Urethral discharge in men
not a trivial symptom

Each month we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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A male patient with urethral discharge, the most obvious symptom of urethritis, may be the only indication that serious sexually transmitted infections (STIs) are circulating in a community. Notifications of *Chlamydia trachomatis* infection, the most common cause of non-gonococcal urethritis, have been increasing over the past few years and the infection is now the most frequently reported bacterial infection of any type in Australia (Figure 1).[1] Chlamydial infection is widespread in all communities, particularly in people under the age of 25 years.

The notifications of gonorrhoea (gonococcal urethritis) have also increased over the five-year period 1996 to 2000 (Figure 1). Unlike *C. trachomatis*, however, infection with *Neisseria gonorrhoeae* is concentrated among homosexually active men, remote indigenous communities and overseas travellers.

The challenge for Australia is to restore the relatively good control of these major sexually

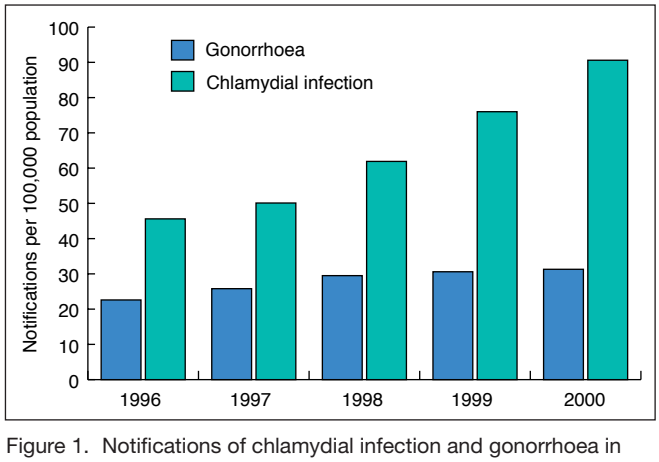
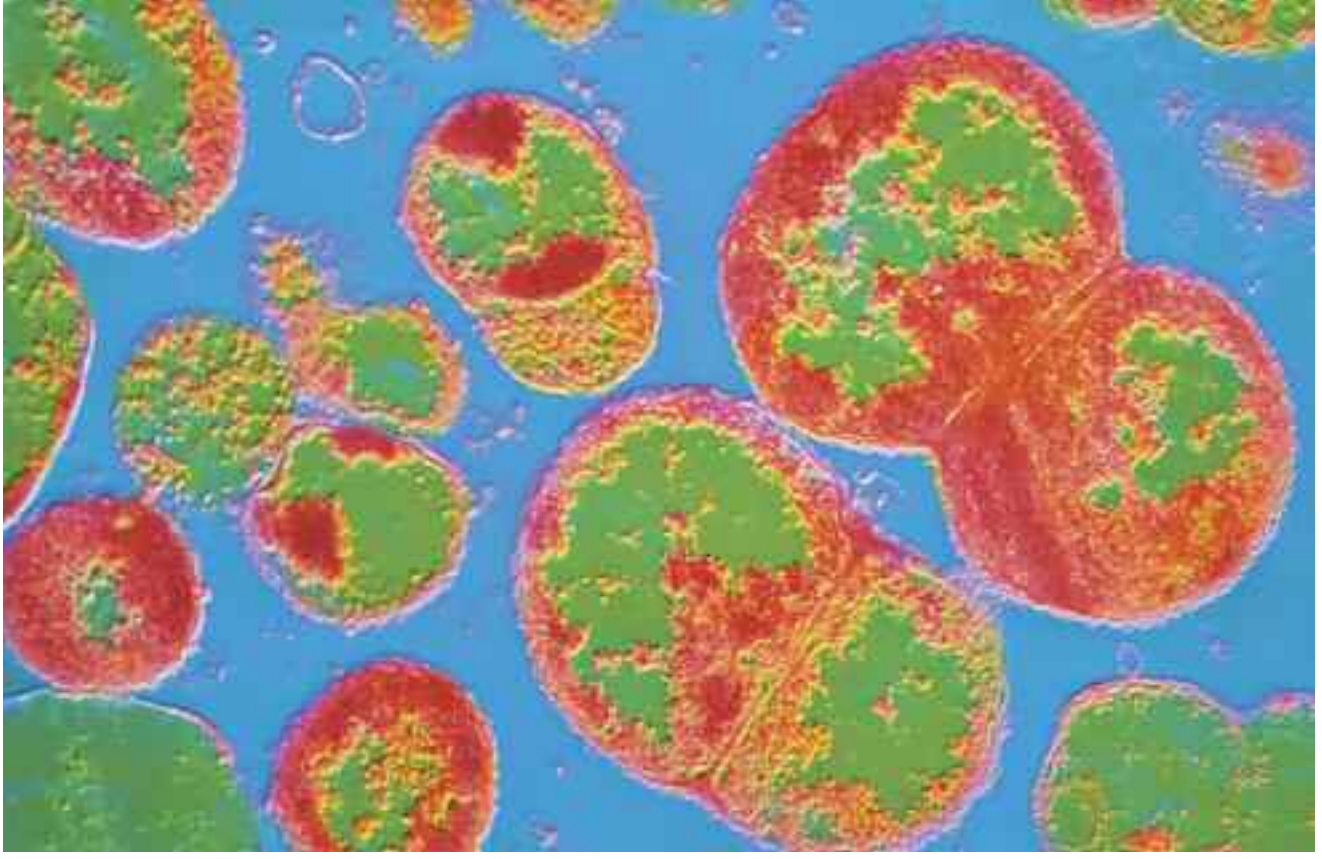


