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Gonorrhoea

GONORRHEA

EPIDEMIOLOGY

- More than 600,000 people are estimated to acquire new gonococcal infections in the United States yearly according to the Centers for Disease Control and Prevention(CDC), although only about half are actually reported through the public health system. This makes gonorrhoea the second most commonly reported infectious disease in the United States, second only to chlamydia.
- The highest rate of reported gonococcal infections is among sexually active teenagers and young adults, aged 15–24.

ETIOLOGY AND PATHOGENESIS

- This infection is due to *Neisseria gonorrhoeae*, a Gram-negative, aerobic, coccus-shaped bacterium typically found in pairs. The organisms are usually visualized intracellular, located within polymorphonuclear leukocytes.
- Gonorrhea is acquired through sexual contact, or, much less commonly, as a result of poor hygiene or by “medical ”use of urine. It can also be transmitted vertically from mother to child during birth, causing an inflammatory eye infection (ophthalmia neonatorum).
- Pathogenesis involves bacterial attachment to columnar epithelial cells by pili or fimbria. The most common sites of attachment include the mucosal cells of the male and female urogenital tracts.
- Humans are the only natural hosts of *N. gonorrhoeae*

ETIOLOGY AND PATHOGENESIS

- Once inside the cell, the organism undergoes replication and can grow in both aerobic and anaerobic environments.
- After cellular invasion, the organism replicates locally, inducing an inflammatory response.
- Outside the cell, the bacteria are susceptible to temperature changes, ultraviolet light, drying, and other environmental factors.
- The outer membrane contains lipooligosaccharide endotoxin, which is released by the bacteria during periods of rapid growth and contributes to its pathogenesis in disseminated infection.

ETIOLOGY AND PATHOGENESIS

- Delay in antibiotic treatment, physiologic changes in host defenses, resistance to immune responses, and highly virulent strains of bacteria contribute to hematogenous spread and disseminated infection
- *N. gonorrhoeae* infection tends to involve mucous membranes predominantly by columnar epithelial cells. The urethra, cervix, rectum, pharynx, and conjunctiva are the areas most commonly involved.

LOCALIZED DISEASE (MEN).

- The incubation period in men is from 2 to 8 days
- Only about 10% of infections are asymptomatic in men
- The most common manifestation of gonococcal infection in men is urethritis, characterized by a spontaneous, often profuse, cloudy or purulent discharge from the penile meatus. Mucosal membrane inflammation in the anterior urethra leads to pain or burning upon urination and meatus erythema and swelling.
- In some cases, there is so much soft tissue inflammation that the entire distal penis becomes swollen, so-called “bull head clap.”
- Testicular pain and swelling may indicate epididymitis or orchitis and may be the only presenting symptom. However, epididymitis is more commonly caused by *Chlamydia trachomatis* or by combined infection with *N.gonorrhoeae*

LOCALIZED DISEASE (MEN).

- Proctitis is a manifestation of gonococcal infection manifesting in those who practice unprotected anoreceptive intercourse. it is most common in MSM. Symptoms may include a rectal mucopurulent discharge, pain on defecation, constipation, and tenesmus. As a result of gonococcal proctitis, MSM are at a higher risk of acquiring HIV infection.
- Pharyngitis caused by *N. gonorrhoeae*. it may be asymptomatic, and may serve as a source for disseminated gonococcal disease. When present, symptoms range from cervical lymphadenopathy, mild-to-moderate pharyngeal erythema, ulceration with pseudomembrane formation

LOCALIZED DISEASE (WOMEN).

- Fifty percent of women infected with *N. gonorrhoeae* are asymptomatic.
- The endocervix is a common site of local infection.
- Symptoms of urethritis include mucopurulent discharge, vaginal pruritus, and dysuria.
- However, vaginitis does not occur except in prepuberty or postmenopausal women because the vaginal epithelium of sexually mature women does not support growth of *N. gonorrhoeae*.
- Other sites of infection include Bartholin's and Skene's glands, which results in swelling and tenderness.
- Organisms may invade the upper genital tract, including the uterus, fallopian tubes, and ovaries, resulting in pelvic inflammatory disease (PID).

LOCALIZED DISEASE (WOMEN).

- pelvic inflammatory disease (PID) occurs in about 10%–40% of uncomplicated gonorrhoea infections in women and is characterized by fever, lower abdominal pain, back pain, vomiting, vaginal bleeding, dyspareunia, and adnexal or cervical tenderness during movement .
- Sequelae of untreated infection include tubo-ovarian abscesses, subsequent ectopic pregnancies, chronic pelvic pain, and infertility due to chronic inflammation with scarring
- Fitz-Hugh–Curtis syndrome, involving inflammation of the liver capsule, is associated with genitourinary tract infection and may be present in up to one-fourth of women with PID caused by either *N. gonorrhoeae* or *C. trachomatis*.
- Presenting symptoms include right upper quadrant pain and tenderness with abnormal liver function tests.
- This syndrome must be distinguished from acute viral hepatitis.

