



Sexually transmitted diseases

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KEYWORDS:

Sexually transmitted diseases; Blood-borne diseases; Ulcerative lesions; Screening partners; Preventive measures Sexually transmitted diseases (STDs) comprise a diverse group that includes blood-borne diseases, sexually transmitted infections (STIs), and ulcerative lesions. This area of medicine has been the cornerstone for many abstinence and safe-sex programs, research into new vaccinations, screening of partners, and infection prevention. Even with these great strides, we still see more and more individuals infected. Recently the Centers for Disease Control and Prevention changed their guidelines for screening in pregnant females regarding hepatitis B and recommendations for prophylaxis of neonates born from hepatitis B virus (HBV)–infected mothers. There is updated information on human papillomavirus (HPV) vaccination for young boys and research on the new HIV vaccination that is projected to curb those who are being infected with HPV and HIV. In addition to growing trends, current treatment, and prevention on sexually transmitted infections, there are now reports of cephalosporin resistance to gonorrhea. Unfamiliarity with ulcerative lesions is common and their presentation is revisited here and expanded for better understanding. Family medicine needs to focus attention both on how to better educate the patient population when screening those who are unknowingly infected, and how to prevent further spread.

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Sexually transmitted diseases (STDs) are one of the most common complaints patients bring to their primary care office. The economic burden of sexually transmitted infections (STIs) in the US is estimated at \$14.1 billion annually in direct medical costs to the health care system. 1 More than 19 million new cases of STIs occur annually in the United States. Chlamydia trachomatis is the most common reportable bacterial STI, with approximately 2.8 million new cases in the US each year and 50 million worldwide.² Gonorrhea and chlamydia infections are common among females ages 15 to 19. STDs are ranked among the top five risks of international travelers, along with diarrhea, hepatitis, and motor vehicle accidents.² Viral infections have been increasing in prevalence; specifically, newly diagnosed herpes simplex virus (HSV) has risen to 500,000 new cases each year. HSV is now one of the most common viral STIs.² One million new cases of human papillomavirus (HPV) are diagnosed every year, and prevalence of this is between 24 and 40 million.² Throughout the US, diagnosis of genital warts has varied from city to city and seems to be fairly equal among men who have sex with men or women.³ Syphilis is seeing a new resurgence in all regions of the US.³ Not all STDs are on this rise; hepatitis B and C are on a downtrend since they were first documented in 1982 and 1992, respectively.⁴ The Centers for Disease Control and Prevention estimated 56,300 new HIV infections had occurred in 2006 in the US; however, the incidence of infection has been stable since the early 2000s.⁵

With the ever-increasing trends and statistics, it is pertinent for all primary care physicians in metropolitan or rural areas to revisit this area of medicine.

The approximate age when coitus first happens in American adolescents is age 16. However, this can be younger in certain young females depending on where they live. Risk factors that should be kept in mind when

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seeing this population are the following: age at first sexual intercourse; time between menarche and first intercourse; sexual activity within early and middle adolescence; multiple partners; new partners; partners with multiple partners; inconsistent use of condoms, especially with established partners; and alcohol/drug use. Primary care physicians should remember the five Ps when obtaining a thorough history regarding their patient's tendencies. Asking whether they are homosexual, heterosexual, or bisexual, as well as how many partners they have had in past two to 12 months is the first 'p,' for Partners. The other four Ps are prevention of pregnancy, protection from STDs, method of sexual practice, and past history of STDs. Please refer to Table 1 SORT Key for current recommendations in practice.

Blood-borne diseases

Blood-borne diseases including hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, and syphilis are still prevalent in the United States.

Hepatitis

Background

HBV and HCV are similar in that they are not only blood-borne diseases and have the same sources of infection but, more importantly, they are contracted through sexual intercourse and the symptoms and signs of both can be mistaken for other viral infections, such as HIV or even common influenza. Sources of HBV and HCV include the following: inoculation of infected blood or blood products; sexual contact; saliva, semen, and vaginal secretions; exposure to blood products before routine testing for HCV; intravenous drug use; and reuse of unsterilized needles, syringes, or medical equipment. Incubation periods vary; HBV's can be anywhere from six weeks to six months and HCV's from six to seven weeks. HBV is a 42-nm hepadnavirus with a partially double-stranded DNA genome consisting of an inner core protein (hepatitis B core antigen [HBcAg]) and outer surface coat (hepatitis B surface antigen [HBsAg]), whereas HCV is a single-stranded RNA virus (hepacivirus).⁷

Clinical manifestations

The onset of symptoms for both types of viral hepatitis can range from abrupt to insidious; symptoms include nausea, vomiting, diarrhea, constipation, fatigue, anorexia, myalgias, arthralgias, weakness, upper respiratory symptoms, low-grade fever, mild abdominal pain, and weight loss. Jaundice usually sets in after five to 10 days subsequent to other symptoms. Stool will start appearing acholic during this phase. Acute illness with HBV subsides after two to

three weeks, with clinical/laboratory recovery by 16 weeks. Hepatomegaly presents in more than half of the patients with HBV/HCV. Splenomegaly is associated with only 15% of patients, along with soft, enlarged lymph nodes in cervical and epitrochlear areas. There is notable neurocognitive impairment in patients with chronic HCV. After some time, elevated serum transaminases in a minority of patients will normalize; however, there will be persistently elevated alkaline phosphatase and bilirubin. If the patient is a smoker, he/she will notice a distaste for cigarettes, matching the rate of their anorexia.

Diagnosis

The appearance of HBsAg in a patient's bloodstream is the diagnosis for HBV, which stays in the blood throughout the clinical illness. Figure 1 from Topley and Wilson's Microbiology and Microbial Infections visualizes the timeline of Hepatitis B viral antigens and antibodies detectability in the blood following acute infection. Persistence for more than six months after the acute illness with HBsAg represents chronic HBV. Anti-HBs is a specific antibody that appears after HBsAg and after HBV vaccine. IgM Anti-HBc appears shortly after HBsAg is detected and its presence indicates diagnosis of acute hepatitis B. In previously inactive chronic hepatitis B, IgM anti-HBc may also reappear during flares. HBeAg and HBV DNA both mirror each other for viral replication and infectivity, with the latter being the more sensitive and precise marker.

