United Kingdom National Guideline for Gonorrhoea Testing 2012

Clinical Effectiveness Group
British Association of Sexual Health and HIV

Guideline Development Group Chris Bignell, Catherine Ison, Mark FitzGerald

Introduction, Scope and Purpose

Gonorrhoea remains a major bacterial sexually transmitted infection. It is caused by the Gram negative bacterium *Neisseria gonorrhoeae*. There is considerable geographic variation in the distribution of gonorrhoea in the UK with the highest rates seen in urban areas of higher deprivation [1]. This geographic variation is reflected in a corresponding wide variation in the prevalence of gonorrhoea in patients attending Genitourinary Medicine and sexual health clinics, with the prevalence exceeding 2% of attendees in high prevalence areas. 50% of new diagnoses of gonorrhoea in England in 2009 were in people aged <25 years and 36% of new diagnoses in men were in men who have sex with men (MSM) [1]. Similar figures are reported in Scotland.

Infection is frequently asymptomatic at the endocervix and urethra in women, and usually asymptomatic in the rectum and oro-pharynx in both men and women [2-4]. Testing for gonorrhoea is an essential investigation in patients presenting to genitourinary medicine and more specialised sexual health clinics (Level 2 in England) with symptoms of genital tract discharge, dysuria and upper genital tract pain. Testing to establish infection status is also a core component of a sexual health check within genitourinary medicine clinics. There is no evidence base to support widespread unselected testing for gonorrhoea in the community [5].

Applicability

This guideline has been designed for use in specialist sexual health clinics in the UK but its principles are also applicable to other healthcare settings where screening or testing for *Neisseria gonorrhoeae* is undertaken. The cautions on population prevalence of the infection should be noted. It complements the 2010 HPA document Guidance for gonorrhoea testing in England and Wales[5]. This guideline should be read in conjunction with the BASHH UK national guideline for the management of gonorrhoea in adults 2010.

Major Changes in 2012 guideline

Significant developments since the publication of the previous guideline in 2006 include:

1) Nucleic acid amplification tests (NAATs) are now used in many clinical services for detecting *Neisseria gonorrhoeae* and widespread clinical experience has been gained with these tests;
2) New NAATs with different nucleic acid targets and improved sensitivity & specificity have been developed and licensed; the HPA has published guidance for gonorrhoea testing in England and Wales and the HPS similar guidance in Scotland[6];
3) There have been clinical reports of treatment failures using many recommended treatments for gonorrhoea and increasing concern about reduced sensitivity of *Neisseria gonorrhoeae* to third generation cephalosporins.

Major new recommendations;

1) NAATs are the test of choice for testing asymptomatic individuals for urethral or endocervical infection with *Neisseria gonorrhoeae*;
2) NAATs are the test of choice for testing rectal and pharyngeal infection in men who have sex with men (MSM);
3) Positive NAATs from extragenital sites and low prevalence populations need confirmation by supplementary testing that uses a different nucleic acid target;
4) The re-introduction of test of cure is recommended as part of the routine follow-up of patients treated for gonorrhoea;
5) Testing by culture remains essential where infection persists after treatment and treatment failure is suspected.

Recommended Tests

No test offers 100% sensitivity and specificity and the prevalence of gonorrhoea in many Genitourinary and sexual health clinics is less than 1%. The prevalence may vary between subgroups of patients even within the same clinic. The testing methodology used should give a positive predictive value (PPV) exceeding 90% [5]. Laboratories used for testing should be appropriately accredited by a nationally approved accreditation scheme, notably by Clinical Pathology Accreditation (UK) Ltd [5] or equivalent

There are two principal ways to detect *Neisseria gonorrhoeae* – by detection of amplified nucleic acid and by culture. *N. gonorrhoeae* can also be visualized by microscopy of Gram stained specimens from the ano-genital mucosae which can be used to facilitate rapid diagnosis in symptomatic patients.

Nucleic Acid Amplification Tests (NAATs)

NAATs have become the most popular screening test for *Neisseria gonorrhoeae* in the UK. They are generally more sensitive than culture, offer testing on a wider range of specimen types and are less demanding in specimen quality, transportation and storage [5-11]. NAATs show high sensitivity (>96%) in both symptomatic and asymptomatic infection [9, 11]. They show equivalent sensitivity in urine and urethral swab specimens from men [12] and in vaginal and endocervical swabs from women[13]. The test sensitivity in female urine is significantly lower and urine is not an optimal specimen in women [5,11,14] (IIB).