LOCALIZED DISEASE (WOMEN).

- Women may also develop proctitis through autoinoculation from cervical discharge or as a result of direct contact from an infected partner's
- The incidence of gonococcal pharyngitis is higher than that in men due to the common practice of fellatio
- It is estimated that, in adolescent women, 11%–26% of cases of gonorrhoea are consist only of asymptomatic pharyngeal infection

NEWBORNS AND CHILDREN

- Neonates may acquire *N. gonorrhoeae* during passage through the birth canal from contact with infected secretions.
- ocular infections are known as ophthalmia neonatorum, and are characterized by profuse, purulent ocular discharge.
- Pharyngeal or genital gonococcal infection in children is often a sign of sexual abuse.

Acute gonorrhoea in a male manifesting as creamy purulent discharge from the urethra. Swelling of the distal shaft characterizes “bull head clap,” which is manifestation of urethral gonococcal infection.

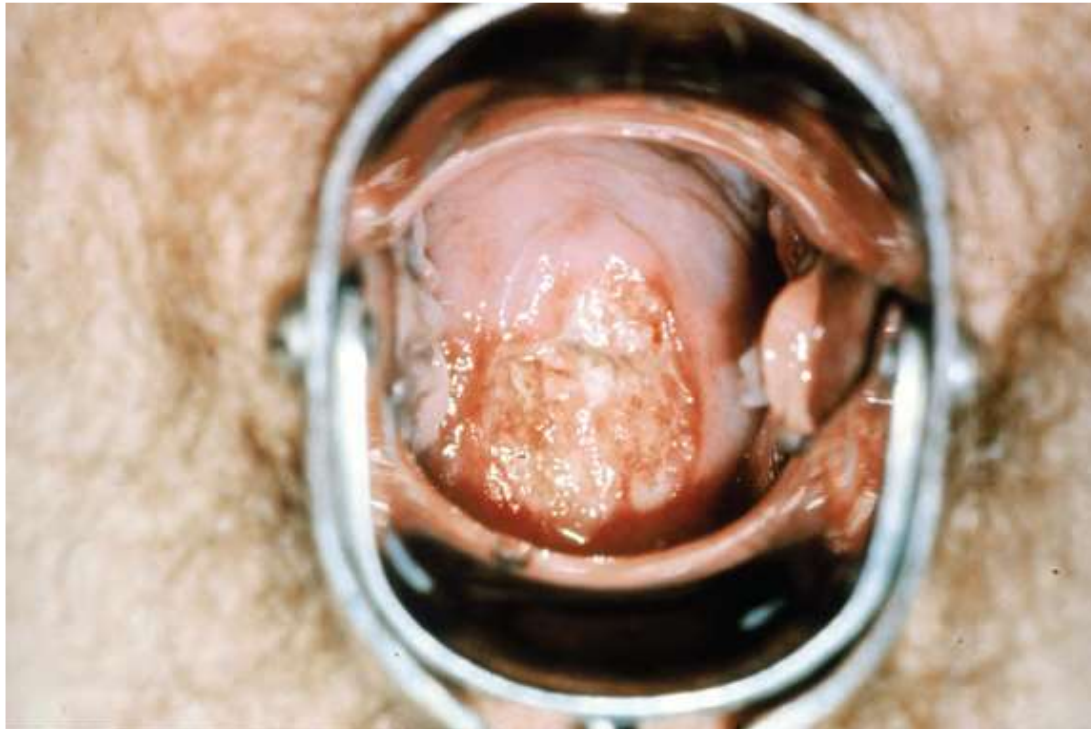


Acute gonorrhoea.

There is a purulent discharge from the urethra and inflammation of the prepuce and glans.



Gonococcal cervicitis showing a mucopurulent discharge with erythema



Gonococcal ophthalmia neonatorum: the purulent discharge may be profuse.



Saxophone penis caused by a periurethral abscess.



Bartholin's abscess: the Bartholin glands are located on either side of the vaginal opening and can become obstructed and/or infected. Gonorrhoea should be considered as a cause.



DISSEMINATED DISEASE

- Spread of infection from the primary site of inoculation to other parts of the body through the bloodstream leads to disseminated gonococcal infection (DGI), also known as gonococemia.
- Disseminated disease occurs in 0.5%–3% of cases and is associated with a classic triad of dermatitis, migratory polyarthritits, and tenosynovitis.
- Pain and swelling may occur in a single joint or in multiple joints asymmetrically.
- Skin findings consist of small- to medium-sized macules or, most typically, hemorrhagic vesicopustules on an erythematous base located on palms and soles or on the trunk and elsewhere on the extremities. The coincidence of some degree of hemorrhage and necrosis led to the term “gun metal gray” to describe the cutaneous lesions of DGI.

