Sexually Transmitted Infections (STIs)

Subjects: Primary Health Care | Infectious Diseases | Public, Environmental & Occupational Health
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Recent estimates of 8 common bacterial, viral, and parasitic sexually-transmitted infections in the United States (chlamydia, gonorrhea, trichomoniasis, syphilis, herpes simplex virus type 2, human papillomavirus, hepatitis B virus, and human immunodeficiency virus) found them to have a combined prevalence of 67.6 million and incidence of 26.2 million. Though preventative health guidelines have clarified screening recommendations for some populations, many bacterial sexually-transmitted infections (STIs) are asymptomatic, leading to missed opportunities for diagnosis and underreporting of disease prevalence and incidence. The best available estimates, published in early 2021, are from 2018. Overall, it is thought that 1 in 5 people in the United States has an STI, with 45.5% of all new STIs occurring in adolescents and young adults. New infections amount to $16 billion in direct medical costs.

sexual health | minority populations | asymptomatic infection | risk | sexually-transmitted infections (diseases) | complications | update

1. Bacterial Infections

1.1. Chlamydia trachomatis

Most people affected by *C. trachomatis* are asymptomatic, which precipitates further spread of the infection. When symptoms do occur, they may include vaginal discharge, vaginal bleeding, dysuria, and/or lower abdominal pain in females, and penile discharge/itch, dysuria, and testicular pain in males [1].

In adolescents and adults, doxycycline 100 mg PO BID × 7 days is now the preferred treatment—one of the most notable updates from the 2015 CDC STI treatment guidelines and reflective of increasing rates of antibiotic resistance. Alternative regimens include azithromycin 1 g PO × 1 or levofloxacin 500 mg PO daily × 7. Although rates of adherence to doxycycline's longer course, compared to azithromycin's single dose, have perennially been called into question [2][3], doxycycline appears to have a higher efficacy rate, even with suboptimal compliance to treatment [4][5]. Indeed, doxycycline is effective against urogenital, rectal, and oropharyngeal infections. Azithromycin, on the other hand, may be less effective against rectal infection [1]. Levofloxacin is still considered to be effective but its use is limited by cost. Erythromycin is no longer recommended due to side effects [1].

Test of cure (i.e., repeat testing 4 weeks after treatment) is not recommended for most patients, but repeat testing 3 months (up to 12 months) after diagnosis and treatment should be performed [1][6].

Patients who are pregnant and found to have chlamydia infection should be treated with azithromycin 1 g PO × 1, although amoxicillin 500 mg PO TID × 7 days is an alternative regimen. Again, erythromycin is not recommended [1].

Chlamydial infection in neonates is treated with erythromycin base or ethyl succinate 50 mg/kg/day divided QID × 14 days. Infants younger than 6 weeks old who have been treated with oral erythromycin or azithromycin should be monitored for infantile hypertrophic pyloric stenosis. Subacute pneumonia in infants, caused by *C. trachomatis,* is treated with erythromycin base or ethyl succinate 50 mg/kg/day divided QID × 14 days; the alternative regimen is azithromycin suspension 20 mg/kg/day once daily × 3 [1].

1.2. Neisseria gonorrhoeae (Gonorrhea)

In females, the most common site of infection with *N. gonorrhoeae* is the cervix. Most affected individuals are asymptomatic, but patients may present with nonspecific symptoms such as pruritis, mucopurulent vaginal discharge, intermenstrual bleeding (metrorrhagia), and/or menorrhagia [1]. Exam findings may range from a normal-appearing cervix to one exhibiting mucosal friability and exuding fluid [1].

Since these signs and symptoms are not specific to *N. gonorrhea*, testing to confirm the diagnosis is recommended [7]. Co-infection with chlamydia is not uncommon [8][9].

Current recommendations for the treatment of gonococcal infections in adults include doubling the dose of ceftriaxone recommended in the 2015 guidelines, with further consideration to the patient's weight. *N. gonorrhoeae* isolates have shown increasing resistance to azithromycin over the last few years, but not to ceftriaxone [10] Test of cure (culture or nucleic acid amplification test [NAAT]) is not necessary for uncomplicated urogenital or rectal infections but is recommended 7-14 days after treatment of pharyngeal gonorrhea[10].

1.3. Syphilis

Caused by the spirochete bacterium *Treponema pallidum*, syphilis is unique in that it goes through three clinical stages if it is not treated. Primary syphilis occurs after infection at the site of inoculation and is characterized by a painless skin ulcer ("chancre") lasting 3–6 weeks. If the infection is not appropriately addressed, syphilis progresses to its second stage, in which a diffuse, nonpruritic macular or papular rash on the extremities and trunk is the most classic symptom [11][12]. Other symptoms in this stage are nonspecific and may include fever, headache, fatigue/malaise, myalgias, and weight loss. Femoral, inguinal, axillary, epitrochlear, and posterior cervical adenopathy are also likely. The dermatologic findings of secondary syphilis are varied, but in addition to the classic rash that is typically seen, "moth-eaten" alopecia may be present [11][12][13][14]. Secondary syphilis may also affect other organs/systems, such as the liver (hepatitis), gastrointestinal system, musculoskeletal system (synovitis, osteitis, periostitis), kidneys (nephrotic syndrome, acute renal failure, acute nephritis), neurological system (headache, cranial nerve deficits, stroke), and eyes (anterior and posterior uveitis, optic neuritis, retinal necrosis) [11]. Latent syphilis is defined as infection with *T. pallidum* shown on serologic testing but without symptoms or clinical manifestations. If the infection occurred within the preceding 12 months (24 months by the World Health Organization's definition), it is considered early latent syphilis. Infection greater than 12 (or 24) months prior defines late latent syphilis, and latent syphilis of unknown duration, although seemingly aptly named, draws ire from some clinicians given its implicit ambiguity [15]. Tertiary syphilis is the symptomatic form of late syphilis and can occur in up to 40% of patients who do not receive appropriate treatment [16]. Symptoms are variable but the most classic symptoms involve the cardiovascular system (aortitis), the central nervous system (general paresis, tabes dorsalis), and the formation of gummas (granulomatous, nodular lesions of any organ) [17].