NAATs are significantly more sensitive than culture for detecting *N. gonorrhoeae* in the rectum and pharynx [15-18] and are the test of choice at these sites in men who have sex with men and other high risk individuals [5,19]. They are not yet licensed for use at these sites and the test used should be validated to comply with CPA accreditation. Available commercial kits differ in their cross-reactivity to commensal *Neisseria* species which may be present at significant levels at these sites, particularly in the pharynx [20]. It is recommended that reactive specimens from the rectum and pharynx are confirmed by supplementary testing using a different nucleic acid target from the original test (IIIC) [5,8,21].

In most Genitourinary medicine clinic settings, positive NAAT results from genital specimens should be regarded as evidence of gonorrhoea[22]. In low prevalence populations (< 1%) the imperfect specificity of NAATs will result in positive tests having a PPV of less than

90% and confirmatory testing will be necessary [5,21]. Clinicians need to be familiar with the test performance of NAATs and be able to interpret results in their clinical setting [23,24].

The swabs used for NAATs and their transport should be as specified by the manufacturer of the test used.

Culture for *Neisseria gonorrhoeae*

Specimens collected from an appropriate site should be cultured onto an enriched medium, usually GC agar base or Columbia agar, supplemented with lysed or chocolatised horse blood or a non-blood based supplement such as IsoVitaleX (Becton-Dickinson) or Vitox (Oxoid) (IIB). If a single medium is used this should contain antimicrobial agents as selective agents to suppress the normal flora and allow the growth of *N. gonorrhoeae* (IIB) [25]. Antibiotic cocktails, available commercially, contain vancomycin or linomycin (to inhibit Gram positive organisms), colistin and trimethoprim (to inhibit other Gram negative organisms) and nystatin or amphotericin (to inhibit Candida spp.). Trimethoprim sensitive strains can occur. The primary isolation medium should be incubated in a CO_2 enriched environment with >90% humidity for 48 hours before discarded as negative. All colonies isolated on specialised media for *Neisseria* that are oxidase positive Gram negative cocci should be further identified using biochemical or immunological tests. With confirmation, culture has a specificity of 100% and PPV of 100%.

Culture for *N. gonorrhoeae* can be used with specimens from all sites and provides a viable organism for confirmatory testing. Direct plating of the specimen and use of transport swabs both give acceptable results [26] (IV). Specimens collected in transport medium should be stored in the refrigerator at 4ºC (as the medium is designed to slow the growth) until transported and should reach the laboratory as soon as possible but no longer then 48 hours from taking the specimen. After this time there will be significant loss of viability of the organism and this could result in a false negative result. Samples may be taken by loop or cotton-tipped swab for culture. Urine is not a suitable sample for culturing the organism. Culture has a sensitivity for urethral and endocervical infection between 85-95% in most laboratories but careful attention is needed with regard to the quality of the specimen, isolation medium and transport to the laboratory to maintain this high level of sensitivity. Culture remains essential for monitoring antimicrobial susceptibility to detect emerging resistance to therapy and in cases of apparent treatment failure.

Microscopy for intracellular Gram-negative diplococci:
Microscopy of Gram-stained smears of urethral discharge in men or endocervical discharge in women can be used as a near patient test to provide an immediate presumptive diagnosis of gonorrhoea (IIB). Microscopy of urethral smears from men with urethral discharge has a high sensitivity (>95%) but is much lower in asymptomatic male patients (50-75%) [2-4]. Microscopy of endocervical smears in women has a sensitivity of between 30-50%. Specificity is high when screened by trained personnel (>99%) [2-4]. *Neisseria* species morphologically identical to *N.gonorrhoeae* can occur at any site. Microscopy has poor sensitivity for detecting rectal infection and is not suitable for identifying pharyngeal infection.