Disseminated gonococcal infection. Tender, hemorrhagic, and necrotic pustules on the fingers and palms.



Disseminated gonococcal infection: early macular lesions progress to pustules and haemorrhagic lesions.



Disseminated gonococcal infection showing a pustule surrounded with erythema.



Disseminated gonococcal infection showing inflammation joints.



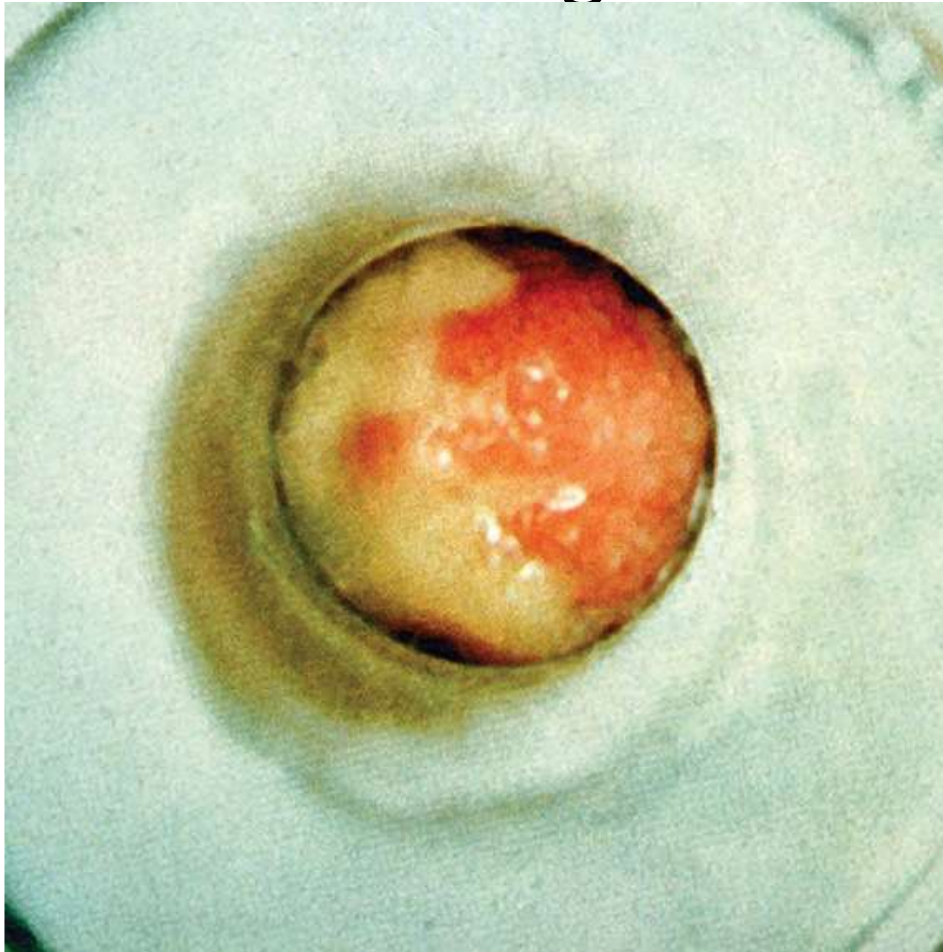
LABORATORY TESTS

- Organisms are Gram-negative, intracellular diplococci inside polymorphonuclear cells
- Gram stain has specificity (>99%) and sensitivity(>95%).
- Gram-negative diplococci can be considered diagnostic for infection with *N. gonorrhoeae* in symptomatic men
- negative Gram stain cannot be considered sufficient for ruling out gonococcal infection in asymptomatic men at high risk for infection.
- Gram stains of endocervical specimen, pharyngeal, or rectal specimen also are not sufficient to detect infection, and, therefore, are not recommended. Vaginal specimen are never recommended for diagnostic , since the vaginal mucosa resists gonococcal invasion.

