Responding to Australia's chlamydia epidemic

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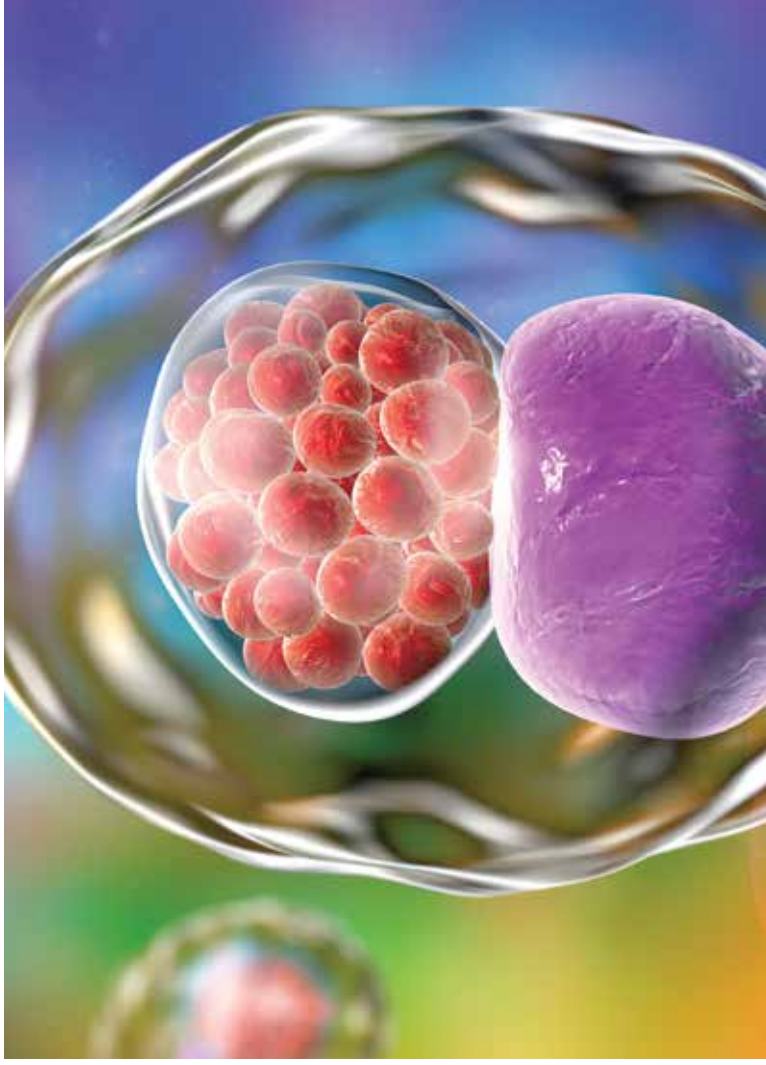
The incidence of *Chlamydia trachomatis* infection has risen steadily over the past decade and remains unacceptably high. Increased opportunistic screening of those most likely to be infected is essential, along with prompt management of the infection and contact tracing.



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Chlamydia trachomatis causes a highly transmissible and mostly asymptomatic sexually transmitted infection (STI), which can lead to significant morbidity if left untreated, particularly in women. It is the most common bacterial STI in Australia, with 86,108 notifications in 2014.[1] Three-quarters of infections occur in young people aged between 15 and 29 years Alarmingly, the notification rate in the Indigenous population is three times that in the general population at 1266 per 100,000 people.[1]

Rectal chlamydial infection is an important risk factor for HIV acquisition in men who have sex with men (MSM). The incidence of chlamydial infection has remained high in this population over the past five years. In 2015, 27% of HIV-positive gay and bisexual men presenting to sexual health clinics in Australia had a new anorectal chlamydial infection.[2]

Addressing the problem

Screening

Public health control of chlamydia is challenging due to the asymptomatic nature of most infections. It is estimated that only 28% of young adults in Australia with new chlamydial infections in 2015 were diagnosed, and of those treated only 26% had a follow-up test.[2] Opportunistic screening of people most likely to be affected is an essential strategy for identifying cases, preventing onward transmission of the infection and reducing the likelihood of sequelae. GPs play an important role in this, as 85% of women and 60% of men between 16 and 29 years of age will visit a GP at least once a year.[3]

Box 1 highlights the populations that should be opportunistically screened for chlamydial infection.[4] If the risk factors are ongoing, consider screening annually. In high-risk MSM, consider testing every three to six months. This group comprises men participating in group sex or any unprotected anal sex; men who use recreational drugs during sex; those who have had more than 10 sexual partners in the past six months; and men who are HIV-positive.