Consequently, pregnant persons with syphilis and an allergy to penicillin should be desensitized and treated with parenteral Penicillin G (PCN G) appropriate to their stage of infection [6]. Note that treatment for neurosyphilis only halts progression—it does not reverse the damage that has already been done.

1.4. Mycoplasma genitalium

Infection with *Mycoplasma genitalium* does not always cause overt symptoms. However, when it does, *M. genitalium* can cause cervicitis, pelvic inflammatory disease (PID), preterm delivery, spontaneous abortion, and infertility in females and urethritis (particularly persistent or recurrent urethritis) in males [1]. It is unclear if *M. genitalium* is associated with epididymitis, prostatitis, or male infertility [1]. As a bacterial culture of *M. genitalium* can take months to grow, NAAT of urine or vaginal/endocervical samples is recommended in symptomatic individuals. The U.S. Food and Drug Administration (FDA)

approved such testing in early 2019 [18][19][20]. Unfortunately, recent research has identified various genetic mutations in *M. genitalium* that result in antimicrobial resistance (AMR) [21][22][23][24]. The prevalence of mutations in the 23S rRNA gene (which allow for macrolide resistance) seems to be increasing worldwide, and more rapidly than topoisomerase/gyrase mutations (parC/gyrA) (which provide fluoroquinolone resistance) [25][26]. Although molecular testing for resistance markers is not yet available in the U.S. [1], increasing resistance to azithromycin has shaped the CDC's treatment recommendations. Since macrolide resistance detection became commercially available in Europe in late 2019 [27], it stands to reason that American clinicians should have access to this testing soon.

Note that the recommended antimicrobial regimens for PID do not cover *M. genitalium*. When PID is diagnosed, empiric treatment should be offered at time of presentation, and, if infection with *M. genitalium* is subsequently discovered, the patient should then receive moxifloxacin 400 mg PO daily × 14 days [6].

1.5. Chancroid

Chancroid, which is caused by the fastidious, gram-negative rod *Haemophilus ducreyi*, is a rare disease. Fewer than 10 cases have been reported annually across the whole United States in recent years [28][29], but its true incidence is difficult to ascertain due to the difficulty with isolation [28]. The pathogenesis of chancroid is poorly understood; however, it is believed to only infect skin that is not intact [30]. Clinical presentations include genital ulcers that will appear approximately 4–10 days after infection [31][28]. The ulcer is preceded by an erythematous papule that rapidly evolves into a pustule, then to the ulcer. Inguinal lymphadenopathy is also present in many cases and is more common in males that are infected compared to females [28].

Given the low incidence of infection, there are no routine screening recommendations for chancroid. Diagnosis of a suspected infection is made using clinical criteria. A probable diagnosis is made if all four of the following clinical criteria are met: one or more painful genital ulcers, no evidence of *T. pallidum* infection, a typical clinical presentation for chancroid (i.e., ulcers and lymphadenopathy), and a negative test (polymerase chain reaction (PCR) or culture) for herpes simplex virus (HSV) [1]. Although a confirmatory culture and PCR testing exist, they are not rapid and often not widely available [32].

1.6. Donovanosis (Granuloma Inguinale)

Formerly known as *Calymmatobacterium granulomatis*, the gram-negative bacterium *Klebsiella granulomatis* is responsible for the genital ulcerative disease donovanosis. Ever since the discovery and widespread utilization of antibiotics, the overall incidence of donovanosis has been decreasing [31][33]. However, because infections are largely limited to a handful of developing countries (e.g., Papua New Guinea, India, Zimbabwe, Brazil), its epidemiology is unclear [31].

Donovanosis typically has an incubation period of 3–40 days, but this period has been reported to be anywhere from 1 to 360 days [33]. A small papule ruptures to form a painless granulomatous lesion, which bleeds easily. Ulcers then extend along skin folds, usually affecting the genital region [31].

1.7. Bacterial Vaginosis (BV)

Bacterial vaginosis (BV) is a common clinical condition in females that is caused by a change in the vaginal flora from the natural *Lactobacillus* species towards more diverse species. Though not always symptomatic, this imbalance in the flora causes a rise in the vaginal pH and, generally, a tacky white/grey vaginal discharge and fishy vaginal odor [34][35]. The characteristic odor can be amplified by mixing a sample of the discharge with potassium hydroxide (KOH); this so-called "whiff test" seems to be fairly reliable [34][36]. Clue cells on microscopy (saline wet mount preparation or gram stain) represent the fourth Amsel criterion, though only 3 of 4 criteria are necessary to confirm the diagnosis of BV [37]. Commercially available molecular diagnostic assays such as direct DNA probes and NAATs can also be used [38].

