

Sexually Transmitted Infection

Editors:

Cynthia S Fok, MD, MPH

Authors:

Vannita Simma-Chiang, MD; Rollin Say, MD, MBA

Last Updated:

Tuesday, February 7, 2023

Keywords

Sexually transmitted infections, genital ulcer diseases, HIV, HPV, ectoparasites

1. Introduction

Sexually transmitted infections (STI), or venereal disease, is a worldwide health issue affecting millions of men and women every year. Urologists play an integral role in the evaluation and diagnosis of STI. These infections may present to the urologist by a specific referral from their primary care physician, self-referral by the concerned patient, or as an incidental finding during evaluation for an unrelated urologic issue. These infections are acquired by sexual contact (genital, oral, or anal contact). The significance of STI has been identified by the AUA: Sexually Transmitted Infections (**STIs**) and has been highlighted in the AUA update series 2017.¹ There are 6 infections that are mandated reportable in every state in the United States: syphilis, chancroid, HIV, gonorrhea, and Chlamydia, and acquired immunodeficiency syndrome (AIDS). The Centers for Disease Control and Prevention (CDC) estimates that nearly 20 million new **STI** are diagnosed annually in the United States.² They also estimate that the total estimated direct cost of STI annually is \$16 billion. While the most recent report indicates an alarming trend of STI affecting people of all races, ages and sexual orientations, it is important to be aware that there are some groups who may be at a higher risk. The CDC identifies the following high risk groups:

- i. **Adolescents and young adults:** Individuals ages 15-24 years account for almost half of all incident STI but only represent 25% of the sexually experienced population in the United States;³
- ii. **Racial and ethnic minorities:** STI disparities are one of the five greatest health disparities for Black communities; and⁴
- iii. **Men who have sex with men (MSM):** These individuals account for ~70% of reported cases of primary and secondary syphilis and more than 50% of HIV-positive individuals.⁵ Pre-exposure prophylaxis (PrEP) can dramatically decrease the risk of acquiring HIV (99% effective) without increasing risk taking behavior.

2. Evaluation

Obtaining a thorough sexual history for diagnosis and evaluation is essential.⁶ An effective strategy for obtaining an STI history are the “five Ps”: partners, practices, prevention of pregnancy, protection from **STI**, and past history of **STI**.

On physical exam, it is important to recognize typical rashes, ulcers, exudates, and warts.⁷ Location of relevant lymph nodes (LN) and palpation of these LN is also important in making a diagnosis. These clinical encounters are also opportunities to provide prevention counseling in a nonjudgmental and empathetic manner. These discussions may include male/female condom use, abstinence and reduction of number of sex partners, vaccination for hepatitis A/B and HPV, spermicides, male circumcision, post-exposure prophylaxis (PEP), and pre-exposure prophylaxis (PrEP). Per CDC recommendations, everyone aged 13-64 years should be tested for HIV at least once. ⁸

3. Presentation

3.1 Cervicitis/Vaginitis

The vaginal epithelium of premenopausal women is well estrogenized and rich in glycogen. Lactobacilli convert glucose into lactic acid to create an acidic vaginal environment (pH 4.0 to 4.5), which maintains normal flora and inhibits growth of pathogenic organisms. Vaginitis is a general term for disorders related to infection, inflammation, or changes in the normal vaginal flora. (Amin and Lee)

Women are often asymptomatic, but signs on pelvic exam may include purulent endocervical exudate or vaginal discharge. Usually a pathogen cannot be identified but the most common organisms include *C. trachomatis* or *N. gonorrhoeae*. Others include the organisms responsible for bacterial vaginosis (BV) *T. vaginalis*, HSV and *M. genitalium*. Diagnostic testing should include microscopic evaluation of an endocervical specimen and testing for *C. trachomatis* and *N. gonorrhoeae*. Women should also be evaluated for BV and trichomoniasis.

3.2 Pelvic Inflammatory Disease (PID)

Lower abdominal and pelvic pain, heavy vaginal discharge with odor, dyspareunia, dysuria and systemic symptoms are usually the presenting symptoms of PID.⁹ Diagnostic criteria include one of the following - pain on cervical motion **or** uterine or adnexal tenderness. The patient should be hospitalized if pregnant, a tubo-ovarian abscess is present, unresponsive to oral antibiotics, **experiencing** nausea/vomiting or high fevers/severe illness, or known to be unreliable in follow up. Fitzhugh-Curtis syndrome occurs in ~10% of PID cases. It leads to perihepatitis with right upper quadrant or pleuritic pain, usually without liver function test (LFT) abnormalities. Adding non-steroidal anti-inflammatories (NSAID) to PID treatment is advised. There is a high rate of infertility, especially if not treated early. Outpatient therapy is ceftriaxone **500 mg intramuscular (IM) once + doxycycline 100 mg orally (PO) twice daily (BID) for 14 days + metronidazole 500 mg PO BID (14 days)**. Inpatient therapy is **ceftriazone 1 gm IV every 24h + doxycycline 100mg PO or by IV every 12 h + metronidazole 500mg PO or by IV every 12 hours** or cefotetan 2 g intravenous (IV) every 12h or cefoxitin 2 g IV every 6h + doxycycline 100 mg PO or IV every 12h. Symptoms should improve within 3 days with PO treatment. All sexual partners in the preceding 60 days should be treated, even if they are asymptomatic.

