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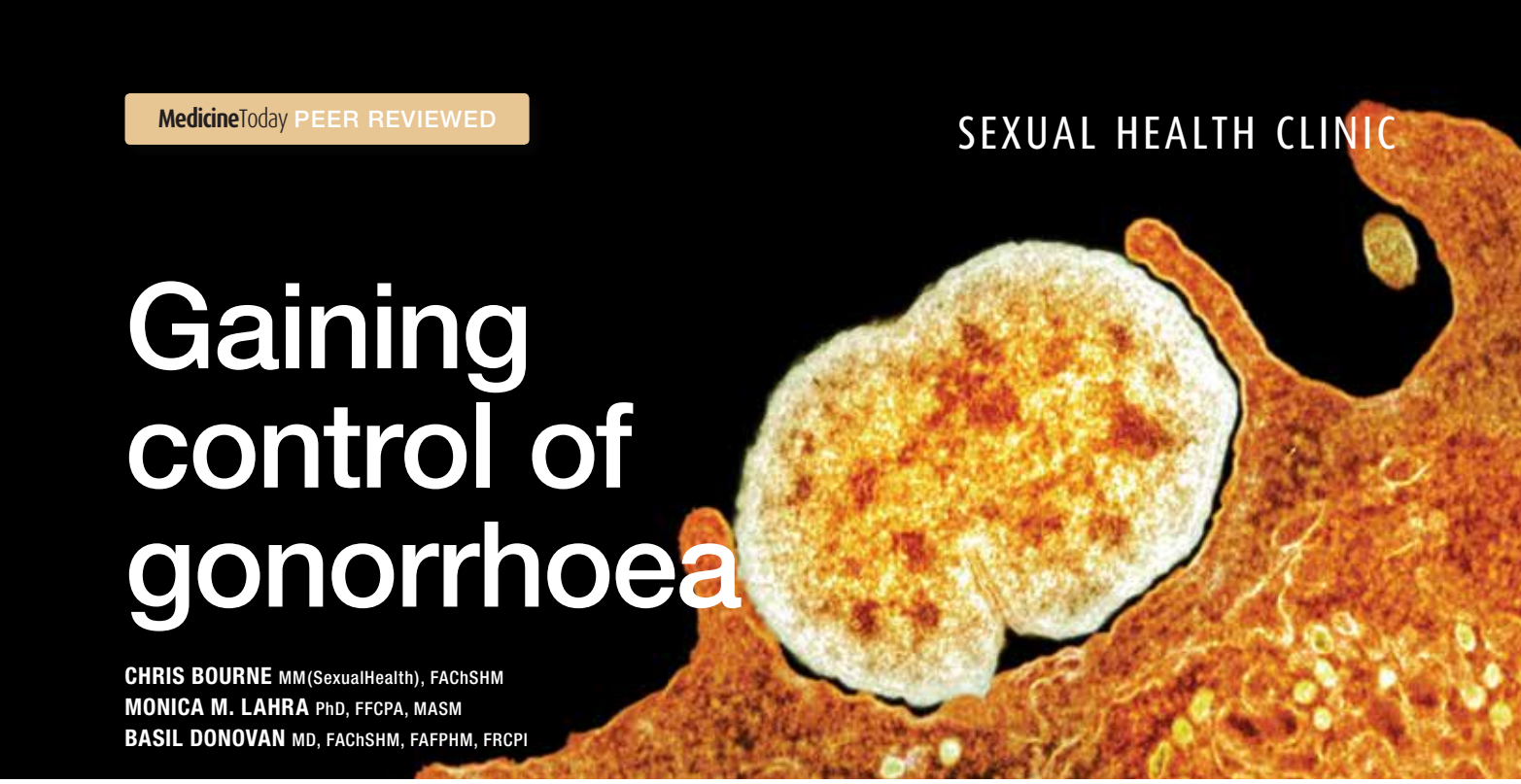
Gaining control of gonorrhoea



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With the increasing resistance worldwide of *Neisseria gonorrhoeae* to antibiotics, new treatment options for gonorrhoea are urgently needed.

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Gonorrhoea is still with us and the number of cases is increasing as the era of extensive drug resistance approaches.[1] This sexually transmissible infection (STI) is caused by the bacterium *Neisseria gonorrhoeae,* and in Australia mainly affects gay men in urban areas and Aboriginal and Torres Strait Islander people in remote locations.[2]

Gonorrhoea is important because of its possible complications, such as upper genital tract disease in women resulting in tubal infertility and increased risk of ectopic pregnancy, epididymitis in men, disseminated infection and, mainly in neonates, eye disease. People with gonorrhoea are often concurrently infected with chlamydia, which is associated with similar complications. Gonorrhoea also promotes the sexual transmission of HIV infection, and the two epidemics frequently coincide.

