The impact of STIs

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Despite being among the easiest infections to treat — the majority require only a single dose of antibiotic for a complete cure — sexually transmitted infections (STIs) remain an important cause of morbidity in the United States and throughout the world.[1] Among the >60 notifiable diseases, the STIs chlamydia and gonorrhea are the two most common.[2] These two STIs are the key cause of preventable infertility among women and, along with other STIs (e.g., genital herpes and syphilis), make the acquisition and transmission of human immunodeficiency virus (HIV) infection three to five times more likely.[3] Recent developments in diagnosing and treating STIs continue to make this field interesting and worthy of review.

Medical laboratories have become increasingly key to diagnosing STIs. Tests previously performed by clinicians (e.g., Gram stain or wet preparation) now are often being performed in the clinical laboratory. In addition, with the advent of nucleic-acid amplification tests (NAATs), more STI tests are of better quality than ever before.[4] These tests can be performed on urine or self-collected swabs, increasing the use of these tests in clinical and non-clinical settings.

Here, we review clinical, diagnostic, and epidemiologic aspects of the major STIs, except HIV, and also discuss STI prevention and examine challenges and developments for the future.

Infections causing cervicitis, PID, proctitis, and urethritis

Chlamydia: An estimated 2.8 million new infections with *Chlamydia trachomatis* occur each year, the majority among persons from ages 15 to 25 years.[5] The Centers for Disease Control and Prevention (CDC) recommends that sexually active women aged <25 years be screened for chlamydia annually. The number of identified cases of chlamydia has continued to increase, probably, in part, as a result of increased testing, but other factors might also be contributors. Despite this, screening and treatment prevent complications (e.g., pelvic inflammatory disease [PID] and other sequelae).[6]

Chlamydial infection can cause a mucoid urethral discharge and painful urination among men or cervicitis among women but is most often asymptomatic. Untreated infections can progress to PID, and approximately 20% of women with PID later have decreased fertility.[7] Recommended treatment for chlamydia among both men and women is a one-time dose of azithromycin (preferred) or doxycycline twice daily for seven to 10 days by mouth.[8]

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Gonorrhea: Gonorrhea was recognized by ancient Greek practitioners who named it for its milky urethral discharge (*gono-* meaning seed or sperm, and *-rhea* meaning flow).[9] In the United States, development of Thayer-Martin media for culture of *Neisseria gonorrhoeae* allowed the institution of national control programs in the 1970s. Thereafter, rates of gonorrhea declined consistently and are now at an historic low.[2] Gonorrhea is increasing, however, in the western United States, and has rapidly developed resistance to multiple classes of antibiotics. Ceftriaxone injection is the only available, universally recommended treatment in the United States, because fluoroquinolone-resistant gonorrhea seems to be rapidly spreading from West to East.[8]

Gonococcal urethritis causes painful urination and discharge, although approximately 25% of men have no symptoms. Among women, gonorrhea can cause cervicitis with vaginal discharge, pain with intercourse, or painful urination; however, approximately half of infected women are asymptomatic. *N gonorrhoeae* can also infect the rectum and throat. Infections at these sites are predominately asymptomatic but can cause proctitis or pharyngitis. Rectal infections increase the risk for HIV acquisition, if a person is exposed through receptive anal sex. Pharyngeal infections usually have minor clinical consequences but can be transmitted to male partners through oral sex.

Gonorrhea can be diagnosed by Gram stain of infected discharge; however, this test is rarely performed except at specialized clinics. Most infections are diagnosed by NAAT of urine or swab specimen or by culture. Although not Food and Drug Administration (FDA)-cleared, NAATs may be used to test pharyngeal and rectal specimens, an important part of screening men who have sex with men (MSM) for STIs.[10]

Nongonococcal urethritis: Nongonococcal urethritis (NGU) is the most common clinical sexually transmitted syndrome among men and is characterized by painful urination with or without discharge. Symptoms can be mild, and patients sometimes complain of itching or tingling of the penis. Signs of inflammation on urine dipstick, Gram stain of urethral discharge, or spun urine sediment make the diagnosis. Approximately 30% of NGU cases are caused by chlamydia, but often no organism is able to be isolated. Other organisms are being recognized as causing NGU, including *Trichomonas vaginalis* and *Mycoplasma genitalium*, as well as multiple oral flora and viruses (e.g., adenovirus).[11]

Infections characterized by genital ulcers

Syphilis: Such historical figures as Columbus, Beethoven, Lincoln, and Nietzsche are all speculated to have suffered from syphilis.[12] Syphilis continues to cause substantial morbidity today. During the 1990s, syphilis epidemics occurred among MSM and among blacks, especially in the southeastern United States. The increase among MSM was fueled by decreased anxiety about HIV and physical health related to the success of HIV treatment,

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the increasing popularity of the Internet to find sex partners, and an emerging crystal methamphetamine-abuse epidemic.[13]

Clinical manifestations of syphilis are varied, and its natural history is complex. The first manifestation is usually a single painless ulcer or chancre at the site of inoculation. After resolution of the chancre, the maculopapular rash of secondary syphilis might appear, along with fever and swollen lymph nodes. After secondary syphilis, patients can remain latently infected for decades with no symptoms. Historically, without treatment, approximately 25% of patients progressed to tertiary syphilis, which can affect the cardiovascular system or brain. Neurosyphilis can develop during any stage and is characterized by visual or hearing loss or, if prolonged, delirium. Diagnosis relies on nontreponemal serologic tests (e.g., rapid plasma reagin [RPR] or venereal disease research laboratory [VDRL]), confirmed by more specific serologic treponemal tests (e.g., fluorescent treponemal antibody-absorption test [FTA-ABS] and *Treponema pallidum* particle agglutination [TPPA]). Treatment for syphilis includes injectable long-acting benzathine penicillin G once for primary, secondary, or latent syphilis of <1-year duration. For syphilis of longer duration, three weekly doses of benzathine penicillin G are necessary. Successful treatment is documented by at least a fourfold decline in VDRL or RPR titer six to 12 months after treatment.[8]