Pregnant women who are found to be infected with hepatitis B e antigen, which is a known marker of increased viral replication and infectivity, have 85% to 90% perinatal transmission rates. ¹¹ In 2004, the United States Preventative Task Force (USPTF) recommended all pregnant women be screened with HBsAg on their first prenatal visit. Prophylaxis is recommended for infants born to mothers who harbor HBsAg. ¹¹ Sensitivity and specificity is greater than 98% in the detection of HBV infection. ⁸ In high-risk, pregnant and non-pregnant females, physicians should consider HCV testing. ¹⁰ Regarding vaccine information and schedules, visit the Centers for Disease Control and Prevention's article on HBV testing; this is outside the scope of this article. ²⁹

HCV antibody enzyme immunoassay, recombinant immunoblot assay, and quantitative HCV RNA polymerase chain reaction (PCR) are diagnostic tests used to detect HCV infection. The most used test is HCV antibody enzyme immunoassay detecting HCV antibodies; confirmation of a positive test should be followed by a recombinant immunoblot assay. The latter detects antibodies to individual HCV antigens having greater specificity, and then combined with viral load to differentiate between a resolving infection and a false-positive enzyme immunoassay. Regarding HCV-infected mothers and lactation, the infection does not appear to transfer from the infected mother to the infant through breast milk. Further questions regarding treatment of mothers and their infants with HBV

| Clinical recommendations* | Evidence rating | References |
|--|-----------------|------------|
| Routine screening of asymptomatic patients who are not at increased risk | A | 9 |
| Persons with HCV should also be vaccinated against hepatitis A and B | С | 9 |
| Pegylated interferon and ribavirin (Rebetol, Merck & Co, Kenilworth, NJ) is standard therapy for chronic HCV | C* | 9 |
| Patients with chronic HCV should avoid alcohol consumption | С | 9 |
| Hepatotoxic drugs should be stopped in chronic HCV and cirrhosis | С | 9 |
| Hepatocellular carcinoma should be considered with chronic HCV and cirrhosis | С | 9 |
| HIV screening should be done using either routine approach for all persons 13 to 64 years old or a risk-based approach, depending on practice setting | С | 13 |
| All pregnant females should be tested for HIV in the first trimester | Α | 13 |
| Second HIV test should be considered in third trimester for pregnant Females, or for those in high-prevalence areas | С | 13 |
| HIV should be confirmed with repeat HIV enzyme-linked immunoorbent assay and Western blot test to document seroconversion within four to six weeks | С | 12 |
| Education and counseling prevention should be provided to HIV patients to reduce the risk of transmission | С | 12 |
| Screening for other STDs (e.g., chlamydia, gonorrhea, syphilis), HBV, HCV, and tuberculosis in patients with acute HIV infection | С | 12 |
| Penicillin is effective in the prevention of congenital syphilis | Α | 10 |
| Tinidazole (Tindamax, Mission Pharmacal, San Antonio, TX) is an appropriate treatment option for metronidazole (Flagyl, Pfizer, Groton, CT)-resistant trichomoniasis | В | 6 |
| Treatment of trichomoniasis has not been shown to decrease the incidence of preterm birth | Α | 10 |
| Quinolones should not be used in the treatment of N. gonorrhoeae infection | C | 6 |
| The use of expedited partner treatment decreases the risk of reinfection for patients | В | 6 |

Recommendation for treatment is "C" because the outcome is a surrogate marker (sustained virologic response) rather than mortality.

A = consistent, good-quality patient-orientated evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-orientated evidence, usual practice, expert opinion, or case series.

For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.xml.

can be found in the CDC's Morbidity and Mortality Weekly Report on immunization strategies to stop the eliminate the spread of HBV.³⁰

treated for N. gonorrhoeae or C. trachomatis infection

Treatment

Screening/Vaccines. The USPTF disapproves the routine screening of asymptomatic patients who are not at increased risk for viral hepatitis. They also found insufficient evidence to recommend for or against routine screening of high-risk patients because studies have not shown a decrease in morbidity and mortality. See Table 2 for a list of blood-borne therapies.

Prognosis and prevention. Potential long-term complications of HBV include liver cancer and cirrhosis. HCV infection has been known to cause cirrhosis in 10% to 20% of those initially infected with acute HCV, which increases the risk of portal hypertension, ascites, hemorrhage, and hepatocellular carcinoma. Factors noted to increase the risk of progression include age less than or equal to 40 years, male gender, coinfection with HBV/HAV, immunosuppression, and daily alcohol use of 3 drinks or more per day (50 grams). Physicians should recommend their pa-

tients stop drinking alcohol and avoid using hepatotoxic drugs if they have known chronic HCV. The rate of hepatocellular carcinoma is increased 20-fold in patients with HCV and cirrhosis. There was a meta-analysis where ultrasound was used to follow the progression to hepatocellular carcinoma in patients with chronic HCV and cirrhosis; sensitivity and specificity were found to be approximately 94%.⁹

HCV transmission can be prevented through use of condoms and education of partners regarding the potential transmission through body fluids. Partners and close contacts are advised to not share toothbrushes or razors.

HIV

Background/clinical manifestations

Primary HIV infection or acute retroviral syndrome, also known as *acute human immunodeficiency virus* infection, occurs just after initial HIV infection before seroconversion. Symptoms of HIV are very difficult to differentiate because they may mimic other viruses, such as influenza. Acute infection may present with fever, rash, malaise, sore throat, fatigue, myalgias/arthralgias, headache, anorexia, pharyngi-

Relative amount in the blood Infectious Immune anti-HBc Total Incubation Symptoms period anti-HBs HBeAc anti-HBe Time Infection After 6 to 12 months 2 weeks to 3 approximately months >20 years 3-6 months

HBV antigens and antibodies in the blood

Figure 1 HBV antigens and antibodies in the blood.

tis, lymphadenopathy, mucocutaneous ulcerations, diarrhea, or a combination of these symptoms. The initial symptoms manifest one to four weeks after transmission, and symptoms may last for two to four weeks. Physical examination is nondiagnostic but may show hepatosplenomegaly.

Diagnosis

Confirmation of HIV infection should made on the basis of repeat HIV enzyme-linked immunoabsorbent assay and Western blot testing to confirm within four to six weeks. ¹² To reduce the risk of transmission, patients with acute HIV infection should receive education and prevention counseling.