While BV is not currently classified an STI, there is evidence that it could be an STI and sexual activity increases the risk of the development of BV [39][40]. Further, females who have BV are more at risk for acquiring other STIs such as HIV, HSV-2, trichomonas, gonorrhea, and chlamydia, and it increases the risk of pre-term delivery in pregnant individuals [39][41].

BV is common in women who have sex with women (WSW) with a prevalence of up to 50% that increases with increasing numbers of sexual partners [42]. BV also tends to be higher in the African-American and Mexican-American ethnicities as compared to females of European descent [38][42].

2. Viral Infections

2.1. Herpes Simplex Virus (HSV)

Genital herpes is a chronic, lifelong infection with one of two serotypes of herpes simplex virus. Compared to HSV-2, infection with HSV-1 has a milder course and fewer recurrences. HSV-1 (which was previously thought to cause only oral lesions) actually causes up to 50% of genital herpes infections [1][43][44], although it is often neglected in prevalence estimates [45]. HSV-1 may be spread to the genitals through oral sex, and both serotypes may be present in anogenital lesions. Transmission occurs via skin-to-skin contact or direct contact with mucous membranes. Asymptomatic viral shedding (i.e., transmission of the virus from an infected person with no visible lesions) is possible, and many people remain asymptomatic once infected. However, a symptomatic outbreak is usually evidenced by clusters of painful or itchy blisters and ulcers, vaginal or penile discharge, inguinal lymphadenopathy, and/or flu-like symptoms [46]. The first episode is usually the most severe and tends to occur within 3 weeks of infection.

Serologic screening for HSV-1 and HSV-2 is not generally recommended; however, testing via type-specific IgG antibodies could be considered for patients with multiple sexual partners, HIV infection, a known partner with genital herpes, or negative HSV cultures with recurrent symptoms or genital lesions. A positive test does not belie the location of the herpetic infection nor reveal when the patient was infected. Testing in patients with active lesions may be performed via viral culture (the current gold standard for urogenital infection) or PCR (the preferred mode of testing if there is concern for HSV infection of spinal fluid) [47][48]. As skin lesions heal, shedding of the virus is reduced, making the viral culture less sensitive and serum testing for type-specific antibodies more helpful in diagnosis and management [46].

Once-daily dosing increases adherence, particularly among adolescents [47]. It is important to note that while treatment decreases clinical symptoms, it does not decrease frequency of recurrence or transmission risk to an uninfected partner (while lesions remain open and uncrusted) [49]. Effective episodic treatment should begin within 24 h of the appearance of lesions during the prodromal phase (30 min to 48 h prior to eruption of a lesion) [46]. Patients with a first episode of genital herpes caused by the HSV-2 serotype are at risk for increased frequency of recurrence; consequently, suppressive therapy may be the preferred initial treatment for HSV-2 infections [47]. Suppressive therapy may also be warranted for those who endure more than 4–6 outbreaks per year or have severe symptoms. Chronic suppressive therapy should be evaluated annually, as frequency of recurrence declines over time [49].

2.2. Human Papilloma Virus (HPV)

Most HPV infections are self-limited; however, persistent infection can lead to warts, cervical cancer in females, and anogenital or oropharyngeal cancer in males, females, or children [49]. There are over 100 subtypes of HPV, of which more than 30 infect the genital tract through skin-to-skin contact between mucous membranes and epithelial tissues [50][51]. Oncogenic (high-risk) strains such as 16 and 18 are associated with cancers whereas low-risk strains such as 6 and 11 are associated with genital warts (condyloma acuminata). Although high-risk strains often infect adolescents, these infections typically resolve within 24 months without symptoms or treatment. Genital warts present as raised, fleshy, painless lesions in

moist areas of the body. Cervical neoplasia will often present with abnormal vaginal bleeding or be discovered on routine screening [47].

Universal screening is recommended for the prevention of cervical cancer in young women. This is performed through cytology—the Papanicolaou or "Pap" smear. The U.S. Preventative Services Task Force (USPSTF) and American College of Obstetricians and Gynecologists (ACOG) recommend obtaining Pap smears starting at age 21, regardless of sexual debut [6][52][53]. Unless there is a concerning finding, screening by cytology is continued every 3 years afterwards until age 29. High-risk HPV infections are less likely to spontaneously resolve in women 30 years of age and older. As such, co-testing with HPV DNA is recommended along with cytology every 5 years if results again remain normal for both [6][47]. By comparison, in mid-2020, however, the American Cancer Society (ACS) recommended that Pap smears be performed starting at age 25 and then every 5 years thereafter [54][55]. Abnormal cervical cytology on Pap smear that may progress to cervical intraepithelial neoplasia (CIN), and eventually cervical cancer, should be managed per the American Society for Colposcopy and Cervical Cytology guidelines, which outline subsequent monitoring, colposcope evaluation, and excisional therapy as appropriate [47].

Interestingly, anal Pap smears may also be useful for detecting HPV-associated cytologic changes in the anal tissue of individuals engaging in anal receptive intercourse [56][57].

Over time, genital warts may resolve spontaneously, remain unchanged, or increase in size and number, making the treatment goal simply to remove these growths. Treatment does not eradicate HPV. Neither condoms nor treatment eliminate infectivity, either. However, strains that lead to genital warts should not lead to cervical cancer [50].