3.3 Epididymitis/Orchitis

Usually unilateral in nature, symptoms of epididymo-orchitis consist of pain and swelling of the testicle. It is important to rule out testicular (or spermatic cord) torsion, as this is a surgical emergency. **Common causative** organisms consist of *C. trachomatis*, *N. gonorrhoeae*, ***M. genitalium*** or enteric organisms (***Escherichia coli***). This clinical syndrome can be acute or chronic, with chronic defined as pain for at least 3 months. Chronic infectious epididymitis can be seen in granulomatous disease, most commonly, *Mycobacterium tuberculosis* (TB). Therapy for acute epididymitis is dependent on the etiology of the infection. Infection most likely caused by chlamydia or gonorrhea consists of ceftriaxone **500 mg IM in a single dose + doxycycline 100 mg PO twice daily (10 days)**. For acute epididymitis caused by gonorrhea, chlamydia or enteric organisms (men who practice insertive anal sex), the treatment is **ceftriaxone 500mg IM x 1 + levofloxacin 500mg PO daily (10 days)**. For acute epididymitis most likely caused by enteric organisms only, then treatment is **levaquin 500mg PO daily for 10 days**.

3.4 Proctitis/Proctocolitis/Enteritis

Symptoms of proctitis include **tenesmus, rectal bleeding, abdominal pain, diarrhea, rectal mucus and painful bowel movements**. Common organisms include ***N. gonorrhoeae*, *C. trachomatis D-K*, *C. trachomatis L1-L3* (LGV), *T. pallidum*** and HSV (**especially severe among HIV+ patients**). Other causes include **Campylobacter, Shigella, Entamoeba, CMV and *Giardia lamblia***. Treatment should target the isolated organism.

3.5 Urethritis

(see **Table 1**)

Urethritis, or urethral inflammation, can be asymptomatic, but may include dysuria, urethral discharge and urethral pruritus. Urethritis is usually divided into two common groups: gonococcal and non-gonococcal urethritis (NGU). *Neisseria gonorrhoeae* is the most common gonococcal organism. **Common non-gonococcal organisms** include: Chlamydia

trachomatis, *Mycoplasma genitalium*,¹⁰ *Trichomonas vaginalis* and *Ureaplasma urealyticum*.¹¹ Urethral discharge should be examined using nucleic acid amplification testing (NAAT) and PCR if available.

Table 1. Sexually Transmitted Syndromes (Urethritis/Cervicitis/Vaginitis)

STI	Symptoms	Diagnosis	Treatment
Gonorrhea	<ul style="list-style-type: none"> - Most asymptomatic - Thin discharge from penis - Mucoid, purulent, or mucopurulent discharge in endocervical canal - Burning sensation during urination (Dysuria) - Women- Pelvic Inflammatory Disease (PID) 	<ul style="list-style-type: none"> - Endocervical Culture - Urethral Culture - Urine Nucleic Acid Amplification Testing (NAAT) (Sensitivity 80-90%) 	<p>Dual therapy</p> <p>Ceftriaxone 500mg IM <i>AND</i> Azithromycin 1g PO x1 <i>OR</i> Doxycycline 100mg PO x 7 days</p> <p>If second-line regimen used, must do test of cure within 2 weeks</p> <p>Treat partners</p>
Chlamydia	<ul style="list-style-type: none"> - Often asymptomatic - Proctitis, urethritis, reactive arthritis, conjunctivitis - Women- PID, cervicitis - Men- epididymitis 	<ul style="list-style-type: none"> - NAAT (gold standard) - May use on endocervical, urethral, urine, vaginal, rectal and pharyngeal culture - Urine preferred site in men 	<p>Doxycycline 100mg PO BID x 7 days <i>OR</i> Azithromycin 1g PO x1 <i>OR</i> Levofloxacin 500mg PO daily x 7 days</p> <p><i>(For pregnant patients:</i> <i>Azithromycin 1g PO x 1</i> <i>OR</i> <i>Amoxicillin 500mg PO TID x 7 days)</i></p> <p>Treat partners</p>
Mycoplasma genitalium	<ul style="list-style-type: none"> - 30% associated with: - non-gonococcal urethritis (NGU) - cervicitis - PID 	<ul style="list-style-type: none"> - NAAT 	<p>Azithromycin 1g PO x1</p>
Trichomonas vaginalis	<ul style="list-style-type: none"> - Men - Most often asymptomatic, NGU - Women - diffuse, malodorous or yellow-green vaginal discharge 	<p>Culture and PCR NAAT</p>	<p>Metronidazole 2g PO x1 (men) <i>OR</i> Tinidazole 2g PO x1 <i>OR</i> Metronidazole 500mg PO BID x 7 days (women)</p>

			<p>BID x 7 days (women)</p> <p>Treat partners from preceding 60 days</p>
Bacterial vaginosis	<ul style="list-style-type: none"> - Thin, white, discharge with "fishy" odor (whiff test) - Causes vaginitis, cervicitis and may increase risk of PID 	<ul style="list-style-type: none"> - PCR - Gram stain—clue cells on microscopy - Amsel criteria: clue cells, pH vaginal fluid >4.5, fishy odor with 10% KOH (positive Whiff test), thin white discharge 	<p>Metronidazole 500mg PO BID x7 days</p> <p>OR</p> <p>Metronidazole gel 0.75%, one 5gm applicator intravaginally, 1 x day for 5 days</p> <p>OR</p> <p>Clindamycin cream 2%, one 5 gm applicator intravaginally, at bedtime for 7 days</p> <p>OR</p> <p>Clindamycin 300mg PO BID x 7 days</p> <p>Do NOT need to treat sexual partners</p>