MedicineToday 2017; 18(9): 54-57

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Contact tracing and testing

Chlamydial infection is highly transmissible with a likelihood of transmission per act of heterosexual sex of between 6 and 17%.[5] About two-thirds of those with a long-term partner who is infected with chlamydia also have the infection.[6] This highlights the importance of both chlamydia contact tracing and testing patients for reinfection three months after treatment. Data on how infectious people remain over time are limited but available data suggest that women can remain infected for over a year, whereas men usually clear the infection within six months.[6] Transmissibility via oral sex is uncommon although possible, particularly in MSM.

Clinical presentation

In women

C. trachomatis can cause both cervicitis, which may be characterised by a mucopurulent cervicovaginal discharge, and urethritis. Up to 5% of women with untreated chlamydial infection may develop pelvic inflammatory disease (PID), which places them at risk of future fertility complications such as tubal factor infertility and ectopic pregnancy.[7]

Anal sex between heterosexual couples is becoming more common and anorectal chlamydia has been reported in women, including those who report no practice of anal sex. Although self-reporting may not give a true estimation of this practice in heterosexual relationships, the possibility of auto-inoculation from existing urogenital tract infections has been postulated as a mechanism for acquisition. However, it is currently not recommended to routinely screen women for anal infection unless they work in the sex industry.

In men

Symptomatic men with chlamydial infection typically develop dysuria with or without urethral discharge. The urethral discharge may be clear or mucopurulent. If there is a delay in treatment, men can develop epididymo-orchitis which is usually unilateral. *C. trachomatis* can also cause anorectal and, less commonly, pharyngeal infections in MSM. As with genital infections, most anorectal infections are asymptomatic. Symptomatic MSM may present with an acute proctitis characterised by anorectal pain and a bloody or mucoid anal discharge.

1. WHO TO SCREEN FOR CHLAMYDIAL INFECTION[4]

- Sexually active young heterosexual people (<30 years)
- Men who have sex with men (any age)
- People with 3 or more sexual partners in the past 12 months
- People who had a sexually transmitted infection (STI) diagnosed in the past 12 months
- People whose sexual partner has been diagnosed with any STI, including chlamydial infection
- Patients with an increased risk of STI complications (e.g. those undergoing termination of pregnancy or IUD insertion)
- Patients with symptoms or signs of chlamydial infection
- Anyone requesting a sexual health check
- Parents of a baby with neonatal ophthalmia

TABLE 1. SUMMARY OF PREFERRED SPECIMEN TYPES FOR SCREENING FOR CHLAMYDIAL INFECTION USING NUCLEIC ACID AMPLIFICATION TESTS[8]

Specimen	Comments
Women	
Endocervical swab	Preferred to vulvovaginal swabs if a clinician is performing a speculum examination
Vulvovaginal swab	Specimen of choice when a genital examination is not otherwise warranted; self-collected specimens preferred
First-void urine sample	Not recommended as this may miss up to 10% of infections diagnosed by endocervical or self-collected vulvovaginal swabs
Anorectal swab	If patient reports anal sex or anorectal symptoms; either self-collected or clinician-collected specimens are acceptable
Men	
First-void urine sample	Self-collection of specimens is possible
Anorectal swab	MSM only; self-collected specimens preferred
Oropharyngeal swab	MSM only; should be collected by a clinician

Abbreviation: MSM = men who have sex with men.