Screening

The CDC recommends that all persons between ages 13 and 64 be routinely screened for HIV at least once regardless of risk, with repeat testing annually for those who are high risk (e.g., intravenous drug users and their sexual partners, persons who exchange sex for money/ drugs, commercial sex workers, and those in adult correctional facilities, sex partners of HIV-infected, homosexual males, history of STDs, and those with multiple sex partners during pregnancy). 13 All pregnant women should be tested for HIV in their first trimester according to recommendations by the USPSTF. 10 High-risk pregnant women should also be re-tested for HIV in their third trimester. 10 Laws pertaining to consent processes vary from state to state and can be found on the Compendium of State HIV testing Laws. 13 Recently the CDC stated in their HIV guidelines that routine HIV pre-test counseling or separate written consent was no longer needed; however, every patient should be informed when an HIV test is offered and given an opportunity for open discussion.

Any patient with acute HIV infection should be screened for tuberculosis and other STIs, including chlamydia, gonorrhea, syphilis, and HBV/HCV.

Treatment/Vaccines

For treatment options, please refer to the Table 2. With regard to vaccination, the problem with HIV is that there is a latent phase in its infectious process, which allows latent CD4⁺ T cells to be established early in the acute infection, thus not allowing HIV to be easily eradicated like other viruses. Research has been underway for a vaccine against HIV.¹⁴

Prevention

Condom use, limiting drug and alcohol intake (because use of both can impair judgment), and using alternative sexual practices that do not deal with exchanging body fluids are the mainstays to prevent the contraction of HIV. Homosexual patients should be warned of serosorting, in which identification of a potential sex partner is based on their HIV status, which may lead to unprotected sex if the potential partner states they are HIV-negative.

Syphilis

Background/Clinical manifestations

Treponema pallidum is the spirochete that causes syphilis and after onset of infection has an incubation period of 10 to 90 days. Contact with infectious lesions or body fluids hastens spread of the disease. Other modes of infection include through vertical transmission and blood transfusion. Primary disease is denoted by a single, painless, indurated ulcer at the site of inoculation appearing about three weeks after contact and lasting for four to six weeks. The location of the ulcer can be found on the glans, corona, or perianal area on men and on the labial or anal area in women. Bilateral, nontender inguinal, or regional lymphadenopathy

| Table 2 | Blood-borne therapies | |
|---------|---|---|
| Disease | Treatment | Notes |
| HBV | Supportive including bed rest and intravenous fluid therapy with 10% glucose | None |
| HCV | Gold standard for treatment of chronic HCV is pegylated interferon (i.e., alfa-2a, alfa-2b) and ribavirin (Rebetol)*; length of tx based on genotype of HCV and virologic response to therapy | Before beginning therapy a CBC, CMP, UA, TSH, urine Beta HCG, viral load, genotype, HIV, and PT/PTT/INR need to be done as therapy has been associated leukopenia, thrombocytopenia, and autoimmune thyroiditis; Rebatol is renally cleared and therefore a baseline serum BUN/Cr should be done prior to treatment especially in those with renal insufficiency; Thirty percent of patients will experience depression, emotional labiality, or anger with HCV therapy, but rarely is it associated with suicidal ideation or hallucinations |
| HIV | acute infection is often supportive. For initial therapy two NRTIs along with either NNRTI (e.g., efavirenz) or a PI/r (e.g. lopinavir) are recommended | Questions regarding HIV therapy is available on the AIDS info website at http://www.aidsinfo.nih.gov/guidelines/default.aspx Guidelines are updated frequently |

CBC = complete blood count; CMP = complete metabolic profile; UA = urine analysis; TSH = thyroid-stimulating hormone; HCG = human chorionic gonadotropin; PT = prothrombin time; PTT = partial thromboplastin time; INR = International Normalized Ratio; BUN = blood urea nitrogen; Cr = creatinine; NRTI = nucleoside reverse transcriptase inhibitors; NNRTI = nonnucleoside reverse transcriptase inhibitors; PI/r = ritonavir-boosted protease inhibitor.

Information taken from references 9, 10, and 16.

*Patients with chronic HCV and anemia, renal insufficiency, active alcohol use/or substance abuse, autoimmune hepatitis, decompensated cirrhosis, pregnancy, severe cardiopulmonary disease, uncontrolled major depression, or untreated hyperthyroidism are not suitable candidates for treatment.

also is often seen. Ulcers and adenopathy are predominantly painless and heal without treatment, therefore remaining unnoticed. This is defined as *latent syphilis*. The first year of the latent phase is called *early latent syphilis*. The time after the first year is referred to as *late latent syphilis* or *latent syphilis* of *unknown length*.

Secondary syphilis begins four to 10 weeks after the appearance of the ulcer and can be seen for as long as 24 months after the initial infection. Manifestations of secondary syphilis are mucocutaneous, constitutional, and parenchymal signs and symptoms.² Physicians should have a high index of suspicion if patients complain of fever, pharyngitis, or arthralgias, and on examination are found to have lymphadenopathy. Early manifestations consist of maculopapular rash that is seen on the trunk and arms along with generalized nontender lymphadenopathy.² A papular rash will eventually accompany the primary rash after several days or

weeks. This rash is associated with endarteritis and can become necrotic and pustular.²

One of the hallmarks of the rash is that it can also affect the palms of the hands and soles of the feet. In the intertriginous area, these papules can become large and erode, to create condyloma lata lesions, which are extremely infectious.² These can be confused with condylomata acuminata lesions because they appear flat, raised, and painless when found on mucosal areas.¹⁷ Hepatitis and immune complexinduced glomerulonephritis are other less common manifestations of secondary syphilis. Syphilis that remains untreated in one-third of patients will progress to tertiary syphilis, which is very rare in industrialized countries, except for occasional cases reported in HIV patients. Syphilis can become systemic and affect almost any organ or system—especially the skeletal, central nervous, integumentary, and cardiovascular systems.² Aortitis, meningitis, uveitis, optic neuritis, general paresis, ta-

| Table 3 Patient-applied therapies | | | | |
|-----------------------------------|--|---|--|--|
| Medication | Application | Notes | | |
| Podofilox 0.5% solution/or gel | Applied twice daily for 3 days, then off for 4 days; optional repeat of treatment cycle 4 times* | No more than 0.5 mL of solution used per week and wart area not >10 cm ² | | |
| Imiquimod 5% cream | Applied three times per week at bedtime for 16 weeks; do not apply to the vaginal area† | Area washed well 6-10 hours after application | | |

^{*}Demonstration of podofilox solution in the office may be helpful.

