Gonorrhea

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Introduction

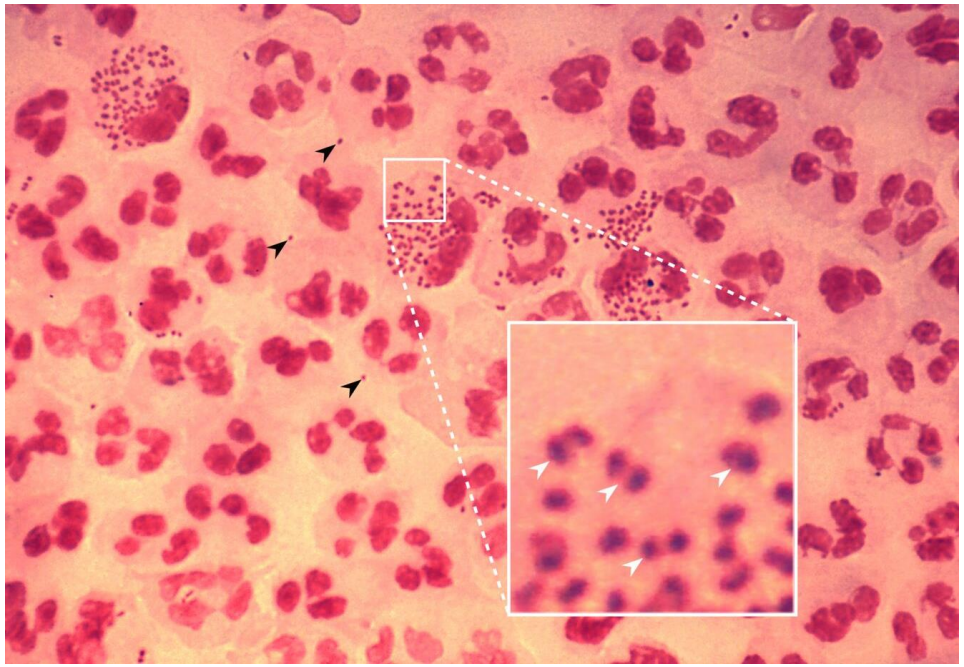
- **Definition:** Sexually transmitted infection caused by *Neisseria gonorrhoeae*
- **Significance:** Second most commonly reported infectious disease in the US after Chlamydia
- **Global Impact:** Approximately 87 million new infections worldwide annually (820,000 cases per year in the US)