The propensity of *N. gonorrhoeae* to become resistant to antibiotics stems from its ability to share mutations with other organisms, including other *Neisseria* species (particularly in the throat), indiscriminate antibiotic use in many settings and undetected infections leading to a greater reservoir. This propensity has been demonstrated over time with the development of resistance to multiple classes of antibiotics, eliminating the effective use of oral single agent treatments in most settings and necessitating the introduction of parenteral ceftriaxone as first-line management. However, the steady increase in mean minimum inhibitory concentration values for ceftriaxone over the past decade and early signs of treatment failure in Australia and elsewhere have prompted a co-ordinated global response, including revision of gonorrhoea treatment guidelines.[1,3] New treatment options are urgently needed and are being explored. In the meantime, we need to enhance our efforts to bring gonorrhoea under control.

TRANSMISSION

Gonorrhoea is vastly more infectious than HIV infection, and practices designed to avoid transmission of HIV (such as oral sex) do not prevent the transmission of *N. gonorrhoeae*. Although receptive anal intercourse among men who have sex with men (MSM) remains high risk for transmission of the causative organism of gonorrhoea, other receptive anal practices (such as fingering) also provide a means of transmission.[4] Updated advice recommends all MSM should have anal swabs even if they do not report unprotected anal intercourse (Table).[5] The rising notifications in men point to a poor control of gonorrhoea among MSM (Figure). Although not as dramatic as in men, the rising notifications in women are also of concern; these diagnoses are occurring in both remote and urban settings. Gonorrhoea is 30 times more common in Indigenous than nonIndigenous Australians.

Gonorrhoea has been well controlled among sex workers in Australia for many years, prompting the Victorian Government to relax its mandatory monthly screening requirement (Table). However, as unprotected fellatio is becoming increasingly common in the sex industry,[6] throat swabs should now be routine.

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TABLE. GONORRHOEA SCREENING AND MANAGEMENT: RECENT CHANGES

Category	Previously	Now
Population testing		
Men who have sex with men (MSM)	Throat and anal (if unprotected sex reported) swabs, and urine (if urethral symptoms present)	Throat and anal swabs, and urine at least annually regardless of whether condoms used. Test every three to six months if patient reports multiple partners[5]
Female sex workers	Vaginal swabs every three to six months (monthly in Victoria). Throat swab if unprotected oral sex reported	Throat and vaginal swabs every three to six months (three-monthly in Victoria). Anal swab as indicated
Indigenous people	Test all 15- to 29-year-olds living in remote areas at least annually, plus older individuals at high risk	Test all 15- to 29-year-olds living in remote areas at least annually, plus older individuals at high risk. Increase opportunistic testing (linked to chlamydia testing) in other areas
Heterosexual people	Test if known contact with gonorrhoea, urogenital symptoms, sexual contact overseas	Test if known contact with gonorrhoea, urogenital symptoms, sexual contact overseas. Now linked to chlamydia testing
Specimen		
Collection	Mainly collected by doctor	Mainly collected by patient if asymptomatic (with guidance)
Testing technology	Separate specimens taken for testing for gonorrhoea by culture and chlamydia by NAAT	Single specimen taken for combined gonorrhoea–chlamydia NAAT test. Collect specimen for culture testing (for antibiotic sensitivities) before treating patients with a positive NAAT
Management		
Treatment	Ceftriaxone 250 mg intramuscularly – single dose (dissolved in 1% lignocaine)*	Ceftriaxone 500 mg intramuscularly (in 1% lignocaine) plus azithromycin 1 g orally – single doses*
Partner management	Instruct patient to inform all sexual partners	Instruct patient to inform all sexual partners (a contact tracing tool is available on the NSW STI Programs Unit website – (www.stipu.nsw.gov.au/page/General_Practice_Resources/STI_Clinical_Management_2). Advise patient of supportive websites: – www.letthemknow.org.au (heterosexual people) – www.thedramadownunder.info/notify (MSM) – www.bettertoknow.org.au (Indigenous people)
Follow up	Test-of-cure by culture one week after treatment	Test-of-cure by NAAT at two weeks after treatment. Confirm that partners have been properly assessed. Offer three-monthly SMS reminders for retesting high-risk MSM

ABBREVIATIONS: MSM = men who have sex with men; NAAT = nucleic acid amplification test; STI = sexually transmitted infection.
*Higher doses or longer courses for ophthalmic, disseminated or pelvic infections.

