining

- The presence of multiple pairs of bean-shaped, Gram-negative diplococci within a neutrophil is diagnostic specially in men
- Sensitivity & specificity
 - Symptomatic males: >92%.
 - Asymptomatic males and females: 40–50% (due to reduced bacterial load)
- it 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.



Diagnosis

2. Culture

In men

- the best specimen is urethral **exudate** or **urethral scrapings** (obtained with a loop or special swab).

In women

- **Cervical, urethral, or vaginal swabs**
- Swabs may be streaked directly (delay not more than 4 hours).
- The most common medium is **Martin–Lewis agar**, an enriched selective chocolate agar. Contains antibiotics active against Gram-positive and negative bacteria at concentrations that do not inhibit *N. gonorrhoeae*.
- They may be identified as *Neisseria* by demonstration of typical Gram stain morphology and a positive oxidase test.

Diagnosis

3. Direct detection

DNA amplification methods that detecting gonococci in clinical specimens without culture

Vaccine

No vaccine, why?

- Given vaccination is meant to mimic natural infection to induce similar immune responses, this is problematic.
- The humoral [i.e., antibody] response to *N. gonorrhoeae* is complicated” and little is known about T cell immunity to *N. gonorrhoeae*.

Case study

History

- **Robert 33-year-old** who presents to his doctor reporting **a purulent urethral discharge and dysuria for 3 days**
- New female sex partner for 2 months (**the last intercourse being 3 days ago**).
- Also had a **one-time** sexual encounter with a woman he **met 3 weeks ago**.
- No history of urethral discharge or STDs, no ulcers or rectal discomfort. Negative HIV test 1 year ago.

Case study

Physical Exam

- Normal vital signs
- Chest, heart, musculoskeletal, and abdominal exams within normal limits
- No flank pain, normal rectal exam, no ulcers or rashes
- The genital exam reveals a reddened urethral meatus with a purulent discharge, without lesions or lymphadenopathy.

Questions

1. Which laboratory tests are appropriate to order or perform?
2. What should be included in the differential diagnosis?
3. What is the appropriate treatment regimen?

Case study

Results of laboratory tests:

- **Gram stain:** Gram-negative diplococcus associated with neutrophils
- Urethral culture: showed growth of a Gram-negative diplococcus that was oxidase-positive. Biochemical and FA conjugate testing confirmed this isolate to be *N. gonorrhoeae*.

differential diagnosis:

- PCR for *Chlamydia*: negative
 - RPR: nonreactive
 - HIV antibody test: negative
- 4) What is the diagnosis based on all available information?

Case study

Follow-up

- Notify all sexual partners to be tested for infection. They should be treated or tested so the infection is not passed back and forth.
- Patients should be tested 72 hours after they finish all the antibiotics
- Avoid sexual intercourse until therapy is completed and both partners no longer have symptoms
- Get tested for other sexually transmitted diseases, especially Chlamydia and human immunodeficiency virus (HIV).

Treatment

- Treat both sides of the relation and contacts
- Strains of *N. gonorrhoeae* that are completely resistant to penicillins are now common throughout the world, although the prevalence varies from country to country.
- Ceftriaxone or cefixime are recommended as first-line therapy, but these drugs are expensive and may not be affordable in developing countries.
- Alternatives to cephalosporins and penicillin include fluoroquinolones (e.g. ciprofloxacin), azithromycin, tetracyclines, co-amoxiclav
- Single-dose therapy appears adequate for uncomplicated cases of acute genital gonorrhoea in men and women.
- Cefixime + Doxycycline or azithromycin to cover for Chlamydia
- In disseminated gonococcal disease and any complicated infection, treatment for 7-10 days is necessary.