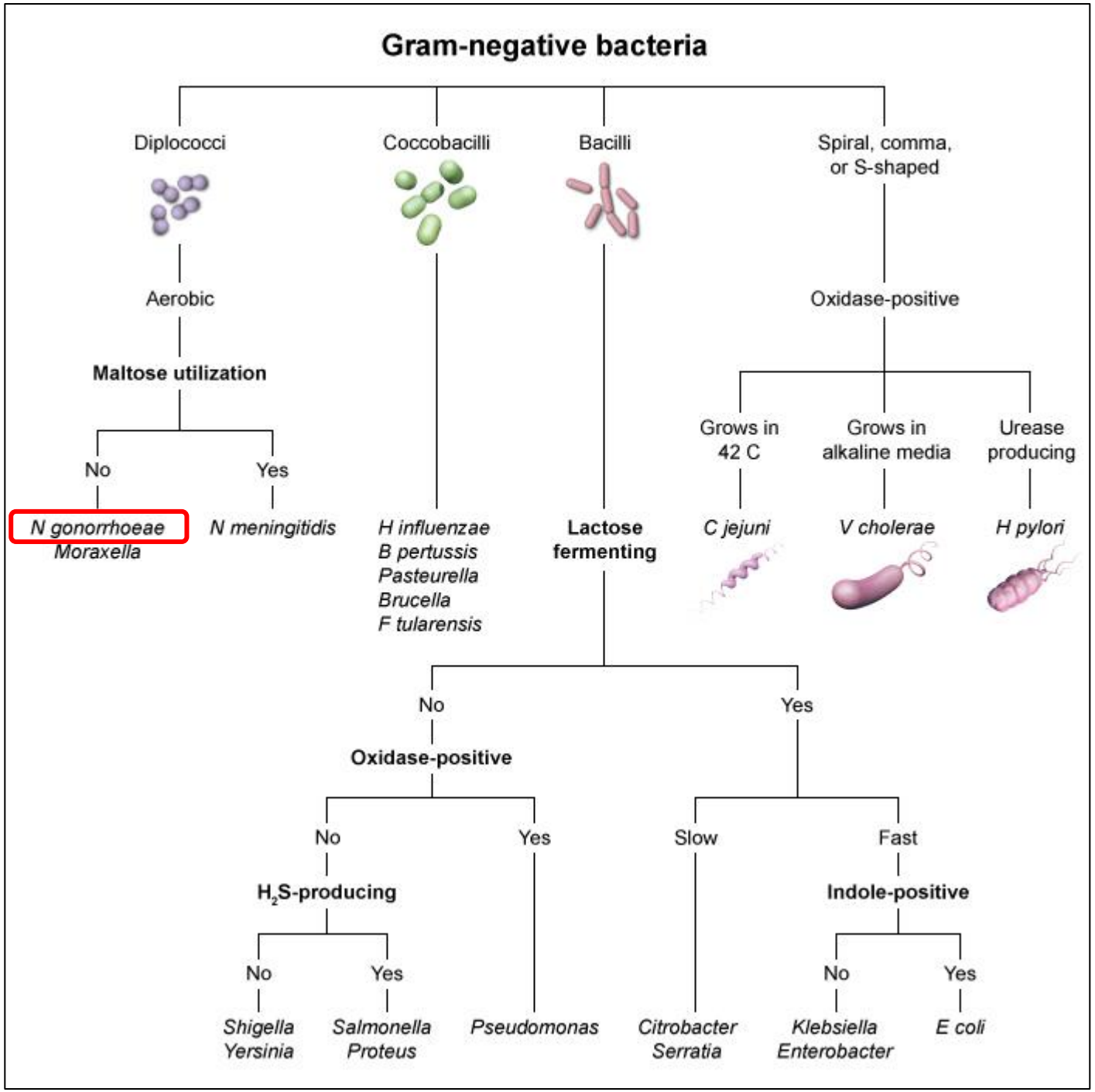
Epidemiology

- **Incidence:** ~820,000 cases per year in the US
- **Age Distribution:** Primarily 15-24 years of age
- **Risk Groups:**
  - Men who have sex with men (MSM)
  - Individuals with low socioeconomic status
  - Persons with multiple sexual partners
- **Trends:** Increasing antibiotic resistance globally
- Gonorrhea is commonly asymptomatic, especially in females, which increases the risk of spread and complications

Etiology and Pathogenesis

- **Pathogen:** *Neisseria gonorrhoeae* (gonococcus)
  - Gram-negative, intracellular, aerobic diplococci
  - Non-spore forming, non-motile
  - Oxidase positive
- **Virulence Factors:**
  - Pili: Attachment to mucosal epithelium
  - Opa proteins: Invasion of epithelial cells
  - IgA protease: Breaks down secretory IgA
  - Porin protein: Mediate host cell invasion
  - Lipooligosaccharide (LOS): Endotoxic activity
- **Incubation Period:** 2-8 days



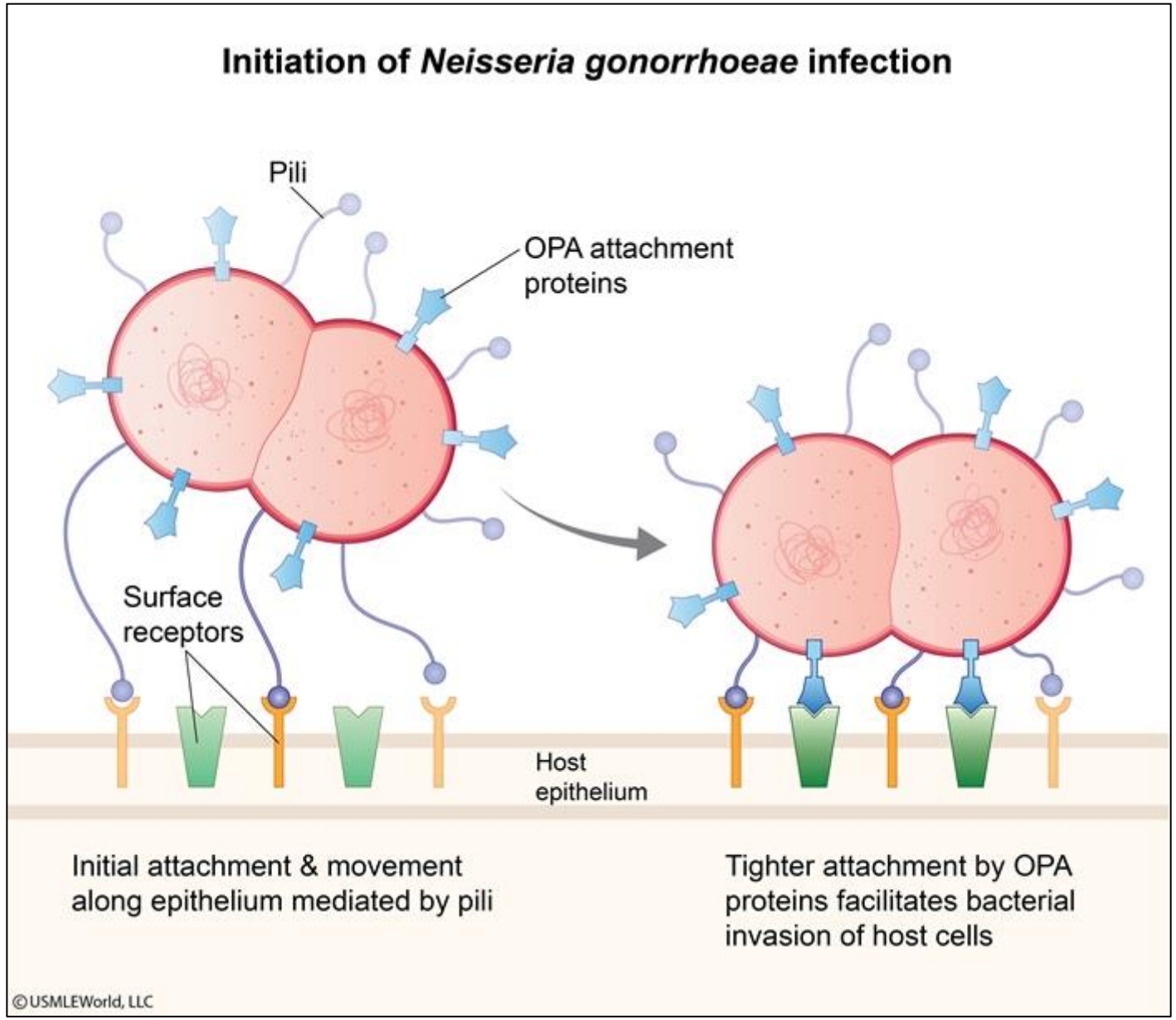

Gram-negative bacteria
Diplococci
Coccobacilli
Bacilli
Spiral, comma, or S-shaped
Aerobic
Maltose utilization
No
Yes
N gonorrhoeae
Moraxella
N meningitidis
H influenzae
B pertussis
Pasteurella
Brucella
F tularensis
Lactose fermenting
Oxidase-positive
Grows in 42 C
Grows in alkaline media
Urease producing
C jejuni
V cholerae
H pylori
No
Yes
Oxidase-positive
No
Yes
H2S-producing
No
Yes
Shigella
Yersinia
Salmonella
Proteus
Pseudomonas
Slow
Fast
Citrobacter
Serratia
Indole-positive
No
Yes
Klebsiella
Enterobacter
E coli

