**Sexually Transmitted Diseases**

**Uncomplicated Gonorrhea**

* Gonorrhea is caused by ***Neisseria gonorrhoeae***, a Gram-negative diplococcus.
* The ***highest incidence*** of gonorrhea is in men aged 20 to 24 years and in females aged 15 to 19 years and aged 20 to 24 years.
* ***Additional risk factors*** for gonorrhea include

 low socioeconomic status, urban residence, unmarried marital status, illicit drug use, inconsistent condom use, new or multiple sex partners, prostitution, and a history of gonorrhea or other sexually transmitted infections

* After ***one or two episodes of unprotected vaginal*** intercourse with an infected prostitute, **a man** has approximately a 50% risk of acquiring a urethral infection;
* The prevalence of infection in **women** who are secondary sex contacts of infected men is as high as 80% to 90%

**Signs and Symptoms: Males**

* gonorrhea usually becomes **clinically apparent 1 to 7 days** after contact with an infected source.
* **A purulent discharge** associated with dysuria is the first sign of infection;
* The discharge may become **more profuse and blood tinged** as the infection progresses.
* **Patients with asymptomatic** or minimally symptomatic disease may serve as **reservoirs** for the infection, evading treatment for prolonged periods of time.
* *At one time, only females were thought to have asymptomatic gonorrhea, but now it is known that men may be asymptomatic carriers as well.*

 **Females**

* ***Because the endocervical canal is the primary site*** of urogenital gonococcal infection in women, the most common symptom is vaginal discharge.
* Many women infected with gonorrhea have abnormalities of the cervix, including purulent or mucopurulent endocervical discharge, erythema, friability, and edema of the zone of ectopy.
* ***Pelvic inflammatory disease (PID)*** is a serious complication and can lead to infertility and chronic pelvic pain.
* ***The assessment of signs and symptoms*** in women with gonorrhea often is confounded by prevalence of coexisting infection, especially with ***Chlamydia trachomatis*** or ***Trichomonas vaginalis***.
* Although lower genital tract symptoms in women may disappear, ***they remain carriers*** of N. gonorrhoeae and should be treated.
* ***Complications of urogenital gonorrhea in pregnancy*** include spontaneous abortion, premature rupture of the fetal membranes, premature delivery, and acute chorioamnionitis.
* Other complications include gonococcal arthritis , conjunctivitis, and ophthalmia neonatorum in the newborn.

**Diagnosis: Males**

* **cultures are recommended for all patients** to permit isolation and testing of the bacteria for antibiotic susceptibility

 **Females**

* **an endocervical culture**, which is positive in 80% of women with gonorrhea and is still considered the “gold standard.”
* **Nucleic acid amplification tests (NAATs**), such as polymerase chain reaction (PCR), may yield sensitivities and specificities in the 90% to 100% range, but results must be confirmed with endocervical culture in low-prevalence communities

**Treatment:**

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| **CDC Recommendations for Treatment of Uncomplicated Gonorrhea** |
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| ***Presentation*** | ***Drugs of Choice (% Cured)*** | ***Dosage*** | ***Alternative Regimens*** |
| Urethritis, cervicitis,a rectal | Ceftriaxone (98.9) | 125 mg IM once | Cephalosporin single dose regimensc |
| Cefixime (97.4)b | 400 mg PO once |
| Pharyngeal | Ceftriaxone | 125 mg IM once |  |

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* Many strains of N. gonorrhoeae exhibit plasmid-mediated ***resistance to*** ***penicillin and tetracycline*** (penicillinase-producing N. gonorrhoeae [PPNG] and/or tetracycline-resistant N. gonorrhoeae [TRNG]; .
* a single dose of intramuscular (***IM) ceftriaxone*** is preferred for the treatment of gonorrhea. ***Cefixime 400 mg orally*** as a single dose is also recommended
* Because a high percentage of patients with gonorrhea are also coinfected with C. trachomatis, a ***single dose of azithromycin*** or a 7-day course of doxycycline is recommended to be taken concurrently for a presumed infection.
* ***Spectinomycin*** was the recommended treatment option for gonorrhea in those with either penicillin or cephalosporin allergies.

**Prescribing Patterns:**

* ***ceftriaxone 125 mg, followed by the fluoroquinolones*** ciprofloxacin and ofloxacin, were the most commonly prescribed agents
* ***Cefixime is currently*** only available in a generic suspension (100 or 200 mg/5 mL) form. preferred agent for uncomplicated gonorrhea.
* no single-dose therapy for gonorrhea and chlamydia is highly effective, additional concurrent therapy needs to be administered. ***Azithromycin or doxycycline*** are effective for concomitant chlamydia coinfection. Single-dose azithromycin 2 g PO has been used to treat concurrent gonorrhea and chlamydia, but it is more expensive, poorly tolerated because of increased gastrointestinal (GI) side effects, and less effective than standard combination therapy

**Sexual Partners:**

* All partners who have had sexual exposure to patients with gonorrhea within 60 days should be treated.
* If the patient has not been sexually active for 60 days, the most recent sexual partner should be treated. This is especially true when the partner is pregnant because gonorrhea during pregnancy is associated with chorio amnionitis and prematurity, as well as neonatal infection.
* Pregnant women can be treated safely with ***cephalosporins*** and ***azithromycin*** for gonorrhea and Chlamydia. Doxycycline should be avoided during pregnancy.