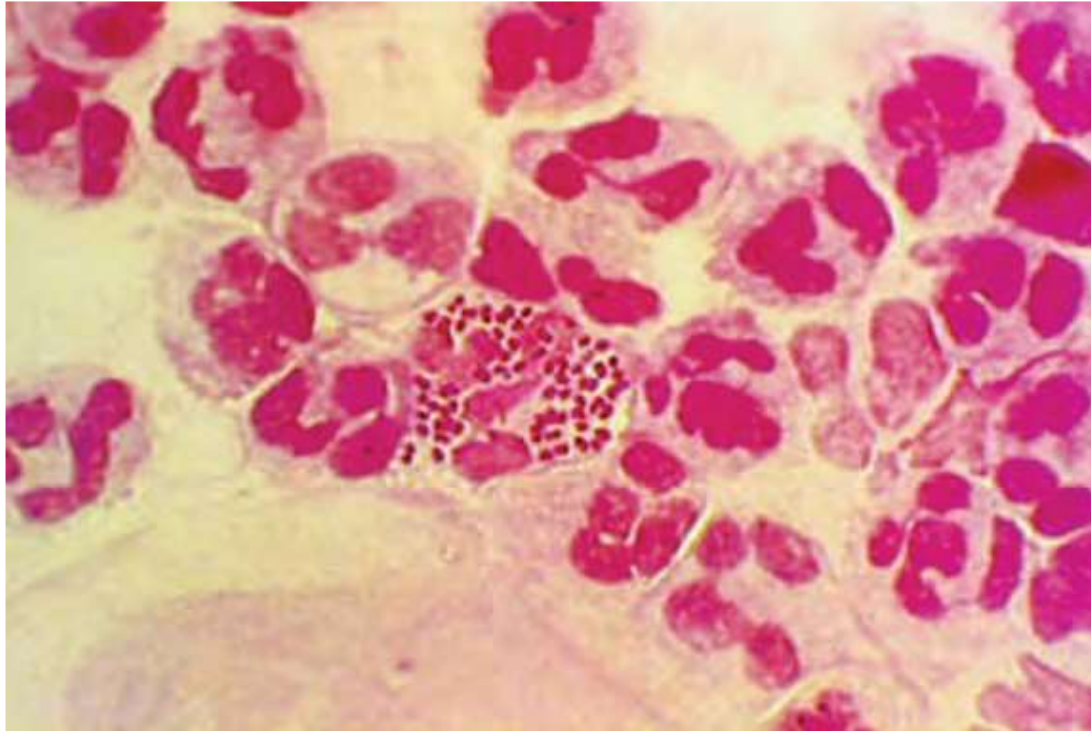
LABORATORY TESTS

- Bacterial culture has been the “gold standard” diagnostic test for years.
- The US Food and Drug Administration has approved certain chemiluminescence DNA probes that can be used on endocervical or urethral specimens for diagnosis of gonorrhea. However, distinguishing gonococcal from nongonococcal infection may be difficult with DNA probes.
- nucleic acid amplification tests are highly sensitive and specific and may be able to detect even the presence of one organism.
- diagnosis by any nonculture method does not allow for antibiotic sensitivity testing.
- In DGI, cultures, and if available, nucleic acid amplification testing, should be done on blood, joint fluid, and skin lesions.

Gonococcal proctitis: proctoscopy reveals an inflamed mucosa and a purulent discharge.



Gram staining of a urethral smear demonstrating intracellular and extracellular Gram-negative diplococci



DIFFERENTIAL DIAGNOSIS

- Localized: Urinary tract infection; Chlamydia; Gonorrhea; Pelvic inflammatory disease; Trichomoniasis; Herpes simplex virus; Bacterial vaginosis; Vaginitis; Mycoplasmal infection; Orchitis and epididymitis; Lymphatic occlusion due to pelvic neoplasm
- Systemic: Septic arthritis; Rheumatoid arthritis; Psoriatic arthritis; Hepatitis B and C; Behçet disease; Reiter syndrome; Lyme disease; Rheumatic fever
- Always Rule Out: Tubo-ovarian abscess; Ectopic pregnancy; Pregnancy; Appendicitis; Coinfection with syphilis and HIV; Sexual abuse (in children)

COMPLICATIONS

- Permanent sequelae of gonococcal infection in women may be infertility as a result of untreated pelvic inflammatory disease (PID).
- Untreated disseminated gonococcal infection (DGI) can lead to septic arthritis.
- Meningitis and endocarditis are rare manifestations of DGI

TREATMENT

- Ten percent to 30% of people with gonococcal infection are coinfecting with Chlamydia
- Due to the increased prevalence of antimicrobial resistance, quinolone are no longer recommended for the routine treatment of any gonococcal infections
- **Treatment of Localized , Uncomplicated Gonococcal Infection of Cervix, Rectum**

Single dosage of any of the following:

- Ceftriaxone, 125 mg IM; Cefixime, 400 mg orally

Alternative single-dose cephalosporin may be considered, as Cefotaxime 500 mg IM, with probenecid 1.0 g orally

TREATMENT

- for chlamydia, add either: Azithromycin, 1 g orally in a single dose; Doxycycline, 100 mg orally twice a day for 7 days
- The recommended regimen for DGI is ceftriaxone, 1 g IM or IV every 24 hours, continuing for 24–48 hours.
- Patients with allergy to later generation cephalosporins can be managed with spectinomycin. Fluoroquinolones can be considered, but only if sensitivity to this class of drugs has been established by culture

Management of Disseminated Gonococcal Infection.