Pathogenesis 1

- *N gonorrhoeae* is primarily transmitted through sexual contact; howevever, vertical transmission can occur during vaginal delivery. *N gonorrhoeae* has multiple virulence factors that allow it to cause local and disseminated disease.
- The bacteria invade epithelial cells, causing cell death, inflammation, and the characteristic purulent discharge associated with gonorrhea.
- Dissemination can occur through the bloodstream, leading to systemic symptoms in severe cases.
- The process of pathogenesis involves the following: (*next slide*)

Pathogenesis 2

1. **Attachment and invasion** (*figure slide 8*): *N gonorrhoeae* expresses a number of surface molecules that allow it to attach to host epithelial cells and neutrophils.
   - **Pili**: proteinaceous projections on the outer surface of the bacterium, allow it to attach to epithelial cells.
   - **Lipooligosaccharides (LOS):** attach to receptors on urothelial cells and sperm. This attachment to sperm may contribute to male-to-female transmission of infection.


Initiation of *Neisseria gonorrhoeae* infection
Pili
OPA attachment proteins
Surface receptors
Host epithelium
Initial attachment & movement along epithelium mediated by pili
Tighter attachment by OPA proteins facilitates bacterial invasion of host cells
©USMLEWorld, LLC

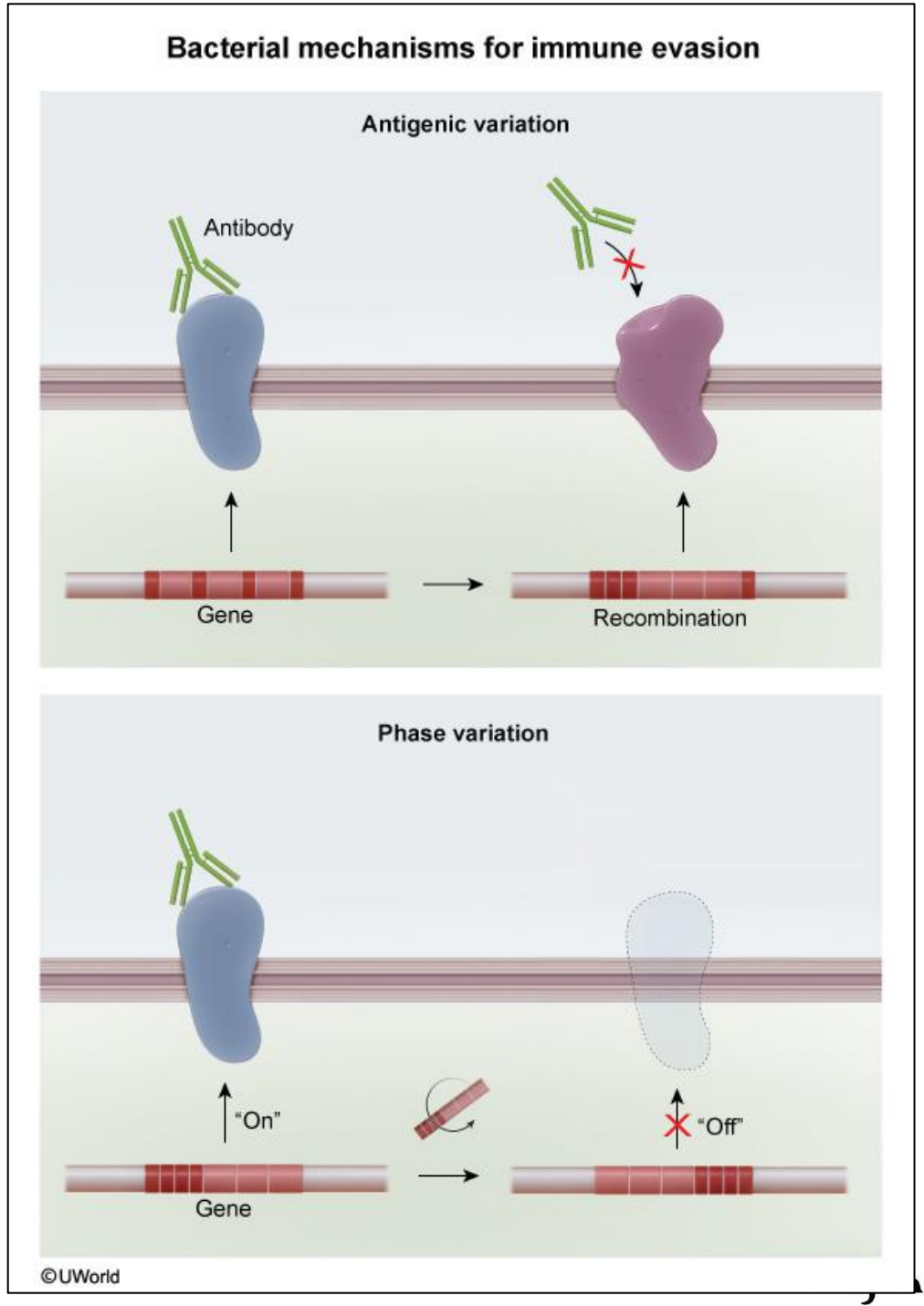
Pathogenesis 3

2. **Dissemination:** Some strains of *N gonorrhoeae* express a membrane porin protein (PorB1A) that can downregulate the complement system, allowing the bacterium to be relatively resistant to complement-mediated killing. These strains can disseminate through the bloodstream and cause disease distant from the site of inoculation.

