

Emerging issues in the management of **chlamydia** and **gonorrhoea**

New evidence suggests that a seven-day course of doxycycline may be more appropriate than a stat dose of azithromycin as a first-line treatment for chlamydia infection. Despite a seven-day course being less convenient for patients, increased use of doxycycline may help reduce the high rates of transmission and Re-infection with chlamydia in New Zealand. Pharyngeal swabs to test for chlamydia and gonorrhoea should be considered due to increasing rates of pharyngeal gonorrhoea infection, particularly in men who have sex with men.

Chlamydia is the most commonly reported STI in New Zealand

The highest rates of *Chlamydia trachomatis* infection are reported in young people; 82% of cases reported to the Institute of Environmental Science and Research (ESR) between 2013 and 2017 were in people aged 15-29 years.¹ Data suggest that by age 38 years, one in three females and one in five males in New Zealand acquire a chlamydia infection at least once.²

Re-infection is common

Re-infection rates for chlamydia are high.³ For example, data from laboratory testing services covering the Wellington region, collected from 2012 to 2015, found that 18% of people who tested positive for chlamydia or gonorrhoea infection retested positive within the next six weeks to six months.³

Untreated rectal chlamydia in females is likely to be an important source of Re-infection

Men who have sex with men (MSM) have typically been the focus of attention for investigating for rectal chlamydia infection. However, data from studies conducted over the last ten years shows that rectal chlamydia in females is likely to be an overlooked source of Re-infection.

Many women with genital chlamydia also have rectal infection: A meta-analysis of 14 studies, conducted in the UK, USA, Canada, Australia and Europe, found that on average 68% of females with genital chlamydia infection were also positive for rectal infection.⁴ In contrast, rectal infection in the absence of genital infection is uncommon; approximately 2% of females across these studies tested positive for rectal but not genital infection.⁴

Most people with rectal chlamydia infection are asymptomatic: At least 90% of females and 70% of MSM with rectal chlamydia infection are asymptomatic.^{5,6}

In females, rectal infection does not depend on sexual practices: Studies have found no association between rectal chlamydia infection in females and whether they have engaged in anal intercourse.⁷ This suggests that rectal infection arises in many females due to spread of genital infection to rectal tissue, rather than transmission from sexual practices.

Doxycycline is more effective for treating rectal chlamydia

A single stat dose of azithromycin is currently the recommended first-line antibiotic regimen for treating genital chlamydia infection, and it is effective in 94% of patients.⁸⁻¹⁰ An alternative treatment is a seven day course of doxycycline, which is effective in 97% of patients with genital chlamydia infection.⁸⁻¹⁰

Since both regimens offer similar effectiveness and azithromycin is a one-off dose that is often given in the clinic at the time of the appointment, it has typically been used first-line as a treatment for patients with genital chlamydia infection and for treating sexual contacts.⁹

However, azithromycin is less effective at treating rectal chlamydia infection than doxycycline.^{11, 12} A meta-analysis reported that the average efficacy of a stat dose of azithromycin for treating rectal chlamydia was 83%, compared to >99% for a seven day course of doxycycline.¹¹

Azithromycin use can lead to resistance in other STIs

Mycoplasma genitalium is an emerging cause of STIs such as persistent urethritis in males, and cervicitis and pelvic inflammatory disease in females.¹³ Data suggest that the use of single dose azithromycin regimens can lead to the emergence of resistance in *M. genitalium*.¹³ Therefore, since this organism shares similar sites of infection as chlamydia, reducing the use of azithromycin as a first-line treatment for chlamydia infection may help prevent resistance in *M. genitalium*.

 For further information on *Mycoplasma genitalium*, see: "*Mycoplasma genitalium*: considerations for testing and treatment in primary care" www.bpac.org.nz/2019/mycoplasma-genitalium.aspx

What does this evidence mean for routine treatment of chlamydia infection in females?

The emerging evidence that asymptomatic rectal chlamydia infection is common in females, and is less responsive than genital infection to a stat dose of azithromycin, suggests that this may be an important cause of recurrent or persistent chlamydia infection.

Consider prescribing doxycycline, 100 mg twice daily for seven days, first-line: This regimen is estimated to be effective for approximately 97% of females with either genital or rectal chlamydia.⁸ Although azithromycin is less effective, it still results in clearance for the majority of patients and may be an appropriate option if there is concern that a seven day course of doxycycline will not be completed.

New evidence creates a dilemma for testing in females: Currently, anorectal swabs are recommended for females who report engaging in anal intercourse.^{9, 10} In addition, current guidelines recommend retesting for cure for patients with rectal chlamydia.

However, data suggest that reported sexual practices are not a useful guide for deciding whether rectal swabbing is necessary. Collecting rectal swabs for all female patients would increase the invasiveness of testing and result in a large number of additional tests. In addition, if all females who tested positive for rectal infection were asked to return for a test of cure this would create an additional burden on patients due to the time and cost of reattending.

A pragmatic approach would be to:

- Collect genital swabs*
- Assume that females who test positive for genital chlamydia may also have rectal infection
- Prescribe doxycycline, 100 mg twice daily for seven days

Testing for cure, using both genital and anorectal swabs, could then be reserved for patients at high risk of Re-infection or consequences from Re-infection, such as if sexual contacts have not been treated, if insertion of an intrauterine device is planned, or there are concerns regarding adherence to a seven-day regimen.