Recommendations

- NAATs are the recommended tests for urine in men, non-invasively collected samples (e.g. vulvo-vaginal swab) and for identifying rectal and pharyngeal infection in MSM (IIa, B). For endocervical and urethral specimens NAATs offer higher sensitivity and less demanding specimen handling than culture but deny the opportunity for antimicrobial sensitivity testing.
- Culture remains a sensitive test for clinician taken genital specimens and is essential for patients with persisting symptoms or signs after treatment to exclude antimicrobial resistance.
- Microscopy of Gram-stained endocervical and urethral smears has low (40-60%) sensitivity in screening asymptomatic patients and is not recommended for routine practice.
- A culture should be taken in all cases of gonorrhoea diagnosed by NAAT's prior to antibiotics being given, if possible, so that susceptibility testing can be performed and resistant strains identified.

Recommended Sites for Testing

Mucosal sites associated with symptoms (discharge and/or pain) or signs (discharge and/or inflammation) should be tested for *Neisseria gonorrhoeae*

.

Screening. Current clinical practice in the UK for screening asymptomatic heterosexual individuals for gonorrhoea utilizes a single test and the sensitivity and convenience of NAATs: a first pass urine is collected from men and a vulvovaginal swab (which may be self taken) from women. Urine can be used in women but is sub-optimal. There is no data to confirm the adequacy of this approach. Culture testing in women identified the urethra as the only site of infection in 6% [27,28]. Sampling the endocervix and urethra continues to be recommended when testing women by culture. There is little recent data quantifying the additional contribution of routinely taking rectal [29] and pharyngeal specimens when screening women, although sampling should be considered at these sites where there is a history of direct exposure[1]. There are no data on the minimum incubation period necessary to exclude infection but it is pragmatic to align it with the recommendation for chlamydia: that a test should be done when the patient presents and if the exposure was within the last two weeks, repeated two weeks after exposure.

Endocervix

In women, the endocervix is the principal site sampled, either directly during speculum examination or indirectly by a vulvovaginal swab. Samples taken directly from the endocervix are suitable for culture, NAATs and microscopy. Water based gel lubricants that are sterile and do not contain bacteriostatic or bactericidal additives appear not to affect cultures or NAATs for *Neisseria gonorrhoeae* [30].

Urethra

In men, the urethra is the principal site sampled, either directly from the urethral meatus or indirectly in a first pass urine sample. Samples directly taken from the urethra are suitable for microscopy, culture and NAATs. For sampling, a loop or cotton-tipped swab is introduced 1-2cm into the urethral orifice. A higher sensitivity for microscopy is reported for urethral samples taken with a plastic loop compared to those taken with a cotton-tipped swab [28.]

In women, sampling the urethra is only recommended to complement testing with endocervical culture and after hysterectomy.

Rectum

Rectal testing should be dictated by symptoms and history of direct sexual exposure. The rectum can be sampled by culture and NAATs. NAATs offer significantly enhanced sensitivity compared with culture in MSM and are the test of choice in this patient population [5,15,16,19]. Confirmatory testing is recommended for positive results [5]. The use of NAATs on rectal samples may require local validation to comply with CPA accreditation. Anorectal samples from patients without symptoms may be obtained by blindly passing a moist swab 2 to 4 cm into the anal canal, using lateral pressure to try and avoid any faecal mass [31] (IIIB). Swabs with heavy faecal contamination should be discarded. In symptomatic patients, proctoscopy may aid diagnosis and allow specimens to be obtained under direct vision. Obtaining smears under direct vision improves the low sensitivity of microscopy [32] (IIIC) to aid immediate diagnosis.

Oropharynx

Oropharyngeal testing should be dictated by symptoms and history of direct sexual exposure. For men, the pharynx should be sampled if the man has been the active provider of fellatio, but not if he is only the active provider of cunnilingus. Specimens are obtained by wiping a swab over the posterior pharynx, tonsils and tonsillar crypts. Samples can be tested by culture (although sensitivity is low) and NAATs. NAATs are not approved for testing for *N. gonorrhoeae* in the pharynx but offer significantly enhanced sensitivity compared with culture in MSM and other high risk individuals [15,16,18,19] . They are the test of choice in these patient populations and confirmatory testing is recommended for positive results [5]. The use of NAATs on pharyngeal samples may require local validation to comply with CPA accreditation.