3. **Evasion of host immune defense:**
   - Antigenic variation occurs in outer membrane structures, including pili, porin proteins, and LOS, allowing for repeated infection without recognition by the immune system.
   - The carbohydrate portions of bacterial LOS are molecularly similar to host glycolipids (molecular mimicry), preventing the host immune system from recognizing them as foreign.
   - *N gonorrhoeae* also produces IgA protease, which destroys host IgA antibodies.

Immune evasion

- Gonorrhea infection generates IgA and IgG antibodies against the bacteria; however, these antibodies provide limited or no protective immunity against future infections due to an extremely high rate of antigenic variation in bacterial surface molecules (eg, porins, Opa proteins, lipooligosaccharide).



Transmission

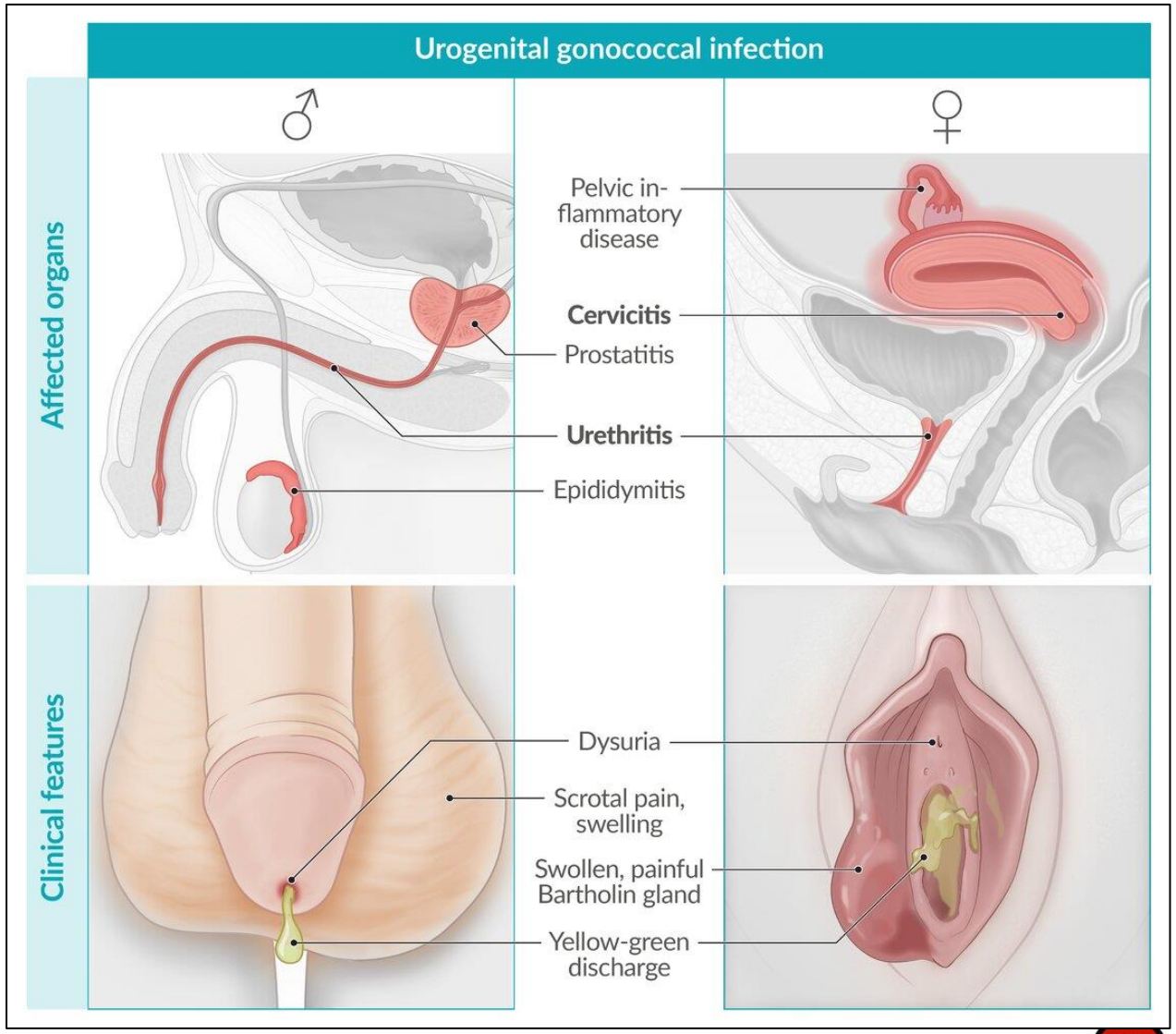
- **Transmission Routes:**
  - Sexual contact (oral, genital, anal)
  - Perinatal (vertical transmission)
  - Auto-inoculation (e.g., eye)

Risk Factors

- **Risk Factors:**
  - High-risk sexual behaviors
  - Lack of barrier protection
  - Multiple sexual partners
  - Previous STIs
  - Young age
  - Substance abuse
- **Host Factors:**
  - Complement deficiencies
  - Menstruation (increased risk of ascending infection)

Clinical manifestations

- Male urogenital infection
- Female urogenital infection
- Extragenital infection
- Disseminated infection
- Neonatal infection



Clinical manifestations - Male urogenital infection

- **Urethritis:** Infection of the urethra is frequently asymptomatic but may cause purulent urethral discharge and dysuria.
- **Epididymitis:** Infection of the epididymis can lead to unilateral scrotal pain and swelling that improves with elevation of the testes.
- **Prostatitis:** Infection of the prostate can cause fever, pelvic and perineal pain, and dysuria.

