A lateral flow assay for *Neisseria gonorrhoeae*: a step forward for an inexpensive biomarker-based diagnosis of *N gonorrhoeae* at the point of care?

At least one million curable sexually transmitted infections (STIs) are acquired daily, and their long-term consequences affect reproductive health, psychological health, neonatal health, and fertility.[1] In 2020, 82·4 million new gonorrhoea infections were estimated to have occurred in adults aged 15–49 years, with the African subcontinent reporting the highest prevalence of infection.[2] A significant weakness in estimating the global burden of gonorrhoea has been the lack of quality data from many regions, caused by the unavailability and access to appropriate diagnosis, treatment, and care; inaccessibility of information about STIs; and stigma associated with seeking health care.[3] Although gonorrhoea is treatable, *N gonorrhoeae* has developed resistance to all classes of antibiotics over many decades; in most regions ceftriaxone is the single recommended antibiotic for the treatment of uncomplicated infections.[4] Cases of gonorrhoea resistant to this antibiotic have been documented and might be increasing in some areas,[4] and there are currently no vaccines against *N gonorrhoeae*.[4] Prompt diagnosis and antibiotic treatment of gonococcal infections is how infections are cured, and transmission is minimised and eliminated.

Diagnostic options for gonorrhoea include microbiological methods (microscopy and culture with associated biochemical tests or other test formats) or expensive nucleic acid amplification tests. In lower-income settings, there is often reduced or no diagnostic capability, and these areas rely on syndromic management of infections, a strategy which is based on clinical signs of infection followed by treatment. Syndromic management can result in overtreatment, especially in women, leading to antimicrobial resistance and stigmatisation of the patient.[5] Several molecular point-of-care platforms with high sensitivity and specificity, such as the Xpert *Chlamydia trachomatis* and *N gonorrhoeae* (CT/NG) PCR assay, are being used worldwide.[6] An inexpensive, easy-to-use, and accurate lateral flow point-of-care test could offer tremendous progress in the diagnosis of *N gonorrhoeae*, ultimately providing the basis for moving away from the syndromic management practice. Presently there are no point-of-care biomarker-based tests for antigen detection approved to detect *N gonorrhoeae*.[4,7]

In *The Lancet*, Remco P H Peters and colleagues[8] report the results of their cross-sectional study where a novel lateral flow assay (LFA) was evaluated in 400 participants recruited from five primary care clinics in South Africa (200 male patients with urethral discharge and 200 female patients with vaginal discharge). The test performed better in male patients (first void urine specimens; sensitivity 96·1% [95% CI 91·2–98·3]; specificity 97·2% [90·4–99·2]) than in female patients (nurse collected vaginal swabs; sensitivity 91·7% [78·2–97·1]; specificity 96·3% [92·2–98·3]). The authors propose that the LFA performed less well in the female cohort because vaginal swab specimens have various cells, bacteria, and vaginal fluids that could interfere with the binding process. The limit of detection for this LFA point of care was $1–3 \times 10^5$ colony forming units (CFU) per mL.[9] In women, the number of gonococci recovered from the cervicovaginal area has been reported to average $1{\cdot}45 \times 10^5$ CFU.[10] Another study[11] showed that the mean gonococcal load in urine swabs was $4{\cdot}5 \pm 1{\cdot}0$ $\log_{10}$ CFU per mL ($3{\cdot}1 \times 10^5$) and vaginal swabs had an average of $4{\cdot}3 \pm 1{\cdot}0$ $\log_{10}$ CFU per mL. Specimens with a load lower than these averages might not be detectable with the new LFA. The LFA met the REASSURED criteria for diagnostics[12]—ie, it offered real-time connectivity with the electronic reading device, ease of specimen collection, and was accurate, user friendly, rapid, robust, and affordable. As stated by the authors, at a current price of less than US$3, its cost and portability will encourage expanded access to diagnostics.

Nevertheless, limitations of the study, as the authors discuss, include a midsize diagnostic study; samples were selected from only one district which raises the requirement for further testing in different geographical areas; and the need for standardised gold standard reference tests to compare performance. Future

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evaluations could include repeating test performance with standardised specimen collection methods in different populations at higher risk for infection, such as trans women, sex workers, men who have sex with men, and incarcerated populations; testing in both low-income and high-income settings; and evaluations in studies with larger (>1000) sample sizes. With current global evidence and preference for self-sampling for the human papilloma virus, chlamydia, and gonorrhoea,[13] self-sampling could help with expanding access in women and transgender populations, who might prefer this convenient and discreet option. As shown in modelling studies,[14] repeat testing with a highly sensitive test can help expand screening coverage to 80%, and help reduce prevalence of *N gonorrhoeae* to under 1%.

This promising first report on a high-performing LFA for *N gonorrhoeae* offers the potential for same-day test and treatment services in outreach settings, and for pathogen-targeted prescribing that could reduce antimicrobial resistance. This could also reduce complications of untreated gonorrhoea for different at-risk populations. In conclusion, an accurate and easy to use LFA-based point-of-care assay could advance policy changes and recommendations for the diagnosis of gonococcal infections, improve world statistics on prevalence, reduce gonococcal transmission and antimicrobial resistance, and make diagnostics accessible in lower-income settings. This would significantly reduce the global burden of gonorrhoea.

We declare no competing interests.

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