[†]This cream should not be applied to the vaginal area because it has been associated with chronic ulceration. Pregnant females are strongly recommended to not use podofilox (Condylox, Watson Pharmaceuticals, Inc., Parsippany, NJ), imiquimod (Aldara, Meda Pharmaceuticals, Somerset, NJ), and podophyllin creams.

Information taken from references 2, 10, and 17.

| Medications | Applications | Advantages/disadvantages | Notes |
|---------------------------------------|--|--|---|
| Cryotherapy with liquid nitrogen | Used for multiple treatments from a single-use disposable applicator. Lesions are 10-20 cm depending on the product and are followed-up in 1-2 weeks to repeat therapy | Unlike liquid nitrogen, the probe temperature is not low enough to cause deep tissue injury | Long shelf life; some warts may need 2 or more applications |
| Electrosurgery | _ | _ | _ |
| Laser Therapy | _ | _ | Carbon dioxide laser alternative for surgical excision |
| Podophyllin resin 20%-1% | Used once and washed thoroughly 1-4 hours after treatment; may repeat treatment on a weekly basis as needed | _ | In benzoin mixture; no open lesions or wounds caused by toxicity; amount <0.5 mL of podophyllin or an area of <10 cm ² of warts per session |
| Trichloroacetic acid (TCA) | Cotton tip applicator at 1-2- week intervals | Not used for large or keratinized warts; patients will complain of burning sensation that resolves in 2-5 minutes | Excess solution should be dabbed off with talcum powder or baking soda |
| Bichloroacateic acid (BCA) 10%-90% | Cotton tip applicator at 1-2- week intervals | Not used for large or keratinized warts; patients will complain of burning sensation that resolves in 2-5 minutes | Excess solution should be dabbed off with talcum powder or baking soda |
| Surgical excision | _ | Large area or large warts can be addressed at one time | Electrocautery or sharply removed with tangential incision; bleeding controlled with electrocautery or silver nitrate sticks; lesions in or around the urethral meatus may suggest urethral or bladder condyloma, warranting cystourethroscopy; lesions on urethra or bladder should be cystoscopically excised |

5-fluorouracil cream causes ulceration and acquired adenosis and is therefore no longer recommended. Topical application of Bacille Calmette-Guerin has shown to be promising; however, larger studies are needed to evaluate the safety and efficacy.

Information taken from references 2 and 17.

ble dorsalis, and gummas of skin and skeleton are some of the sequalae associated with tertiary syphilis.²

Diagnosis

For primary and secondary lesions, dark-field microscopy and direct fluorescent antibody (DFA) are tests used to diagnose syphilis. Non-treponemal serologic testing with rapid plasma regain (RPR) or venereal disease research laboratory (VRDL) are most commonly used for screening.² The sensitivity is 78% and 86% for RPR and VDRL, respectively, in primary syphilis; 100% for both in secondary syphilis; and more than 95% in tertiary syphilis.² False-positive results can be 1% to 2% and need to be confirmed with treponemal testing using *T. pallidum* particle agglutination or florescent treponemal antibody absorbed.² Falsenegative results on both the treponemal and nontreponemal methods may result if the patient is also infected with HIV.

To follow disease activity, RPR and VDRL should be performed in the same laboratory.

Screening

The USPSTF recommends all pregnant women and people who are at high risk to receive screening.^{2,17} All patients positive for syphilis should consider HIV, HBV, HCV, gonorrhea, and chlamydial testing on the basis of CDC recommendations.² There are strong recommendations by the USPTF against routine screening of asymptomatic persons who are not at increased risk for syphilis infection.¹⁷

Treatment

Treatment of choice is a single dose of benzathine penicillin G 2.4 million U intramuscularly (i.m.). After 24 hours of treatment with penicillin, patients may have head-

| Medication | Initial | Suppressive | Episodic |
|--------------|--|---------------------------------------|--|
| Acyclovir | 400 mg 3 times daily or 200 mg 5 times daily for 7-10 daily | 400 mg twice daily | 200-800 mg every 6-12 hours for 5 days |
| Famciclovir | · | 250 mg every 8-12 hours for 7-10 days | 125 mg twice daily for 5 days |
| Valacyclovir | 1 g twice daily for 7-10 days | 500 mg or 1 g daily | 500 mg 1g every 12-24 hours for 3-5 days |

aches, myalgia, fever, tachycardia, and increased respiratory rate, collectively called the Jarisch-Herxheimer reaction.² Patients with penicillin allergy can consider doxycycline 100 mg orally twice daily, tetracycline 500 mg four times daily for 14 days, or ceftriaxone 1 g i.m./intravenously (IV) daily for eight to 10 days.⁶ Benzathine penicillin injection (IV) of 2.4 million U should be repeated weekly for a total of three doses. Doxycycline/tetracycline are extended for four weeks for patients with tertiary, latent, or late latent syphilis. Patients with neurosyphilis are treated with aqueous crystalline penicillin G 3 to 4 million U IV every four hours for 10 to 14 days, or penicillin G procaine 2.4 million U i.m. daily plus probenecid 500 mg orally four times daily, each given for 10 to 14 days. Patients with sulfa allergy cannot be given probenecid. Nontreponemal antibody titers at six and 12 months should be followed. A repeat cerebrospinal fluid examination should be done at three to six months after therapy and every six months afterward until normal results are obtained.²

Sexually transmitted infections

Trichomoniasis

Background/clinical manifestations

The incubation period for *Trichomonas vaginalis* is anywhere from four to 28 days. This flagellated protozoan can live in the vagina, urethra, Bartholin glands, Skene's glands, and prostate. It cannot inhabit the rectum or mouth. In males, this organism may go unnoticed; however, some men have urethral discharge, dysuria, and urinary urgency. For women with T. vaginalis infection, symptoms include sudden onset of frothy white or green foul-smelling vaginal discharge, pruritus, erythema, dyspareunia, suprapubic discomfort, and urinary urgency.^{2,10} When infection becomes chronic, erythematous lesions are sometimes noted on the exocervix.¹⁷ T. vaginalis has been linked to increased risk of HIV transmission and adverse birth outcomes such as premature labor in pregnant females and low birth weight.^{2,10,17} On physical examination, frothy discharge and the characteristic "strawberry vulva" and/or "strawberry cervix" may be seen.