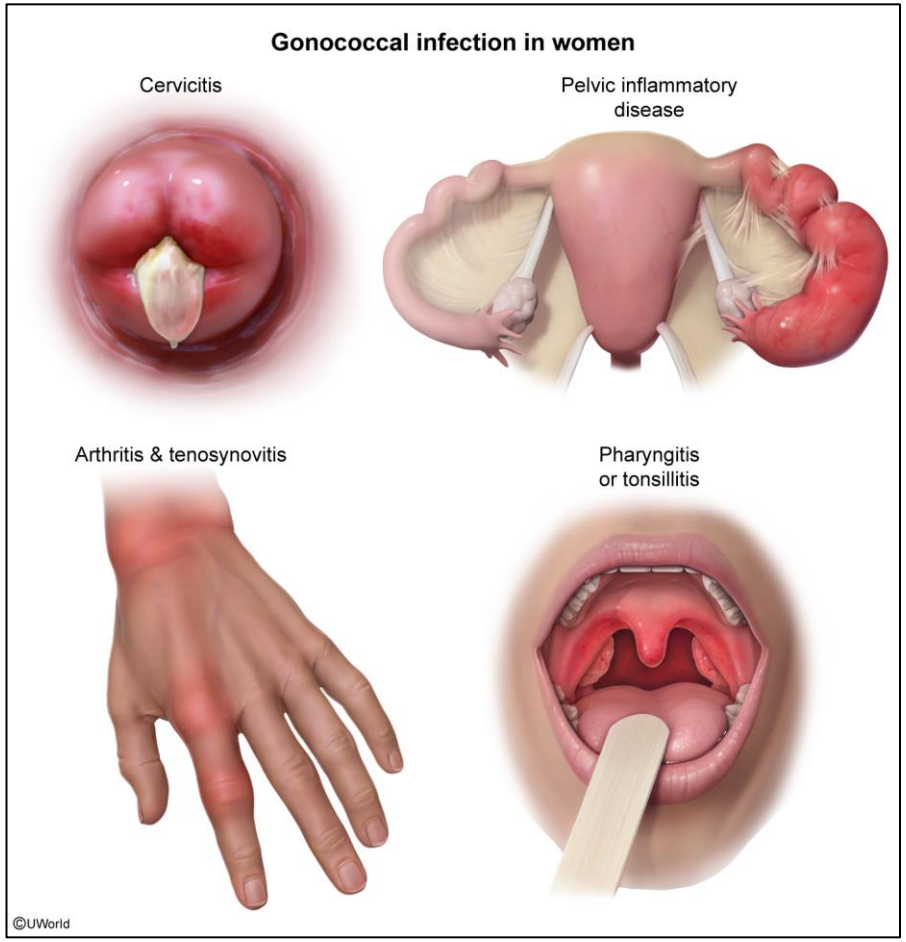
Purulent urethral discharge

Clinical manifestations - Female urogenital infection (1)

- **Cervicitis (*figure next slide*):** Cervical infection is most commonly asymptomatic. When symptomatic, patients often have purulent or mucopurulent cervical discharge.
- **Urethritis:** Inflammation of the urethra usually occurs with concomitant cervicitis. It is typically asymptomatic but may cause urinary symptoms (eg, dysuria, urinary frequency).
- **Urogenital infections during pregnancy:** Infection can increase the risk for complications, including intraamniotic infection, preterm prelabor rupture of membranes, preterm delivery, and spontaneous abortion.

Clinical manifestations - Female urogenital infection (1)

Infectious cervicitis
Colposcopy view of the ectocervix
The ectocervix is erythematous and there is purulent discharge from the external os.



Clinical manifestations - Female urogenital infection (2)

- **Pelvic inflammatory disease (PID) (** *table next slide***):** PID is a polymicrobial infection of the upper genital tract (ie, uterus, fallopian tubes, and ovaries) in which *N gonorrhoeae* is a common contributing pathogen. About 15% of cases of gonococcal cervicitis progress to PID. PID causes pelvic or abdominal pain that may be accompanied by fever, abnormal uterine bleeding, and mucopurulent cervical discharge.
- PID leads to scarring of the fallopian tubes and an increased risk for infertility and ectopic pregnancy.

Clinical manifestations - Female urogenital infection (2)

Pelvic inflammatory disease	
Symptoms	• Lower abdominal pain • Abnormal bleeding
Risk factors	• Multiple sexual partners • Age 15-25 • Previous pelvic inflammatory disease • Inconsistent barrier contraception use • Partner with sexually transmitted infection
Physical examination	• Fever >38.3 C (>100.9 F) • Cervical motion, uterine, or adnexal tenderness • Mucopurulent cervical discharge
Treatment	• Inpatient: IV broad-spectrum antibiotics • Outpatient: PO broad-spectrum antibiotics
Complications	• Tuboovarian abscess • Infertility • Ectopic pregnancy

