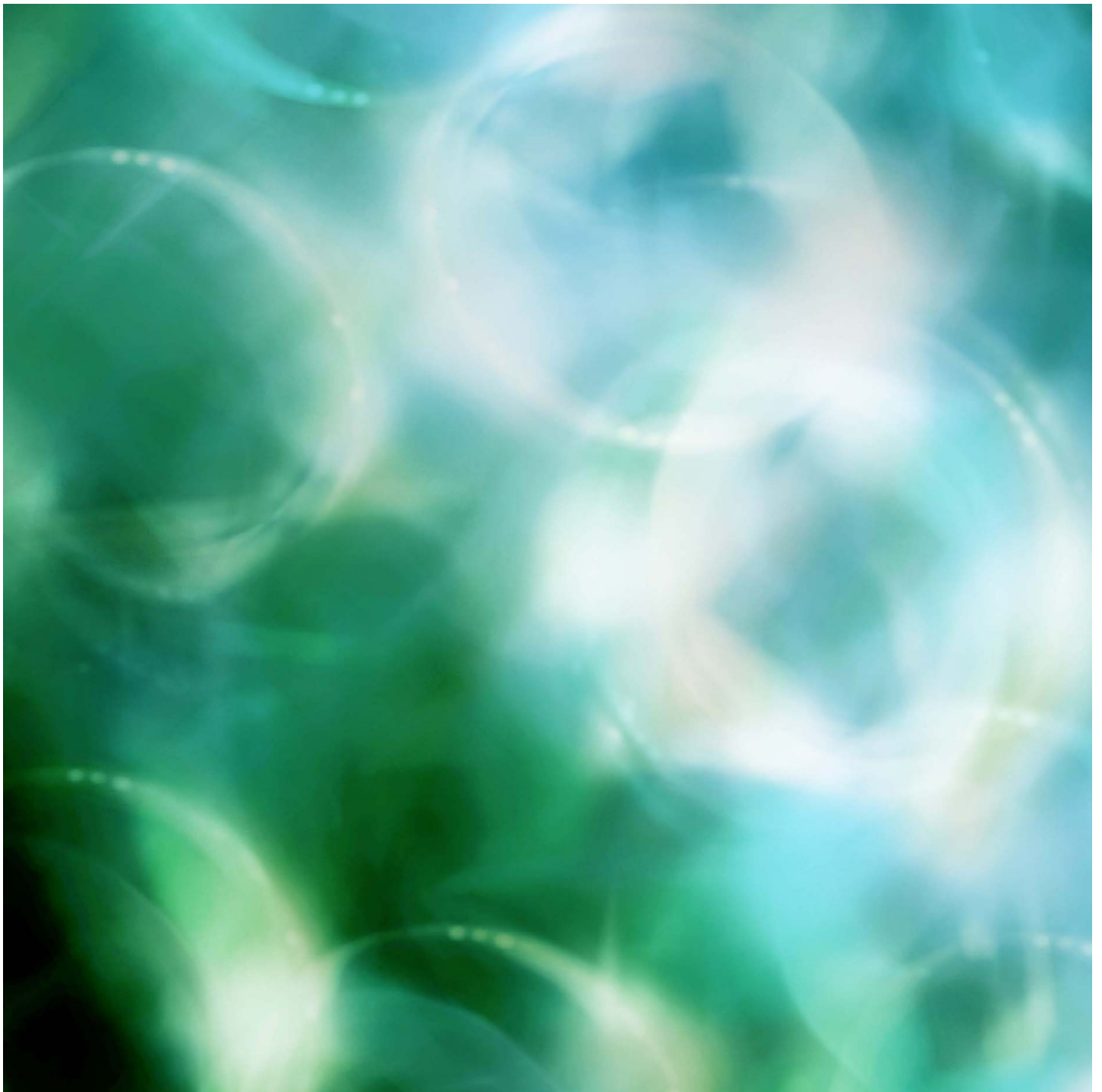




Guidance for gonorrhoea testing in England and Wales



Expert group

	Representing	Affiliation
Sarah Alexander	Health Protection Agency	Sexually Transmitted Bacteria Reference Laboratory, Centre for Infections
Chris Bignell	British Association of Sexual Health & HIV (BASHH)	Nottingham University Hospitals, NHS Trust
Fiona Boag	British Association of Sexual Health & HIV	Chelsea & Westminster Hospital
Jan Clarke	National Chlamydia Screening Advisory Group	Dept GU Medicine, Leeds General Infirmary
Mark Fitzgerald	Clinical Effectiveness Group, BASHH	Dept GU Medicine, Musgrove Park Hospital, Somerset
Gwenda Hughes	Health Protection Agency	STI Surveillance, Centre for Infections
Catherine Ison (Chair)	Health Protection Agency	STBRL, Centre for Infections
Kay Orton	Department of Health	Department of Health
Sue Skidmore	National Chlamydia Screening Programme	Shrewsbury and Telford NHS Hospital Trust
Shylaja Thomas	Health Protection Agency	Public Health Specialist Registrar. Eastern Region Public Health Training Programme

Introduction

The isolation of the causative organism, *Neisseria gonorrhoeae*, has been the 'gold standard' for the diagnosis of gonorrhoea for many years and can have a high sensitivity and specificity, but the organism is intolerant of problems with transportation or isolation methods resulting in a reduced sensitivity. In recent years, a number of factors have driven a change towards molecular detection using nucleic acid amplification tests (NAATs), including:

- A greater tolerance of NAATs to inadequacies in specimen collection or storage, compared to culture.
- Increasing pressure on genitourinary medicine (GUM) clinics to reduce waiting times and so increase throughput of patients.
- Desire to screen for sexually transmitted infections in non-GUM settings, particularly in young people under 25 years, as part of the National Chlamydia Screening Programme roll-out.