Herpes: Genital herpes infects approximately 45 million Americans. Primary infection is characterized by fever, painful vesicles or ulcers and, commonly, neurologic symptoms. Primary infection is followed by milder recurrences among the majority of persons. Severity and frequency of recurrences vary considerably but typically diminish over time. Although patients shed more virus during outbreaks, patients shed intermittently outside of symptomatic outbreaks, and asymptomatic shedding transmits the majority of new infections. Diagnosis is made by culture or polymerase chain reaction (PCR) detection of herpes simplex virus (HSV) from a lesion. Type-specific serology is also increasingly being used to identify infected persons. Though there is no cure, treatment with acyclovir or valacyclovir can decrease the duration and severity of symptoms and can reduce the chances of transmitting infection. As with other STIs, HSV infection facilitates the transmission and acquisition of HIV infection.

Other causes of genital ulcers: Other ulcerative STIs include chancroid, caused by *Haemophilus ducreyi*, and lymphogranuloma venereum (LGV), caused by L serotypes of *C trachomatis*. These infections are rare in the United States, although outbreaks of LGV proctitis have occurred recently among MSM in Europe.[14] Chancroid and LGV are characterized by inguinal lymphadenopathy.

Other STIs

Hepatitis B: Hepatitis B virus (HBV) can be transmitted sexually and is approximately 100 times more transmissible than HIV. Approximately 15% to 20% of all new HBV infections occur among MSM.[15] Although condoms probably protect against sexually acquired HBV, vaccination is the most effective strategy, and all adults who are at risk should be vaccinated. Since 1991, CDC has recommended that all newborns receive routine HBV vaccination.

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Human papillomavirus: Human papillomavirus (HPV) has recently attracted substantial attention because of the development of PCR-based HPV assays and the FDA approval of a new HPV vaccine. In total, 40 types of HPV can infect the genital tract. HPV-16 or -18 causes >70% of cervical cancers worldwide, whereas HPV-6 or -11 causes >90% of genital warts. These four types are included in the newly approved vaccine. HPV infection is extremely common and is transmitted through vaginal or anal sex, but not through oral sex, because genital HPV types cannot infect the mouth.

The majority of infections are self-limited and asymptomatic; however, certain HPV infections result in genital warts, and others, ultimately, result in cervical, anal, vulval, or penile cancer. Genital warts are treated mainly for cosmetic reasons by using cryotherapy, topical destructive agents, or surgery. Treatment often must be repeated for complete resolution; however, recurrence is common.

Sequelae of HPV infection are usually mild or avoidable with routine Papanicolaou or Pap testing. HPV testing is not routinely recommended among men, and reassurance and condom promotion are the mainstays of HPV counseling.

Prevention efforts

Preventing STIs relies primarily on reducing risky sexual behavior and timely identification and treatment of infections. Primary prevention through consistent and correct condom use has been demonstrated to be highly effective in preventing and can reduce the risk of gonorrhea, chlamydia, trichomonas, genital herpes, and HPV. Condoms might be effective for other STIs, but well-executed studies are lacking. Efforts at secondary (e.g., partner management) prevention have been improved in recent years. Originally developed for syphilis control, partner notification, counseling, and treatment programs seek to find and treat as many infected sex partners as possible to prevent reinfection and further spread. Expedited partner therapy (EPT), in which an infected patient is given antibiotics (or a prescription) for his sex partners is becoming more commonplace, although legal hurdles to providing medications to partners exist in certain jurisdictions. EPT decreases repeat STIs and is endorsed by CDC.[16]

Another secondary prevention measure is widespread screening and treatment. Chlamydia-screening programs have resulted in increased screening, but more screening of difficult-to-reach populations, who are often at highest risk, is needed. Programs to screen incarcerated young adults and school-based screening have demonstrated promise in this regard.

Challenges

A major challenge in the control of STIs is to address racial disparities. In the United States, black women have rates of chlamydia, gonorrhea, syphilis, and HIV that are seven, 15, 14, and 21 times higher than white women, respectively.[2,17] Similar disparities exist among men. STI programs should do more to eliminate racial disparities in STIs by providing focused programs that meet the needs of populations at increased risk while also assuring access to prevention and care for everyone.

Using the Internet for meeting sex partners has allowed more frequent partner change and more anonymous partners, but the Internet also provides opportunity for education and intervention. In San Francisco and other locations, persons with an STI can notify partners electronically (*www.inspot.org/gateway.aspx*). Also in San Francisco, a text-messaging referral service for adolescents and young adults provides information on STI resources (*www.sexinfo.org*). Methamphetamine abuse has also increased STI spread. Erectile dysfunction medications used recreationally, often with methamphetamine, have added to continued disease transmission among certain groups.

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New technologies will continue to help in STI control. NAATs are now available for *T vaginalis* and *M genitalium*. Testing for antibiotic resistance by molecular methods will become increasingly important. Molecular techniques will also be used for molecular epidemiology, allowing tracking of STI genotypes throughout sexual networks.

The HPV vaccine is expected to be the next successful vaccine against an STI (the first was for HBV). If this vaccine performs as expected and is made widely available throughout the world, it might be among the most important public-health advances of the 21st century. Although no other STI vaccines are ready for clinical trials, work continues on vaccines for HSV, chlamydia, and gonorrhea. □

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Editor's Note: The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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