Clinical manifestations - Extragenital infection

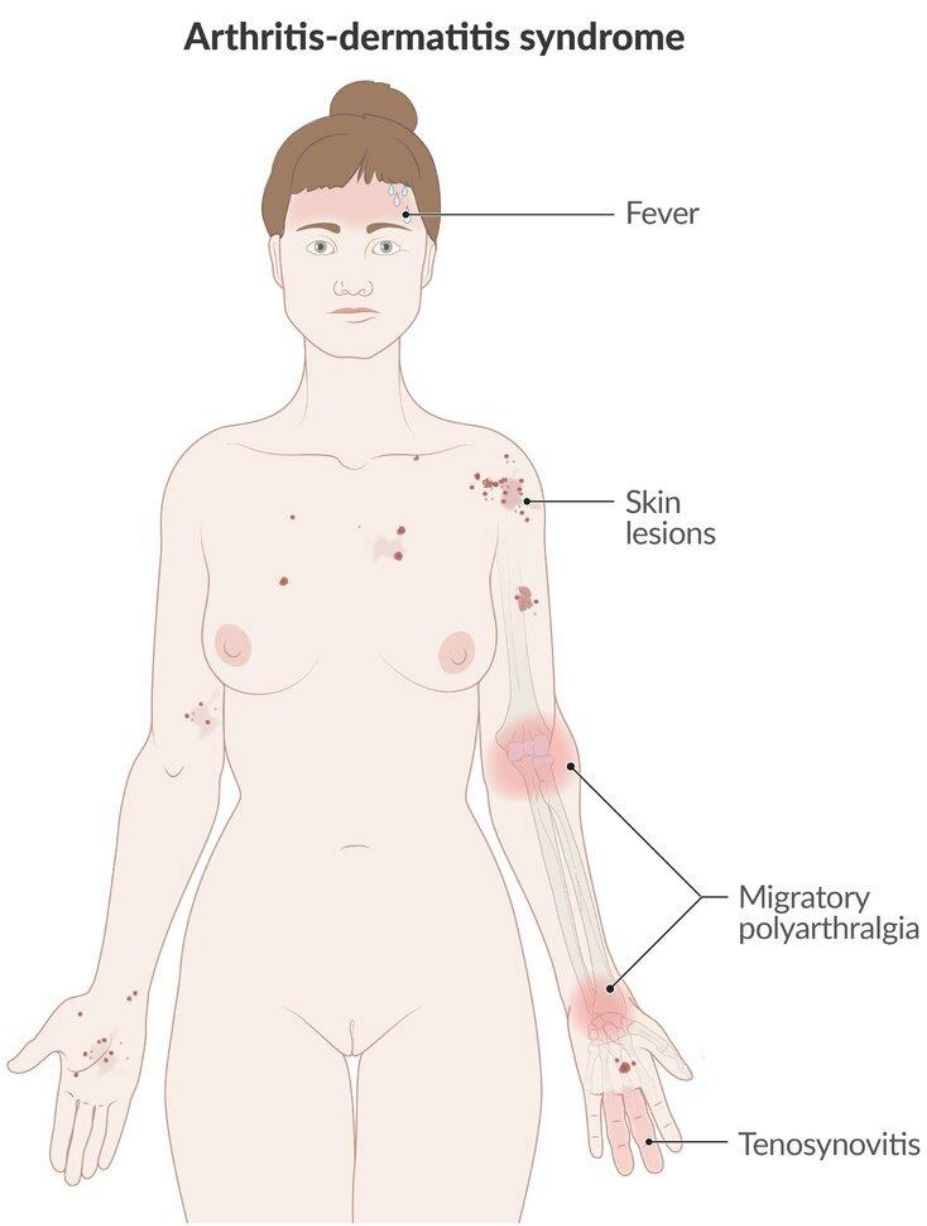
- **Gonococcal proctitis (** *table next slide*): Rectal infection can occur through receptive anal intercourse and via proximal spread from the vagina. Manifestations typically include tenesmus, mucopurulent anal discharge, and pruritus; rectal fullness, bleeding, anorectal pain, and constipation can also occur.
- **Gonococcal pharyngitis:** Infection can occur with oral sex; patients have sore throat and cervical lymphadenopathy; some may have associated tonsillar exudates.
- **Gonococcal conjunctivitis:** This severe infection can threaten vision; it is typically caused by autoinoculation from genital infection and presents with profuse mucopurlent conjunctival discharge, eyelid edema, and injection of the conjunctiva.

Clinical manifestations - Extragenital infection

Gonococcal proctitis	
Transmission	• Receptive anal intercourse • Direct spread from the vagina
Manifestations	• Mucopurulent anal discharge, occasional rectal bleeding • Tenesmus, constipation • Pruritus, rectal pain, rectal fullness
Diagnosis	• Nucleic acid amplification test of rectal swab
Treatment	• Ceftriaxone + doxycycline (to cover *Chlamydia*)

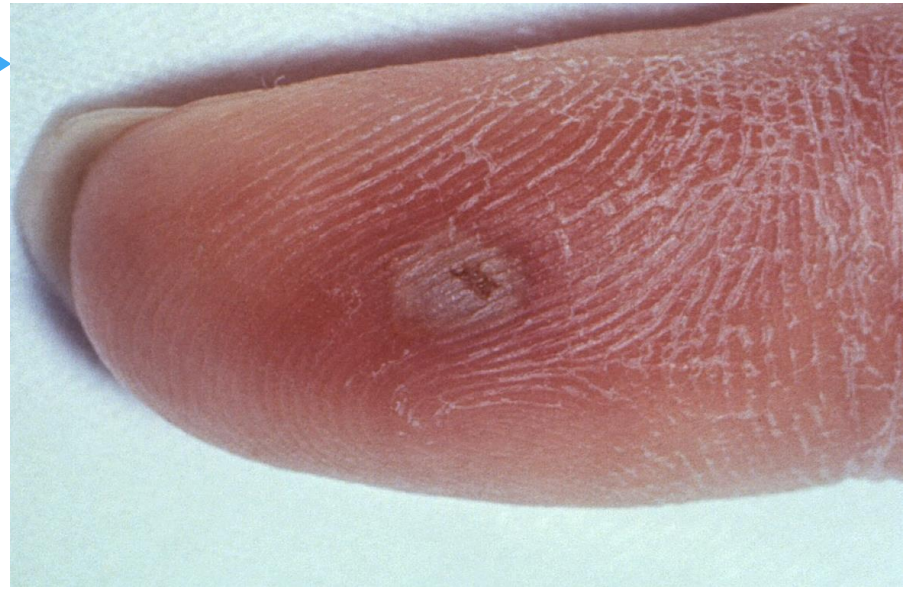
Clinical manifestations - Disseminated infection

- **Arthritis-dermatitis syndrome** (eg, tenosynovitis, dermatitis, polyarthralgia): Patients have migratory polyarthralgia that tends to be asymmetric and can affect small and large joints, painless skin lesions (typically pustules), tenosynovitis, and fever. Symptoms usually begin within several weeks of infection, but most patients do not have symptoms of genital infection. Arthritis-dermatitis syndrome is the most common presentation of disseminated infection and can progress to purulent arthritis if untreated.
- **Purulent arthritis:** Sudden onset of pain and swelling of one or more distal joints (eg, wrists, knees, ankles) is seen.