Individuals with external anal or perianal warts should be evaluated for intra-anal warts. Vaginal, cervical, intra-anal, and urethral meatus warts should only be treated by a clinician with the following additional recommendations: A cryoprobe should not be used in these areas, cervical and intra-anal warts warrant specialist consultation, and TCA/BCA should not be used at the urethral meatus [1][58].

2.3. Molluscum Contagiosum (MC)

Though not specifically mentioned in the CDC guidelines, MC can be transmitted by any form of skin-to-skin contact. Caused by a poxvirus, MC is characterized by clusters of smooth, flesh-colored papules, usually featuring a central umbilication (divot), and found on the trunk, axillae, or groin. This benign condition is common in adolescents and is typically self-limited. Diagnosis is made based on clinical appearance; however, excisional biopsy may also lead to a diagnosis in atypical cases [59].

MC is frequently seen in immunocompromised individuals, for whom it has increased presence on the face compared to immunocompetent patients. MC has the potential to become disseminated in HIV-positive individuals and even poses risk for disfigurement in patients with AIDS, as lesions can be greater than 1 cm in size [59].

2.4. Hepatitis

The hepatitis A virus (HAV) is primarily transmitted via fecal–oral routes and may arise from oral–anal sexual contact. Infection with hepatitis A is typically self-limited; however, acute illness may include fever, jaundice, and gastrointestinal upset. The hepatitis B virus (HBV) is transmitted through seminal fluid, vaginal fluid, or blood and may present as an acute, self-limited illness or a chronic infection [60]. The current adolescent population in the United States has increased immunity secondary to routine immunization against HBV during infancy. People who remain at risk include men who have sex with men (MSM), injection drug users, the unimmunized, and those whose immunity has waned. The hepatitis C virus (HCV) is typically a blood-borne infection and is uncommon among adolescents in the United States [61]. Acute hepatitis C infection progresses to liver disease in approximately 60–70% of patients; the remainder experience spontaneous cure within 6–12 months, with patients having either had symptoms of a mild viral syndrome or no symptoms at all [61].

Routine screening for HAV is not recommended; however, routine vaccination starting at age 2 (or age 1 if HIV-positive or other risks for infection are present) is advised [62]. Initiation of the hepatitis B vaccination series is universally recommended for medically stable infants within 24 h of birth [60]. Individuals not previously immunized should be vaccinated, especially those at high risk. Serologic screening (antibody titers) and revaccination (boosters) are generally not necessary, although healthcare personnel and hemodialysis patients may need such testing and repeat inoculation [60]. All patients seeking initiation of HIV Pre-Exposure Prophylaxis (PrEP) should be screened for hepatitis B by hepatitis B surface antigen (HBsAg), and any patient entering care for HIV should be screened for hepatitis B with HbsAg as well as hepatitis B surface antibody (HbsAb) and hepatitis B core antibody (HbcAb). In general, all adults should be screened for HCV at least once in their lifetime, and pregnant individuals should be screened with each pregnancy. Routine periodic testing is recommended for current injection drug users and individuals receiving maintenance hemodialysis. Further, the CDC recommends that anyone who requests testing for Hepatitis C infection should receive it, as many risk factors (e.g., HIV-positive serostatus) can be stigmatizing [63].

Hepatitis A is treated with supportive care; Hepatitis B and C should be treated by healthcare providers with expertise in the treatment of hepatitis, such as infectious disease and/or gastrointestinal physicians [61].

3. Parasitic Infections

3.1. Scabies

Scabies infection is caused by the *Sacroptes scabiei* mite, and sexual contact is one mode of transmission. After mating, the male mite dies and the female mite burrows under the skin, where she remains for the rest of her lifespan (1–2 months) laying eggs. Larvae emerge 2–3 days after the eggs are laid and will cut through the burrows to the skin surface to mate and multiply [64][65]. Symptoms may not develop until six weeks later, when a hypersensitivity reaction develops to the mites' feces. During this asymptomatic period, others may become unknowingly infected through direct sexual or non-sexual contact. Mites can be transferred after about 15–30 min of close contact with an infected person or fomite (e.g., clothing, linens, or towels) [64]. Symptomatic dermatologic manifestations of infection include small linear groupings of erythematous, pruritic papules and are commonly seen between the fingers and on the anterior wrists, elbows, axillae, buttocks, genitalia, and breasts. Due to the hypersensitivity reaction, patients may also have excoriations, eczema, and pyoderma. Diagnosis is confirmed by identification of mites, their eggs, and/or fecal pellets in microscopic evaluation of a skin scraping suspended in oil or through dermoscopy [64].

No universal screening recommendations for scabies exist; however, patients living in overcrowded conditions, tropical regions, or those who have poor hygiene, poor nutritional status, homelessness, or dementia are at increased risk for scabies [64].

