ARTICLE

Updating the management of sexually transmitted infections

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SUMMARY

The control of sexually transmitted infections relies on case-finding and treatment of sexual contacts to prevent further transmission.

Screening for infections should be tailored to the demographic and sexual risk of the individual.

For most sexually transmitted infections, screening is performed on self-collected, non-invasive samples using highly sensitive molecular assays. These are quick and inexpensive.

Shorter courses of antivirals for genital herpes are now recommended.

New chemoprophylactic strategies for preventing HIV transmission have emerged, including treatment to prevent transmission and the use of antiretrovirals for pre-exposure prophylaxis.

Introduction

In Australia, most sexually transmitted infections are managed in primary care. The rates of infections continue to rise despite years of safe sex promotion, non-invasive screening and the availability of tests that allow self-collected samples.[1]

Rates of newly acquired HIV infection have increased, and gonorrhoea notifications almost doubled between 2008 and 2012. In 2013, the highest number of syphilis cases ever was recorded. Conversely, in the same year, chlamydial infections decreased for the first time in nearly 15 years. Genital warts in young women are also declining following the introduction of the human papillomavirus (HPV) vaccination.[1]

The emergence and spread of resistance to therapies among sexually transmitted bacteria and viruses now threaten our ability to effectively control infections (including HIV) in the longer term. Australian guidelines[2] are available for managing sexually transmitted infections, and Therapeutic Guidelines: Antibiotic has recently been updated.[3]

Screening

Effective management of sexually transmitted infections relies on timely, accurate diagnosis. As most infections are asymptomatic, screening is important for identifying new cases. Guidelines[2] and screening tools[4] outline who should be screened (Box), what infections they should be screened for and which tests should be done. Populations vary geographically and the local epidemiology of infections may highlight other at-risk groups. Examples of these include prisoners and backpackers.[5-7] For most asymptomatic 'check-ups', a brief discussion to ascertain sexual practices, and non-invasive or self-collected samples are appropriate and acceptable.

Screening for chlamydia and hepatitis B is recommended for all groups. Gonorrhoea screening should also be performed in young sexually active Aboriginal and Torres Strait Islander people. Gonorrhoea, HIV and syphilis screening is recommended for men who have sex with men, people who inject drugs and sex workers. People who inject drugs should also be screened for hepatitis C.[4]

Men who have sex with men

For men who have sex with men, Australian guidelines recommend serological screening for syphilis and HIV, hepatitis A and hepatitis B (in non-vaccinated individuals), and hepatitis C (people with HIV, or those with a history of injecting drug use). Updated guidelines include testing for chlamydial and gonococcal infection in the oropharynx and anorectum. Oropharyngeal and anorectal swabs should be obtained for gonorrhoea and chlamydia, and a first-catch urine sample for chlamydia.

Box Who should be offered screening for sexually transmitted infections? [4]

- Anyone requesting a screen
- Sexually active people under 29 years
- Men who have sex with men
- Sex workers
- People who inject drugs

Testing is advised up to four times a year if the man is HIV positive or there is a history of the following:

- unprotected anal sex
- more than 10 sexual partners in the preceding six months
- group sex
- recreational drug use during sex.

Any sex in the previous year should prompt at least annual screening.[8]

Testing symptomatic patients

Sexual history and physical examination play an important role for symptomatic patients, including those with complex presentations. When an infection is identified, exclude all other sexually transmitted infections by screening and treat any that are detected.

Contact tracing

Contact tracing or partner notification identifies asymptomatic cases of infection, interrupts transmission and prevents reinfection.[8] It is an integral part of the management of sexually transmitted infections and is facilitated by ensuring confidentiality and using a non-judgemental manner. Contact tracing is a priority for HIV infection, syphilis, gonorrhoea and chlamydial infection, but is not generally useful or required for genital herpes and warts.

The time period over which to trace previous sexual contacts depends on the pathogen. The diagnosing clinician is responsible for initiating the discussion about contact tracing. Most commonly, the patient will notify their own sexual contacts (patient referral). This can be done anonymously via contact-tracing websites using texting and email messaging, or directly by telephone or face-to-face. Alternatively, with consent of the index patient, the doctor, delegate or other health agency can notify the sexual contacts (provider referral). Again, the identity of the index case may remain confidential. A mix of patient and provider referral may be appropriate with numerous contacts. Guidance for contact tracing is available online.[9,10]

Chlamydia

Chlamydia continues to be of concern, particularly in young people – nearly 60% of all notifications are in people aged 15–24 years old. Teenage girls are three times more likely to be infected compared to their male counterparts. Most infections remain asymptomatic and untreated. This is associated with significant long-term sequelae and screening is essential for diagnosis. It is recommended in all sexually active people less than 30 years old (<35 years old if indigenous Australian), for men who have sex with men at any age, and as part of antenatal screening depending on individual risk.

Testing for chlamydia is quick and most samples can be self-collected. Nucleic acid amplification tests (NAATs) are the preferred method. Depending on sexual behaviour, samples include first-catch urine, and blind vulvo-vaginal (preferred to urine for females), rectal and pharyngeal swabs.