- Recommended Regimen: Ceftriaxone 1 g IM or IV every 24 hours (intravenous route preferred)
- Alternative Regimens
 - Cefotaxime (1 g IV every 8 hours)
 - Ceftizoxime (1 g IV every 8 hours)
 - Spectinomycin (2 g IM every 12 hours)

Treatment of Gonococcal Infection in Neonates

- Ceftriaxone, 25–50 mg/kg/day IV or IM in a single daily dose for 7 days, or for 10–14 days if meningitis is documented. Or
- Cefotaxime, 25 mg/kg IV or IM every 12 hours for 7 days, or for 10–14 days if meningitis is documented

CHLAMYDIA

CHLAMYDIA

- Infection with *C. trachomatis* is the most common reported STD in the United States
- The highest rates of infection reported are in women between the ages of 15 and 24 years.
- Risk factors are similar to those related to gonococcal infections, and include young age, new or multiple sex partners, unprotected sexual intercourse, and low socioeconomic and education.

CHLAMYDIA

- *C. trachomatis* is a nonmotile, Gram-negative, intracellular organism with 15 serotypes: A through C cause chronic conjunctivitis and are endemic in Africa and Asia, D through K cause urogenital tract infections, and L1 through L3 cause lymphogranuloma venereum.
- Chlamydia are obligate intracellular bacteria characterized by two distinct morphologic forms: (1) the small metabolically inactive and infectious elementary body, and (2) the larger metabolically active and noninfectious reticulate body

CHLAMYDIA

- Urogenital tract infection is the area most commonly affected in men and women
- Transmission is through oral, anal, or vaginal intercourse with symptoms occurring 1–3 weeks after exposure. However, asymptomatic infection occurs in up to 80% of women and 50% of men.
- Various serotypes have been associated with an increased risk of cervical squamous cell carcinoma, suggesting that Chlamydia species may act as a cofactor with oncogenic, high-risk HPV in neoplastic transformation.
- Newborns can be infected from passage through the birth canal of an infected mother.

CLINICAL FINDINGS

- The most common manifestation of disease is urethritis, characterized by a watery or mucoid discharge from the urethra that may be associated with dysuria in both men and women.
- Note that the discharge due to Chlamydia is classically less purulent, less profuse, and less spontaneous when compared to urethral gonorrhoea.
- Rectal infection may result in proctitis in both men and women; symptoms resemble those seen with gonococcal proctitis.
- In men younger than age 35 years, *C. trachomatis* is the most common cause of epididymitis. Thus, aside from urethral discharge, men may also present with unilateral scrotal pain and swelling.

CLINICAL FINDINGS

- In women, the columnar epithelium of the endocervix is commonly affected. Other symptoms, beside those of urethritis, include intermenstrual or postcoital bleeding and persistent lower abdominal pain.
- As with gonococcal infection, a severe complication in women that can result in sterility is pelvic inflammatory disease (PID), with ascending infection to the uterus and fallopian tubes.
- In the United States, chlamydial species are currently the most common causes of PID.
- Symptoms may include fever, lower abdominal pain, back pain, vomiting, vaginal bleeding, dyspareunia, and adnexal or cervical motion tenderness on physical examination.
- Sequelae of untreated infection include tubo-ovarian abscesses, ectopic pregnancies, chronic pelvic pain, and infertility due to chronic inflammation with scarring.

CLINICAL FINDINGS

- Newborns may develop conjunctivitis and pneumonia after being infected from passage through the birth canal.
- Signs of ophthalmia neonatorum may include injected conjunctivae, purulent discharge, or swollen eyelids.
- Subacute, a febrile pneumonia as a consequence of neonatal chlamydial infection usually presents after 1–3 months. Symptoms include cough and wheezing

Chlamydial urethritis with meatal erythema and a mucopurulent discharge.