3.2. Pubic Lice

Lice are parasites that can infest hair-bearing areas, such as the pubic region (*Phthirus pubis*). They have a low profile and cannot fly or jump, thus requiring close contact for transmission. The female louse survives for up to one month and lays 8–10 eggs per day at the junction of the skin and hair. The eggs mature into adults within 20 days and are found at the base of the hair shaft [64]. Pediculosis (infection with lice) also often causes a delayed hypersensitivity reaction leading to intense pruritus 4–6 weeks after first exposure. This intense pruritus leads to scratching, excoriation, and potentially cellulitis. Body lice should be expected in patients who have poor hygiene and/or live in crowded conditions and present with genital pruritus [64]. Diagnosis may be made by identification of body lice or nits on the person or in the seams of their clothing. If pubic lice are identified, those patients should be evaluated for other STIs [64].

First-line topical treatments for pubic lice include permethrin 1% lotion (trade name Nix) and pyrethrins 0.3%/piperonyl butoxide 4% shampoo (trade name Rid), both of which are available OTC. Compared to scabies infection, treatment of pubic lice uses a less potent formulation of permethrin, and the chemical is only applied to affected areas and washed off after 10 min. Alternative treatments for pubic lice are available by prescription and include malathion 0.5% lotion and oral ivermectin. Limited data on ivermectin use in pregnant and breastfeeding patients disfavor its use in those populations [1]. Note, too, that dosing of oral ivermectin differs for pediculosis capitis and pediculosis corporis. Sexual partners from the previous 1–3 months should also be treated. In addition to topical or oral medications, clothing and bedding should be laundered in hot water and patients should be instructed to bathe regularly for treatment to be effective and lasting [64].

3.3. Trichomonas vaginalis

Trichomonas vaginalis is a protozoan transmitted through unprotected oral, vaginal, or anal sex. It is the third most common cause of vaginitis and often associated with other infections. Distinguishing characteristics of vaginitis due to trichomoniasis are yellow-green, malodorous, frothy vaginal discharge with an elevated pH > 4.5. Females may also have urethritis and irritation of the vulva along with a “strawberry cervix” due to punctate hemorrhages and tiny ulcerations of the cervix. Males are typically asymptomatic; however, they may present with urethritis [47][46].

All symptomatic individuals—and especially those with high-risk behaviors—should be tested for *T. vaginalis*. In contrast to a wet mount, NAAT has very high sensitivity and high specificity for female vaginal, endocervical, or urine specimens. TMA (transcription-mediated amplification) assays are acceptable testing modalities for male urine or urethral swabs [66][67]. However, as these tests are often expensive and can take several days to result [68], microscopic evaluation through wet mount preparations is the most common method for diagnosis despite requiring immediate evaluation (less than 1 h) of the specimen for optimal results [47].

The preferred treatment for *T. vaginalis* infection is metronidazole, with the exact dosage/regimen depending on the patient’s sex. Sexual partners of those diagnosed with trichomoniasis are recommended to undergo treatment [47][46]. Persistent or recurrent infections may reflect reinfection or drug resistance and warrant adjustment in pharmacotherapy. As with BV, pregnant patients should avoid tinidazole, and breastfeeding is not advised for 72 h after single-dose tinidazole treatment [1].

4. Fungal Infections

4.1. Vulvovaginal Candidiasis (VVC)

VVC is common in females, with 75% of women experiencing at least one episode in her lifetime. Typically caused by the opportunistic pathogenic yeast *Candida albicans*, VVC presents as vaginal pruritis with a thick, white vaginal discharge of normal pH and associated vulvar burning, dyspareunia, and dysuria. Diagnosis can be made through visual examination or upon discovery of budding yeast and/or pseudohyphae on microscopic evaluation of the vaginal discharge [1][46]. although there may be a role for their use (especially in complicated cases), per the CDC’s most recent guidance, most molecular assays for VVC are not yet FDA-approved [1].

Most OTC treatments use 1–14 doses of intravaginal azoles (e.g., miconazole). Oral fluconazole (150 mg, given once and then repeated in 72 h if needed) is available by prescription and can be used depending on infection severity, recurrence, and associated co-morbidities [46]. It should be avoided during pregnancy but can be used while breastfeeding.

4.2. Tinea Cruris

Also not specifically mentioned in the CDC guidelines, tinea cruris (commonly known as “jock itch”) often affects adolescent males and leads some to worry they have contracted a more severe infection. The term “tinea” refers to a fungal infection and may be caused by dermatophytes such as *Trichophyton, Microsporum,* or *Epidermophyton* [69]. In young males, infection

commonly presents as a pruritic, erythematous rash on the upper thigh opposite the scrotum, brought about by heat and friction in a moist area. Diagnosis is often made through appearance; however, a KOH preparation may be used for detection in atypical presentations [69].

Twice-daily topical treatment with OTC or prescription creams such as terbinafine (trade name Lamisil) or butenafine (trade name Lotrimin) for 10–14 days is preferred. It is important to note that nystatin is effective for candidiasis but most tinea infections are resistant to it. Oral antifungals (itraconazole 200 mg PO daily or terbinafine 250 mg PO daily × 3–6 weeks) may be used for severe or refractory cases, or in immunocompromised patients [70].