* Either a self-collected vulvovaginal swab for females who are asymptomatic or who do not wish to be examined, or a clinician-collected endocervical swab for those who are symptomatic.^{9, 10}

To reduce Re-infection, trace and treat sexual contacts:

Sexual contacts from the previous three months should be contacted, treated empirically, preferably with a seven day course of doxycycline, and offered testing for STIs.⁹

What does this evidence mean for routine treatment of chlamydia infection in males?

Testing recommendations for men who have sex with men are unchanged: routine testing for rectal and pharyngeal chlamydia and gonorrhoea infection as part of a sexual health check remains appropriate in this high-risk population.^{9, 10, 14} Rectal chlamydia infection is more common than urethral infection in MSM, is often asymptomatic, and can increase the risk of HIV transmission.^{14, 15} In addition to rectal swabs,

collecting swabs to routinely test for pharyngeal chlamydia or gonorrhoea infection is recommended in MSM (see below). For patients with positive rectal or pharyngeal test results, testing for cure is recommended.⁹ Doxycycline is also the recommended treatment for rectal chlamydia in males.

For heterosexual males with urethral chlamydia, prescribing a seven-day course of doxycycline is also likely to be preferable, as azithromycin use can contribute to the development of resistance in *M. genitalium*, a cause of urethritis. Unlike for heterosexual females, there are currently no data to suggest that heterosexual males with genital chlamydia have high rates of rectal infection.

Rates of gonorrhoea are increasing, including rates of pharyngeal infection

The current national rate of gonorrhoea infection is approximately 100 cases per 100,000 population, with higher rates in males than females. Incidence has increased in recent years, with a greater proportion of positive gonorrhoea tests from pharyngeal swabs in males.¹⁶ A key reason for increasing rates of gonorrhoea, particularly in large urban areas, is likely to be higher transmission among MSM.¹⁶

Pharyngeal infection is typically asymptomatic, and is thought to play an important role in the development of antibiotic resistance in *N. gonorrhoea*.^{10, 17} This is because antibiotic treatment leads to the development of resistance in oral bacteria, which are then able to pass resistance genes to *N. gonorrhoea* in the pharynx.¹⁷

In males, genital gonorrhoea infection is usually symptomatic. Testing for asymptomatic infection is not necessary in heterosexual males, however, it should be offered at least once a year as part of a routine sexual health check in MSM, due to high rates of gonorrhoea in this population.^{9, 14} Collected samples should include rectal and pharyngeal NAAT swabs and a first void urine sample to test for chlamydia and gonorrhoea infection.^{9, 14} Collecting pharyngeal swabs in heterosexual males may be appropriate if there is a high degree of suspicion,

e.g. if a sexual contact has had a chlamydia or gonorrhoea infection.

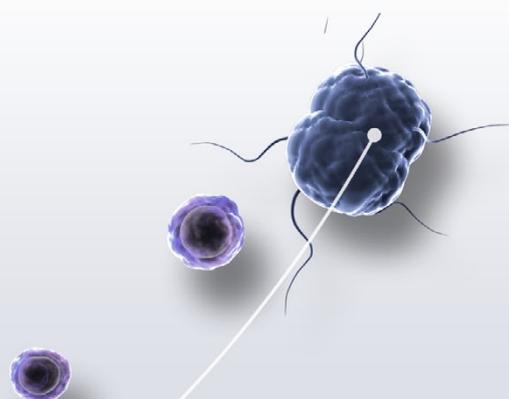
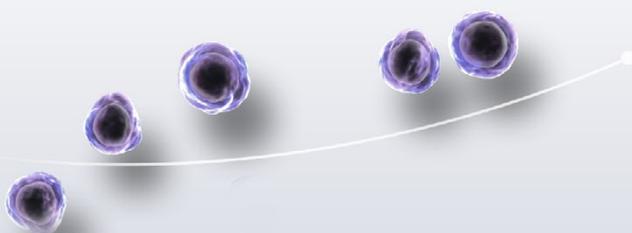
In females, testing for genital gonorrhoea infection is recommended during a sexual health check, as up to 80% of females with genital gonorrhoea infection are asymptomatic.¹⁰ Collecting pharyngeal swabs may be appropriate if there is a high degree of suspicion, e.g. if a sexual contact has had a chlamydia or gonorrhoea infection.

The recommended first-line treatment for gonorrhoea infection is the same for genital, rectal or pharyngeal infections: ceftriaxone, 500 mg intramuscular injection, and azithromycin, 1 g stat.⁹

The recommended first-line treatment for pharyngeal chlamydia infection is the same as for rectal chlamydia: doxycycline, 100 mg twice daily, for seven days.⁹

Summary checklist:

- Asymptomatic rectal infections with chlamydia are common in females, most often not related to anal intercourse, and may serve as a reservoir for genital re-infection
- Doxycycline is more effective than azithromycin for treating genital or rectal chlamydia and should be considered as a first-line treatment option for females and males with chlamydia
- There are increasing rates of pharyngeal gonorrhoea infection in males
- Collecting pharyngeal swabs to test for chlamydia and gonorrhoea is recommended as a routine part of a sexual health check for men who have sex with men
- For heterosexual patients, collect pharyngeal swabs if they are a sexual contact of someone with chlamydia or gonorrhoea



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