TESTING

Nucleic acid amplification tests (NAATs) are now the test of choice for gonorrhoea at all anatomical sites. NAATs have the advantages of being more sensitive and more transportable than culture testing, and can be used with patient self-collected specimens (Table). Self-collection of samples saves time and embarrassment and the samples give as accurate results on NAAT testing as clinician-collected samples.[7] Combined chlamydia–gonorrhoea NAATs reduce the number of specimens required and this testing is now used routinely by most Australian laboratories. Previous concerns about false-positive NAAT results for gonorrhoea have been largely addressed by technological advances and improved laboratory protocols.

Although physical examination and culture is recommended for symptomatic patients, offering self-collected sampling for NAAT when there are no symptoms can improve gonorrhoea detection. In MSM, up to two-thirds of gonorrhoea infections can be missed if only the urine is sampled. Any patient considered at risk

of gonorrhoea should also be routinely tested for chlamydia, syphilis, HIV infection and hepatitis B (unless vaccinated).

Unfortunately, just at a time when antibiotic resistance is becoming an increasing problem, these improvements in test technology have seen a shift away from culture testing – the only method that currently allows for assessment of antibiotic sensitivities. It is recommended that culture samples are taken before treatment is commenced in a person with a positive result on NAAT or in those who clinically appear to have gonorrhoea.

Gonococcal DNA clears relatively quickly from urogenital sites and a test of cure by NAAT is now recommended two weeks after treatment, with confirmation by culture if the follow-up NAAT is positive. Follow-up throat swabs are particularly important as throat gonococcal infections are the most difficult to clear and the throat is a site where bacterial species mix and potentially share genes coding for antimicrobial resistance.

TREATMENT

In Australia the treatment recommendation for uncomplicated gonorrhoea at all anatomical sites is ceftriaxone 500 mg intramuscularly plus azithromycin 1 g orally, both as single doses, to raise the barrier to the emergence of further resistance to extended spectrum cephalosporins and also to treat potential chlamydia co-infection (Table).[8] The only exception is in some remote areas where penicillin (amoxycillin 3 g plus probenicid 1 g orally) is still effective. Oral cephalosporin, quinolone and tetracycline antibiotics are largely ineffective and should no longer be used.

PARTNER MANAGEMENT

Ensuring sexual partners of people diagnosed with gonorrhoea are properly and promptly managed is critical to the control of this STI. Contrary to perceived wisdom, patients are willing to contact their recent sexual partners to enable them to be tested and treated for STIs, and view contact tracing as the 'right thing to do'.[9] Most contacted partners are grateful about being informed. Patients need to be advised that infected partners will probably be asymptomatic and at risk of complications.

Targeted websites are now available that enable patients to contact partners with an educational phone text message (SMS) or email (Table). Public sexual health services can also assist with contact tracing if required. Contacts should be given treatment for gonorrhoea without waiting for test results.

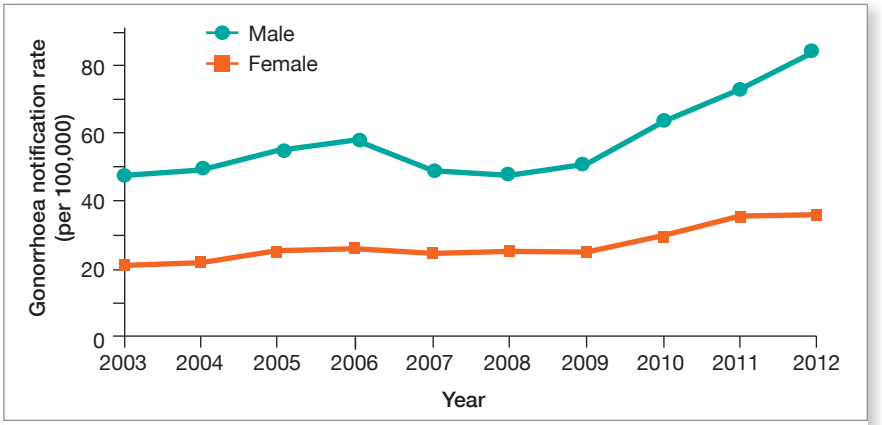

Figure. Gonorrhoea notifications, Australia, 2003 to 2012.
Source: National Notifiable Disease Surveillance System

CONCLUSION

Gonorrhoea remains a challenging condition, especially with the increasing resistance worldwide of the causative bacterium to antibiotics. The treatment recommendation in Australia for individuals with gonorrhoea is now ceftriaxone intramuscularly plus azithromycin orally, both as single doses, and prompt management of sexual partners. This treatment also treats potential chlamydia co-infection.

New treatment options are urgently needed and are being explored. It is of paramount importance that gonorrhoea is brought back under control in Australia before extensively drug-resistant infections become the norm, potentially further increasing the rates of HIV infections. MT

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COMPETING INTERESTS: Associate Professor Lahra and Professor Donovan are chief investigators on an NHMRC-funded project investigating gonococcal drug resistance. Dr Bourne: None.