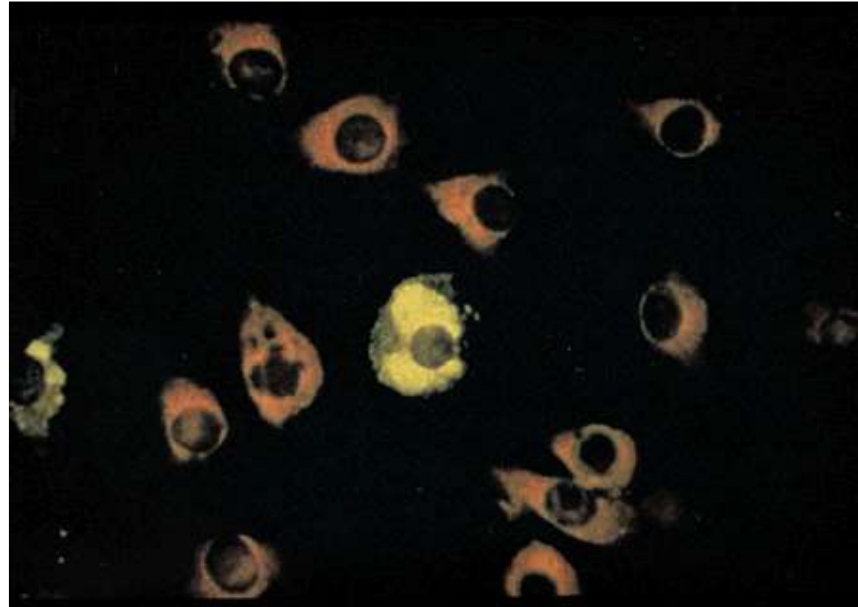
LABORATORY TESTS

- chlamydial infection was diagnosed by tissue culture with specimens obtained from the endocervix in women, urethra in men, and rectum, or conjunctivae.
- More rapid and sensitive tests have replaced culture in recent years
- A direct fluorescent antibody test, which is highly specific, can be performed on endocervical and penile urethral specimens with rapid results.
- Enzyme immunoassays, which are less specific than the direct fluorescent antibody test

LABORATORY TESTS

- Less invasive tests involving nucleic acid hybridize and nucleic acid amplification, such as PCR and ligase chain reaction, are more commonly being used to detect even small amounts of chlamydial DNA in urethra, vagina, endocervical swabs and in first voided urine samples.
- It should be noted that the nucleic acid amplification and hybridize tests are less precise for chlamydial detection from rectal and oropharyngeal sites than from genital sites.
- The CDC recommends annual screening of all sexually active women under the age of 25 and for older women with risk factors(e.g., those who have a new sex partner or multiple partners).

Detection of *Chlamydia trachomatis* by direct immunofluorescence.



TREATMENT

- Azithromycin, 1 g orally in a single dose or Doxycycline, 100 mg orally twice a day for 7 days

Alternative regimens:

- Erythromycin base 500 mg orally, four times daily for 7 days
- Erythromycin ethylsuccinate 800 mg orally, four times daily for 7 days
- Ofloxacin 300 mg orally, twice daily for 7 days
- Levofloxacin 500 mg daily for 7 days

Recommended treatment for pregnant women:

- Azithromycin 1 g orally as a single dose
- Amoxicillin, 500 mg orally three times a day for 7 days

Recommended treatment for ophthalmia neonatorum:

- Erythromycin base or ethylsuccinate 50 mg/kg/day orally, divided into four doses daily, for 14 days

GENITAL MYCOPLASMAS

GENITAL MYCOPLASMAS

- Species of Mycoplasma are the smallest, free-living, self-replicating bacteria.
- These organisms developed by degenerative evolution from lactobacilli, and lack a cell wall. These organisms have ability to colonize the respiratory and urogenital tracts of humans.
- Seven mycoplasmal strains have been isolated from the genital tract: **(1) Mycoplasma hominis and (2) Mycoplasma genitalium are commonly identified**, while (3) Mycoplasma fermentans, (4) Mycoplasma penetrans, (5) Mycoplasma pneumoniae, (6) Mycoplasma primatum, and (7) Mycoplasma spermatophilum are rare at this site.

GENITAL MYCOPLASMAS

- Forty percent to 80% of sexually active women in the United States have urogenital infections with *Ureaplasma* organisms. *M. hominis* has also been isolated in 20%–50% of sexually active women. Newborns may be infected by passage through the birth canal of an infected mother.
- While the most common cause of symptomatic NGU remains *Chlamydia* sp., the genital mycoplasmas may also cause this disorder. *Ureaplasma* organisms have been found to be the cause of over 20% of nonchlamydial NGU, while *M. genitalium* accounts for 10%–20% of cases of nonchlamydial NGU.

ETIOLOGY AND PATHOGENESIS

- The bacteria can attach to and penetrate epithelial cells by adhesion proteins on the back of the cell body.
- All genital mycoplasmas multiply as parasites, as they are unable to complete various metabolic reactions
- Cholesterol is required for growth and is taken from the epithelial cell; ureaplasmas need urea as well.
- Because of their parasitic nature and specific nutritional requirements, Mycoplasma species tend to remain localized to mucosal surfaces.
- Disseminated infection is rare and tends to occur only in immunocompromised hosts or by trauma of the epithelium .
- There is no clear relationship between genital mycoplasma and epididymitis and/or prostatitis.