- Dual detection of *N. gonorrhoeae* and *Chlamydia trachomatis*.
- High sensitivity and specificity of NAATs and faster turnaround times for results, compared to culture.
- Use of non-invasive specimens with NAATs, which facilitates screening in both GUM and non-GUM settings.

However, there has been confusion over the correct algorithm for incorporating molecular testing in different settings and this document has been produced by an expert group to provide evidence-based guidance. It is also supported by a paired laboratory standard method which gives technical advice (1).

The document provides:

- **Key points**, giving relevant background information.
- **Recommendations** for testing for gonorrhoea.
- **Rationale** for the recommendations.
- **References**.

Key points

1. Both identification of individuals with gonorrhoea, and testing to establish infection status, are important components of good sexual health.
2. Identifying cases of gonorrhoea, administering effective antibiotic treatment and notifying partners will interrupt transmission and prevent spread of antimicrobial resistance.
3. The prevalence of gonorrhoea is very low in the general population, but significantly higher in certain defined subpopulations.
4. Sequelae (such as upper genital tract infection) caused by *N. gonorrhoeae* are uncommon, but serious. Gonorrhoea is known to facilitate the transmission of HIV.
5. All current NAAT platforms will detect *Neisseria gonorrhoeae*, in addition to *Chlamydia trachomatis*, and will be used by many laboratories. Attention must be given to their correct use and their limitations. No test is 100% sensitive or specific and patient consent is required when using them in opportunistic screening settings.
6. Rectal and pharyngeal specimens contain higher levels (than genital sites) of closely related *Neisseria* sp, which have the capacity to cause false positive results when NAAT platforms are used.