***Anorectal and Pharyngeal Gonorrhea***

* The most prevalent bacterial STD among the **homosexual male** population is gonorrhea.
* **Rectal infection** occurs rarely in strictly heterosexual men, whereas in the  male **homosexual population, anorectal (25%) and pharyngeal (10%–25%)** gonococcal infections occur more often.9,36
* Because pharyngeal and anorectal gonococcal infections are often **asymptomatic,** a **large reservoir of carriers** in the homosexual male population may exist,
* **diagnosed only** with more sensitive DNA amplification techniques
* **The treatment of choice** for patients with anorectal and/or pharyngeal gonorrhea is ***ceftriaxone 125 mg IM*** as a single dose).

***Azithromycin or doxycycline*** should be given to those with rectal gonorrhea to treat possible coexisting rectal chlamydial infection.

* Patients with either anorectal or pharyngeal gonorrhea should be **advised to avoid further unprotected** sexual activity and should be counseled and tested for infection with HIV.

***Pelvic Inflammatory Disease***

* **The term** pelvic inflammatory disease (PID) commonly refers to a **variety of inflammatory disorders of the upper female reproductive tract.**
* **PID also has been** used to connote an infection that traverse the sterile endometrium and ascend to the fallopian tubes.
* **Acute salpingitis** also may be used to describe an acute infection of the fallopian tubes.

 Therefore, the terms PID and salpingitis are used interchangeably in this discussion to denote an acute infection involving the fallopian tubes.

* **Most cases of PID are caused** by ***C. trachomatis and N. gonorrhoeae.***6 Some micro-organisms that comprise the vaginal flora are also associated with PID, including Gardnerella vaginalis, H. influenzae, and Streptococcus agalactiae.

**Signs and Symptoms**

**The onset of symptoms of abdominal pain** attributable to PID caused by either *gonococci or chlamydia often occurs soon after the menstrual period.*

* **Symptoms of PID**, if present, Vaginal discharge, menorrhagia, dysuria, and dyspareunia.
* **Signs include cervical motion** tenderness, uterine tenderness, or adnexal tenderness.
* **Temperatures above 101°F**, abnormal cervical or vaginal mucopurulent discharge, white blood cells (WBC) on saline microscopy of vaginal secretions, elevated erythrocyte sedimentation rate, or an elevated C-reactive protein support a diagnosis of PID
* **After a single episode of PID**, tubal occlusion and fibrosis secondary to fallopian tube inflammation (salpingitis) result in 12% infertility, 25% infertility **after two episodes**, and 50% infertility after **three or more** episodes.
* **Other sequelae** include ectopic pregnancy (9%) and chronic pelvic pain (18%).57 The risk of ectopic pregnancy is increased approximately eightfold after one or more episodes of PID.

**Diagnosis and Treatment**

* **Treatment should be initiated immediately** after diagnosis of PID to prevent clinical sequelae;
* ***For inpatient treatment,***

 ***(IV) cefotetan 2 g*** every 12 hours or

 ***IV cefoxitin 2 g*** every 6 hours for at least 24 hours

Once clinical improvement is noted, parenteral therapy may be discontinued and ***PO doxycycline 100 mg*** every 12 hours can continue to complete 14 days of therapy.

* ***For outpatient treatment,***

 ***IM ceftriaxone 250 mg*** as a single dose ***or***

 ***IM cefoxitin 2 g*** as single dose (***with probenecid 1 g PO × 1)***

**plus** ***PO doxycycline 100 mg*** twice a day for 14 days

 **with or without *PO metronidazole 500 mg*** twice daily for 14days.

* A ***tetracycline derivative*** or an alternative agent that is active against C. trachomatis should be included in the treatment of PID; however, monotherapy with a tetracycline is not recommended because of the lack of activity against Gram-negative aerobic and anaerobic organisms and N. gonorrhoeae.
* Both ***oral and IV doxycycline*** have similar bioavailability tometronidazole; therefore, doxycycline should be given PO whenever possible because IV administration may be painful.6 Substantial clinical improvement is usually seen within 3 days after initiation of therapy.
* Clindamycin plus gentamicin can be used alternatively in penicillin-allergic and pregnant females

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| **Antimicrobial Regimens Recommended by the CDC for Treatment of Acute Pelvic Inflammatory Disease** |
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| ***Treatment Setting, Drugs, Schedule*** | ***Advantage*** | ***Disadvantage*** | ***Clinical Considerations*** |
| **Inpatient** |
| **Regimen A**Cefotetan 2 g IV Q 12 hr or cefoxitin 2 g IV Q 6 hr plus doxycycline 100 mg IV or POa Q 12 hrContinue doxycycline (100 mg PO BID) after discharge to complete 14 days of therapy | Optimal coverage of *N. gonorrhoeae* (including resistant strains) and *C. trachomatis* | Possible suboptimal anaerobic coverage | Penicillin-allergic patients also may be allergic to cephalosporins; doxycycline use in pregnant patients may cause reversible inhibition of skeletal growth in the fetus and discoloration of teeth in young children |
| **Regimen B**Clindamycin 900 mg IV Q 8 hr plus gentamicin loading dose IV or IM (2 mg/kg) followed by a maintenance dose of 1.5 mg/kg Q 8 hrbContinue clindamycin 450 mg PO QID or doxycycline 100 mg PO BID after discharge to complete 14 days of therapy | Optimal coverage of anaerobes and Gram-negative enteric rods | Possible suboptimal coverage of *N. gonorrhoeae* and *C. trachomatis* | Patients with decreased renal function may not be good candidates for aminoglycoside treatment or may need a dosage adjustment |
| **Alternative regimen**Ampicillins/sulbactam 3 g IV Q 6 hr plus doxycycline 100 mg PO or IV Q 12 hr | Optimal coverage of *N. gonorrhoeae* and *C. trachomatis* | Inadequate coverage of anaerobes necessitates use of metronidazole or ampicillin/sulbactam | Not appropriate in pregnancy or in young children |
| **Outpatient** |
| **Regimen A**Ceftriaxone 250 mg IM in a single dose plus doxycycline 100 mg PO BID for 14 days with or without metronidazole 500 mg PO BID for 14 days or cefoxitin 2 g IM in a single dose and probenecid, 1 g PO administered concurrently in a single dose plus doxycycline 100 mg PO BID for 14 days with or without metronidazole 500 mg PO BID for 14 days or other parenteral third-generation cephalosporins (e.g., ceftizoxime or cefotaxime) plus doxycycline 100 mg PO BID for 14 days with or without metronidazole 500 mg PO BID for 14 days | Good to excellent coverage of *N. gonorrhoeae* and optimal coverage of *C. trachomatis* | Possible suboptimal anaerobic coverage necessitating the addition of metronidazole | Optimal cephalosporin is unclear; more complicated regimen requiring combination of parenteral and oral therapies |