Uncomplicated genital or pharyngeal chlamydia infection should be treated with a single dose of oral azithromycin 1 g. Doxycycline 100 mg twice daily for seven days is recommended for rectal infection. Contact tracing is advised, as is a test for reinfection at three months.

Gonorrhoea

While most men with urethral gonorrhoea are symptomatic, endocervical, oropharyngeal and anorectal infections are often asymptomatic. Screening for gonorrhoea is important as HIV acquisition is three times more likely in men who have sex with men with rectal gonorrhoea.[11] Gonorrhoea continues to be of concern in Aboriginal and Torres Strait Islander people, and travellers returning from high-prevalence countries. Sex workers providing oral sex should be screened for oropharyngeal gonorrhoea every three months.

As with chlamydia, NAATs are the preferred screening method. They can be performed on first-catch urine, and blind vulvo-vaginal (preferred in women), anorectal and oropharyngeal samples. Before treatment, request culture and sensitivity testing for men with purulent urethral discharge, and from all sample sites found to be positive for *Neisseria gonorrhoeae*.

Treatment includes a single dose of ceftriaxone 500 mg intramuscularly and azithromycin 1 g orally. Contact tracing and a test of cure are advised after treatment, particularly where first-line therapy is not administered. For the test of cure, culturing the organism is preferred over testing with NAATs. Culture testing can be conducted at one week, but testing with NAATs should be delayed until three weeks after treatment. Patients should be tested again for reinfection three months after treatment.

Growing antimicrobial resistance to treatments for *N. gonorrhoeae* has been documented in Australia and there are concerns about treating this organism in the future.

Mycoplasma genitalium infection

Although less prevalent than chlamydia in most studies, *M. genitalium* is established as a sexually transmissible cause of urethritis and cervicitis.

There is increasing evidence that it can cause pelvic inflammatory disease.

Genital mycoplasma polymerase chain reaction (PCR) assays allow for quick and self-collected testing and are Medicare rebatable. Suitable samples include first-catch urine in men and endocervical swabs for women. Currently, there are no recommendations to sample the rectum or oropharynx.

The current treatment is a single dose of azithromycin 1 g. However, there is increasing concern that this may induce macrolide resistance in *M. genitalium*. A test of cure should be performed four weeks after treatment is completed.

Genital herpes

It is estimated that only one-fifth of adults infected with genital herpes (type 1 or type 2) experience classical features such as recurrent blisters followed by ulceration and healing. There is a high prevalence of type 1 (seroprevalence 80%) and type 2 (seroprevalence 12%, estimates up to 25–30%) infection in Australia. Much of the management concerns counselling and health education. PCR testing of a genital swab from potential lesions is the gold standard for diagnosing genital herpes.

For recurrent herpes episodes, antiviral regimens have become shorter allowing patients more choice for managing their infection (see Table). Comparison studies have shown therapeutic equivalence for three drugs that differ only in dosing schedules and cost.[3,12] Viral replication in recurrent infections is short-lived and standard five-day regimens offer no therapeutic advantage over shorter courses.[12-16] The majority of patients will not require any treatment. However, when episodic therapy is unsuitable, suppressive treatment is an option (see Table).

HIV

Regular screening for populations with ongoing risk is advised. These include:

- men who have sex with men
- injecting drug users
- sexual contacts of people with HIV infection
- people diagnosed with a sexually transmitted infection, viral hepatitis or tuberculosis
- people with multiple sex partners or recent change of partner
- people reporting high-risk behaviours in high-prevalence countries
- migrants from high-prevalence countries.

Pregnant women should have HIV screening at their first antenatal visit. Testing should be done for anyone requesting it.[17]

Increasing HIV rates have prompted a change in the approach to treatment. Patients are now being treated earlier. This benefits the individual, and is also a public health benefit by preventing transmission.

Treatment as prevention

The efficacy of 'treatment as prevention' for HIV was shown in a multinational trial of serodiscordant couples. When the infected partner immediately commenced (rather than deferred) antiretroviral therapy and adhered to treatment, the virus was rapidly suppressed and HIV transmission was reduced by 96%. Early treatment was also associated with a 41% reduction of HIV-related clinical events.[18]

For prophylactic treatment to be effective, early diagnosis through expanded testing is essential. In 2012, the first rapid HIV test (Determine HIV combo) was approved. The test is a point-of-care antibody/antigen assay that can provide results in 20 minutes. It performs well in established infection, but has low sensitivity in early infection (<70%) and is inferior to routine conventional enzyme-linked immunosorbent assays performed on patient sera.[19]

In 2012, antiretroviral prophylaxis (pre-exposure prophylaxis or antiretrovirals for at-risk HIV-negative individuals to prevent transmission) with daily tenofovir and emtricitabine was approved for high-risk individuals in the USA. This included sexually active men who have sex with men (not in a monogamous partnership) who, in the last six months, had anal sex without a condom, a sexually transmitted infection or an HIV-positive partner.[20,21]