Recommendations

1. There is no evidence base to support widespread unselected testing for gonorrhoea in the community.
2. Laboratories undertaking dual testing should be CPA-accredited and provide timely turnaround of results to the clinician.
3. Laboratories must ensure that they use recommended algorithms when testing for gonorrhoea.
4. The prevalence of gonorrhoea in most areas is low. Therefore, the testing algorithm should give a positive predictive value of >90%. This will usually require a supplementary test with a different nucleic acid target.
5. Dual NAATs can be used with a range of genital samples taken invasively and non-invasively. Urine from women is not the optimal sample for detection of *N. gonorrhoeae*.
6. NAATs have a superior sensitivity to culture for the detection of *N. gonorrhoeae* in extra-genital specimens. All GC-positive NAATs from extra-genital specimens must be confirmed by a supplementary test with a different target. Care should be taken to use a NAAT which exhibits little cross-reactivity, to reduce misdiagnosis.
7. Care must be taken in both clinic and laboratory settings to avoid contamination with extraneous DNA or rRNA, which could cause false positive results.
8. Care pathways must be in place to ensure prompt and effective treatment of gonorrhoea and contact tracing in all settings. In non-GUM settings, referral into specialist STI clinics is recommended for appropriate treatment and partner notification, and to complete a full STI screen, including HIV testing.
9. Culture is necessary in patients with signs and symptoms compatible with gonorrhoea and/or with a confirmed NAAT result, so that susceptibility testing can be performed and resistant strains identified.

Rationale

Gonorrhoea is primarily an uncomplicated infection of the lower genital tract and is believed to be symptomatic in most men (90-95%) and asymptomatic in approximately 50% of women. If gonorrhoea goes undetected, or is inadequately treated, it can lead to complicated infection of the upper genital tract. This presents as prostatitis or epididymitis in men and salpingitis or pelvic inflammatory disease in women and is more common in women than men, due to the asymptomatic nature of the primary infection. Complicated gonococcal infection is uncommon in the UK. The total number reported in 2008 was 348 cases, of which 248 were from women, compared with 3,834 cases of complicated chlamydial infection, of which 2,828 were from women (2). It is possible that this is under-reported, as many of these infections will present to emergency departments, rather than sexual health clinics.

Complicated gonococcal and chlamydial infections both have the serious sequelae of infertility and ectopic pregnancy. Gonorrhoea is known to facilitate the acquisition and transmission of HIV. As gonorrhoea prevalence is high in men who have sex with men (MSM), who are also at high risk of acquiring HIV, early detection and treatment is of paramount importance.

Aims of testing:

The key objectives when testing for any sexually transmitted infection are to:

- Promote good sexual health.
- Guide individual patient management.
- Ensure effective treatment.
- Break the transmission chain.
- Prevent serious sequelae.

Screening for gonorrhoea

There is no evidence base to support widespread unselected screening for gonorrhoea, and evidence for selective community screening in UK settings is sparse. Data for all STIs is limited outside GUM clinic returns and prevalence studies are rare. Gonorrhoea diagnoses and subsequent complications are uncommon, compared with chlamydia. Immediate benefits to health from diagnosis of gonorrhoea, and subsequent reduction of risk of HIV onward transmission or acquisition, may be seen as supportive of an intervention, but the cost and adverse effects of screening also need to be considered.

The prevalence of gonorrhoea infection varies widely between and within communities and patient populations. Inner-city residents, GUM attendees, military personnel, prisoners and MSM have a higher prevalence of infection than

the general population (2, 3). Localised interventions targeted at these high-risk core groups is likely to be more cost-effective and beneficial than unselected community screening.

Distribution of gonorrhoea

The prevalence of gonorrhoea across England and Wales is variable among individuals attending GUM clinics and there is limited information regarding the prevalence among individuals attending non-GUM settings (4-6).

Laboratory standards

Laboratories must be appropriately accredited by a nationally approved accreditation scheme, such as Clinical Pathology Accreditation (UK) Ltd (<http://www.cpa-uk.co.uk/>), now part of the United Kingdom Accreditation Service (UKAS). They must also be seen to comply with the international standards for medical laboratory accreditation, ISO 15189.