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**Complicated Gonorrhea**

***Disseminated Gonococcal Infection(DGI)***

**Signs and Symptoms**

* The most common manifestation of gonococcemia is the ***gonococcal arthritis–dermatitis*** syndrome or ***disseminated gonococcal infection (DGI)***
* Symptoms include fever, occasional chills, a mild tenosynovitis of the small joints,  and skin lesions;

**Treatment**

* **Patients with gonococcal arthritis** and bacteremia should be hospitalized for treatment with ***ceftriaxone 1 g IV daily*** until clinical improvement, such as decreased fever and pain, is sustained for 24 to 48 hours,
* **switched to an appropriate oral agent**. ***cefixime 400*** mg daily for 7 days is currently recommended
* **Symptoms and signs of tenosynovitis** should be improved markedly within 48 hours.
* **Septic gonococcal arthritis** with purulent synovial fluid may require repeated aspiration and resolves more slowly.

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| **Treatment of Disseminated Gonococcal Infectiona** |
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| ***No Penicillin Allergy*** |
| **Parenteral** |
| Ceftriaxone 1 g IV or IM Q 24 hr or cefotaxime 1 g IV Q 8 hr or ceftizoxime 1 g IV Q 8 hr and doxycycline 100 mg PO BIDb or erythromycin base 500 mg PO QIDb (if pregnant) |
| **Oral** |
| Cefixime 400 mg PO BID |
| ***Penicillin Allergy*** |
| **Parenteral** |
| Spectinomycin 2 g IM Q 12 hr and doxycycline 100 mg PO BIDb or erythromycin base 500 mg PO QIDb (if pregnant) |
| aDuration of treatment is 7 days.bFor possible concomitant chlamydial infection, treat for 7 days.Adapted from reference 6. |

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***Treatment of Gonococcal Endocarditis and Meningitis***

* Gonococcal endocarditis and meningitis, occurring in only 1% to 3% of DGIs,
* **require high-dose IV** therapy such ***as ceftriaxone (1–2 g IV*** every 12 hours) for 10 days or more in the case of meningitis and for 4 weeks in the case of endocarditis

***Treatment of Neonatal Disseminated Gonococcal Infe*ction:**

* Neonatal DGI and meningitis can be treated with either ***ceftriaxone or cefotaxime f***or 7 days;
* if meningitis is documented, 10 to 14 days of treatment is required. Ceftriaxone is given at 25 to 50 mg/kg (IV or IM) Q 24 hr and cefotaxime is given at 25 mg/kg (IV or IM) Q 12 hr.

**Chlamydia trachomatis**

* **C. trachomatis** was first isolated from patients with lymphogranuloma venereum (LGV
* **Women are three times** more likely than men to be infected with Chlamydia
* **If left untreated**, chlamydial infection in women can lead to serious sequelae such as PID, ectopic pregnancy, and infertility.
* **Asymptomatic infection** is also observed in both men and women; however, routine screening is only recommended for sexually active women at least 25 years old and women with risk factors for infection (e.g., multiple sexual partners, new sexual partners). Screening sexually active men in settings with a high prevalence of the infection.6

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| **Clinical Parallels Between Genital Infections Caused by N. gonorrhoeae and C. trachomatis: Resulting Clinical Syndromes** |
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| ***Gender*** | ***Site of Infection*** | ***N. gonorrhoeae*** | ***C. trachomatis*** |
| ***Male*** | Urethra | Urethritis | NGU, postgonococcal urethritis |
| Epididymis | Epididymitis | Epididymitis |
| Rectum | Proctitis | Proctitis |
| Conjunctiva | Conjunctivitis | Conjunctivitis |
| Systemic | DGI | Reiter syndrome |
| ***Female*** | Urethra | Acute urethral syndrome | Acute urethral syndrome |
| Bartholin gland | Bartholinitis | Bartholinitis |
| Cervix | Cervicitis | Cervicitis |
| Fallopian tube | Salpingitis | Salpingitis |
| Conjunctiva | Conjunctivitis | Conjunctivitis |
| Systemic | DGI | Arthritis-dermatitis (Reiter syndrome) |

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* ***clinical syndromes*** are cervicitis, urethritis, bartholinitis, endometritis, salpingititis, and perihepatitis in women, and urethritis, epididymitis, prostatitis, proctitis, and Reiter syndrome in men.
* Only **azithromycin and doxycycline** have cure rates.
* Agents mentioned as alternatives include erythromycin, ofloxacin, and levofloxacin, **but not** the penicillins, cephalosporins, aminoglycosides, clarithromycin, ciprofloxacin, or metronidazole.