Figure 1. Notifications of chlamydial infection and gonorrhoea in Australia, 1996-2000.[1]

IN SUMMARY

- **Increasing notifications of chlamydial infection and gonorrhoea indicate that Australia is losing control of these sexually transmitted infections (STIs), with serious implications for sexual partners and enhanced HIV transmission.**
- **Opportunistic testing in general practice of asymptomatic young men who are at high risk of STIs, as well as women, is one way to help restore control of these infections.**
- **DNA testing of first void urine for *Chlamydia trachomatis* has revolutionised the assessment of these men. DNA testing for *Neisseria gonorrhoeae* is available but needs further evaluation.**
- **Single oral dose treatment with azithromycin is appropriate for most men with nongonococcal urethritis, while the ever-evolving antibiotic resistance of *N. gonorrhoeae* makes single dose intramuscular ceftriaxone the treatment of choice for gonorrhoea.**
- **The diagnosis of urethritis, chlamydial infection or gonorrhoea in a man should act as a trigger to ensure that his sexual partner(s) are also assessed.**



Neisseria gonorrhoeae: CNRI, SCIENCE PHOTO LIBRARY

transmissible infections that existed at the beginning of the 1990s. In this article we outline how GPs can contribute to regaining control of these pathogens.

Why is urethritis serious?

In its own right urethritis is usually not a serious condition for most men. Indeed, it is sometimes treated as trivial by patients and doctors alike. Yet the consequences for the untreated sexual partners are frequently serious and costly, even if these consequences may not manifest for years (Table 1). Also, urethritis from any cause is important because of the potential promotion of the sexual transmission of HIV.[2,3]

The causes of urethritis vary considerably in their public health importance (Table 2). *C. trachomatis* and *N. gonorrhoeae*, for example, are actively sought because a high proportion of infected men and their sexual partners will develop disease, the most common and serious among women being pelvic inflammatory disease with all its sequelae. Preliminary indications are that *Mycoplasma genitalium* also fits into this category.[4] By contrast, *Ureaplasma urealyticum* is a ubiquitous organism in the normal vagina that may occasionally be responsible for disease in men. *Trichomonas vaginalis* can cause a low-grade

Table 1. Complications of urethritis

Diseases that may develop in untreated sexual partners of men with urethritis
Cervicitis
Urethritis
Pelvic inflammatory disease
Chronic pelvic pain
Tubal infertility
Ectopic pregnancy
Proctitis
Perihepatitis
Conjunctivitis

Note: *Neisseria gonorrhoeae* and, occasionally, *Chlamydia trachomatis* colonise the throat, but they do not appear to cause pharyngitis.
Neither infection causes prostatitis.