In addition, the laboratory should show active participation in an External Quality Assurance (EQA) programme.

Detection of *N. gonorrhoeae*

Genital specimens

The choice of approach and method used for detection of *N. gonorrhoeae* should be decided by considering the prevalence of gonorrhoea in the local population.

In the population being tested, any testing algorithm should give a positive predictive value (PPV) of >90%. In low-prevalence populations it will be necessary to use a supplementary/confirmatory test to achieve an acceptable PPV (7).

The specimen type and sampling site used should be validated for the test used. Some commercial kits are not approved for use on all specimen types but, if validation data is available and validation files (8) are completed, this complies with CPA accreditation.

The methodology used should comply with the standard method for use of GC NAATs (1). Isolation of *N. gonorrhoeae* from a patient with a positive molecular test should be obtained (where possible), so that sensitivity testing can be performed to ensure that appropriate treatment has been given.

Urines are not considered a suitable sample for culturing for *N. gonorrhoeae* and are not recommended (9). However, urines are used widely for screening for *C. trachomatis* and so may be tested additionally for *N. gonorrhoeae*. NAATs can detect *N. gonorrhoeae* in urine in both men and women but, in

women, the sensitivity varies between commercial kits and is lower than if an endocervical or self-taken vulvovaginal swab is used

Extra-genital specimens

Culture for *N. gonorrhoeae* is now known to be inferior to use of NAATs (10, 11).

NAATs are the method of choice for extra-genital sites in men who have sex with men (MSM) and other high-risk individuals (11). However, rectal and pharyngeal specimens contain higher levels of closely related *Neisseria* sp. and care should be taken to use a NAAT which exhibits little cross-reactivity (12).

It is essential that a positive result using NAATs with either a rectal or pharyngeal specimen is always confirmed using a supplementary test with a different target, to prevent high numbers of false positives (1).

Use in low-prevalence groups should be undertaken with extreme caution.

Validation data is not available for specimens taken from the conjunctiva.

Handling of the specimen

Nucleic acid amplification tests are extremely sensitive and will detect very small amounts of DNA or rRNA. Detection does not necessarily indicate that the organism is viable.

Care should be taken to regularly clean (or decontaminate) both clinic and laboratory areas where positive specimens have been collected or processed.

Clinics should be aware that it is possible for DNA or rRNA to be transferred to inanimate objects during specimen collection, either by the clinician or the patient, which could then be transferred to another patient's specimen.

Laboratories must have decontamination protocols in place to prevent cross-contamination between samples during processing.

Turnaround times

The turnaround time for a test includes the time taken for the specimen to reach the laboratory, performing (and confirming where appropriate) and reporting the test result, and delivering the result report to the clinician.

The turnaround time in the laboratory, from receiving the sample to issuing a report, should be:

- Primary test: two working days.
- Confirmed positive: three to five working days.

If delay is envisaged, an interim report should be issued.

The overall turnaround time, from taking the sample from the patient, to the clinician receiving the results, should be no more than seven working days.

Care pathways

Before a GC NAAT service is offered, a care pathway, which includes notifying the patient of the result, appropriate treatment and partner notification, needs to be in place. It is recommended practice that a patient should be managed (that is, from the specimen being taken to the patient receiving treatment) within 14 working days (13).

Antimicrobial resistance

The national surveillance programme in England and Wales, GRASP, ([Gonococcal Resistance to Antimicrobials Programme](#)) has identified continual high levels of resistance to ciprofloxacin, previous first-line treatment, and emergence of decreased susceptibility to cefixime and ceftriaxone, the third generation cephalosporins (14) currently recommended for therapy (15). It is, therefore, recommended that antimicrobial susceptibility testing is necessary, both for patient management and surveillance purposes, and is essential to guide appropriate therapy to interrupt transmission of resistant infection. Susceptibility testing for either purpose will require a viable organism and it is essential to retain culture facilities and expertise to enable testing.