Diagnosis/Screening

Culture is the most sensitive and specific method for diagnosis. ¹⁷ The vaginal or seminal secretions will have a basic pH when tested on nitrazene paper. There is 60% to 70% sensitivity with microscopic inspection of vaginal secretions. ^{2,6} In men, a urethral swab or microscopic examination of urine are taken for culture. There are two new Food and Drug Administration–approved point-of-care tests called Osom Trichomonas Rapid Test and BD affirm VPIII Microbial Identification Test, both of which have a sensitivity of more than 83% and specificity of more than 97%; however, there is concern for false-positive results in regions of low disease prevalence. ⁶ There are no screening recommendations for trichomoniasis, especially in asymptomatic women. ¹⁰

Treatment

Treatment consists of metronidazole or tinidazole. Metronidazole 2 g is effective as a single dose and is associated with a 90% to 95% cure rate. Common side effects are gastrointestinal problems. In this case, metronidazole 500 mg twice daily for seven days is better tolerated. Physicians must counsel their patients to abstain from alcohol consumption while on therapy and also 24 hours after completion of treatment. There is approximately 2.5% to 5% of *T. vaginalis* isolates that harbor some level of resistance to metronidazole, therefore allowing the use of tinidazole in such cases.

Tinidazole has a longer serum half-life and better penetration into the genitourinary tissues, making it a potential treatment for metronidazole-resistant trichomoniasis. If a patient is taking tinidazole, alcohol consumption should be withheld for 48 hours after treatment.

Physicians will need to repeat testing in five to seven days and 30 days if symptoms fail to resolve or if a failure of treatment is suspected.² If the latter is true, then repeat metronidazole 500 mg twice daily for seven days or 2 g once a day for three to five days may be attempted. There is metronidazole gel for intravaginal application; however, it should be noted that it is 50% less effective than oral treatment.² Sexual partners should be treated even if they are asymptomatic.

Chlamydia

Background/Clinical manifestations

Of all the sexually transmitted infections, Chlamydia trachomatis remains the most commonly reported bacterial infection, with an estimated 2.8 million new cases in the United States each year.² Virulent serotypes include D, E, F, G, H, I, J, and K. The incubation period ranges anywhere from three to 14 days. Approximately 50% of men will have lower urinary tract symptoms as a result of urethritis, epididymitis, or prostatitis, and they will notice clear/white urethral discharge.² In women, 75% will be asymptomatic, with 40% progressing to pelvic inflammatory disease (PID).^{2,17} Purulent or mucopurulent endocervical exudates or sustained endocervical bleeding are sometimes the only abnormalities noted on pelvic examination.² Some women may have only post-coital or abnormal vaginal bleeding. When PID is evident, concern exists for scarring of the fallopian tubes, which puts patients at risk for recurrent PID infections, ectopic pregnancy, pelvic pain, and infertility. 2,17,19

Diagnosis/Screening

For diagnosis in women, this can be done by one of the following: nucleic acid amplification test (NAAT) performed on an endocervical swab specimen or urine sample, an unamplified nucleic acid hybridization test (DNA probe), an enzyme immunoassay (EIAs), or DFA test on endocervical swab culture. NAAT is the test of choice for urethral, cervical, vaginal, and urine specimens because of its high sensitivity and exceptional specificity. However, this test is expensive and may not be readily available but is noninvasive and therefore preferred. The DNA probe test is an option when NAAT is not available or is too expensive for patient. It is now recommended to screen all females up to the age of 25, and sexually active adolescents yearly.

Treatment

Patients can be treated with either azithromycin 1 g orally once 10,20 or seven days of doxycycline 100 mg orally twice daily, which are both equally effective. To Cure rates for these drugs are 97% and 98%, respectively. Other alternatives include erythromycin base 500 mg four times daily, erythromycin ethylsuccinate 800 mg four times daily, ofloxacin 300 mg twice daily, or levofloxacin 500 mg daily for seven days. Patients will need to refrain from sexual intercourse until both their and their partner's treatment is complete or seven days after single-dose therapy is given. A test-of-cure is urged after three weeks from treatment, regardless of which medication is used. If patients were sexually active, all sexual contacts within 60 days of the onset of symptoms or diagnosis of chlamydia should be notified and examined.

Gonorrhea

Background/Clinical manifestations

Caused by a gram-negative diplococcus, Neisseria gonorrhoeae has an incubation time of three to 14 days. Men and women carry 10% and 40% risk of infection after one exposure, respectively.² More than 50% will be asymptomatic. 17 Men will have symptoms involving the lower urinary tract that will be accredited to urethritis, epididymitis, proctitis, or prostatitis, with mucopurulent urethral discharge. Women will have symptoms of vaginal and pelvic discomfort, dysuria, abnormal vaginal discharge that is yellowish in color, erythema, edema to the genitals, burning, or pruritus of the vaginal area. Those who engage in anal intercourse may be subject to tenesmus, pruritus, and bloody/ mucoid discharge. Pharyngeal infections will initially be asymptomatic but will eventually progress into odynophagia.¹⁷ Regardless of symptoms, PID and its consequences are potential risks. It is now recommended to screen all females up to the age of 25, and sexually active adolescents yearly. 10 The systemic manifestations of this infection arthritis, dermatitis, meningitis, and endocarditis—are rare.

Diagnosis/Screening

Diagnosing gonorrhea includes performing NAAT or culture in Thayer-Martin media by endocervical swab in women and intraurethral swab in men per CDC guidelines. Also, individuals considered to be in a high-prevalence area should consider testing regardless of age.

Treatment

The recommended treatment for gonorrhea is ceftriaxone 125 mg i.m. as a single dose, which gives high, sustained blood levels that result in cure in more than 99% of uncomplicated cases.² An alternative is cefixime 400 mg single dose¹⁰; however, the tablet form is no longer available in the US and only the suspension form exists.² Cefuroxime 500 mg i.m., cefoxitin 2 g i.m. with probenecid 1 g, or cefotaxime 500 mg i.m. are all alternative single-dose regimens. The resistance to cephalosporins stems from chromosomal mutations previously seen to relate resistance to beta-lactam antimicrobials and mosaic penicillin-binding protein (penA).²¹

For patients with penicillin and cephalosporin allergy, a single intramuscular dose of spectinomycin 2 g is a recom-

mended alternative but is not available in the US. Pharyngeal infection is not susceptible to spectinomycin.² There is increasing resistance to the use of azithromycin 2 g single oral dose in uncomplicated infections.² It is an option for those patients with well-documented allergic reactions to penicillin and cephalosporin.