Table 2. Causes of acute urethritis in men*

Cause	Proportion of acute urethritis cases
Chlamydia trachomatis	20 to 30%
Neisseria gonorrhoeae	5 to 10%
Mycoplasma genitalium	10 to 20%
Ureaplasma urealyticum	10 to 20%
Trichomonas vaginalis	<1%
Respiratory flora, e.g. *Neisseria meningitidis* and *Haemophilus influenzae*	1 to 2%
'Sterile' – e.g. chronic catheterisation and Reiter's syndrome	1 to 2%
Unknown	Up to 40%

*The relative contribution of each organism varies between populations. These are estimates for a typical Australian city in 2002.

Table 3. Presentations of urethritis in men

- Asymptomatic
- Dysuria (minimal to severe)
- Urethral discharge (minimal and transient, through to heavy)
- Scrotal pain (epididymitis)
- Reactive arthritis
- Conjunctivitis

Figure 2. Mucoid discharge of nongonococcal urethritis.

Figure 3. First-void urine of a man with asymptomatic urethritis. The 'threads' are mucopurulent casts of the urethra which are passed with the urine.

urethritis in men but is rare in all but remote parts of Australia. Oral sex can occasionally lead to respiratory flora inducing urethritis in men but this is not well studied.

A man presenting with symptoms of urethritis or who is at risk of the condition should trigger a comprehensive response that ensures the correct assessment and management of that individual and also his immediate contacts. For the busy GP this man may be the best indication that serious STIs are circulating in the immediate community.

Figure 4. Frank purulent discharge of gonococcal urethritis.

Is urethritis present?

Urethral discharge is the most obvious of the symptoms of urethritis (Table 3). Yet, even in specialist services, as few as 85% of men with gonococcal urethritis and 50% of men with chlamydial urethritis report symptoms.[5] Out in the community – particularly in remote and rural areas – only a small proportion of men with these infections report any symptoms.[6] Some men may only present because they think they are at risk of an STI (typically HIV) or their sexual partner has complications that may be associated with urethritis: most young women with pelvic inflammatory disease have a partner with asymptomatic urethritis.

Investigation of suspected urethritis

Physical examination in a supine position of a man with suspected urethritis may reveal only a slight discharge after 'milking' of the urethra or purulent threads in the first-void urine (a specimen which brings with it the contents of the urethra) – if there are any signs at all (Figures 2 and 3). A purulent, yellow to green discharge indicates probable gonococcal urethritis (Figure 4).

An overview of the management of suspected urethritis is given in the flowchart on page 69, and specific details are given below.

Diagnosis of urethritis

Urethritis is formally defined by the presence of five or more polymorphonuclear leucocytes (PMNL) per high powered field [1000X] of a smear of expressed urethral discharge or, if there is no discharge visible, a smear of a swab taken 0.5 to 1 cm into the distal urethra. The smear is made onto a glass slide, air dried, Gram stained and viewed using light microscopy.

The PMNL count in the smear may be unrepresentative (i.e. reduced) if urine has been passed within an hour or so of testing.

Testing for specific causes of urethritis

Men with evidence of urethritis and men who are asymptomatic but at high risk of STIs should be tested for both *N. gonorrhoeae* and *C. trachomatis* (Table 4).

Gonococcal urethritis

Gram staining of a discharge smear from a patient with gonococcal urethritis will usually show Gram-negative diplococci within polymorphonuclear leucocytes. The diagnosis is confirmed by isolating *N. gonorrhoeae* by culture. *Neisseria meningitidis*, an uncommon cause of urethritis (Table 2), can produce an identical clinical and microscopic appearance – culture differentiates between the species.