References

1. Workowski, K.A.; Bachmann, L.H.; Chan, P.A.; Johnston, C.M.; Muzny, C.A.; Park, I.; Reno, H.; Zenilman, J.M.; Bolan, G.A. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm. Rep. 2021, 70, 1–187.
2. Adimora, A.A. Treatment of Uncomplicated Genital Chlamydia trachomatis Infections in Adults. Clin. Infect. Dis. 2002, 35 (Suppl. S2), S183–S186.
3. Kong, F.Y.S.; Hocking, J.S. Treatment challenges for urogenital and anorectal Chlamydia trachomatis. BMC Infect. Dis. 2015, 15, 293.
4. Kang-Birken, S.L. Challenges in Treating Chlamydia trachomatis, Including Rectal Infections: Is it Time to Go Back to Doxycycline? Ann. Pharm. 2021.
5. Suarez, J.D.; Snackey Alvarez, K.; Anderson, S.; King, H.; Kirkpatrick, E.; Harms, M.; Martin, R.; Adhikari, E. Decreasing Chlamydia Reinfections in a Female Urban Population. Sex Transm. Dis. 2021, 48, 919–924.
6. Screening Recommendations and Considerations Referenced in Treatment Guidelines and Original Sources. Available online: https://www.cdc.gov/std/treatment-guidelines/screening-recommendations.htm (accessed on 20 December 2021).
7. Barlow, D.; Phillips, I. Gonorrhoea in women: Diagnostic, clinical, and laboratory aspects. Lancet 1978, 1, 761.
8. Dicker, L.W.; Mosure, D.J.; Berman, S.M.; Levine, W.C. Gonorrhea prevalence and coinfection with chlamydia in women in the United States, 2000. Sex Transm. Dis. 2003, 30, 472–475.
9. Gonorrhea/Chlamydia Co-Infection. Available online: https://www.vdh.virginia.gov/content/uploads/sites/10/2016/01/SSuN-Fact-Sheet-CT-Coinfection-04-05-13-1.pdf (accessed on 25 December 2021).
10. St. Cyr, S.; Barbee, L.; Workowski, K.A.; Bachmann, L.H.; Pham, C.; Schlanger, K.; Torrone, E.; Weinstock, H.; Kersh, E.N.; Thorpe, P. Update to CDC's Treatment Guidelines for Gonococcal Infection, 2020. Morb. Mortal. Wkly. Rep. 2020, 69, 1911–1916. [Google Scholar] [CrossRef]
11. Baughn, R.E.; Musher, D.M. Secondary Syphilitic Lesions. Clin. Microbiol. Rev. 2005, 18, 205–216.
12. Syphilis–CDC Fact Sheet (Detailed). Available online: https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm (accessed on 26 December 2021).
13. Qiao, J.; Fang, H. Moth-eaten alopecia: A sign of secondary syphilis. CMAJ 2013, 185, 61.
14. Wu, M.Y.; Li, J. Syphilis presenting with moth-eaten alopecia. CMAJ 2021, 193, E126.

15. Peterman, T.A.; Kahn, R.H.; Ciesielski, C.A.; Ortiz-Rios, E.; Furness, B.W.; Blank, S.; Schillinger, J.A.; Gunn, R.A.; Taylor, M.; Berman, S.M. Misclassification of the Stages of Syphilis: Implications for Surveillance. Sex Transm. Dis. 2005, 32, 144–149.
16. Kollmann, T.R.; Dobson, S. Syphilis. In Infectious Diseases of the Fetus and Newborn; Remington, J.S., Klein, J.O., Wilson, C.B., Nizet, V., Maldonado, Y.A., Eds.; Saunders: Philadelphia, PA, USA, 2011; pp. 524–563.
17. Clark, E.G.; Danbolt, N. The Oslo study of the natural course of untreated syphilis: An epidemiologic investigation based on a re-study of the Boeck-Bruusgaard material. Med. Clin. N. Am. 1964, 48, 613.
18. FDA Permits Marketing of First Test to Aid in the Diagnosis of a Sexually-Transmitted Infection Known as Mycoplasma genitalium. Available online: https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-test-aid-diagnosis-sexually-transmitted-infection-known-mycoplasma (accessed on 31 December 2021).
19. Nucleic Acid Based Tests. Available online: https://www.fda.gov/medical-devices/in-vitro-diagnostics/nucleic-acid-based-tests#microbial (accessed on 31 December 2021).
20. Shipitsyna, E.; Unemo, M. Profile of the FDA-approved and CE-IVD-marked Aptima Mycoplasma genitalium assay (Hologic) and key priorities in the management of M. genitalium infections. Exp. Rev. Mol. Diag. 2020, 20, 1063–1074.
21. Anderson, T.; Coughlan, E.; Werno, A. Mycoplasma genitalium Macrolide and Fluoroquinolone Resistance Detection and Clinical Implications in a Selected Cohort in New Zealand. J. Clin. Microb. 2017, 55, 3242–3248.
22. Gaydos, C.A. Mycoplasma genitalium: Accurate Diagnosis is Necessary for Adequate Treatment. J. Infect. Dis. 2017, 216 (Suppl. S2), S406–S411.
23. Ke, W.; Li, D.; Tso, L.S.; Wei, R.; Lan, Y.; Chen, Z.; Zhang, X.; Wang, L.; Liang, C.; Liao, Y.; et al. Macrolide and fluoroquinolone associated mutations in Mycoplasma genitalium in a retrospective study of male and female patients seeking care at a STI Clinic in Guangzhou, China, 2016–2018. BMC Infect. Dis. 2020, 20, 950.
24. Pitt, R.; Unemo, M.; Sonnenberg, P.; Alexander, S.; Beddows, S.; Cole, M.J.; Clifton, S.; Mercer, C.H.; Johnson, A.M.; Ison, C.A.; et al. Antimicrobial resistance in Mycoplasma genitalium sampled from the British general population. Sex Transm. Infect. 2020, 96, 464–468.
25. Cools, P.; Padalko, E. Emerging macrolide resistance in Mycoplasma genitalium. Lancet Infect. Dis. 2020, 20, 1222–1223.
26. Machalek, D.A.; Tao, Y.; Shilling, H.; Jensen, J.S.; Unemo, M.; Murray, G.; Chow, E.P.F.; Low, N.; Garland, S.M.; Vodstrcil, L.A.; et al. Prevalence of mutations associated with resistance to macrolides and fluoroquinolones in Mycoplasma genitalium: A systematic review and meta-analysis. Lancet Infect. Dis. 2020, 20, 1302–1314.
27. Van Der Pol, B. Resistance Guided Therapy for Mycoplasma genitalium: Application of Macrolide Resistance Testing Results (Slide Deck). Available online: https://www.cidrap.umn.edu/sites/default/files/public/downloads/resistance_guided_therapy_for_mycoplasma_genitaliu (accessed on 1 January 2022).
28. Lewis, D.A. Epidemiology, clinical features, diagnosis and treatment of Haemophilus ducreyi-a disappearing pathogen? Expert Rev. Anti-infect. Ther. 2014, 12, 687–696.