In the last 10 years, there has been an increasing emergence of quinolone-resistant N. gonorrhoeae (QRNG).⁶ Asia, the Pacific Islands, Hawaii, and California are areas where QRNG is most prevalent. However, now this is seen in other areas of the US. As of April 2007, the CDC no longer recommended the use of quinolones in the treatment of gonorrhea.^{2,17} QRNG is more commonly seen in homosexual men than in heterosexual men (23.8% vs. 2.9%, respectively); however, there is still an increasing rate of QRNG among heterosexual persons.^{6,22} Use of azithromycin and spectinomycin are options for cephalosporinresistant infections; however, azithromycin is becoming resistant and spectinomycin will be available in the future for clinical use.²² There are further studies into other antimicrobials such as aminoglycosides, rifampin, carbapenems, and other new cephalosporins with a broader spectrum of activity underway.

Sexual activity should be avoided for seven days after treatment. Patients with persistent symptoms should be reevaluated by culture, and positive isolates need to undergo antimicrobial susceptibility testing. ¹⁷ Laboratories should report treatment failures or resistant gonococcal isolates to the CDC through state and local public health authorities. Uncomplicated gonococcal infections that are treated and respond to cephalosporin do not require a test-of-cure. ¹⁷ However, it is recommended to do a test-of-cure for pregnant women if symptoms persist, or if there is a concern of re-infection. Test-of-cure should be performed three weeks after treatment. ¹⁰ As in patients with chlamydia, all partners exposed to gonococcal infection in the previous 60 days should be referred for evaluation and treatment.

Human papillomavirus (HPV)

Background/Clinical manifestations

Condylomata acuminata, or genital warts, are caused by HPV and are spread only through skin-to-skin contact. There are more than 100 subtypes, with as many as 30 that are transmitted through the genital-to-genital contact. Risk factors for this include having multiple sexual partners, early age onset of sexual intercourse, and having a sexual partner with HPV. The common types for genital warts are types 6 and 11, which are visible on physical examination. They can appear anywhere on the external genitalia. They can also be found on the cervix, vagina, urethra, anus, and mucous membranes (e.g., conjunctiva, mouth, and nasal passages). They appear as flesh-colored, flat, verrucous, or papillary lesions. People will typically be infected with more than one type. Of the known types that cause cancer (e.g., 16, 18, 31, 33, 35, 39, 45, and 51), types 6 and 11 are

of low risk for invasive canreinoma of the external genitalia.² In HIV-infected women, HPV progresses quickly, therefore allowing cervical cancer to be considered an AIDS-defining illness.² Smoking is an independent risk factor in increasing dysplastic progression and malignancy in both men and women. For women with HPV, they may have nonspecific symptoms: vulvodynia, pruritus, or malodorous vaginal discharge. Female patients with internalized warts may experience pain, bleeding, or difficulty with intercourse.¹⁷ Men will most often be asymptomatic.

Diagnosis

Visualization or palpation of nontender flat or pedunculated papillomatous genital lesions confirms the diagnosis of HPV. ¹⁰ If there is any doubt, biopsies should be done in all cases where atypical, pigmented, indurated, fixed, or ulcerated warts are seen. ¹⁰ Warts that are treated but persist in immunocompromised patients warrant biopsy. ^{2,10,17}

Screening

Currently the CDC recommends patients with genital warts be informed that HPV and recurrence is common in sexually active individuals and the incubation period can be long and erratic. Therefore, the length of infection and methods of prevention are not definitively known.²

Treatment

There are several factors that go into deciding what treatment will be used, such as size, number, and location of the wart along, with the patient and physician preference. Knowing that in some cases genital warts resolve without treatment, makes observation an option to treatment. When HPV infection is diagnosed by colposcopy, biopsy, or through the detection of HPV by laboratory test, but there are no genital warts or cervical squamous intraepithelial lesion (SIL); treatment is not recommended for subclinical genital HPV infection. ¹⁷ Please refer to Tables 3 and 4 for both Patient versus Physician applied therapies.

Prevention

In addition, patients should be told that regular and consistent use of condoms will decrease the chance of exposure to this infection.

Across the various types of treatment, there is a similar response rate of 60% to 80% and the preference of treatment depends on physician training as well as availability of the method. Patients need to be warned that there is a 30% recurrence rate.

Vaccines

Currently there are two virus-like vaccines that protect against HPV. The quadrivalent Gardasil (Merck & Co., Whitehouse Station, NJ) protects against HPV types 6, 11,

16, and 18. This formulation was approved in June 2006 to prevent HPV-associated conditions such as cervical cancer, cervical cancer precursors, and anogenital warts. Cervarix (GlaxoSmithKline, London, UK), a bivalent vaccine, is a newly licensed vaccine that is directed against HPV to prevent cervical cancer and was approved by the Advisory Committee on Immunization Practices (ACIP).¹⁸ The bivalent version protects against types 16 and 18. There was 100% efficacy for preventing vaccine type-related grade 2 or 3 cervical intraepithelial neoplasia, adenocarcinoma in situ, external genital warts, and vulval/vaginal intraepithelial neoplasia with the quadrivalent vaccine in those patients without prior infection who were vaccinated without delay using the vaccination series protocol.² If a person is infected with one or more vaccine HPV types before vaccination, they will be protected against disease caused by remaining vaccine HPV types.²

The CDC's Advisory Committee on Immunization Practices currently recommends routine vaccination of females aged nine to 26 with three doses of Gardasil at 0, 2, and 6 months for the quadrivalent version before sexual activity or known exposure to HPV. Recently, the ACIP allowed physicians to vaccinate males aged nine to 26 years with Gardasil to prevent genital warts.¹⁸

Females aged 10 to 25 years should receive the Cervarix vaccination with routine immunizations starting at 11 to 12 years of age. The series of three dose of Cervarix are given at 0, 1 and 6 months. "Catch-up" time period is in patients between the ages of 13 and 26 and 13 and 25, respectively for Gardasil and Cervarix, who have not been previously vaccinated or who have not completed the three-vaccine series. ¹⁸ On the contrary, the American Cancer Society does not recommend vaccination for women ages 19 to 26 because the probability of an increased number of lifetime sexual partners reduces efficacy. ² Immunocompromised and immunosuppressed patients can safely receive the vaccinations because they do not contain live viruses.