TABLE 2. TREATMENT REGIMENS FOR CHLAMYDIAL INFECTIONS[4]

Infection	Treatment
Uncomplicated urogenital and oropharyngeal infections	• Single 1 g dose of oral azithromycin or oral doxycycline 100 mg twice a day for seven days
Rectal chlamydial infection	• Oral doxycycline 100 mg twice a day for seven days • If doxycycline contraindicated or adherence issues: single 1 g dose of oral azithromycin followed by a second 1 g dose one week later • If laboratory confirms anorectal LGV infection: extend doxycycline course from one to three weeks
Epididymo-orchitis	• Oral doxycycline 100 mg twice a day for 14 days • If doxycycline allergy or adherence issues: single 1 g dose of oral azithromycin followed by a second 1 g dose one week later • If gonorrhoea not excluded at time of treatment: add single 500 mg dose of intramuscular ceftriaxone to azithromycin regimen; add single dose of intramuscular ceftriaxone 500 mg plus single 1 g dose of oral azithromycin to doxycycline regimen
Pelvic inflammatory disease	• Intramuscular ceftriaxone 500 mg plus single 1 g dose of oral azithromycin plus oral metronidazole 400 mg twice a day for 14 days plus oral doxycycline 100 mg twice a day for 14 days • If doxycycline contraindicated (e.g. pregnancy, doxycycline allergy) or adherence issues: replace doxycycline with an additional dose of azithromycin one week after the first azithromycin dose

Other chlamydia-associated conditions

In adults associated syndromes include perihepatitis (Fitz-Hugh–Curtis syndrome), prostatitis, reactive arthritis and conjunctivitis. Chlamydial conjunctivitis and pneumonitis may occur in neonates exposed via vertical transmission.

Laboratory diagnosis

Modern diagnosis relies on molecular-based laboratory detection of *C. trachomatis* using highly sensitive nucleic acid amplification tests. The exquisite sensitivity of these tests has made it possible for patients to take their own vulvovaginal (women), first-void urine (men) or anal swabs (Table 1).[8] Several studies have demonstrated that the quality of patient-collected specimens for *C. trachomatis* detection are as good as, or in some studies better than, clinician-collected swabs. Self-collection of specimens also prevents embarrassment for many patients and has improved patient acceptability of STI screening. However, there are still situations where it is preferable for the clinician to collect the specimen (Table 1).

Managing complications

Pelvic inflammatory disease

Diagnosis

All women diagnosed with chlamydial infection or presenting with an abnormal discharge should be questioned about the presence of symptoms of PID, which may include fever, low abdominal or pelvic pain, deep dyspareunia, abnormal vaginal bleeding and worsening dysmenorrhoea. Those women with suggestive symptoms should undergo a pelvic examination. PID is a clinical diagnosis and a low index of suspicion is necessary because symptoms can vary from mild to severe.

A diagnosis is made if there is new-onset pelvic pain coupled with cervical motion tenderness and adnexal or uterine tenderness. The absence of cervical motion tenderness on examination has a strong negative-predictive value for PID. On the other hand, the presence of tenderness has a relatively low positive-predictive value as this clinical finding is compatible with several differential diagnoses. Ectopic pregnancy must be excluded in all cases of acute pelvic pain with a urinary pregnancy test. Urgent referral is required if the test is positive. A urine dipstick is also helpful to exclude urinary tract infection.

Treatment

Given the potential for serious complications, it is better to over treat than under-treat PID. Most cases of PID will respond quickly to antibiotics (Table 2); therefore, careful follow up will identify those who may require further investigation with pelvic ultrasound to identify alternative diagnoses. Women whose symptoms do not resolve should be referred to a gynaecologist. Women should be referred urgently to the emergency department if they are septic, if they have a pelvic mass or if ectopic pregnancy or appendicitis cannot be confidently excluded (a surgical emergency). Intrauterine devices can be left in situ initially but should be removed after 48 to 72 hours in those who are not responding to antibiotic treatment. Appropriate specialist advice should be sought.

Acute chlamydia proctitis

In all cases of acute chlamydia proctitis, a request for further testing for lymphogranuloma venereum (LGV) should be indicated on the laboratory request form. Check your laboratory's requirements as to whether an additional anal swab is required. LGV is caused by the *C. trachomatis* serovars L1, L2 or L3 rather than the usual D through to K chlamydial serovars responsible for oculogenital infections. LGV requires a longer course of doxycycline than non-LGV anorectal chlamydial infections. LGV is uncommon but outbreaks have been reported in MSM, particularly HIV-infected MSM, and NSW Health has recently reported an increase in cases of LGV.[9] Specialist advice concerning the management of LGV is available from sexual health clinics.