29. Chancroid—Reported Cases and Rates of Reported Cases by State/Territory in Alphabetical Order, United States, 2015–2019. Available online: https://www.cdc.gov/std/statistics/2019/tables.htm (accessed on 25 December 2021).
30. Ussher, J.; Wilson, E.; Campanella, S.; Taylor, S.L.; Roberts, S.A. Haemophilus ducreyi causing chronic skin ulceration in children visiting Samoa. Clin. Infect. Dis. 2007, 44, e85–e87.
31. Korzeniewski, K.; Juszczak, D. Travel-related sexually transmitted infections. Int. Marit. Health 2015, 66, 238–246.
32. Chancroid (Haemophilus ducreyi) 1996 Case Definition. Available online: https://wwwn.cdc.gov/nndss/conditions/chancroid/case-definition/1996/ (accessed on 20 May 2019).
33. O'Farrell, N. Donovanosis. Sex Transm. Infect. 2002, 78, 452–457.
34. Cohrssen, A.; Anderson, M.; Merrill, A.; McKee, D. Reliability of the Whiff Test in Clinical Practice. J. Am. Board Fam. Med. 2005, 18, 561–562.
35. Klebanoff, M.A.; Schwebke, J.R.; Zhang, J.; Nansel, T.R.; Yu, K.F.; Andrews, W.W. Vulvovaginal symptoms in women with bacterial vaginosis. Obstet. Gynecol. 2004, 104, 267.
36. Thulkar, J.; Kriplani, A.; Agarwal, N. Utility of pH test & Whiff test in syndromic approach of abnormal vaginal discharge. Indian J. Med. Res. 2010, 131, 445–448.
37. Hainer, B.L.; Gibson, M.V. Vaginitis: Diagnosis and Treatment. Am. Fam. Physician 2011, 83, 807–815.
38. Coleman, J.S.; Gaydos, C.A. Molecular Diagnosis of Bacterial Vaginosis: An Update. J. Clin. Microbiol. 2018, 56, e00342-18.
39. Fethers, K.A.; Fairley, C.K.; Hocking, J.S.; Gurrin, L.C.; Bradshaw, C.S. Sexual risk factors and bacterial vaginosis: A systematic review and meta-analysis. Clin. Infect. Dis. 2008, 47, 1426.
40. Morris, M.C.; Rogers, P.A.; Kinghorn, G.R. Is bacterial vaginosis a sexually transmitted infection? Sex. Transm. Infect. 2001, 77, 63–68.
41. Flynn, C.A.; Helwig, A.L.; Meurer, L.N. Bacterial vaginosis in pregnancy and the risk of prematurity: A meta-analysis. J. Fam. Pract. 1999, 48, 885.
42. Allsworth, J.E.; Peipert, J.F. Prevalence of bacterial vaginosis: 2001–2004 National Health and Nutrition Examination Survey data. Obstet. Gynecol. 2007, 109, 114.
43. Kriesel, J.D.; Hull, C.M. Herpes Simplex Virus Infection. In Netter's Infectious Diseases; Jong, E.C., Stevens, D.L., Eds.; Saunders: Philadelphia, PA, USA, 2012; pp. 110–116.
44. Wald, A.; Brown, J.M. Genital Herpes. In Women and Health; Goldman, M.B., Hatch, M.C., Eds.; Academic Press: San Diego, CA, USA, 2000; pp. 311–323.
45. Kreisel, K.M.; Spicknall, I.H.; Gargano, J.W.; Lewis, F.M.; Lewis, R.M.; Markowitz, L.E.; Roberts, H.; Johnson, A.S.; Song, R.; St. Cyr, S.B.; et al. Sexually transmitted infections among US women and men: Prevalence and incidence estimates, 2018. Sex Transm. Dis. 2021, 48, 208–214.
46. Straub, D.M. Sexually Transmitted Diseases in Adolescents. Adv. Pediatrics 2009, 56, 87–106.
47. Gibson, E.J.; Bell, D.L.; Powerful, S.A. Common sexually transmitted infections in adolescents. Prim. Care Clin. Off. Pract. 2014, 41, 631–650.
48. Strick, L.B.; Wald, A. Diagnostics for herpes simplex virus: Is PCR the new gold standard? Mol. Diagn. Ther. 2006, 10, 17–28.