Ulcerative lesions

There are several STIs characterized by the presence of genital ulcers, most commonly herpes simplex virus (HSV), chancroid, lymphogranuloma venereum, and granuloma inguinale. Other differential diagnoses to be considered with ulcerative lesions that are non-sexually-transmitted include Behçet's syndrome, drug reaction, erythema multiforme, Crohn's disease, lichen planus, amebiasis, trauma, and carcinoma. High-risk considerations for ulcerative diseases are: homosexuality, sex workers, young patients, pregnant females, women who have had a hysterectomy, and sexual contact with those who are affected.

Herpes simplex virus (HSV)

Background/Clinical manifestations

HSV is one of the most common viral STIs, with 50 million people currently infected. HSV is incurable. Genital

herpes is caused by HSV-2 in 85% to 90% of cases and HSV-1 in 10% to 15% of cases.² HSV-1 is the source of common cold sores but can be transmitted via oral secretions during oral-genital sex, and 75% of infected persons are silently infected.² The incubation period ranges from 1 to 26 days. Those individuals infected with nongenital HSV-1 in childhood may be protective to some degree against subsequent genital HSV-2 infection in adults.

HSV-1 and 2 generally present in the same way. They appear as a group of vesicles on an erythematous base not following a neural distribution. HSV lesions are painful vesicles to the mouth, genitals, or anus, and are typically shallow. Multiple lesions are generally present and patients have tender, bilateral inguinal lymphadenopathy. The lesions are usually accompanied by flu-like symptoms and localized or regional pain, tingling, and burning lasting from two to 24 hours. 17 Patients with vesicles in the anal region rarely have sacral radiculomyelopathy, which can be seen with primary anal HSV.² In women who have lesions around the urethra, they can expect transient urinary retention, along with the appearance of ulcers on the cervix, introitus labia, vagina, vulva, perineum, and surrounding skin. Within 14 to 21 days, the vesicles rupture, leading to ulceration and crusting, and eventually heal without scarring.¹⁷ Recurrent breakouts are not as painful or severe and involve ulceration to the genital and/or anal areas. Complications of this disease include: pneumonitis, disseminated infection, hepatitis, meningitis, and encephalitis.² Asymptomatic shedding is most likely to occur in the third to twelfth month after initial clinical presentation, which increases the risk of transmission.²

Diagnosis

Diagnosis cannot be made from clinical presentation alone. The gold standard for diagnosis is viral tissue culture with subtyping. ^{2,10,17} PCR is only reserved for HSV encephalitis or for neonatal infections because the results are more rapid than viral culture, and physicians should be aware that PCR is costly and has limited availability. ^{10,17} The use of routine serologic screening is not recommended.

Treatment

Medication must be started either during the prodrome or within one day of the onset of lesions; this should decrease the duration of the outbreak by one to two days. Suppressive therapy has shown to be effective in preventing 80% of recurrences and decreases the frequency and duration of recurrences, as well as viral shedding. Clinical studies involving single-, two-, and three-day treatments of oral antivirals may be just as effective as traditional longer treatments for genital herpes. Valacyclovir 500 mg twice daily for three days, acyclovir 800 mg three times daily for two days, and famciclovir 1 g twice daily for one day showed a decrease in the number of days for lesion healing and duration; however the number of patients who ceased to participate in the study was significant. Topical therapy has not been proven effective to address HSV infections.

Please refer to Table 5 for further information regarding HSV treatment.

Prevention

Patients need to refrain from sexual activity while having breakouts or symptoms and need to be counseled that even when they are not having symptoms, it is still possible to transmit infection. Currently, development is underway of a vaccine based on mucosal immunity.¹⁷

Chancroid

Background/Clinical manifestations

Haemophilus ducreyi is the etiologic bacterium leading to infection with chancroid, which is the most common STI worldwide.² The incidence of chancroid is greater in men than in women.² The lesions are tender papules that can progress into painful undermined purulent ulcers. They can be single or multiple in the vulvovaginal or penile area with a friable base with gray or purulent disheveled borders.² Lymph nodes are regional, painful, suppurative, and unilateral.^{2,24} The incubation time is one to 21 days.

Diagnosis

This bacterium is fastidious and difficult to culture. The culture medium required is not always available, and sensitivity remains less than 80%. ^{2,24} Use of Gram stain to detect short, fine gram-negative streptobacilli in short, parallel chains, or using PCR can be done if needed. ²

There are four major criteria that need to be met: presence of one or more painful ulcer, presence of lymphadenopathy, a negative syphilis evaluation or negative serologies at least seven days after the onset of symptoms, and negative HSV culture from culture ulcer exudates.² There is dual infectivity with syphilis or HSV at a rate of 10%; therefore these individuals should be screened. There are recommendations for screening of HIV and syphilis at the time of diagnosis and three months after treatment if the patient is initially negative.²

Treatment

Treatment of choice is azithromycin 1 g or ceftriaxone 250 mg i.m. Alternatives include: ciprofloxin 500 mg twice daily for three days or erythromycin 500 mg three times daily for seven days. However, with the latter two, there has been resistance reported in some areas. Known HIV status or uncircumcised men with ulcers below the foreskin will have a slower healing trend.² Failure to treatment has been reported in patients who are immunosuppressed because of HIV infection, in uncircumcised individuals, and in Africans treated with single doses of ceftriaxone or fleroxacin.²⁴ Patient follow-up in five to seven days and sexual partners should be evaluated if

they had intercourse either two weeks before or during the eruption of the ulcer. Patients often need relief from painful lymph nodes, and needle aspiration or incision and drainage of the nodes is permitted.

Lymphogranuloma venereum

Background/Clinical manifestations

This disease is caused by Chlamydia trachomatis types L1, L2, and L3. It is rare in the US, but parts of Africa, Asia, South America, and the Caribbean are common endemic areas. These lesions are a single, painless vesicle or papule that progresses to an ulcer on the penis, anus, or vulvovaginal area.25 The initial stage of the disease process includes painful, unilateral, suppurative inguinal lymph nodes and constitutional symptoms for two to six weeks; systemic symptoms can persist after the genital lesion heals.² These lymph nodes can in turn become matted, progressing to fistulous tracts during the secondary stage of lymphogranuloma venereum. In the final stage of this disease, if left untreated, it can progress to chronic inflammation and destruction of tissue such as fistulae, strictures, and chronic proctocolitis, mimicking inflammatory bowel disease (IBD); and chronic granulomatous conditions of the external genitalia including lymphoedema and elephantiasis that are irreversible with antibiotic therapy alone.²⁵ The incubation period is between three and 30 days.