CLINICAL FINDINGS

- Patients with genital mycoplasma infections may go undiagnosed because these organisms may produce symptoms that are usually attributed to other, more common causative agents such as Chlamydia.
- As with chlamydia, various genital mycoplasmas infections can result in urethritis, cervicitis, PID, endometritis, salpingitis.
- Infection with these organisms needs to be considered if workup for the more commonly isolated organisms is negative.
- Physical findings and symptoms are indistinguishable from those seen with chlamydial NGU.

LABORATORY TESTS

- Laboratory tests for genital mycoplasmas may be limited because most specimens must be sent to reference laboratories.
- Culture specimens should be obtained from the urethra or first voided urine in men, and from the cervix, urethra, and vagina in women.
- Polymerase chain reaction (PCR) assay is required to detect *M. genitalium*, and may also be used to identify other *Mycoplasma*.
- Because *Mycoplasma* does not possess a cell wall, Gram stain will not detect these organisms.

TREATMENT

- Because these organisms lack a cell wall, they are resistant to β -lactam and cephalosporin antibiotics.
- Treatment for genital mycoplasmas is similar to treatment for chlamydia. *M. genitalium* is the most difficult of these organisms to treat, with failure rates ranging from 67% (levofloxacin) to 16% (single dose azithromycin).

Trichomonas vaginalis

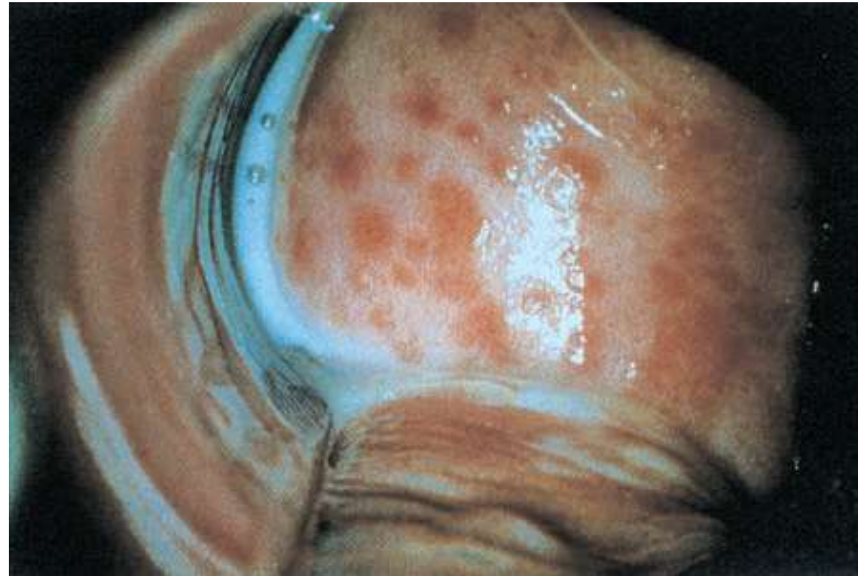
ETIOLOGY AND PATHOGENESIS

- *Trichomonas vaginalis* causes a condition called trichomoniasis, which affects about 2–3 million women annually in the United States.
- It is difficult to estimate the number of men infected because most infections in men are asymptomatic.
- Trichomoniasis is an STD caused by parasitic protozoa that infects mucosal epithelium, causing microulceration.
- In women, organisms may be isolated from the vagina, urethra, cervix, Bartholin's and Skene's glands, and bladder.
- In men, organisms may be found in the external genital area, anterior urethra, epididymis, prostate, and semen. Most men are asymptomatic carriers
- The incubation period is usually between 4 and 28 days.
- In women, manifestation of infection ranges from an asymptomatic carrier state to inflammatory vaginitis

CLINICAL FINDINGS

- Women may complain of a malodorous, yellow–green vaginal discharge, vulvar pruritus, swelling and erythema, dyspareunia, lower abdominal discomfort, or dysuria
- Infection tends to occur in sexually active women and men.
- Men are usually asymptomatic, although some may complain of urethral discharge and dysuria or urinary frequency.
- Both men and women may be asymptomatic carriers.
- Newborns may become infected from passage through the birth canal of an infected mother.
- On physical examination, punctate hemorrhage may be seen on the vaginal wall and cervix. A term commonly associated with such hemorrhages is “colpitis macularis” or “strawberry cervix”. This is a specific sign of trichomoniasis, but is also seen in 1%–2% of women during a regular pelvic exam.

Trichomonas vaginalis infection:
“strawberry”
appearance of cervix with punctuate
bleeding erosions.