3.6 Gonorrhea

Gonorrhea is caused by the gram negative diplococcus bacteria *Neisseria gonorrhoeae*. It can be contracted during vaginal, oral or anal sex with an infected partner. In men, it is most often asymptomatic, but patients may experience dysuria or mucopurulent discharge. They may present with urethritis or epididymitis. In women, early symptoms can be mild, whereas later symptoms can cause irregular bleeding, dysuria, mucopurulent discharge and low abdominal/pelvic pain. If untreated, it can lead to PID. Gonorrhea may also affect the throat, eyes, blood, skin and joints. Disseminated gonococcal infection presents as a few skin lesions limited to the extremities which progress to bulla, petechiae and necrotic lesions. Commonly infected joints include wrists, ankles and joints of the hands and feet. The **incubation** period is 2 - 6 days. Diagnosis can be made either by culture (Thayer-Martin or chocolate agar) or NAAT of the infected fluid. In women, endocervical samples have higher sensitivity than urine samples, which both can be used. NAAT are commonly used to detect rectal gonorrhea although the CDC recommends using culture for diagnosis.

Treatment for gonorrhea is ceftriaxone **500 mg IM once** and one dose of oral azithromycin 1 gram,¹² which also serves as dual therapy to treat the common co-infection with *C. trachomatis*.¹² If a patient is allergic to cephalosporins, then the recommended treatment is 2 grams of azithromycin with either 320 mg oral gemfloxacin or 240 mg intramuscular gentamicin. Dual therapy is cost effective and increases patient compliance.¹³ Empiric treatment should be considered for patients at high risk of being lost to follow-up. All sexual partners should be treated to avoid reinfection and must avoid sex until treatment is complete.

3.7 Chlamydia

Chlamydia is caused by the intracellular *Chlamydia trachomatis* and most commonly affects the urogenital tract. Serotypes L1–L3 cause lymphogranuloma venereum (LGV- see section 5.4), whereas strains D through K cause urethritis, epididymo-orchitis (E-O), cervicitis, and pelvic inflammatory disease (PID).

Men will present with symptoms which include dysuria, urethral discharge, and epididymitis. *C. trachomatis* is most common cause of epididymitis in young men.

Most women with chlamydia have minimal **or no** symptoms; however, symptoms can include an odorless, mucoid vaginal discharge and dysuria. Physical findings in women include cervicitis with a cloudy mucoid discharge from the os, and the cervix tends to bleed easily when scraped. Untreated infection can lead to PID. A rare complication of untreated chlamydial infection is Reactive Arthritis Syndrome, which includes the triad of urethritis, conjunctivitis and painless mucocutaneous lesions. In men, diagnosis is most often made with NAAT on urogenital or rectal samples. In women, diagnosis is most often made using NAAT on endocervical or urine samples, which has both high sensitivity and specificity. NAAT is NOT a culture so sensitivities to antibiotics cannot be obtained. Pharyngeal infections can occur and may be diagnosed with NAAT, as long as the test has been validated.

Treatment for uncomplicated urogenital infections include doxycycline 100 mg PO twice daily **x7 days OR azithromycin 1 g PO once OR levofloxacin 500mg PO daily x 7 days**. For pregnant patients treatment is **azithromycin 1 g PO once OR amoxicillin 500mg PO TID x 7 days**. Empiric treatment should be considered for patients at high risk of being lost to follow-up. As mentioned in the earlier section (4.6), chlamydia often coexists with gonorrhea, so patients routinely receive empiric treatment for both organisms. All sexual partners should be treated to avoid re-infection.

3.8 Bacterial Vaginosis (BV)

BV is the most common genital infection in reproductive-age women. It is a polymicrobial syndrome in which anaerobic bacteria replace the normal vaginal flora. BV is associated with having multiple partners or a new sexual partner, douching, and lack of condom use. Studies have shown that women with BV are at increased risk for acquiring other STIs. BV is also associated with increased complications after gynecologic surgery or pregnancy. Diagnosis is made by Amsel diagnostic criteria or Gram stain. Clinical diagnosis requires three of the following: clue cells (**vaginal epithelial cells studded with adherent coccobacilli**), vaginal fluid pH > 4.5, fishy odor with 10% KOH addition (**whiff test**), and thin white discharge that coats vaginal walls. Treatment is with metronidazole 500 mg PO twice daily (7 days), OR

metronidazole gel 0.75% vaginal suppository once a day (5 days) OR clindamycin cream 2% vaginal suppository once daily (7 days). Treatment of sexual partners is not necessary, as it has not been shown to prevent recurrence.