A urine test that uses DNA amplification for detecting gonorrhoeal DNA has recently become available. However, it needs further evaluation, especially

Initial management of suspected urethritis in men

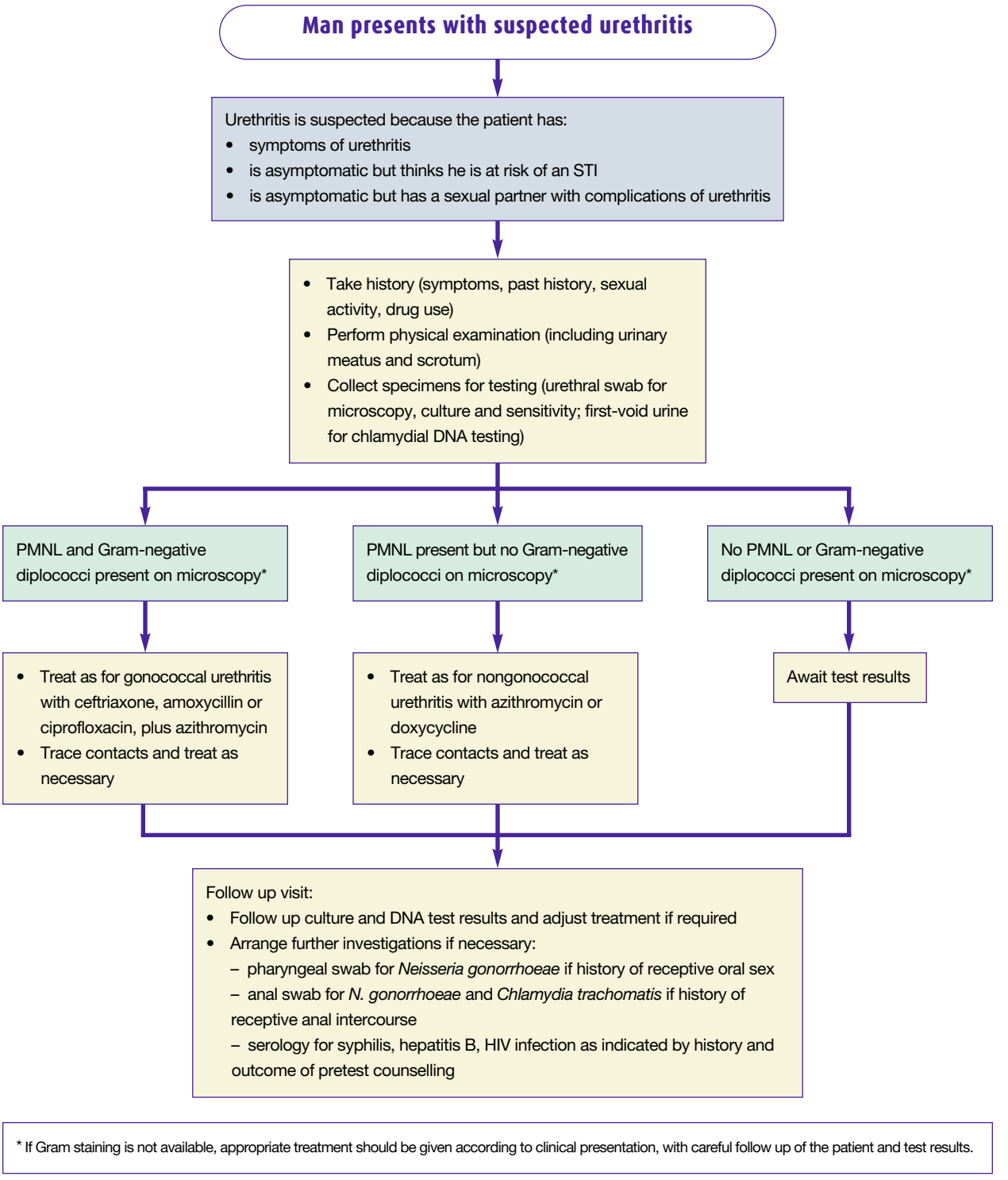


Table 4. Guidelines for chlamydial testing in men

Testing for *C. trachomatis* is recommended in the following situations:

- symptoms or signs of infection
- sexually active adolescent
- unprotected sex with a new partner
- partner with known or suspected STI
- any current STI

with regard to its specificity, and at the moment its use is mainly confined to high-risk populations.

Nongonococcal urethritis

Tests that use DNA amplification (polymerase chain reaction, ligase chain reaction, strand displacement amplification, and or transcription-mediated amplification) are much more sensitive and specific in detecting *C. trachomatis* than older tests that rely on culture, immunofluorescence or enzyme immunoassay. DNA tests are now widely available for *C. trachomatis* and have superceded older testing methods. DNA testing is more acceptable to the patient as it can be performed on the first-void urine.

M. genitalium and *U. urealyticum*, other common bacterial causes of nongonococcal urethritis, can only be reliably tested for by DNA amplification. However, such tests are not generally available for these bacteria.

Table 5. Antibiotic regimens for urethritis

Uncomplicated gonorrhoea

- Ceftriaxone 250 mg intramuscularly as a single dose – effective against all strains (so far)
- Ciprofloxacin 500 mg orally as a single dose – increasing resistance emerging; useful for cephalosporin allergy or isolate known to be sensitive
- Amoxycillin 3 g orally with probenecid 1 g orally as a single dose – effective if isolate is known or likely to be sensitive to penicillin
- Consider concurrent treatment for chlamydia infection

Non-gonococcal urethritis, including uncomplicated C. trachomatis infection

- Azithromycin 1 g orally as a single dose – highly effective, good compliance
- Doxycycline 100 mg orally 12-hourly for 10 days – if intolerant to macrolides

Urethritis: key points for rural and remote GPs

The key messages concerning urethritis for GPs in rural and remote settings are:

- All evidence suggests that both chlamydial infection and gonorrhoea are more common in many rural and remote settings than in Australian cities, in both indigenous and non-indigenous people.[10] Most of these infections are asymptomatic.
- Stoicism, shyness, limited access to health services and lack of awareness of the importance of urethral symptoms may be contributing to these high prevalences.
- Testing of first-void urine for chlamydial and gonococcal DNA can substitute for formal clinical assessment of a man if he is shy of a physical examination.
- Oral ciprofloxacin can be used for gonorrhoea acquired in remote areas, plus azithromycin for all men with urethritis regardless of the cause.
- Empirical treatment for trichomoniasis should be considered for men whose urethral symptoms fail to resolve because of the high prevalence of this infection in remote areas.

Tests to be avoided

Inappropriate testing of men with urethral symptoms is common. Serology for *C. trachomatis* should be avoided because it fails to confirm or exclude infection. Men with uncomplicated *C. trachomatis* infection may never develop antibodies, while a positive antibody test may only indicate a previous infection or a cross-reaction with another *Chlamydia* species.

Midstream urine examination and culture is only indicated if there are bladder symptoms, such as frequency or suprapubic pain, or if epididymitis is suspected.

Treatment

Men with frank urethral discharge are often treated on clinical grounds before the test results are available. Usually, but not invariably, the diagnosis is obvious – with nongonococcal urethritis most likely in an urban heterosexual man with a mucoid discharge, and gonorrhoea more likely in a man with a frank purulent discharge who has a history of homosexual, overseas or remote area contact (see Figures 2 and 4). It is best to wait for the laboratory results in cases where the diagnosis is not obvious.