***1-Nongonococcal Urethritis (NGU)***

* causative organisms identified include C. trachomatis ,U. urealyticum , M. genitalium , T. vaginalis , and no identifiable cause in up to 20%.

**Signs and Symptoms**

* **Chlamydial urethral** infection is **completely asymptomatic** more often than gonococcal urethral infection.
* **The incubation period** for gonococcal urethritis is 2 to 7 days, whereas the incubation period for NGU is typically 2 to 3 weeks.
* If there is objective evidence of a **urethral discharge** (expressed by milking the urethra), the diagnosis of NGU is made by excluding the presence of N. gonorrhoeae by Gram stain and/or culture.

**Treatment**

* therapy with ***azithromycin*** should be initiated to cover for both M. genitalium and Chlamydia.
* ***Doxycycline*** 100 mg PO BID for 7 days may also be prescribed.
* Both azithromycin and doxycycline are considered equally effective against NGU
* ***Erythromycin base 500 mg*** PO QID or erythromycin ethylsuccinate 800 mg PO QID for 7 days are alternative .

**Recurrent Infection**

* patients experience recurrent or persistent urethritis within 1 to 2 weeks after treatment
* ***metronidazole*** or ***tinidazole 2 g*** PO as a single dose **plus** a single 1 g dose of ***azithromycin*** if not used for the initial episode.
* Older men with epididymitis more often are infected with ***Escherichia coli*** .If testicular tenderness is present with urethritis, epididymitis is caused by chlamydia or gonorrhea
* a single dose of ***ceftriaxone 250 mg IM plus doxycycline 100 mg*** PO twice for 10 days.
* For a nonsexually transmitted etiology of epididymitis, ***ofloxacin*** 300 mg PO BID ***or levofloxacin*** 500 mg PO once daily for 10 days may be used.6

**Sexual Partners -**empirical treatment of women who are sexual partners of men with NGU is recommended with the same doxycycline regimen used for NGU.

***2-.Lymphogranuloma Venereum LGV***

**Etiology and Signs and Symptoms**

* **The cause** of LGV is usually C. trachomatis serovars L1, L2, or L3, which is different from those serovars responsible for chlamydia urethritis.
* **Three stages** of LGV infection are recognized in heterosexual men.

=***stage I***, a small genital papule or vesicle appears between 3 and 30 days after exposure. The patient usually is asymptomatic; the ulcer heals rapidly and leaves no scar.

***=Stage II*** is characterized by acute, painful lymph adenitis with bubo formation (the inguinal syndrome); it often is accompanied by pain and fever,.

 Without treatment, the buboes may rupture, forming numerous sinus tracts that drain chronically.

Adenopathy above and below the inguinal ligament results in the “groove sign.”

Patients in this stage also may present with an anogenitorectal syndrome, which is accompanied by proctocolitis and hyperplasia of intestinal and perirectal lymphatic tissue.

***= stage II*** LGV Late or tertiary manifestations include perirectal abscesses, rectovaginal fistulae (in women), rectal strictures, and genital elephantiasis.

 Appropriate treatment of stage II LGV usually prevents these late complications.

An acute anorectal syndrome of LGV occurs in homosexual men who acquire the infection through rectal receptive intercourse. In these cases, a primary anal ulcer may be noted with associated inguinal adenopathy (anal lymphatics drain to inguinal nodes). Subsequently, acute hemorrhagic proctocolitis occurs with tenesmus, rectal pain, constipation, and a mucopurulent, bloody rectal discharge. Rectal biopsy may show granulomatous colitis, mimicking Crohn disease. Perirectal pelvic adenopathy also occurs.

**Treatment**

* ***doxycycline 100 mg*** PO BID or

***erythromycin base 500*** mg PO QID for 21 days.

* Surgical intervention may be needed for later forms of the disease.

**Syphilis**

Syphilis is caused by the spirochete, ***Treponema pallidum***

**Clinical Stages**

**1-Primary Stage**

* **incubation period - 3 weeks** , T. pallidum can be demonstrated in the lymph and blood.
* **The primary chancre** develops at the site of inoculation as a painless papule that becomes ulcerated and indurated. The ulcer is nontender and filled with spirochetes
* **The differential diagnosis** of genital ulcers also includes *chancroid and genital herpes*. Syphilis can be differentiated from herpes by

- a nonpainful versus painful lesion,

- a papular versus vesicular appearance,

-and single versus multiple lesions.

 Chancroid is more difficult to differentiate from syphilis, although chancroid tends to have a more tender lesion, jagged border, and striking inguinal lymphadenopathy.

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**2-Secondary Stage**

* Approximately 6 weeks after a chancre first appears,
* patient begins to manifest signs of macular lesion. The lesion is round or oval, occurs primarily on the trunk, and is rose or pink in color.
* As lesions mature, they become papular or nodular with scaling (the so-called papulosquamous rash). Generalized lymphadenopathy usually is present, and patching alopecia may be seen.

**3-Latent Stage**

* asymptomatic persons with serologic evidence for syphilis have latent syphilis.
* The latent stage is divided into ***two phases***:

=the early latent (<1 year's duration) and

= late latent (>1 year's duration).