Urogenital and oropharyngeal infections

Table 2 summarises the treatment regimens for chlamydial infections. For uncomplicated infections the azithromycin and doxycycline treatment regimens outlined in the table have been shown to be equally effective. However, there is evidence that suggests the one-week course of doxycycline has marginally higher efficacy than single-dose azithromycin in treating men with urethritis.[10] Single-dose azithromycin offers ease of dosing, better tolerability and less issues with adherence. Doxycycline is contraindicated in women who are pregnant or breastfeeding; therefore, in these women azithromycin must be used.

First-line treatment for rectal chlamydial infections is oral doxycycline 100 mg twice daily for seven days (Table 2). A recent meta-analysis of treatment for rectal chlamydial infections showed that a single 1 g dose of azithromycin was considerably less effective than a one-week course of doxycycline.[11]

All patients should be told not to resume sexual activity until they and their partners have completed their treatment regimen. If patients were treated with a single dose of azithromycin, they should not resume sexual activity for a week afterwards. Recall all patients at three months for a reinfection test. In cases of rectal infection or pregnancy, perform an additional test-of-cure four weeks after treatment.

Partner management

Contact tracing is a high priority for patients with chlamydial infections given the ease of transmission, potential for serious complications and very high notification rates. Patients should be advised that all sexual partners in the past six months should be notified, tested and offered presumptive treatment. There are patient websites that give practical information on how to notify partners as well as providing an anonymous SMS service for those who feel unable to notify their partners directly (Box 2).

Patient-delivered partner therapy

Although best practice is to encourage patients to convince their partners to present to a doctor, this is not always successful. Patient-delivered partner therapy (PDPT) with azithromycin can be considered if partners are unlikely to attend for testing and treatment. In this circumstance the index patient takes an azithromycin prescription for their sexual partner without that partner having to attend for a medical consultation. Azithromycin delivered as a single dose has a high safety profile and is associated with very few adverse events. Allergic reactions are rare and it is rated a category B1 drug in pregnancy and breastfeeding.

The practice of PDPT is supported by the Australian Chapter of Sexual Health Medicine, a Chapter of the Royal Australian College of Physicians; the Australian Society of HIV, Hepatitis and Sexual Health Medicine; and the Australian Society of Infectious Diseases. It is also supported by legislation in Victoria, the Northern Territory and New South Wales. However, the one disadvantage of the PDPT approach is that sexual partners are infrequently screened for STIs, which has implications for their own sexual health and that of their other sexual contacts.

PDPT should always be provided with clear written instructions for the partner. This should include:

- consumer medicine information about azithromycin
- information about chlamydia
- advice about seeking medical care, particularly if the partner has symptoms suggestive of chlamydial infection
- emphasis on the importance of attending for STI screening.

PDPT has particular value in treating male partners of young women diagnosed with chlamydia where the risk of reinfection carries concern for their future fertility. PDPT should be prescribed cautiously for partners in whom other STIs are likely to be present, such as MSM, and for pregnant partners, as these people require clinical assessment. Clinical guidelines and clinician factsheets on contact tracing can be downloaded from the Australian Society of HIV, Hepatitis and Sexual Health Medicine website (Box 2).

2. USEFUL CONTACT TRACING WEBSITES

For patients

- Let Them Know
  www.letthemknow.org.au
- The Drama Down Under (for men who have sex with men)
  www.thedramadownunder.info

For clinicians

- Australasian contact tracing guidelines
  www.contacttracing.ashm.org.au

Conclusion

Reduction of the unacceptably high rates of chlamydial infection in Australia remains a public health priority. Due to the asymptomatic nature of chlamydial infections, it is important to use every opportunity to screen individuals in high-risk groups, including young people, MSM and Indigenous people. Screening with highly sensitive nucleic acid amplification tests has enabled patients to collect their own specimens.

Treatment consists of either single-dose azithromycin or one week of doxycycline; however, doxycycline is preferred to treat rectal infections and non-gonococcal urethritis in men. Tests for cure and reinfection should be undertaken as indicated in local guidelines. Consideration of PDPT in selected cases is supported legally in some states and may go some way to reduce the ongoing spread of this infection. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: None.

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