Antiretroviral prophylaxis is not currently subsidised in Australia, but there are projects evaluating the implementation of this strategy. Almost all of the pre-exposure prophylaxis trials have studied daily

Table **Treatment regimens for genital herpes** [3]

Drug	5-day regimens for initial infection	Episodic treatment for recurrent infection	Suppressive treatment
Aciclovir	400 mg orally, 8-hourly for 5 days	800 mg 3 times daily for 2 days	200–400 mg orally, 12-hourly
Famciclovir	250 mg, 8-hourly for 5 days	1 g orally, 12-hourly for 1 day	250 mg orally, 12-hourly
Valaciclovir	500 mg orally, 12-hourly for 5 days	500 mg orally, 12-hourly for 3 days	500 mg daily

tenofovir alone or tenofovir and emtricitabine as a fixed-dose combination. Outcomes have been mixed. This appears to depend on adherence. In studies involving drug monitoring, if a drug was detected, efficacy ranged from 70–92%.[22-25]

Human papillomavirus

Genital human papillomavirus (HPV) infection may manifest as genital warts, premalignant lesions or squamous cell carcinomas. Pre-malignant and cancerous changes may occur in the cervix, vulva, anus and, less commonly, the vagina. HPV is more prevalent in people with HIV so cervical screening should be performed annually in these women.

The prevalence of genital warts and cervical dysplastic lesions has substantially declined in young people since the introduction of the quadrivalent HPV vaccine. It is hoped that this will translate to a decrease in cervical and other HPV-related cancer rates. Research is ongoing to determine if anoscopy screening will reduce anal cancer in HIV-infected men who have sex with men.

Syphilis

Rates of infectious syphilis increased from 5/100 000 in 2004 to 14/100 000 in 2013.[1] This was almost exclusively in men who have sex with men. Others at increased risk include indigenous Australians and people from endemic countries where infection is typically asymptomatic. These cases are usually detected by serology in the latent phase.

Presentation depends on the stage of infection. Infectious syphilis describes both primary infection, characterised by the classic chancre, and secondary syphilis which may present with a constellation of signs and symptoms such as malaise, rash, condylomata lata (wart-like lesions) and patchy alopecia. Serology remains the mainstay of diagnosis. However, in very early infection, serology can be negative. In these cases, direct detection of *Treponema pallidum* by PCR may be useful.

Hepatitis A

Rates of hepatitis A infection remain stable at below 1.3/100 000. This is punctuated by occasional outbreaks most commonly associated with travel, food-borne disease, and household and institutional contacts.[1] Sexually transmitted hepatitis A infections occur almost exclusively in men who have sex with men, and New South Wales accounts for approximately 7% of all notified cases.[26] Large outbreaks recorded in the early 1990s (New South Wales, Victoria and South Australia) and mid 1990s (Sydney) have prompted the recommendation of vaccination for all homosexually active men.[27-31]

Hepatitis B

It is estimated that nearly 220 000 Australians are living with chronic hepatitis B, often acquired during childhood. Over 40% of these people remain undiagnosed.[1,32] Rates of newly acquired infections are slowly decreasing, due in part to infant and childhood immunisation. Chronic infection mostly affects people from endemic countries. Limited data suggest that about 70% of newly acquired infections occur in Australian-born individuals.[33] Although injecting drug use is the most commonly reported exposure risk for new infection, it is estimated that sexual transmission (homosexual and heterosexual) accounts for 15–25% of cases.[33-35]

Hepatitis B is a preventable infection and vaccination should be considered for everyone, but particularly for:

- sex workers
- people who inject drugs
- men who have sex with men
- HIV-positive and other immunocompromised people
- household and sexual contacts of people with chronic hepatitis B
- Aboriginal and Torres Strait Islander people
- people with hepatitis C or other chronic liver disease
- travellers
- people from endemic countries
- prisoners
- people at occupational risk.

Hepatitis C

Some traumatic sexual practices have been implicated in sexual transmission of hepatitis C, particularly among HIV-positive men who have sex with men. In men who have sex with men, hepatitis C is more common in those who are HIV positive than those who are HIV negative (6.08/1000 vs 1.48/1000 person years).[36] Key risk factors include fisting, shared use of sex toys, group sex, recreational drug use during sex, current or previous sexually transmitted infections (particularly ulcerative infections) and inconsistent condom use.

The risk of transmission between heterosexuals is extremely low. Prospective studies of serodiscordant partnerships report incidence rates ranging from zero transmissions to up to 12/1000 person years.[37-42]

While percutaneous exposure accounts for the majority of newly acquired infections, an Australian study reported 18% of transmission due to sexual exposure. Of these, 14% were heterosexual partnerships and 86% occurred in men who have sex with men (nearly all HIV positive).[43]

Conclusion

GPs play a key role in caring for patients with sexually transmitted infections. Effective management involves identifying and screening at-risk individuals, prescribing therapy, following up for test of cure and test of reinfection, and initiating contact tracing with the patient. GPs can also educate patients about unsafe sex and encourage regular screening for those at ongoing risk.

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