**4-Tertiary Stage**

* Morbidity and mortality of syphilis involving the skin, bones, central nervous system, and cardiovascular system.
* Infectious granulomas (gummas), the characteristic lesions of tertiary syphilis,

**Neurosyphilis**

* asymptomatic early or late, meningeal, parenchymatous, or gummatous.
* Although neurosyphilis has been a rare complication for more than 40 years because of the widespread of use of penicillin, *syphilitic meningitis, an early form of neurosyphilis*, may be increasing among HIV-positive patients.
* Late neurosyphilis may be asymptomatic or accompanied by a variety of manifestations;

**Treatment**

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| **Treatment Guidelines for Syphilis** |
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| ***Stage*** | ***Recommended Regimen*** | ***Alternative Regimen*** |
| **Early (primary, secondary, or early latent)a** | Benzathine penicillin G 2.4 MU single dose IM | Doxycycline 100 mg PO BID for 14 days *or*Tetracycline 500 mg PO QID for 14 days *or*Ceftriaxone 1 g IM/IV QD for 8 to 10 days *or*Azithromycin 2 g PO ×1 dose |
| **Late latent or latent syphilis of unknown duration** | Lumbar puncture | Lumbar puncture |
| If CSF normal: Benzathine penicillin G 2.4 MU/wk ×3 wk IM | If CSF normal: Doxycycline 100 mg PO BID for 28 days *or*Tetracycline 500 mg PO QID for 28 days |
| If CSF abnormal: Treat as neurosyphilis | If CSF abnormal: Treat as neurosyphilis |
| **Neurosyphilisb (asymptomatic or symptomatic)** | Aqueous penicillin G 18–24 MU IV QD ×10–14 daysc | Procaine penicillin 2.4 MU IM QD plus probenecid 500 mg PO QID, both for 10–14 days |
| **Congenital** | Aqueous penicillin G 100,000–150,000 U/kg/d, administered as 50,000 U/kg/dose IV Q 12 hr during the first 7 days of life, and Q 8 hr thereafter for a total of 10 daysd*or*Procaine penicillin G 50,000 U/kg/dose IM a day in a single dose for 10 days | If CSF normal: benzathine penicillin G 50,000 U/kg/dose IM in a single dose |
| **Syphilis in pregnancy** | According to stage | According to stage |

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* ***Penicillin G*** is the drug of choice for the treatment for all stages of syphilis
* recommended therapy for primary, secondary, or latent syphilis is a single, ***IM 2.4 MU dose of benzathine penicillin G***.
* If penicillin is contraindicated, ***tetracycline (500 mg PO QID***) or ***doxycycline (100 mg PO BID)*** for 2 weeks are the main alternatives.
* If the patient is allergic to penicillin, a 14-day regimen of ***azithromycin (500 mg PO QD)*** or ***ceftriaxone (500 mg IM QD***) may be used *. an alternative regimen of azithromycin 2 g in one dose or ceftriaxone 1 g IM or IV for 8 to 10 days*.
* **Neurosyphilis** can present at any stage of syphilis. can be treated with ***procaine penicillin (2.4 MU IM/d)* plus *probenecid (500 mg*** PO every 6 hours) for 10 to 14 days
* penicillin-allergic nonpregnant patients receive ***either doxycycline*** 200 mg PO BID or ***tetracycline*** 500 mg PO QID for 30 days.

**Neonatal Syphilis**

* Infants born to mothers who have been treated for syphilis during pregnancy should be carefully examined at birth, at 1 month, every 2 to 3 months for 15 months, and then every 6 months
* ***Aqueous penicillin G 50,000 U/kg per dose IV*** every 12 hours should be used during ***the first 7 days of life*** and every 8 hours thereafter for a total of 10 days.
* ***Procaine penicillin G 50,000 U/kg per dose IM*** daily for at least 10 days is an alternative regimen

**Chancroid**

* Chancroid or soft chancre is a painful genital ulcer disease that often is associated with tender inguinal adenopathy.
* It is caused by ***Haemophilus ducreyi***, a Gram-negative bacillus. Chancroid is endemic in developing countries

**Signs and Symptoms**

* A painful genital ulcer appears 3 to 10 days after exposure and begins as a tender, red papule that becomes pustular and ulcerates within 2 days. ulcer may be covered by a grayish or yellow exudate.
* Multiple ulcers and tender inguinal lymph nodes,

**Treatment**

* ***Azithromycin 1 g PO*** for 1 dose, ***ceftriaxone 250 mg IM once***, ***ciprofloxacin 500 mg PO BID*** for 3 days, or ***erythromycin base 500*** mg PO TID for 7 days.
* Follow-up should occur 3 to 7 days after treatment is initiated. Depending on the size of the ulcer ,larger ulcers may require longer than 2 weeks.6

**Genital Herpes**

* **Genital herpes** and **neonatal herpes** primarily are the result of HSV-2 infections.
* However, up to 50% of all reported cases of primary genital herpes are due to HSV-1 infections acquired **through oral sex**.

The initial, primary disease is a **gingivostomatitis** characterized by vesicles in the oral cavity and occasionally an elevated temperature; life-threatening encephalitis or keratitis may appear during this interval.