Urine

Urine is an easily obtained non-invasive sample and is the sample of choice when testing asymptomatic men using a NAAT. The first 15 to 30 mls of urine is collected after urine has been held for at least an hour. Urine is not suitable for culture. In women, the sensitivity of urine testing by NAATs is lower than vulvovaginal or endocervical swabs and urine is not a specimen of choice in women [5-8,33] (IIB).

Vagina

Patient taken vulvovaginal swabs and clinician taken endocervical swabs are equally suitable for detecting *N. gonorrhoeae* when tested by NAATs. Vulvovaginal swabs are the sample of choice for screening asymptomatic women for gonorrhoea.

Neisseria gonorrhoeae may infect the vaginal mucosa of prepubertal girls because the vagina is lined with columnar epithelium in pre-pubertal girls. Vaginal samples should be cultured in these circumstances in view of the implications of the diagnosis and to provide diagnostic certainty.

Bartholin's duct

When a Bartholin's abscess is present, purulent material expressed from the duct may be cultured and stained for microscopy.

Ophthalmic and systemic sites

Ophthalmic samples are suitable for culture. Specimens are obtained after cleaning excess, exudates by wiping a swab over the lower eye lid. NAATs are not licensed for this site and there is no data to validate their use on the conjuctiva.

Proving infection in patients with suspected disseminated gonococcal infection (DGI) can be difficult. The diagnosis of DGI is made on the basis of positive blood or synovial culture or, in a patient with the typical clinical syndrome and negative blood or synovial culture results, on the basis of gonococci isolated from another site. Genital and pharyngeal samples should be taken and have a higher yield in identifying the presence of *N. gonorrhoeae* than blood cultures[34,35](IIIC).

Factors which alter tests recommended or sites tested

Sexual History

Testing in heterosexual men and women focuses on the genital tract. Infection may be asymptomatic and all sexually active heterosexuals requesting screening for sexually transmitted infection at a genitourinary medicine clinic should receive a genital tract test for gonorrhoea. The prevalence of pharyngeal infection in patients attending genitourinary clinics in the UK is believed to be low and there is no evidence to support routine pharyngeal testing of heterosexuals who disclose oro-genital sexual activity. Data from a high-risk female population in the Netherlands show a prevalence of isolated pharyngeal infection of < 0.3%[36]. Rectal testing in women practicing anal sex is indicated in the presence of symptoms consistent with rectal infection and after sexual assault with anal penetration. The additional contribution of a rectal test to a vulvovaginal or endocervical NAAT test to determine the infection status of asymptomatic women is small even in a high-risk population[36]. A history of condom use for intercourse is not an indication to omit testing for gonorrhoea.

Risk Groups

- Men who have sex with men

  Tests should be taken from all sites (urethra, rectum and oropharynx) potentially exposed to infection as directed by the sexual history (recommendation C). Rectal infection may be acquired by transmission from the oropharynx in the absence of penetrative anal intercourse [37].

- Sex workers

  Test all sites potentially exposed to infection as indicated by sexual history. A history of condom use should not deter testing at exposed sites.

- 'Young' patients

  Testing in post-pubertal young men and women follows that in adults. Young people may be intimidated by the prospect of invasive tests and may prefer non-invasive options when available, notably urine testing. Cultures and implementation of chain of evidence should be considered if there is prospect of legal proceedings for sexual abuse.

Other groups:

- Pregnant women

  Screening tests as for heterosexual women.

- Women with history of hysterectomy

A urethral swab for culture offers a better yield than high vaginal culture [38]. No comparative data was found on testing urine, urethral swab and vaginal swabs by NAATs.

- Patients who are known contacts of gonorrhoea

Test all sites potentially exposed to infection as indicated by the sexual history. Microscopy may be worthwhile even if the patient is asymptomatic.

Recommendation for Frequency of Repeat Testing in an Asymptomatic Patient

The minimum time interval between exposure and when to test for gonorrhoea has not been determined (see above). Symptoms may develop within a few days and the incubation period for detection by culture is said to be 2 to 7 days.