References

1. Health Protection Agency (2010). *Detection of Neisseria gonorrhoeae using Molecular methods*. National Standard Method QSOP 62 Issue 1 (<http://www.hpa-standardmethods.org.uk/documents/qsop/pdf/qsop62.pdf>)
2. Health Protection Agency. STI annual data tables. London. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1203348026613 (accessed 09-02-2010).
3. Delpech V, Martin IM, Hughes G, Nichols T, James L, Ison CA. Epidemiology and clinical presentation of gonorrhoea in England & Wales: Findings from the Gonococcal Resistance to Antimicrobials Surveillance Programme 2001-2006. *Sex Transm Infect.* 2009;85:317-21.
4. Stanley B, Todd A. Testing for *Neisseria gonorrhoeae* by nucleic acid amplification testing of chlamydia samples using Roche Cobas Amplicor in

a rural area in the north of England does not find more gonorrhoea in primary care. *Sex. Transm Infect* 2005;**81**:518

5. Lavelle SJ, Jones KE, Mallinson H, Webb AM. Finding, confirming, and managing gonorrhoea in a population screened for chlamydia using the Gen-Probe Aptima Combo2 assay. *Sex Transm Infect* 2006;**82**:221-224
6. Gopal Rao G, Bacon L, Evans J, Dejahang Y, Michalczyk P, Donaldson N and on behalf of Lewisham Chlamydia and Gonococcus Screening Programme. Prevalence of *Neisseria gonorrhoeae* infection in young subjects attending community clinics in South London. *Sex. Transm. Inf* 2008; 84:117-121
7. Whiley DM, Garland SM, Harnett G et al. Exploring 'best practice' for nucleic acid detection of *Neisseria gonorrhoeae*. *Sexual health* 2008;5:17-23
8. Health Protection Agency (2008). *Commercial and in-house diagnostic tests: evaluations and validations*. National Standard Method QSOP 23 Issue 4.1. http://www.hpa-standardmethods.org.uk/pdf_sops.asp.
9. Cook RL, Hutchinson SL, Otergaard L, Braithwaite RS, Ness RB. Systematic review: noninvasive testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. *Ann Intern Med* 2005;142:914-25
10. Whiley DM, Tapsall JW, Sloots TP. Nucleic acid amplification testing for *Neisseria gonorrhoeae*: an ongoing challenge. *J Mol Diagn* 2006;8:3-15
11. Alexander S. The challenges of detecting gonorrhoea and Chlamydia in rectal and pharyngeal sites: could we, should we, be doing more? *Sex Transm Infect*. 2009;85:159-160
12. Palmer HM, Mallinson H, Wood RL, Herring AJ. Evaluation of the specificities of five DNA amplification methods for the detection of *Neisseria gonorrhoeae*. *J Clin Microbiol* 2003; 41:835-7.
13. Standards for the management of sexually transmitted infections (STIs). Published by Medical Foundation for AIDS & Sexual Health (MEDFASH) ISBN 978-1-905545-42-1 January 2010
http://www.medfash.org.uk/publications/documents/Recommended_standards_for_sexual_health_services.pdf (accessed 10/2/10)
14. GRASP Steering Group. [The Gonococcal Resistance to Antimicrobials Surveillance Programme \(GRASP\), Year 2008 collection](#). London, Health Protection Agency 2009.
http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1245914960426 (accessed 10/2/10)
15. Bignell C. National guideline on the diagnosis and treatment of gonorrhoea in adults 2005. www.bashh.org/guidelines (accessed 3/2/10)

Health Protection Agency

Central Office

7th Floor

Holborn Gate

330 High Holborn

London WC1V 7PP

www.hpa.org.uk

For information or queries relating to this document please contact:

catherine.ison@hpa.org.uk

February 2010

© Health Protection Agency

This publication is also available in large print



Corporate member of
Plain English Campaign
Committed to clearer communication.

339