**Signs and Symptoms**

* Most initial episodes, especially in the male, are symptomatic. usually start about 1 week after the initial exposure
* **prodromal signs** of tingling, itching, paresthesia, and/or genital burning.
* followed by the appearance **of numerous** **vesicles.** The vesicles eventually erupt, resulting in painful genital ulcers.
* The pain and edema can be severe enough to result in dysuria and urinary retention.
* Bilaterally distributed lesions of the external genitalia are characteristic. lesions can occur on the buttocks, thighs, and urethra.
* Asymptomatic or mucopurulent cervicitis .Rectal and perianal HSV-2 infections. Herpes simplex virus proctitis ,Symptoms include anorectal pain and discharge, tenesmus, and constipation.
* **Recurrent infections** are shorter in duration (average, 1 week); local symptoms such as pain and itching last 4 to 5 days and the lesions themselves last 7 to 10 days.
* **Transmission of HSV** occurs by

**=** direct contact with active lesions or from a symptomatic or asymptomatic person shedding virus at a peripheral site, mucosal surface, or secretion.1

= Genital HSV-2 infections usually are acquired through sexual (vaginal or anorectal) intercourse, whereas genital HSV-1 infections are acquired via oral–genital sexual practices

**Treatment**

* Currently, ***only acyclovir (ACV), famciclovir (FCV), and valacyclovir (VCV)*** are used to treat and prevent genital herpes outbreaks.
* **The ideal anti-HSV agent** should

(a) prevent infection,

(b) shorten the clinical course,

(c) prevent the development of latency,

(d) prevent recurrence in patients with established latency,

(e) decrease transmission of disease, and

 (f) eradicate established latent infection.

 To date, no agent has been successful in achieving all of these goals.

* **All three agents**, ACV, FCV, and VCV, are for the short-term treatment of some HSV infections.
* primary genital herpes, ***IV ACV (5 mg/kg Q 8 hr)*** significantly reduced signs and symptoms of disease by a mean of 5 days, .
* For patients with HIV, ***ACV 400 mg PO three times daily, FCV 500 mg twice daily, or VCV 500 mg twice daily*** for 5 to 10 days have been used for recurrent episodes.
* Currently, IV therapy is recommended only for patients with severe genital or disseminated infections who cannot take oral medication.

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| **Antiviral Chemotherapy of Genital HSV-2 Infections** |
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|  | ***Acyclovir*** | ***Valacyclovir*** | ***Famciclovir*** | ***Duration*** | ***Comments*** |
| First clinical episode | 400 mg PO TID *or*200 mg PO 5 per day | 1 g PO BID | 250 mg PO TID | 7–10 days | May extend treatment duration if healing is incomplete |
| Episodic recurrent infection | 400 mg PO TID *or*200 mg PO 5 per day *or*800 mg PO BID | 500 mg PO BID *or* 1 g QD | 125 mg PO BID | 5 days | Most effective if initiated within the first 24 hr of onset of lesions or during the prodrome |
| Daily suppressive therapy | 400 mg PO BIDa | 500 mg PO QD*b or*1 g PO QD | 250 mg PO BID | Daily | Reduces the frequency of genital herpes recurrences by ≥75% among patients who have frequent recurrences (i.e., ≥6 recurrences per year); use should be reevaluated at 1 yr |
| Severe disseminated | 5–10 mg/kg IV Q 8 hr | Not indicated | Not indicated | Variable | Hospitalize and treat until clinical resolution of symptomsFollow-up IV therapy with PO ACV to complete 10 days |
| HIV-infected: episodic | 400 mg PO TID *or* 200 mg 5 per day | 1 g PO BIDc | 500 mg PO BID | 5–10 days | Treat until clinical resolution of lesions |
| HIV-infected: suppressive | 400–800 mg PO BID or TID | 500 mg PO BIDd | 500 mg PO BID |  |  |

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**Patient Education and Counseling**

* Most genital herpes infections **heal spontaneously** unless the patient is immunocompromised or the lesions have become infected secondarily.
* The patient should be instructed to keep the involved areas clean and dry.
* To prevent autoinoculation, the patient should be told not to touch the lesions and to wash his hands immediately afterward if he comes in contact inadvertently.
* Local anesthetics provide relief from the pain of genital lesions, but they should be avoided if possible because they counteract efforts to keep the lesions dry.
* Local corticosteroid therapy is contraindicated because it may predispose the patient to secondary bacterial infections.

**Genital Warts**

* ***Human papilloma virus HPV***, primarily types 6 and 11, are the cause of genital warts, or ***condylomata acuminata***.
* The goal of HPV therapy is the **removal of symptomatic warts**.
* Several therapeutic options are

***podofilox 0.5% solution*** or gel and ***imiquimod 5% cream*** and topical treatments (***podophyllin 10%–25%, trichloroacetic acid 80%–90%, and cryotherapy***),

***surgery (laser or scalpel***), and

***intralesional interferon***.

 None of these treatments has been shown to eradicate HPV .

**Podophyllin**, compounded as a 10% to 25% solution in tincture of benzoin,. After application, it is washed off 3 to 4 hours later and then reapplied once or twice a week until the warts have disappeared. Podofilox 0.5% solution or gel, the active component of podophyllin resin, may be applied by the patient with a cotton swab, or podofilox gel with a finger, to visible genital warts twice a day for 3 days, followed by 4 days of no therapy.

A total of four cycles, 0.5 mL/day, or application of an area larger than 10 cm2 should not be exceeded.

Podophyllin is potentially neurotoxic if absorbed in large amounts.

**Imiquimod i**nduces cytokines and activates the cell-mediated immune system**.** A 5% cream may be applied with a finger at bedtime three times per week  for up to 16 weeks. It is usually left on for 6 to 10 hours before it is washed off with soap and water.