49. Wangu, Z.; Burstein, G.R. Adolescent Sexuality: Updates to the Sexually Transmitted Infection Guidelines. Pediatric Clin. N. Am. 2017, 64, 389–411.
50. Juckett, G.; Hartman-Adams, H. Human Papillomavirus: Clinical Manifestations and Prevention. Am. Fam. Phys. 2010, 82, 1209–1214.
51. Skoulakis, A.; Fountas, S.; Mantzana-Peteinelli, M.; Pantelidi, K.; Petinaki, E. Prevalence of human papillomavirus and subtype distribution in male partners of women with cervical intraepithelial neoplasia (CIN): A systematic review. BMC Infect. Dis. 2019, 19, 192.
52. Cervical Cancer Screening. Available online: https://www.acog.org/womens-health/faqs/cervical-cancer-screening (accessed on 10 October 2021).
53. Cervical Cancer: Screening. Available online: https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cervical-cancer-screening (accessed on 10 October 2021).
54. ACS's Updated Cervical Cancer Screening Guidelines Explained. Available online: https://www.cancer.gov/news-events/cancer-currents-blog/2020/cervical-cancer-screening-hpv-test-guideline (accessed on 10 October 2021).
55. The American Cancer Society Guidelines for the Prevention and Early Detection of Cervical Cancer. Available online: https://www.cancer.org/cancer/cervical-cancer/detection-diagnosis-staging/cervical-cancer-screening-guidelines.html (accessed on 10 October 2021).
56. Lindsey, K.; DeCristofaro, C.; James, J. Anal Pap smears: Should we be doing them? J. Am. Acad. Nurse Pract. 2009, 21, 437–443.
57. Young, C.; McCormack, S. Anal Cancer Screening in High-Risk Populations: A Review of the Clinical Utility, Diagnostic Accuracy, Cost-Effectiveness, and Guidelines; CADTH Rapid Response Report: Summary with Critical Appraisal; CADTH: Ottawa, ON, Canada, October 2019; Available online: https://www.cadth.ca/sites/default/files/pdf/htis/2019/RC1212%20Anal%20Cancer%20Screening%20Update%20Final.p (accessed on 29 December 2021).
58. Yanofsky, V.R.; Patel, R.V.; Goldenberg, G. Genital Warts: A Comprehensive Review. J. Clin. Aesthet. Dermatol. 2012, 5, 25–36.
59. Crow, E.; Claudius, I. Human Immunodeficiency Virus-Associated Rashes. In Life-Threatening Rashes; Rose, E., Ed.; Springer: Cham, Switzerland, 2018; pp. 167–184.
60. Schillie, S.; Vellozzi, C.; Reingold, A.; Harris, A.; Haber, P.; Ward, J.W.; Nelson, N.P. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR 2018, 67, 1–31.
61. Wood, S.M.; Salas-Humara, C.; Dowshen, N.L. Human Immunodeficiency Virus, Other Sexually Transmitted Infections, and Sexual and Reproductive Health in Lesbian, Gay, Bisexual, Transgender Youth. Pediatric Clin. N. Am. 2016, 63, 1027–1055.
62. Nelson, N.P.; Weng, M.K.; Hofmeister, M.G.; Moore, K.L.; Doshani, M.; Kamili, S.; Koneru, A.; Haber, P.; Hagan, L.; Romero, J.R.; et al. Prevention of hepatitis A virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. MMWR 2020, 69, 1–38.
63. Testing Recommendations for Hepatitis C Virus Infection. Available online: https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm (accessed on 10 October 2021).

64. Gunning, K.; Kiraly, B.; Pippitt, K. Lice and Scabies: Treatment Update. Am. Fam. Phys. 2019, 99, 635–642.
65. Parasites–Scabies. Available online: https://www.cdc.gov/parasites/scabies/index.html (accessed on 2 December 2021).
66. Nye, M.B.; Schwebke, J.R.; Body, B.A. Comparison of APTIMA Trichomonas vaginalis transcription-mediated amplification to wet mount microscopy, culture, and polymerase chain reaction for diagnosis of trichomoniasis in men and women. Am. J. Obstet. Gynecol. 2009, 200, 188.e1–188.e7.
67. Schachter, J.; Chernesky, M.A.; Willis, D.E.; Fine, P.M.; Martin, D.H.; Fuller, D.; Jordan, J.A.; Janda, W.; Hook, E.W. Vaginal Swabs Are the Specimens of Choice When Screening for Chlamydia trochomatis and Neisseria gonorrhoeae: Results from a Multicenter Evaluation of the APTIMA Assays for Both Infections. Sex Transm. Dis. 2005, 32, 725–728.
68. Hobbs, M.M.; Seña, A.C. Modern diagnosis of Trichomonas vaginalis infection. Sex Transm. Infect. 2013, 89, 434–438.
69. Edwards, S. Balanitis and balanoposthitis: A review. Genitourin Med. 1996, 72, 155.
70. Ely, J.W.; Rosenfeld, S.; Seabury Stone, M. Diagnosis and Management of Tinea Infections. Am. Fam. Phys. 2014, 90, 702–710.