3.9 Trichomoniasis

Trichomoniasis is the most common non-viral STI in the US.¹⁴ The causative organism is *Trichomonas vaginalis*, which is a flagellated protozoa. Infection is more common in women than in men, and disproportionately¹⁴ affects African American women (13% prevalence) as compared to Caucasian women (1.8% prevalence). *T. vaginalis* infection is associated with an increased risk of HIV infection as well as adverse pregnancy outcomes. Most patients have few or no symptoms, but some have vaginal discharge that may be diffuse, foul-smelling, and yellow-green. On examination, women may have the classic “strawberry cervix,” though this is non-specific. The most common method for diagnosing *Trichomonas vaginalis* is microscopic evaluation of wet preparations of genital secretions, which may show motile, flagellated protozoa and white blood cells. **Nucleic acid amplification tests (NAAT)** outperform the traditional wet mount microscopy, detecting 3-5 times more infections. Approved by the FDA in 2019, the **Aptima CV/TV assay** has demonstrated clinical sensitivity and specificity of 95-100%. More recently, point-of-care diagnostic tests are being used. The recommended treatment regimen is metronidazole 500mg PO BID (7 days **for women**) or metronidazole 2g PO x 1 (men) OR tinidazole 2 g PO in a single dose. All sexual partners should be treated. **Retesting is recommended within 3 months due to high rate of reinfection among treated women (17%).**

4. Genital Ulcer Diseases (GUD)

Genital ulcers are most commonly due to an infectious process such as Herpes Simplex Virus (HSV) and *Treponema pallidum* (syphilis). *Haemophilus ducreyi*, *Chlamydia trachomatis*, *Klebsiella granulomatis*, Epstein-Barr virus, tuberculosis, amebiasis and leishmaniasis are less common causes of genital ulcers. (see **Table 2**)¹⁵ Patients presenting with a genital ulcer should undergo laboratory evaluation for STIs such as HSV and syphilis (Appendix 6). High risk patients should also undergo evaluation for HIV, chlamydia, gonorrhea, and hepatitis C and B. Biopsy is warranted for recalcitrant lesions and lesions suspicious for neoplasms or when diagnostic evaluation is negative or non-specific. ¹⁶

Table 2. Genital Ulcer Disease

STI	Pain	Symptoms	Diagnosis	Treatment
Chancroid	YES	<ul style="list-style-type: none"> - Indurated, genital ulcers and tender suppurative inguinal adenopathy - "kissing lesions" on thighs 	<ul style="list-style-type: none"> - Culture 	<p>Azithromycin 1g PO x1 OR Ceftriaxone 250mg IM x1</p> <p>Treat all partners in preceding 60 days</p>
Herpes Simplex Virus (HSV)	YES	<ul style="list-style-type: none"> - Multiple, superficial, vesicular or ulcerative lesions with clean, erythematous base - HSV-2 and 1 	<ul style="list-style-type: none"> - PCR (gold standard) - Antigen detection - Culture - Tzanck smear (less sensitive) 	<p>First clinical episode: Acyclovir 400mg PO three times daily 7-10 days OR Famciclovir 250mg PO three times daily OR Valacyclovir 1g PO twice daily</p> <p><i>Recurrence:</i> Acyclovir 800mg PO twice daily OR Famciclovir 125mg PO three times daily OR Valacyclovir 1g PO twice daily</p> <p><i>Also suppressive daily for recurrent therap</i></p>
Granuloma Inguinale (Donovanosis)	NO	<ul style="list-style-type: none"> - Progressive, "serpiginous" ulcerative lesions without LAD 	<ul style="list-style-type: none"> - Tissue biopsy 	<p>Doxycycline 100mg PO BID x 3 weeks OR Azithromycin 1g PO q week x 3</p>

Lymphogranuloma venereum (LGV)	NO	<ul style="list-style-type: none"> - Short-lived genital ulcer with painful suppurative inguinal LAD - Outbreaks associated with proctitis among MSM - Serotypes L1-L3 	<ul style="list-style-type: none"> - NAAT/Culture for chlamydia - if positive send serology 	<p>Doxycycline 100mg PO BID x 3 weeks</p> <p>OR</p> <p>Azithromycin 1g PO q week x 3 weeks</p> <p>OR</p> <p>Erythromycin base 500mg PO QID for 3 weeks</p>
Syphilis	NO	<ul style="list-style-type: none"> - Single chancre with heaped-up borders and clean base; painless LAD - Later phases include rash, hair loss, cardiac or neurologic damage 	<ul style="list-style-type: none"> - RPR/VDRL or EIA are used for screening - Nontreponemal tests <ul style="list-style-type: none"> a. VDRL b. RPR - Treponemal tests* <ul style="list-style-type: none"> a. TPPA, b. FTA-Abs, c. EIA d. CIA <p>* once positive usually for life</p>	<ul style="list-style-type: none"> - IM or IV penicillin (depending on stage) treatment of choice - Penicillin must be used in pregnant women - Jarisch-Herxheimer reaction is an acute febrile reaction with headache and myalgia within 24 hours of treatment initiation

Reference Websites

<https://www.cdc.gov/std/syphilis/>

<http://web.archive.org/web/20090412202456/http://www.soc.ucsb.edu/sexinfo/?article=stds&refid=006>

4.1 Chancroid

The causative organism for chancroid is a gram-negative rod, *Haemophilus ducreyi*, which is transmitted sexually by direct contact with purulent lesions. It is less frequently seen in the US but remains prevalent in underdeveloped regions of Asia, Africa and the Caribbean.¹⁷ This infection is characterized by painful, necrotizing genital ulcers that may be accompanied by inguinal lymphadenopathy. The lymphadenopathy can be painful, suppurative and often may fistulize.¹³ “Kissing lesions” may be seen on thighs. Gram stain of exudates may reveal short, plump, GNR but culture remains the gold standard. Treatment is with a single dose azithromycin OR ceftriaxone. Treat all partners from the preceding 60 days. 10% of patients have a secondary STI such as Herpes virus or Syphilis.¹³

