

Editorial

Asymptomatic non-chlamydial, non-gonococcal urethritis — an iatrogenic disease?

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Around the middle of the twentieth century, specialist services began routinely screening asymptomatic men with a urethral smear for gram staining. The practice persists in over 90% of United Kingdom services in line with national guidelines.¹ If the smear reveals ≥ 5 polymorphs in five or more oil-immersion fields then a diagnosis of non-gonococcal urethritis (NGU) is made, despite the absence of symptoms or a specific pathogen. Some will even fish out threads or debris from an asymptomatic man's first-void urine and stain these, in this case looking for ≥ 10 polymorphs/oil-immersion field. An alternative is a leucocyte esterase test on the urine. Thus (arbitrarily) a new disease was created; necessitating counselling, antibiotic treatment, contact tracing, and frequent psychosocial dilemmas.

The Americans generally go easy on the tracing of contacts of cases of asymptomatic NGU in the absence of a specific organism (*C. trachomatis*) being documented.² While agreeing on the microscopic criteria for asymptomatic urethritis, in contrast to the UK neither the American nor the Australian guidelines advocate urethral smears for microscopy for asymptomatic men, though neither guidelines actually advise against the practice.^{3,4} Perhaps technology has advanced to the point where this time-consuming and often problematic diagnosis of asymptomatic non-chlamydial, non-gonococcal urethritis (NCNGU) (and its active pursuit in the clinic) needs to be reappraised.

First, we need to ask why did the practice start in the first place? After glancing over their shoulders, a few senior UK genitourinary physicians have intimated their sceptical view that the process was devised 'to keep the statistics up in the clinics'. By the 1950s, the introduction of penicillin had made large inroads into the major concerns of the time — gonorrhoea and syphilis. The tactic worked. NGU filled the gap and the comprehensive network of UK clinics was preserved. In the meantime, in the USA, the practice did not become as widespread and much of their clinical

network was de-funded. But these days the UK clinics are straining under a massive and growing clinical burden — yet more reason to question a traditional practice with a fading rationale.

Second, there was a strong hunch (confirmed by the 1970s) that NGU often indicated an important infection (namely *C. trachomatis*) with serious consequences for sexual partners, and chlamydial urethritis is commonly asymptomatic. At the time (in the absence of any other test for *C. trachomatis* infection) this provided a compelling argument for screening for asymptomatic NGU. However, these days, a specific test for *C. trachomatis* is part of the routine work-up in specialist services,¹ so all the urethral smear now contributes is the diagnosis of asymptomatic NCNGU. Additionally, as control programmes take effect, *C. trachomatis* tends to contribute shrinking proportions (typically < 20%) of acute NGU cases and even smaller proportions of asymptomatic NGU cases.²

The only consistently documented causes of NCNGU are *Mycoplasma genitalium*⁵ and *Trichomonas vaginalis*⁶ [the latter largely confined to areas of high prevalence (Table 1)] but we don't routinely test for these organisms. The reasons that we don't screen for these infections are because the pathogenicity of *M. genitalium* has been unclear until recently⁵ while *T. vaginalis* tends to be uncommon in those services that can afford to test for it. There may be a scattering of other specific causes of NCNGU (Table 2)^{7–11} but there is no debate that we don't know the cause of most cases. Thus we find ourselves in the odd predicament of having constructed and been required to manage an asymptomatic condition with generally no known cause and no known consequences.

Some may chose to continue the practice of urethral smears with the justification that a sinister (as yet undiscovered) pathogen is lurking in the urethrae of these men and that they wouldn't otherwise get treated. But the treatments most commonly used for NGU or NCNGU in the public sectors in the UK and the USA (tetracyclines) have no effect on *T. vaginalis* and, on preliminary experience, a

Table 1. Confirmed causes of male urethritis of public health importance

Cause
<i>Neisseria gonorrhoeae</i>
<i>Chlamydia trachomatis</i>
<i>Mycoplasma genitalium</i> ⁵
<i>Trichomonas vaginalis</i> ⁶

high failure rate for *M. genitalium*.¹² We have no way of knowing if this yet-to-be-discovered pathogen is susceptible to our undirected antibiotics — this hardly qualifies as evidence-based medicine.

Another proffered justification for urethral microscopy of asymptomatic men relates to clinic dynamics. It is claimed that more men (some of whom harbour *C. trachomatis*) get treated sooner so that they have less opportunity to infect others and are at less risk of being lost to follow-up without treatment. There is scant recent evidence for this supposition.¹³ A nucleic acid amplification test for *C. trachomatis* takes 1–4 h (equivalent to getting most patients treated in 1 or 2 days in real terms) which is hardly a major public health hazard. What about the resources and distress involved in counselling men diagnosed with asymptomatic NGU (*C. trachomatis* test pending) who have to be told that they ‘may or may not’ have a sexually transmissible infection, when we know in advance that they usually don’t? Compounding the poor positive predictive value of microscopy for the presence of major NGU pathogens is its poor sensitivity.¹⁴ What about the other potentially infected patients who have to wait for extended

periods (often several working days) for appointments, in part because of the inherent inefficiency of the fractured double-consultation needed to deliver the gram-stain result? What about the physical discomfort due to the collection of the urethral smear and its effect on future health-care seeking behaviour? Cost effectiveness and patient acceptability studies are needed.

Nevertheless, the art of the gram-stained smear need not be lost. The smear remains relevant for urethrally symptomatic men, for the assessment of male contacts of women with pelvic inflammatory disease and of men suspected of having epididymitis or reactive arthritis, as well as men participating in research into urethritis.

Given the current limitations in our knowledge, if we want to do the best thing by our patients we should be lobbying our laboratories and diagnostic companies for multiplex nucleic acid amplification tests for the substantiated causes of urethritis (Table 1) and consider relegating to history the routine gram-stained urethral smear of the asymptomatic man.

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Table 2. Anecdotal, sporadic or unconfirmed causes of urethritis in men (source: reference 11, unless otherwise indicated)

Infections
<i>Ureaplasma urealyticum</i>
<i>Neisseria meningitidis</i>
<i>Candida albicans</i>
Herpes simplex viruses
Adenoviruses
<i>Haemophilus</i> species
Extension of a urinary tract infection
<i>Bacteroides ureolyticus</i> ⁷
Exposure to bacterial vaginosis ⁸
The absence of a yet-to-be-classified bacterium ⁹
Non-infectious
Reactive arthritis
Urethral stricture
Catheterisation
Stevens-Johnson syndrome
Chemicals
Tumours
Prior urethritis, particularly in association with chlamydial heat-shock protein 60 kD ¹⁰
? Condoms/allergy

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