BASHH

GC NAATs: is the time right?

The laboratory diagnosis of gonorrhoea has historically been achieved by the isolation and identification of the causative agent, *Neisseria gonorrhoeae*. Currently it remains the gold standard because it demonstrates a high sensitivity and specificity and provides an organism for susceptibility testing to inform therapy. The obvious disadvantages of culture are that it requires good transport and isolation procedures and an invasive sample.

The increasing interest in the use of nucleic acid amplification tests (NAATs) for the detection of *N gonorrhoeae* has, in part, resulted from the widespread use of NAATs for the detection of *Chlamydia trachomatis*, both for testing genitourinary medicine patients and for screening as part of the National Chlamydia Screening Programme (NCSP). Non-invasive specimens are tested by the NCSP, and are also attractive for genitourinary medicine clinics, with the continued pressure on clinic time and resources. All of the NAATs for *C trachomatis* can detect *N gonorrhoeae* either simultaneously or using the same sample for little or no extra cost, which has encouraged their use.

NAATs for *N gonorrhoeae* have not proved as robust as those for *C trachomatis* and, at least in the United Kingdom, have been used less often. There are three commercially available kits (BD Probetec; Roche Amplicor; Aptima Combo 2) and a range of unlicensed in-house assays. The sensitivity and specificity of any NAAT is dependent on amplification of a nucleic acid sequence that is totally specific to the target organism. This has proved a challenge for *N gonorrhoeae* because of the close genetic relatedness to other pathogenic and commensal neisseriae, and is reflected in the specificity of the test. The sensitivity and specificity of available licensed tests are high except with urines from women,[1] but in low prevalence populations the positive predictive value may still be unacceptably low (table 1). Gonorrhoea, unlike chlamydia, is believed to be concentrated in core groups and so the prevalence is likely to vary between populations.

The reporting of a false positive result should be avoided and therefore any positive gonococcal NAAT result should be confirmed, as is also recommended for *C trachomatis*. Isolation is the only method that confirms the presence of *N gonorrhoeae* and should always be used for evaluation of a new test. In instances where it is not possible to confirm using culture then all positive results should be repeated with a supplementary test that is of equal sensitivity and specificity to the original test. Ideally repeat testing should utilise an additional sample from the patient tested with a NAAT, which has a different target. However this is not always achievable and repeat testing of the same sample with the same or different target or repeat testing with the same target are less suitable alternatives. If NAATs are to be used routinely for the detection of *N gonorrhoeae* it is essential that quality assurance is established to detect problems within an individual laboratory and to ensure consistency between different laboratories. Quality assurance schemes would need to include a variety of specimen types and gonococcal strains to ensure sensitivity and a range of commensal neisseriae to test the specificity.

One of the main concerns if NAATs were to replace culture is the issue of testing rectal or pharyngeal specimens. Most NAATs have a lower specificity and hence are not licensed for use with these specimens. Culture must, therefore, be maintained for accurate diagnosis, even if a laboratory is using NAATs for testing all genital samples. This raises two issues: are there sufficient resources for NAATs and culture in the same laboratory and will restricted use of culture affect the level of expertise.

An additional concern is the availability of a viable organism for antimicrobial susceptibility testing. The national surveillance programme for antimicrobial resistance (GRASP) is currently dependent on provision of a viable organism to detect emerging resistance as molecular detection of resistance relies on knowledge of the resistance determinant. If NAATs were used more widely it is worrying that the sample size will not remain sufficient to detect changes in the 5% resistance level and be representative. While GRASP will need to respond to such changes, high quality culture methods will need to be maintained to ensure a representative sample for the foreseeable future.

The accurate diagnosis of gonorrhoea to provide effective treatment and interrupt transmission is the goal of both microbiologists and clinicians. Advances in techniques to aid the detection of infectious diseases should be exploited to achieve this aim. The time is right to consider GC NAATs, but we should proceed with caution until we have a strong evidence base.

Recommendations for use of GC NAATs:

- All positive tests must be repeated with a supplementary test
- Positive results should be confirmed by culture (BASHH guideline)
- Rectal/pharyngeal specimens should be cultured
- NAATs should be validated in different populations before use
- NAATs should have a positive predictive value of >90%
- NAATs should not be used in children
- Retain a representative population of gonococcal isolates for antimicrobial susceptibility testing.

Table 1 Testing low prevalence populations

Prevalence	1%	1%
Number screened	1000	1000
Sensitivity	99%	99%
Specificity	99%	99.9%
Total positives	20	11
Total true positives	10	10
Positive predictive value	50%	91%

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REFERENCE

1 **Cook RL**, Hutchison SL, Ostergaard L, *et al.* Systematic review: noninvasive testing for Chamydia trachomatis and Neisseria gonorrhoeae. *Ann Intern Med* 2005;**142**:914–25.