4.2 Herpes Simplex Virus (HSV)

A chronic, life-long viral infection, genital herpes is caused by HSV, a double-stranded DNA virus, with serotypes HSV-1 (most common cause of oral herpes) or HSV-2 (most common cause of genital herpes). Most people have no symptoms or have sub-clinical disease. When symptoms first occur, painful clusters of papules may appear on or near the genitals, rectum or mouth. The first episode is often associated with systemic symptoms and local symptoms (dysuria, discharge or inguinal adenopathy). These lesions then develop into vesicles which are self-limiting and heal in 4 to 6 weeks. Genital herpes often recurs, especially during the first year. Viral culture and PCR assays are the preferred tests for herpes diagnosis. Viral culture sensitivity depends on **the** stage of the lesion and declines as lesions heal. IgM testing for HSV should not be used as IgM is not type-specific. Treatment can control herpes but cannot eradicate it. When patient have their first clinical episode of genital herpes, antiviral therapy includes PO acyclovir OR valacyclovir OR famciclovir (7-10 days). In patients with established genital herpes, daily suppressive antiviral therapy can reduce recurrences, subclinical shedding, and likelihood of partner transmission. Shorter durations of acyclovir, famciclovir, or valacyclovir can be used for episodic therapy for recurrent genital herpes. Topical antiviral therapy is not effective.

Herpes Reference resources:

<http://web.archive.org/web/20080605052535/http://www.soc.ucsb.edu/sexinfo/?article=stds&refid=006>

4.3 Granuloma Inguinale (Donovanosis)

The intracellular organism responsible is *Klebsiella granulomatis* (formerly known as *Calymmatobacterium granulomatis*).¹⁷ It rarely occurs in the US, and is endemic in tropical and developing areas. Initially a papule or nodule, which is soft and often pruritic, arises at the site of inoculation. These lesions progress to large, usually painless, expanding, suppurative ulcers. Characterized by clean, friable bases with distinct raised margins that are highly vascular and bleed easily. Ulcers are classically “beefy red” which eventually become more granulomatous with serpiginous borders. This condition is more commonly seen in the tropics and sub-tropics. Smear or crush preparation can be performed which may reveal Donovan bodies, intracellular inclusions in macrophages. The gold standard for diagnosis is tissue biopsy. Recommended therapy is azithromycin. Alternative regimens include doxycycline OR ciprofloxacin OR erythromycin OR trimethoprim/sulfamethoxazole (3 weeks or until lesions have completely healed).

4.4 Lymphogranuloma venereum (LGV)

LGV is caused by *Chlamydia trachomatis* serotypes L1-L3. When acute proctitis or proctocolitis in women or in MSM is present, suspect LGV. Symptoms may include anal discharge, rectal ulcers/bleeding, fever, anorectal pain, tenesmus and constipation. Initially, patients may have herpetiform genital ulcers or papules. Then, 2-6 weeks later may form tender fluctuant inguinal or femoral lymphadenopathy (buboes).¹³ Clinical evaluation should include digital rectal exam (DRE) and anoscopy if possible. Complications of LGV proctocolitis can mimic inflammatory bowel disease and include chronic colorectal fistulas and strictures¹⁸ LGV can be detected by NAAT or PCR. Treatment is doxycycline 100 mg PO twice daily for 21 days. An alternative regimen is **azithromycin 1 gm PO once a week for 3 weeks** or **erythromycin 500mg PO QID for 21 days**.

4.5 Syphilis

The causative organism for syphilis is *Treponema pallidum*, a spirochete. In order to help guide treatment and follow-up, this systemic disease has been divided into stages based on clinical findings. Primary syphilis is characterized by a **firm, painless ulcer or chancre** at the site of inoculation. It lasts 3-6 weeks and heals regardless of therapy but can progress to secondary stage. Secondary syphilis usually starts with a non-pruritic maculopapular rash on the trunk and extremities including the palms and soles. Other symptoms include lymphadenopathy, alopecia, condylomata, and systemic symptoms. If not treated the infection can progress to latent syphilis, which is characterized as early, late latent, or of unknown duration. Neurological involvement can occur at any stage.

Serological tests are the mainstay of diagnosis. There are non-treponemal tests: venereal disease research laboratory (VDRL) and rapid plasma reagin (RPR). Treponemal tests include: *T. pallidum* passive particle agglutination (TPPA), Fluorescent treponemal antibody absorbed (FTA-ABS), enzyme immunoassay (EIA) and chemiluminescence immunoassay (CIA). Two separate types of serologic tests must be used for diagnosis. The CDC recommends non-treponemal tests be used for screening and treponemal tests be used to confirm the diagnosis. However, reverse-sequence testing has become more common. If clinical evidence of neurologic involvement is observed, cerebrospinal fluid (CSF) exam should be performed.

Penicillin remains the mainstay of treatment. Patients with early syphilis (primary, secondary or early latent) should receive a single dose of benzathine penicillin G 2.4 million units IM. Patients should be warned of the Jarisch-Herxheimer reaction consisting of tachycardia, tachypnea, headache, malaise, and fever usually within 24 hours of starting the antibiotic.¹³ Management is with NSAID agents and bed rest.