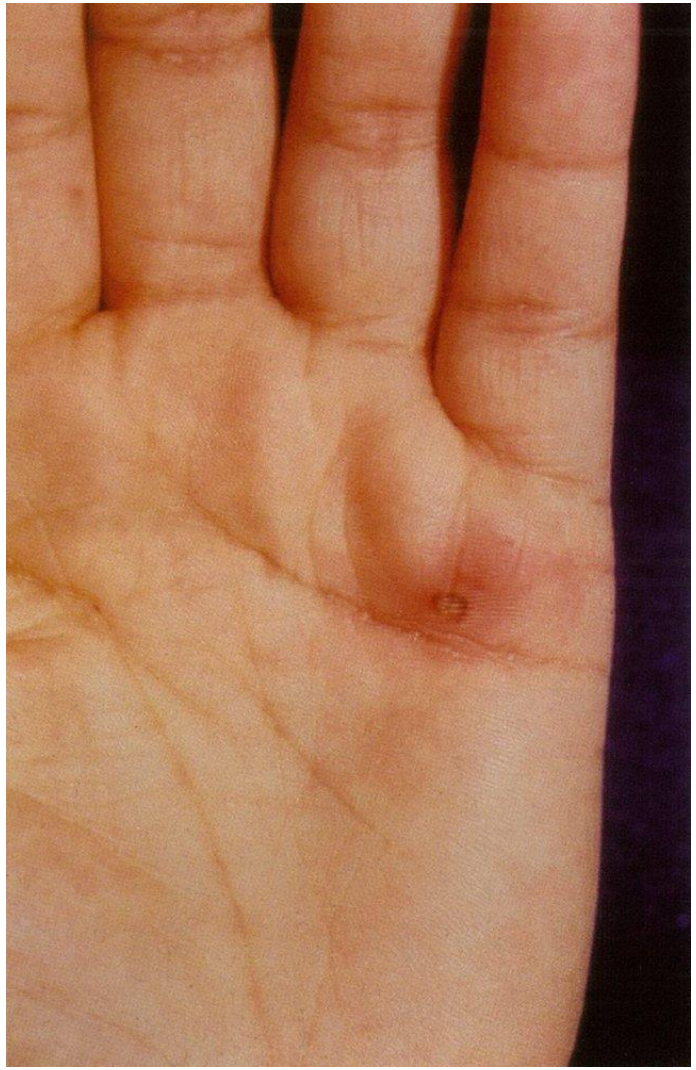


Arthritis-dermatitis syndrome

Gonococcal arthritis



Pustular skin lesion in disseminated gonococcal infection



Pustular skin lesion in disseminated gonococcal infection

Clinical manifestations - Neonatal infection (1)

- **Ophthalmia neonatorum:** This is the most common manifestation of gonococcal disease in newborns and onset occurs several days after birth. It most commonly causes conjunctivitis, with purulent exudate, injection, and edema of the eyelids, and can occasionally progress to corneal ulceration and blindness.
- **Other local infection:** As in adults, infection of the pharynx, vagina, urethra, and anus can occur in infants and may or may not be symptomatic. A scalp abscess can develop in infants of mothers who had intrapartum placement of a fetal scalp electrode, which creates a break in the skin to allow bacterial entry.

Ophthalmia neonatorum: The eyelids are swollen, with purulent exudate forming crusts around them. Below the crusts there may be a large reservoir of pus. Special care should be taken and safety goggles should be worn when examining the eyes.

Clinical manifestations - Neonatal infection (2)