**Cryotherapy** by application of liquid nitrogen can be more effective than podophyllin, but requires special equipment and highly trained personnel to avoid over- or undertreating warts.

**Trichloroacetic acid (80%–90%)** is used topically in the treatment of some genital warts,.

To date**, interferons** are not recommended because of expense, frequent occurrence of toxicity when given systemically, and limited efficacy for intralesional administration.

 Cases refractory to topical drug therapy should be considered for **surgical** treatment.

*Because there are more than 30 types of HPV associated with anogenital disease, a previous HPV infection is not a contraindication to vaccination*

**Vaccines**

* Immunization, however, holds the promise of protecting large numbers of people before they are at risk for STDs as well as targeting those who already have the infection.
* **Hepatitis B** is an example of an STD with a highly effective vaccine that is *now mandatory for school-aged children.*

**Trichomoniasis**

**Signs and Symptoms**

* Trichomoniasis is an STD caused by the ***protozoan T. vaginalis***.
* **The prevalence** in women ranges from 5% to 10% and up to 60% in commercial sex workers.
* Trichomoniasis in women is asymptomatic about 20% to 50% of the time.157 In men, T. vaginalis presumably infects the urethra, although the site of infection (urethra versus prostate) is uncertain. Men with T. vaginalis infection usually are asymptomatic.
* Classic symptoms of trichomoniasis in women include a diffuse, yellow-green discharge with pruritus, dysuria, and a “strawberry” cervix (cervical microhemorrhages).
* Direct microscopic observation of trichomoniasis using a wet mount suffers from low sensitivity, but is up to 99% specific.

**Treatment**

**Metronidazole and Tinidazole**

* first-line treatments given as a ***single 2-g oral*** dose.6 In addition, sexual partners should be simultaneously treated.
* If the 2-g metronidazole dose fails and reinfection is excluded, either ***metronidazole 500 mg PO*** twice daily for 7 days or ***tinidazole 2 g PO as a single dose*** can be used. If either of these regimens fail, either metronidazole or tinidazole 2 g PO daily for 5 days may be used.
* During pregnancy, trichomoniasis is associated with premature rupture of the membranes, preterm delivery, and low birth weight.
* All symptomatic women should be treated with metronidazole 2 g PO as a single dose.
* Metronidazole is classified as pregnancy category B. Tinidazole 2 g PO as a single dose could be suggested as an alternative regimen; however, it is classified as pregnancy category C.

**Vaginitis**

* The term vaginitis refers to such nonspecific vaginal symptoms as itching, burning, irritation, and abnormal discharge that may be caused by infection or other medical conditions.
* The most common vaginal infections are **Bacterial Vaginosis BV** (22%–50% of cases), **vulvovaginal candidiasis (VVC**; 17%–39% of cases), and **trichomoniasis** (4%–35% of cases). However, between 7% and 72% of cases of vaginitis may remain undiagnosed.

**1-Bacterial Vaginosis BV**

* represents the most common cause of vaginal disharge.
* Many sexually active women are infected with G. vaginalis at any one time, yet fewer than 50% are symptomatic or have signs of abnormal vaginal discharge.1
* The evidence for definitive risk factors in BV is inconclusive. Multiple sexual partners,6 a new sexual partner,6 IUDs,

**Treatment**

* Nonpregnant women with symptomatic disease require treatment. ***Oral metronidazole 500*** mg twice a day for 7 days is the most effective treatment of BV. only 82% still report cure after 4 weeks,
* The FDA has approved ***metronidazole extended release 750 mg*** once daily for 7 days and a single dose of ***clindamycin intravaginal*** cream for the treatment of BV;
* **Ampicillin is no longer** considered an alternative treatment because approximately 50% of women develop recurrent symptoms within 6 weeks.
* ***Clindamycin cream 2%,*** one full applicator (5 g) intravaginally at bedtime for 7 days ***or metronidazole 0.75% gel***, one full applicator (5 g) intravaginally, once daily for 5 days are recommendations.6

**2-Vulvovaginal candidiasis VVC**

* ***Candida albicans*** is the causative organism of VVC in 80% to 92% of cases, with ***C. glabrata and C. tropicalis*** accounting for most of the remaining cases.
* Vulvovaginal candidiasis is **not usually described as an STD** because celibate women can develop VVC; however, the incidence of VVC increases when women become sexually active.

 **Signs and Symptoms;**

* **vulvar and vaginal pruritus**, vaginal soreness, vulvar  burning, dyspareunia, and a thick, white vaginal discharge that appears to be “curdlike”
* **vaginal discharge** associated with VVC is a nonodorous, highly viscous, white discharge that may vary in consistency from curdlike to watery.
* Symptoms may be worse before menses and may diminish with the onset of menses.140
* VVC should be differentiated from other vaginal infections (e.g., BV) because a nonprescription antifungal agent could delay the appropriate treatment of other vaginal infections.