Adult patients with late latent syphilis should receive three doses at 1 week intervals. Neurosyphilis, ocular syphilis, and otosyphilis should be treated with aqueous crystalline penicillin G 18-24 million units daily (10-14 days). Treat partners within varying durations depending on the stage of disease.

5. Ectoparasites

5.1 Pediculosis Pubis (Pubic Lice or Crabs)

Pediculosis Pubis is a wingless insect that can infect people via infested people, clothes, or bedding. Physical exam findings include maculae ceruleae (blue gray macules) on skin. Treat with topical permethrin 1% cream **rinse (apply to affected areas and wash off 10 minutes later) OR pyrethrin with piperonyl butoxide (apply to affected area and wash off after 10 minutes)**. Consider malathion 0.5% lotion (apply to affected area and wash off after 8 - 12 hours) or oral ivermectin (250mcg/kg body weight) with treatment failure. Bedding, clothes, towels should be laundered using the heat cycle or dry cleaned. Treat sex partners and household members exposed within the previous 30 days.

5.2 Scabies

The causative organism is the parasitic mite, *Sarcoptes scabiei*. Patients get infected with the mites by contact with an infected person, clothes, or bedding. Symptoms include severe pruritus, especially at night or after bathing. The female mites burrow into the skin, most commonly in intertriginous regions. Treat with topical permethrin cream 5% (wash off after 8 hours) OR ivermectin 200 mcg/kg PO on day 1 and 14 OR **ivermectin 1% lotion (apply to affected areas and then wash off after 8 - 14 hours)**. Rash and pruritus of scabies can persist up to 2 weeks after successful therapy. Crusted scabies is seen mainly in patients with HIV disease or malnourished persons. It is contagious and aggressive. Treat with ivermectin 250 mcg/kg orally on days 1, 15 and 29.

6. Human Papilloma Virus (HPV, Genital Warts, Condyloma acuminata)

Genital HPV is very common. Most sexually active adults get HPV at some point in their lives, although most remain asymptomatic and the infection clears spontaneously. A double-stranded DNA virus, HPV has more than 30 types that cause genital infections: high risk (16, 18) and low risk (6, 11). Types 16 and 18 cause ~70% of cervical cancers, also a significant proportion of vulvar, vaginal, anal and upper airway cancers. Low risk types can cause genital warts, low-grade dysplasia, recurrent respiratory papillomatosis. Risk factors for persistence include age, immunosuppression, smoking,

concurrent infection with multiple types.

Genital warts may need to be biopsied if the diagnosis is uncertain, if the lesion is pigmented or ulcerated, or if the patient is immunocompromised. **Flat-topped lesions and giant condylomata should also be biopsied to rule out squamous cell carcinoma (SCC).** It is not recommended to treat sub-clinical (non-visible) lesions. Exophytic or symptomatic warts should be removed. Treatment does not eradicate the HPV virus and does not affect the risk of cervical cancer. Topical therapies can be applied by the patient and include podofilox 0.5% solution or gel (antimitotic drug), imiquimod 3.75% or 5% cream (immune enhancer, increases cytokines such as TNF- α) and sinecatechins 15% ointment (green tea extract, reduces HPV gene products E6 and E7). Provider-administered therapies include cryotherapy with liquid nitrogen, and trichloroacetic acid (TCA) (chemical coagulation) or bichloroacetic acid (BCA) 80%-90% solution or surgical removal.

Smaller lesions are easier to treat and may reduce recalcitrant condylomata in the future. Lesions on the glans penis may lead to meatal and intraurethral migration of the virus which portends more difficult management. Therefore, cystoscopy may be warranted in patients in whom the glans is affected, urethral symptoms are present, or lower urinary tract symptoms exist. If patients have no symptoms, some have advocated waiting for the glans lesions to heal prior to cystoscopy so as to not transfer HPV virus into the urethra. **For urethral meatal warts options for treatment include cryotherapy with liquid nitrogen or surgical removal. For vaginal, cervical or intra-anal warts, options include cryotherapy, surgical removal, or TCA or BCA 80%-90% solution.**

There are three types of HPV vaccines: 9-valent (6, 11, 16, 18, 31, 33, 45, 52, 58), quadrivalent (6, 11, 16, 18), and bivalent (16, 18). The 9-valent HPV vaccine was approved by the FDA in December 2014. All vaccines are administered in 3 doses over 6 months. These vaccines are preventative, not therapeutic. The vaccines consist of noninfectious, virus-like particles. Efficacy is >97% against CIN 2/3, vulvar and vaginal lesions. The quadrivalent and 9-valent vaccines have >98% efficacy against genital warts. Routine HPV vaccination is recommended for use in all individuals ages 9-26 years old and was recently approved to be used up to age 45 based on provider discretion. There is no need to restart the vaccination schedule for patients who do not follow up on time.

Bowenoid papulosis is a precancerous intraepithelial neoplasm characterized by either solitary or multiple pruritic, smooth-velvety, pigmented papules/plaques. It is **associated mostly with HPV 16** and to a lesser extent other subtypes. A small percentage evolve into invasive SCC. Lesions are contagious and often spontaneously regress. Treatment is only indicated for persistent lesions or if concern for SCC exists.