Gonorrhoea

The gonococcal strains in Australia continue to develop resistance to antibacterial agents, particularly in urban areas. Ceftriaxone (Rocephin) 250 mg, given as a single dose, has increasingly become the treatment of choice for gonorrhoea in urban Australian settings (Table 5). It can

be dissolved in 1 ml of 1% lignocaine and administered as a single intramuscular injection, and is equally effective for cervical, pharyngeal and anal infections.

In many rural and remote areas of Australia or where the sensitivities are already known, amoxycillin 3 g with probenecid (Pro-Cid) 1 g as a single oral dose or ciprofloxacin (Ciproxin) 500 mg as a single oral dose can still be used because resistance is not such a problem in these areas. Most authorities advocate concurrent treatment for chlamydia because co-infection is likely in an increasing proportion of gonorrhoea cases.

Nongonococcal urethritis

Azithromycin (Zithromax) 1 g, given as a single oral dose, has cure rates for uncomplicated nongonococcal urethritis due to *C. trachomatis*, *M. genitalium* and *U. urealyticum* that are similar to a week of doxycycline 100 mg orally, 12-hourly (Table 5). Azithromycin is preferred because of improved compliance, making it more cost-effective. Most relevant respiratory flora are also sensitive to azithromycin.

Men with urethritis secondary to *Trichomonas vaginalis* should be treated with metronidazole (Flagyl, Metrogyl) 2 g, given as a single oral dose.

Contact tracing and counselling

Men with acute urethritis who are well informed by their GP about its asymptomatic nature plus the severe complications of untreated infection in their sexual partners (Table 2) are usually co-operative in ensuring their partners are properly assessed and treated. All recent sexual partners should be examined, investigated and offered similar treatment if required.

Contact tracing must be approached in a sensitive and discrete manner, as patients are usually anxious that their confidentiality is protected. Further information on techniques is available in the *Australasian Contact Tracing Manual*.[7] Professional assistance with the process can also be provided by local sexual health services. Treating urethritis provides an ideal opportunity for addressing the man's future risks of contracting a STI and for encouraging safer sex.

Follow up

The follow up consultation, normally a week after treatment initiation, is the ideal time to confirm with the patient that he understands his infection and to ensure that his sexual partners have been managed properly.

Whatever the treatment, all patients treated for gonorrhoea should have a follow up test at one to two weeks to check that cure has been achieved. Treated chlamydial urethritis has a high cure rate and antibiotic resistance is rare. In addition, DNA tests remain positive for several days after treatment. Retesting the patient to ascertain cure of chlamydial urethritis is, therefore, not routine. Nevertheless, because of high reinfection rates, if the patient re-attends after four weeks opportunistic re-testing for *C. trachomatis* should be considered. A prompting note in the medical record may be helpful.

Urethral symptoms may take a few days to weeks to settle after initial treatment, although they normally continue to improve after treatment. In cases where symptoms persist or recur following initial treatment for urethritis, further limited investigation and antibiotic therapy may be necessary. As a significant pathogen is only rarely implicated in persistent urethritis, excessive or invasive investigations and serial antibiotics should be avoided because they have never proven to be of any benefit and may only exacerbate patient anxiety. The patient should be asked if reinfection is possible. In difficult cases, or where complications may be present or the patient is particularly concerned, specialist consultation with a sexual health physician can be considered.

Conclusion

Even though the tests and treatments for urethral pathogens are improving, we seem to be losing control of these major infections in Australia – as shown by the increasing numbers of notifications of infections. In part, this may be because only a tiny proportion of the population now see themselves at risk of HIV/AIDS and most young men have never even heard of *C. trachomatis*.[8,9]

Increasing vigilance by GPs, particularly lowering the threshold for testing young men and women at high risk of STIs, will be central to regaining some control. Key messages for GPs in rural and remote settings, where chlamydial infection and gonorrhoea may be more common, are given in the box on page 70.

Considering infected men as a symptom of a broader problem affecting their partners and their social circle, rather than as isolated clinical entities, is essential to improving our control of these infections. MT

A list of references is available on request to the editorial office.

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