**Physiological Vaginal Discharge and Symptomatic Normal pH Vulvovaginitis**

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| **Characteristics of Vaginal Discharge** |
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| ***Characteristics*** | ***Normal*** | ***Candidiasis*** | ***Trichomoniasis*** | ***Bacterial Vaginosis*** |
| Color | White or clear | White | Yellow-green | White to gray |
| Odor | Nonodorous | Nonodorous | Malodorous | Fishy smell |
| Consistency | Floccular | Floccular | Homogeneous | Homogeneous |
| Viscosity | High | High | Low | Low |
| pH | -4.5 | 4–4.5 | 5–6.0 | >4.5 |
| Other s |   | Thick, curdlike | Frothy | Thin |

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**Treatment :**

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| **Products Available for the Treatment of Candida Vulvovaginitis** |
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| ***Drug*** | ***Availability*** | ***Trade Names*** | ***Dosing Regimens*** |
| **OTC Products** |
| Butoconazole | 2% vaginal creama | Femstat 3 | *Nonpregnant women:* Administer 1 applicatorful intravaginally QHS for 3 consecutive days*Pregnant women during second and third trimesters:* Administer 1 applicatorful intravaginally QHS for 7 consecutive days |
| Clotrimazole | 1% vaginal creama | Gyne-Lotrimin 7; Mycelex-7; Sweet'n Fresh Clotrimazole 7; various generics | Administer 1 applicatorful intravaginally QHS for 7 consecutive days |
| Miconazole | 2% creama | Monistat 7; Femizol-M; various generics | Administer 1 applicatorful intravaginally QHS for 7 consecutive days |
| 100-mg vaginal suppositoriesa | Monistat 7 | Insert 1 suppository intravaginally QHS for 7 consecutive days |
| 200-mg vaginal suppositoriesa | Monistat 3 | Insert 1 suppository intravaginally QHS for 3 consecutive days |
| 1200-mg vaginal suppositoriesa | Monistat 1 Daytime Ovule | Insert 1 suppository intravaginally HS for 1 dose only |
| Tioconazole | 6.5% vaginal ointment | Vagistat-1, generics | Administer 1 applicatorful intravaginally at HS for 1 dose only |
| **Prescription Products** |
| Butoconazole (sustained release) | 2% vaginal creama | Gynazole 1 | *Nonpregnant women:* Administer 1 applicatorful HS for 1 dose only |
| Clotrimazole | 100-mg vaginal tablets | Gyne-Lotrimin; Mycelex-7; Sweet'n Fresh Clotrimazole 7; various generics | Insert 1 tablet intravaginally QHS for 7 consecutive days |
| 100-mg vaginal tablets | Gyne-Lotrimin; Mycelex-7; Sweet'n Fresh Clotrimazole 7; various generics | Insert 2 tablets intravaginally QHS for 3 consecutive days |
| Fluconazole | 150-mg oral tablet | Diflucan tablet | Take 1 tablet PO for 1 dose only |
| Nystatin | 100,000 U vaginal tablet | Mycostatin; Nystatin; various generics | Insert 1 tablet intravaginally QHS for 14 consecutive days |
| Terconazole | 0.4% vaginal creama | Terazol 7 | Administer 1 applicatorful intravaginally QHS for 7 consecutive days |
| 0.8% vaginal creama | Terazol 3 | Administer 1 applicatorful intravaginally QHS for 3 consecutive days |
| 80-mg vaginal suppositoriesa | Terazol 3 | Insert 1 suppository intravaginally QHS for 3 consecutive days |

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**=Vaginally Administered Azoles**

* The available ***azole antifungals*** are equally effective in treating VVC with cure rates between 80% and 90% when a full course of therapy is completed.
* All the azole antifungal products are superior to nystatin.

**=Oral Azoles**

* ***Fluconazole (Diflucan***), administered as a single 150-mg oral dose, is the only oral antifungal agent currently recommended

**=Other Treatments for ACUTE Vulvovaginal Candidiasis**

* ***Boric acid (600-mg capsules)*** inserted high in the vagina at bedtime for 14 days is effective for the treatment of VVC, but vaginal burning and irritation occur in approximately 4% of women
* ***Gentian violet*** preparations also have limited use in the treatment of candidiasis because they stain clothing and bed linens and cause local irritation and edema

**Adverse Effects Associated With Azoles**

* azoles are associated with minimal adverse reactions, many of which are similar to the symptoms women report from candidiasis infections. *Thus, it can be difficult to differentiate disease symptoms from adverse drug reactions.*
* Vulvovaginal irritation, itching, burning, and pelvic cramps are commonly associated with vaginal administration of azoles
* Miconazole has also been associated with headaches, allergic contact dermatitis, and skin rashes; clotrimazole with vulvovaginal pruritus, dyspareunia, and bloating; butaconazole with vulvovaginal pruritus (0.9%), burning (2.3%), soreness, discharge, and swelling; terconazole with headaches (21%–30%), dysmenorrhea (6%), genital pain (4.2%), and pruritus (2.3%–5%); and tioconazole with burning (6%) and itching (5%).
* Oral fluconazole has been associated with headache (13%), nausea (7%), abdominal pain (6%), diarrhea, dyspepsia, dizziness, taste perversion, angioedema, and rare cases of anaphylactic reactions.151

**Recurrent Vulvovaginal Candidiasis**

* Treatment of recurrent C. albicans vulvovaginitis should focus on a prolonged (7- to 14-day) course of topical therapy or

 a three dose regimen of oral fluconazole (100, 150, or 200 mg) administered every 3 days

* A 6-month maintenance regimen should be initiated after remission has been achieved.

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| **Maintenance Regimens for Recurrent Vulvovaginal Candidiasis** |
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|  | ***Dose*** | ***Frequency*** |
| Topical agents |
|    Clotrimazole | 200 mg | Twice weekly |
|    Clotrimazole vaginal suppositories | 500 mg | Weekly |
| Oral agents |
|    Fluconazole tablets | 100, 150, or 200 mg | Weekly |

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