Diagnosis

NAAT for *C. trachomatis* swab specimens with specific molecular typing and culture is commonly implemented; however, they are not specific for *L. venereum* caused by *C. trachomatis*. If a patient has symptoms, then specific typing is required and contact with the state health department is needed. Complement fixation or indirect-fluorescence antibody titers can confirm the diagnosis; \geq 64 units is diagnostic of infection with complement fixation. Direct immunofluorescence is a test licensed for detection of *C. trachomatis* from rectal swabs from symptomatic patients; however, this is a technically difficult test and has low sensitivity.

Treatment

Treatment includes doxycycline 100 mg twice daily (compliance may be better) or erythromycin 500 mg four times daily for three weeks. There is insufficient data using azithromycin 1 g by mouth weekly for three weeks as an alternative to treatment. Enlarged lymph nodes may need incision and drainage or aspiration to avoid femoral or inguinal ulceration.

Granuloma inguinale

Background/Clinical manifestations

Granuloma inguinale, or donovanosis, is caused by infection with Klebsiella granulomatis, formerly known as Donovania granulomatis, and Calymmatobacterium granulomatis; it was recently renamed after studies involving comparative DNA sequencing.²⁶ Granuloma inguinale presents as a painless shallow ulcer at the primary site of inoculation (genital, oral, anal, or at other extra genital locations). The main areas this disease is endemic to are India, Papua New Guinea, areas among Australian aboriginals, Brazil, and South Africa.²⁶ These lesions are characterized by a sharply demarcated, beefy-red, friable base of granulation tissue. Lesions spread by contiguity and there is prominent local lymphadenopathy. Lymphadenopathy can progress to more ulcerative lesions; lymphoedema and genital mutilation with spread of disease locally can result without treatment.²⁶ Rare cases of systemic spread along with secondary infection with spirochete-fusiform bacteria are common, after which the ulcer has purulent, painful, foul-smelling drainage and is subsequently hard to treat. Just as with HSV, there is also transmission to infants during birth with granuloma inguinale.²⁶ The incubation period is between 8 days and 12 weeks with an insidious onset.

Diagnosis/Screening

The use of Giemsa, Wright, and Leishman stains showing Donovan bodies are a few ways to diagnose granuloma inguinale. A quick and useful version of Giemsa stain, Rapi Diff (Biotech Sciences, Ltd., Wigan, Lancashire, UK), is recommended as an easy and steadfast method. If a punch/snip biopsy of ulcer or lymph nodes needs to be completed, then pretreatment of biopsy with vancomycin or metronidazole is recommended. Patients presenting to the physician's office with unusual ulcerations, after other diagnoses have been ruled out and there is a history of travel outside of the US, should be screened. Those in contact with patients who are diagnosed with the disease should be evaluated. There are currently no recommendations to screen asymptomatic patients. ²⁶

Treatment

There are different treatments that can be used to treat disease. Doxycycline 100 mg twice daily, azithromycin 1 g once weekly, ciprofloxin 750 mg twice daily, or erythromycin 500 mg four times daily are recommended regimens that should be given for three weeks or until lesions have healed.²⁷

Screening partners/behavioral counseling for prevention

The main strategies in prevention and control of STDs are education and counseling. There are five keys areas that address sexual health: Partners, Prevention of pregnancy, Protection from STDs, Practices, and Past history of STDs.⁶ People between the ages of 18 and 28 are most at risk for contracting any STD, but particularly between the ages of 15 and 19 for gonorrhea and chlamydia. Physicians should screen homosexual women, just as heterosexual women, as homosexual women are also at risk for developing HPV and squamous intraepithelial lesions. Homosexual women are also at a higher risk for HSV-1 owing to more frequent orogenital activity. Adolescent patients 12 to 14 years of age can legally consent for their own health services for the diagnosis and treatment of STIs. 17 Asking open-ended questions when taking a complete sexual history, using an understandable voice tone/language, and not assuming that married individuals or those in long-term relationships or their partners are in monogamous relationships will help establish a strong patient-physician relationship.¹⁷

Putting condoms in restrooms, at the receptionist desk, or in examination rooms is an assured way to make patients more comfortable and open to discussing their sexual issues. For females whose male partners are reluctant to wear a condom, suggest using a female condom. Female condoms are more expensive, however, but still protect against STIs and HIV.

Expedited partner therapy (EPT) has been used to prevent complications from STIs and the spread of disease.¹⁷ With expedited partner therapy, the sexual partner is given a prescription without being seen or counseled. There were three randomized, control trials in which the CDC evaluated the behavioral and clinical outcomes of EPT compared with traditional treatment programs by patient and physician referral. There was evidence that pointed to EPT as an option in patients with N. gonorrhoeae or C. trachomatis infection. 6 Currently, the CDC recommends that physicians consider using EPT as a way to overcome the barriers to health care access for their patient's sexual partners. 6,20 EPT should not be used in homosexual males because there is a lack of data confirming efficacy in this population and comorbidity (undiagnosed HIV). EPT is practiced in 11 states, potentially allowable in 28 states, and legally prohibited in six states.¹⁷ To find out whether your state allows EPT visit the CDC's site outlining the legal status per state of EPT.17

Goals for behavioral strategy pertain to knowledge, stigma reduction, access to services, and delay of onset of first intercourse, decrease in number of partners, increases in condom sales/use, and decrease in sharing of contaminated injection equipment.²⁸ Physicians can help their patients regarding the stigma associated with testing for HIV by offering it as a part of routine care for prevention instead

of only questioning those who are considered more high risk. 13

Therefore, physicians across the globe should make it their personal goal to screen, educate, and prevent these STDs, rather than brushing the matter off until the next appointment. STDs may be preventable with time, patience, and compassion toward every patient regardless of gender, race, or sexual preference. Providing information regarding STDs in office waiting areas, restrooms, patients' rooms, pharmacies, local health departments, and homeless shelters will not only help prevent but will, more importantly, educate patients on how to be smart and stand up for themselves. In addition, providing information to patients breaks the barriers to screening and treatment. ¹⁶

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