

## Comment and Reply

### Comment on Editorial by B. Donovan: Asymptomatic non-chlamydial non-gonococcal urethritis — an iatrogenic disease (*Sexual Health* 1, 65–67)

#### The role of the urethral Gram stain in non-gonococcal urethritis

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We agree with the comments of Donovan in the August issue of *Sexual Health*, that microscopy of the urethral smear has no place in screening men without symptoms or signs of urethritis, but would also suggest it has a limited role in treatment decisions in men with symptoms of non-gonococcal urethritis (NGU). We have recently completed a case control study of men with urethral symptoms that supports this point.

We compared 80 heterosexual men with symptoms of NGU to 79 controls without symptoms of urethritis.<sup>1</sup> In this study 39% of cases did not have evidence of urethritis [ $<5$  polymorphonucleocytes (PMN) per high power field (hpf)] on their urethral gram stain, despite having symptoms consistent with NGU. Men with urethral symptoms, but no urethritis on Gram stain, still had a higher prevalence of *Chlamydia trachomatis* than the asymptomatic control group (16% versus 1%,  $P < 0.002$ ). First pass urine samples were also collected from the control group without symptoms of urethritis. Among these individuals 18% had evidence of urethritis ( $\geq 10$  PMN per hpf of centrifuged urine), but no urethral pathogens were detected in this group. *Chlamydia trachomatis* was isolated from only one control, and he had no evidence of urethritis on microscopy.

It is time to re-examine the relevance of the laboratory definition of urethritis in men with NGU. Studies pre- and post-introduction of molecular testing, report low sensitivities of the urethral Gram stain in predicting the presence of *Chlamydia trachomatis*. It is apparent that a significant proportion of men with chlamydial infection have  $<5$  PMNs per hpf on their urethral gram stain. Haddow *et al.* recently examined 363 consecutive men attending an STD clinic in the UK, 8% had chlamydia detected by LCR and 26% had 5 or  $>$  PMN pphf.<sup>2</sup> Of the men with chlamydial infection a large proportion, 37%, had  $<5$  PMN pphf on their

urethral smear. While urethral PMN count was associated with the presence of *C. trachomatis*, the urethral gram was only 63% sensitive and 77% specific for chlamydial infection, and dysuria and young age were considered as predictive for chlamydial infection. From the premolecular era, Janier concluded that in men with symptoms of NGU but an absence of urethral discharge, the situation was even worse, and the urethral gram had a sensitivity for *C. trachomatis* of only 29%.<sup>3</sup>

In Australia it is common practice to perform a urethral smear in symptomatic men, to assist in the diagnosis of gonorrhoea, however the decision for treatment is based on the presence of urethral symptoms and not on the urethral PMN count. With increasing evidence that urethral pathogens are common in symptomatic males with normal urethral microscopy, it seems appropriate clinical practice to base treatment on the presence of symptoms of NGU, and not to place great importance on the findings of microscopy. This approach is more relevant and feasible in the majority of clinical settings worldwide, where most clinicians do not have access to onsite microscopy.

#### References

- 1 Iser P, Read TR, Tabrizi SN, Bradshaw CS, Lee D, Horvath L, *et al.* Symptoms of non-gonococcal urethritis in heterosexual men – a case control study. *Sex Transm Dis* (in press).
- 2 Haddow LJ, Bunn A, Copas AJ, Gilson R, Prince M, Ridgway GL, *et al.* Polymorph count for predicting non-gonococcal urethral infection: a model using *Chlamydia trachomatis* diagnosed by ligase chain reaction. *Sex Transm Infect* 2004; 80(3): 198–200. doi: 10.1136/STI.2003.006924
- 3 Janier M, Lassau F, Casin I, Grillot P, Scieux C, Zavaro A, *et al.* Male urethritis with and without discharge: a clinical and microbiological study. *Sex Transm Dis* 1995; 22(4): 244–52.

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# Reply

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Bradshaw *et al.* question the value of a urethral smear in the management of symptomatic non-gonococcal urethritis (NGU). They conclude that risk factors, together with symptoms, may be better guides to treatment.<sup>1,2</sup> As the clinical severity of chlamydial urethritis varies between asymptomatic and symptomatic infection, it is to be expected that any 'cut-off' in polymorph count for diagnostic purposes is necessarily arbitrary.<sup>2</sup> However the distinction between symptomatic and asymptomatic urethritis may be equally grey.

In a case control study, we examined genital symptoms reported by chlamydia-infected men attending our centre (Table 1). The investigator was blinded to the diagnosis of the 363 men with *Chlamydia trachomatis* diagnosed by urine polymerase chain reaction and 363 negative controls. It's worth noting that the presence or absence of such symptoms is not always clear-cut. In eight of the cases, there was uncertainty on the part of the clinician (or a discrepancy between the clinician and triage nurse) over whether symptoms were present or not.

Although we have similar reservations about the indiscriminate use of microscopy of the urethral smear, it may be premature to do away with this test altogether. Many men present with atypical urethral symptoms of indeterminate

significance and a degree of reassurance may be provided to the majority with a 'negative' smear. To those men with a 'positive' ( $\geq 5$  polymorphs) smear, atypical symptoms, and a negative test for *C. trachomatis* we may have imparted a harmful result, but at least any harm will be minimised if we generally limit the intervention of microscopy to men with symptoms.<sup>3</sup> Until the role and clinical spectrum of other pathogens responsible for non-chlamydial NGU becomes clearer, and reliable tests for these become widely accepted, microscopy of the urethral smear (as crude a tool as it is) may be the best we have to sort out men with equivocal symptoms.

## References

- 1 Bradshaw CS, Read TR, Fairley CK. The role of the urethral gram stain in non-gonococcal urethritis. *Sex Health* (in press).
- 2 Haddow LJ, Bunn A, Copas AJ, Gilson R, Prince M, Ridgway M, *et al.* Polymorph count for predicting non-gonococcal urethral infection: a model using *Chlamydia trachomatis* diagnosed by ligase chain reaction. *Sex Transm Infect* 2004; 80: 198–200. doi: 10.1136/STI.2003.006924
- 3 Donovan B. Asymptomatic non-chlamydial non-gonococcal urethritis: an iatrogenic disease? (editorial). *Sex Health* 2004; 1: 65–7.

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**Table 1. Genital symptoms associated with *C. trachomatis* infection in heterosexual men attending a sexual health service**

Symptom		Chlamydia cases No. (%) ( <i>n</i> = 363)	Controls No. (%) ( <i>n</i> = 363)	Odds ratio (95% CI)	<i>P</i> value <sup>A</sup>
Urethral discharge	Yes	130 (35.8)	37 (10.2)	4.9 (3.3–7.3)	<0.001
	No	233 (64.2)	326 (89.8)	1	
Dysuria	Yes	140 (38.6)	45 (12.4)	4.4 (3.0–6.5)	<0.001
	No	223 (61.4)	318 (87.6)	1	
Urethral discomfort	Yes	58 (16.0)	32 (8.8)	2.0 (1.2–3.1)	0.003
	No	305 (84.0)	331 (91.2)	1	
Urinary frequency	Yes	9 (2.5)	6 (1.7)	1.5 (0.5–4.3)	0.454
	No	354 (97.5)	357 (98.3)	1	
Testicular pain	Yes	19 (5.2)	23 (6.3)	0.8 (0.4–1.5)	0.525
	No	344 (94.8)	340 (93.7)	1	

<sup>A</sup>*P* values were determined using the Chi-square test.