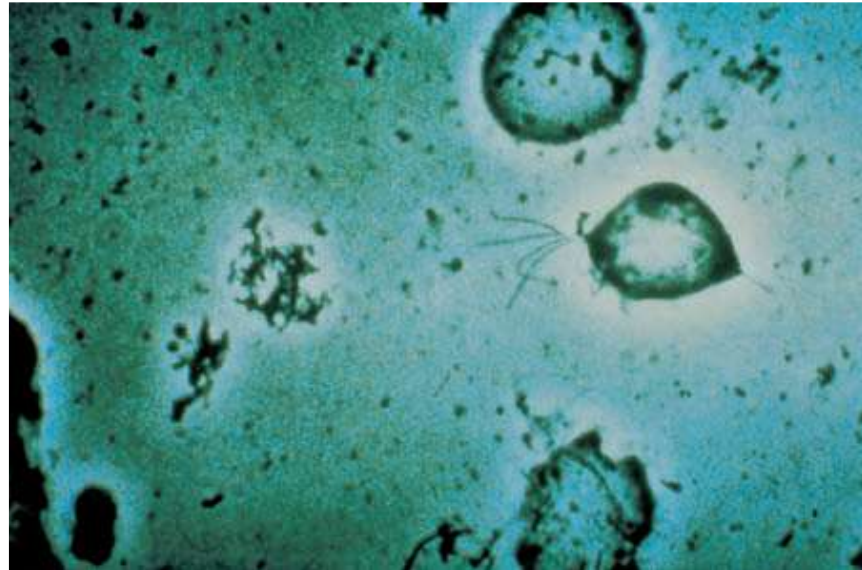


LABORATORY TESTS

There are three basic methods to search for the causative parasite.

- A saline wet mount of a vaginal discharge specimen is the most common diagnostic test.
- The can be visualized microscopically, best by phase contrast or dark-field examination.
- The most sensitive test is anaerobic culture, which usually is positive within 48 hours, and is the preferred detection method.

Trichomonas vaginalis



COMPLICATIONS

- Recently, studies have shown a link between *T. vaginalis* infection and complications in pregnancy, such as premature delivery, early rupture of membranes, and low birth weight in newborns.
- Trichomoniasis has also been associated with an increased risk of HIV transmission.
- Less commonly, it has been linked to atypical pelvic inflammatory diseases.

TREATMENT

- The nitroimidazoles, metronidazole and tinidazole are the only agents approved for treatment of trichomoniasis, the clinical efficacy of both drugs being identical
- Metronidazole, 2 g orally in a single dose Or Tinidazole, 2 g orally in a single dose
- Alternative recommendations Metronidazole, 500 mg orally twice a day for 7 days

BACTERIAL VAGINOSIS

BACTERIAL VAGINOSIS

- BV is the most common vaginal infection in women of childbearing age.
- It is estimated that approximately 16% of pregnant women in the United States may have BV at a given time.
- Women who have never had sex are extremely rarely affected
- BV is a polymicrobial syndrome that occurs when there is an imbalance of the bacterial flora normally present in the vagina.
- It is not known to be transmitted through sexual contact, and the exact etiology has not been defined.

CLINICAL FINDINGS

- As many as 50%–75% of women with BV may be asymptomatic.
- Women with BV may complain of a fishy odor and thin, white or gray vaginal discharge.
- Vulvo-vaginal pruritus and inflammation are rare.
- On physical examination, a milky, homogenous vaginal coating may be seen adherent to the vaginal wall.

LABORATORY TESTS

- According to the Amstel criteria for diagnosis BV, three of the following four must be present:
- (1) thin, homogenous vaginal discharge;
- (2) a positive whiff test, which involves the production of a fishy odor when mixing vaginal fluid with 10% potassium hydroxide;
- (3) vaginal fluid pH greater than 4.5
- (4) the presence of clue cells (epithelial cells covered with bacteria) on microscopic examination.
- Clue cells, being the most reliable indicator of BV, must make up at least 20% of the epithelial cells on saline wet mount.

LABORATORY TESTS

- Another diagnostic test involves the use of Gram staining to distinguish between the normal bacterial flora of Gram-positive rods and lactobacilli from the Gram negative morphotypes seen in BV.
- Due to the variety of bacterial species, culture is not a trustable diagnostic test.

TREATMENT

- Metronidazole, 500 mg orally twice daily for 7 days or
- Metronidazole gel, 0.75%, 5 g intravaginal once daily for 5 days or
- Clindamycin cream, 5%, 5 g intravaginal every bedtime for 7 days

TREATMENT

In pregnant women:

- Metronidazole, 250 mg orally three times daily for 7 days or
- Metronidazole 500 mg orally twice daily for 7 days or
- Clindamycin, 300 mg twice daily for 7 days

Alternative regimens

- Tinidazole 2.0 g orally once daily for 3 days or
- Tinidazole 1.0 g orally once daily for 5 days or
- Clindamycin 300 mg twice daily for 7 days or
- Clindamycin ovules, 100 g intravaginally every night at bedtime for 3 days