Verrucous Carcinoma (Bushcke-Lowenstein Tumor, Giant condyloma) is a low grade, well-differentiated squamous cell carcinoma associated with HPV 6 and 11 that can be locally invasive but non-metastasizing. Surgical resection is difficult as it usually locally invasive and has a high recurrence rate.¹⁹

7. Human Immunodeficiency Virus (HIV)

See Reference 20

7.1 Basic Pathology

Human immunodeficiency virus (HIV) is a retrovirus with RNA as genetic material. HIV invades cells through the CD4 receptor, found on macrophages and T-cells. CD4 is needed to process antigen, so loss of CD4 cells leads to immunodeficiency.²¹

Acute retroviral syndrome occurs 2-4 weeks after exposure, and symptoms resemble mononucleosis with fever, swollen glands, sore throat, and malaise. Anti-HIV antibodies are not yet present, so ELISA testing is negative. Asymptomatic carriage of the virus is of variable duration. Progression can be rapid (< 5 years), typical (10 years), or slow (> 15 years). Case definition of AIDS is an HIV+ person with no other causes of cell mediated immune deficiency with total CD4 count <200 cells/mL, and or any AIDS defining condition, many of which are opportunistic infections

(www.cdc.gov/mmwr/preview/mmwrhtml/rr5710a2.htm).²²

7.2 Clinical Presentation

The symptoms of HIV vary, depending on the individual and the stage of disease. In primary infections, the majority of patients develop a flu-like illness within one or two months of infection. In a clinically latent infection, some patients have persistent swelling of lymph nodes. Otherwise there are no specific signs or symptoms. In early symptomatic HIV infection, mild infections or chronic symptoms such as fever, fatigue, lymphadenopathy, diarrhea, weight loss, cough, and shortness of breath may occur. After progression to AIDS, people may develop signs and symptoms consistent with various opportunistic infections.

7.3 Diagnosis

Anti-HIV antibodies usually develop 3-6 weeks after the infection. Laboratories should conduct initial testing for HIV with an FDA-approved antigen/antibody combination immunoassay that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen (4th generation HIV test) to screen for established infection with HIV-1 or HIV-2 or for acute HIV-1 infection. Specimens with a reactive antigen/antibody combination immunoassay result should be confirmed with an FDA approved antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies

(<https://stacks.cdc.gov/view/cdc/45930>). If acute HIV infection is suspected, an HIV RNA viral load should be sent.

7.4 Treatment

It is difficult to eradicate HIV for two reasons - the presence of viral sanctuaries such as CNS or lymphoid tissue and the high genetic variability of the virus. Anti-retroviral therapy (ART) is used to keep viral load <20-40 copies (depending on assay) of HIV RNA per ml of blood. A combination ART regimen generally consists of two nucleos(t)ide reverse transcriptase inhibitors (NRTIs) plus one active drug from one of the following classes: integrase inhibitor, non-nucleoside reverse transcriptase inhibitor (NNRTIs), or protease inhibitor (PIs) generally boosted with ritonavir. There are currently six pills available as combination therapy.

In early treatment, the immune reconstitution syndrome (IRIS) may be seen, an excessive restored immune response, which leads to systemic symptoms and lymphadenopathy or the appearance/emergence of infections such as tuberculosis or mycobacterial infection or autoimmune disease such as Grave's disease or sarcoidosis.

7.4.1 Nucleotide Reverse Transcriptase Inhibitors (NRTIs)

Nucleotide Reverse Transcriptase Inhibitors (NRTIs) stop conversion of viral RNA to DNA nucleoside analogs. Tenofovir alafenamide (TAF), emtricitabine, lamivudine and abacavir are the common NRTIs used currently. The main toxicities associated with NRTIs are lactic acidosis and peripheral neuropathy. Tenofovir disoproxil fumarate was associated with renal dysfunction and bone loss in ~2% of patients, but toxicity is not a risk with TAF.

7.4.2 Non-Nucleotide Reverse Transcriptase Inhibitors (NNRTIs)

Non-Nucleotide Reverse Transcriptase Inhibitors (NNRTIs) block reverse transcriptase by binding directly to the enzyme. Commonly used NNRTIs are rilpivirine, doravirine and efavirenz, and the main toxicities include skin reactions and hepatitis.

7.4.3 Protease Inhibitors (PI)

Protease Inhibitors (PI) stop precursor proteins from being cleaved into viral proteins. Commonly used are darunavir and atazanavir. The main toxicities include visceral fat accumulation and lipid elevation. PIs may have significant interactions with other drugs. Note: PDE5 inhibitors are metabolized by the same enzyme system, so consideration should be given to decreasing PDE5i dose of medications at commencement of ED therapy or using drugs with short half-lives such as sildenafil or vardenafil (Drug Interaction).

7.4.4 Integrase inhibitors

Integrase inhibitors block the enzyme that inserts the viral genome into the DNA of the host cell. Raltegravir, elvitegravir, dolutegravir and bictegravir are currently approved. The combination tablets that include an integrase inhibitor are triumeq, genvoya and biktaryv. There are generally few side effects but rash, fatigue and myopathies are seen in some

patients.