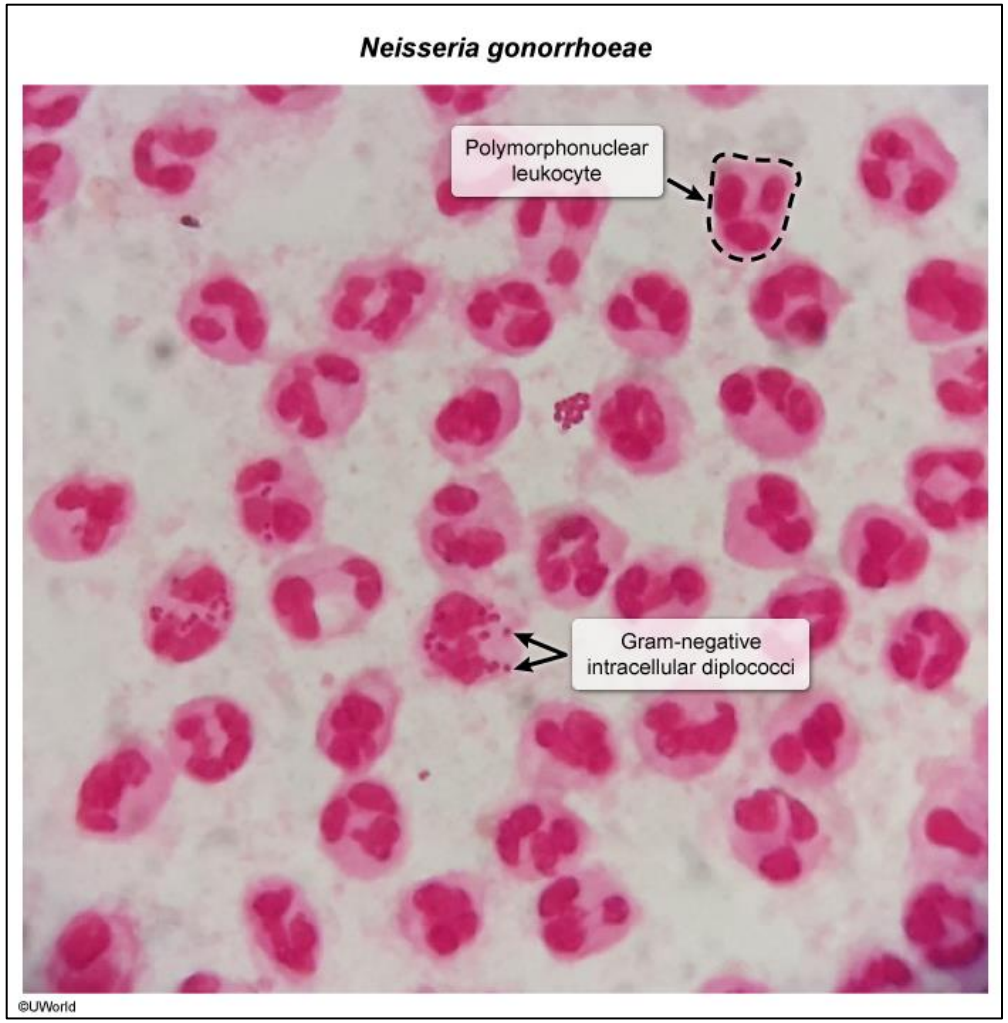
- **Disseminated infection:** Local infection (particularly scalp abscess) can lead to gonococcal bacteremia and disseminated infection, which typically present as arthritis, meningitis, or sepsis.

Diagnosis and laboratory evaluation

- Evaluation of local infection
- Evaluation of disseminated infection
- Evaluation of coinfection

Diagnosis and laboratory evaluation- Evaluation of local infection

- **Nucleic acid amplification testing (NAAT)** is the preferred method for diagnosing gonorrhea due to high sensitivity and specificity rates. In male patients, NAAT can be performed on a first-catch urine specimen or urethral swab. In female patients, NAAT performed on a vaginal or endocervical swab is preferred.
- NAAT, however, does not allow for testing for antimicrobial sensitivity. Therefore Gram stain and culture may be used.
  - A Gram stain demonstrating gram-negative intracellular diplococci is diagnostic (*image next slide*).
  - Culture is typically collected with cases requiring a Gram stain and in cases of cases of suspected treatment failure to evaluate for antibiotic resistance.
  - Culture is performed with **Thayer-Martin media** (results take ~ 48 hours), and swabs can be taken from the penile urethra, cervix, rectum, posterior pharynx, or conjunctival discharge.



Thayer Martin medium

A selective culture medium that favors the growth of Neisseria species. Contains vancomycin (which inhibits the growth of gram-positive organisms), trimethoprim and colistin (which inhibit the growth of gram-negative organisms), and nystatin (which inhibits the growth of fungi).

Diagnosis and laboratory evaluation- Evaluation of disseminated infection

- Diagnosis of disseminated gonococcal infection is made by identification of *N gonorrhoeae* by culture or NAAT performed on a skin lesion (rarely performed), blood, or synovial fluid. Evaluation of patients with suspected disseminated infection should include the following:
  - Urogenital, rectal, and pharyngeal testing: NAAT or culture.
  - Blood cultures.
  - Synovial fluid analysis: This should be performed in patients with an accessible joint effusion. Fluid is sent for NAAT, culture, Gram stain, and white blood cell count.

Diagnosis and laboratory evaluation- Evaluation of coinfection

- Patients diagnosed with gonorrhea should be tested for other sexually transmitted infections, including chlamydia, HIV, and syphilis.

Treatment & Prevention

- Treatment includes a single intramuscular dose of **ceftriaxone**, along with either **tetracycline (eg, doxycycline)** or a macrolide like **azithromycin** to cover potential **chlamydia co-infection**.
- Instruct the patient to avoid all sexual contact until
  - 7 days after treatment of the patient and their sexual partners
  - Symptoms have resolved
- Since Neisseria gonorrhoeae can cause recurrent infections, prevention methods such as consistent **condom use** are essential.

وَلَا تَقْرَبُوا الزِّنَا ۖ إِنَّهُ كَانَ فَاحِشَةً وَسَاءَ سَبِيلًا

Thank You

Summary

Neisseria gonorrhoeae, a **gram-negative diplococcus**, is the causative agent of the sexually transmitted infection, **gonorrhea**. N. gonorrhoeae is **not encapsulated** and can develop in **asymptomatic carriers**. It can infect genitalia, with symptoms ranging from **urethritis**, **prostatitis**, and **epididymitis** in male individuals to **urethritis**, **cervicitis**, **pelvic inflammatory disease (PID)**, and **salpingitis** in those with female reproductive organs. The infection can also affect **newborns** through direct contact during labor and delivery, potentially leading to a **severe eye infection** and blindness.

Diagnosis involves gram staining and culturing of urine, urethral, or endocervical specimens, with **nucleic acid amplification testing (NAAT)** being the test of choice due to its high sensitivity and rapid results. Treatment includes a single intramuscular dose of **ceftriaxone**, along with either **doxycycline** or a macrolide like **azithromycin** to cover potential **chlamydia co-infection**. Since Neisseria gonorrhoeae can cause recurrent infections, prevention methods such as consistent **condom use** are essential.