7.5 HIV/AIDS: Clinical Pearls for the Urologist

See References **23, 24, 25**

(see **Table 3**)

Table 3. HIV/AIDS: Clinical Pearls for the Urologist

Opportunistic infections	<ul style="list-style-type: none">- Genitourinary Tuberculosis - may present with changes in urinary function, scrotal mass, or prostatic induration. Typically found to have pyuria, hematuria, or proteinuria. GU TB can present as renal, genital, or pelvic organ disease²⁶- Bacterial urinary tract infection (UTI) -may need longer course of antibiotics to clear- Viral Infections (BK, Adenovirus, CMV, HHV8)
Hemorrhagic cystitis	<ul style="list-style-type: none">- Caused by viral infections including:<ul style="list-style-type: none">- BK virus (BK was the first patient's initials isolated from a renal transplant patient)- (Gardner et. al)- Adenovirus or- Cytomegalovirus (CMV)
AIDS related malignancies	<ul style="list-style-type: none">- Kaposi's sarcoma (from HHV-8)- Non-Hodgkin's lymphoma- Invasive cervical cancer- Testicular cancer- Renal cell carcinoma- Bowen's disease
Renal dysfunction	<ul style="list-style-type: none">-HIV-associated nephropathy (HIVAN) with focal segmental glomerulosclerosis (FSGS) and severe proteinuria (infrequently seen with the advent of ART)
Urinary retention	<ul style="list-style-type: none">- Can be seen in CNS and peripheral nervous system disease.
Hypogonadism	<ul style="list-style-type: none">- Can occur due to virus, chronic illness and drugs (see testicular atrophy).- For HIV+ men with low Testosterone and weight loss, testosterone replacement is recommended.
Adrenal insufficiency	<ul style="list-style-type: none">- Monitor for need of stress dose steroids at surgery.
Stones	<ul style="list-style-type: none">- Indinavir, other protease inhibitors and efavirenz can cause stones, radiolucent on CT scan.- Treat with hydration and drug cessation.- Some patients may need a ureteral stent and may occur bilaterally.
Rhabdomyolysis	<ul style="list-style-type: none">- Trimethoprim-sulfamethoxazole can cause rhabdomyolysis within 2 weeks of starting the drug in HIV/AIDS patients.
Renal Transplant Concerns	<ul style="list-style-type: none">- HIV+ individuals are still candidates for renal transplant if CD4+ > 200 however they have higher incidence of rejection.

Prevention

- HIV infection rate can be reduced by 60% with circumcision in high prevalence communities (current randomized control data exists only in Africa)

8. RISK OF HIV AND HEPATITIS B/C ACQUISITION

8.1 Occupational Exposure

Urologists are considered high-risk for exposure to bodily fluids.²⁷ All health care workers (HCW) should be immunized against Hepatitis B (three shot vaccine series).²³ Occupational transmission of HIV to HCWs is extremely rare. If exposed to HIV-infected blood at work and untreated, 0.3% will result in infection. The risk is higher for injection needles than for knives or solid needles. A HCW who sustains a “sharps injury” should be evaluated immediately at an employee health service or emergency department.

Universal precautions are essential. **It is important to know that the following fluids are infectious- blood, tissue, semen, vaginal secretions, pus and the following fluids: cerebrospinal, amniotic, pericardial, peritoneal, pleural and synovial fluid.** It is important to use care with passing sharps. Needles should not be recapped. Double gloving may be beneficial. Immediately wash hands and other skin surfaces after contact with blood or body fluid.²⁸

Post-exposure prophylaxis (PEP) for HCWs is recommended when occupational exposures to HIV occur. It should be started as soon as possible and continued for a 4-week duration. PEP medication regimens should contain at least 3 antiretroviral drugs.²⁹ For more information, see current CDC guidelines <https://www.cdc.gov/hiv/risk/pep/index.html> or call National Clinicians Consultation Center, PEP Hotline at **888-448-4911**. Other resources:

<https://www.jstor.org/stable/pdf/10.1086/672271.pdf>, and
<https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm>

8.2 Non-Occupational Exposure

Non-occupational post-exposure prophylaxis (nPEP) is offered when there is a potential exposure to HIV outside the workplace. High risk exposures include needle sharing, intercourse and exposure to infected bodily fluids. Lower risk would be oral sex for women and men with or without ejaculation. Kissing and mouth-to-mouth resuscitation do not warrant nPEP. (See www.hivguidelines.org/pep-for-hiv-prevention/). To be effective, nPEP must begin within 72 hours of exposure. This consists of 3 antiretroviral drugs with the fixed dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200mg plus an integrase inhibitor that should be taken for 28 days. Baseline HIV testing must be done with repeat testing at 4 and 12 weeks. Pre exposure prophylaxis (PrEP) is taken when someone is at ongoing, substantial risk of HIV acquisition. Daily oral PrEP with the fixed dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200mg (Truvada) has been shown to be safe and effective in reducing the risk of HIV acquisition in adults including individuals at substantial risk of HIV acquisition. Daily oral dolutegravir (fixed dose combination of TAF 25mg and FTC 200mg) was approved in individuals at risk for HIV infection excluding those who engage in vaginal sex. HIV infection should be assessed every 3 months; STIs and renal function at least every 6 months. Patients should be encouraged and supported to use PrEP in combination with other effective prevention methods.

<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf>.

9. HELPFUL LINKS

AUA update link (Update Series (2017) Lesson 18: Sexually Transmitted Infections Patient guide links – Urology Care Foundation. <https://www.urologyhealth.org/urologic-conditions/sexually-transmitted-infections>

<https://www.cdc.gov/std/treatment-guidelines/pocket-guide.pdf>

Videos

Sexually Transmitted Infection

Presentations

Sexually Transmitted Infection Presentation 1

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CDC website is always a very helpful place to gather up to date information when dealing with a patient specific issue.
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