Repeat testing should relate to risk rather than to a prescribed frequency. The prevalence of gonorrhoea in the general population is low but there are linked population subgroups at higher risk of infection and re-infection. The chance of contracting gonorrhoea depends largely on membership or contact with these subpopulations [39]. A past history of gonorrhoea is a strong risk factor for re-infection [40,41]. Re-infection rates of 0 to 30.8% have been reported in follow-up studies[40] and about a third of patients with gonorrhoea in England and Wales have a history of previous infection [42]. There is no compelling evidence to support frequent checks in sex workers, who have almost universal condom use at work [43]. No general recommendation on the frequency of repeat testing in asymptomatic patients is suggested. Sexual health checks in relation to new risk exposures are self-evident and commended.

Recommendation for Test of Cure

Progressive creep in minimal inhibitory concentration (MIC) to cephalosporins [44] and reported treatment failures with ceftriaxone and cefixime [45-49] indicate that microbiological cure can no longer be presumed with currently recommended treatments. Test of cure is recommended following treatment for all gonococcal infections (IVC). This is to identify treatment failure, emerging resistance which is predicted to occur on the basis of the past capability/history of *N. gonorrhoeae* and because susceptibility results that indicate potential failure to ceftriaxone and cefixime are not yet defined.

Where resource or practical considerations require TOC to be selective rather than universal, then the following patients should be prioritized –

- Persisting symptoms or signs
- Pharyngeal infection (all treatments are less effective at eradicating pharyngeal infection [50])
- Treatment with anything other than the first-line recommendations
- Pregnant women

Method and timing of test of cure

There is a lack of evidence on optimal timing for test of cure and method of testing. Current opinion and pragmatic considerations suggest that where there are persisting symptoms or signs, testing with culture should be performed at least 72 hours after completion of therapy. If asymptomatic, test with NAAT's where available followed by culture if positive. Test two weeks after completion of antibiotic therapy [52]

Principle Authors

Chris Bignell (Consultant Physician in Genitourinary Medicine)

Nottingham University Hospitals NHS Trust. E-mail: chris.bignell@nuh.nhs.uk
Catherine Ison (Professor of Microbiology)
STBRL, Health Protection Agency, UK. E-mail: Catherine.ison@hpa.org.uk
Mark FitzGerald (Lead Editor, Consultant Physician in Genitourinary Medicine)
Musgrove Park Hospital, Taunton E-mail: mark.fitzgerald@doctors.org.uk

Conflict of Interest
Each of the authors has declared they have no conflict of interest

Stakeholder Involvement
This guideline was developed with involvement of the Bacterial Special Interest Group of BASHH, a group of clinicians and microbiologists with an interest in STIs. There was no patient or public involvement. It was posted on the BASHH website for 3 months for consultation and comments taken into account by the authors and the CEG in preparing the final version.

Timescale for review
2016

Search Strategy
To update this guideline, a Medline search was conducted using the terms "gonorrhoea AND testing", gonorrhea AND diagnosis" and "gonorrhoea AND screening" covering the period January 2006 to December 2010. Duplicates were removed and titles and abstracts in the English language were screened (663). Full articles testing for gonorrhoea in-vitro and in clinical trials were obtained and reviewed. The Cochrane collaboration databases (www.cochrane.org) and the CDC STD treatment guidelines 2010 (www.cdc.gov/std) were reviewed.

Auditable Outcome Measures

- All reactive NAAT tests for gonorrhoea from the pharynx and rectum should be confirmed by supplementary testing. (Standard 100%)
- The percentage of patients, with a positive gonorrhoea NAAT, that also had testing for culture and sensitivity offered. (Standard 100%)
- The percentage of patients offered a test of cure by 2 weeks. (Standard 100%)

Acknowledgements

The BASHH National Audit Group
The Clinical Effectiveness Group
Individuals who contributed to the Consultation – Ade Apoola, Sophie Brady, Rudi Pittrof, Claire Robertson, Peter Watson, Andy Winter

References

1. Health Protection Agency. Health Protection Report HPR 2010; 4 (34) [27 August 2010]. Available at: http://www.hpa.org.uk/hpr/archives/2010/hpr3410.pdf

2. Sherrard J, Barlow D. Gonorrhoea in men: clinical and diagnostic aspects. Genitourin Med 1996; **72:** 422-426.

3. Barlow D, Phillips I. Gonorrhoea in women: diagnostic, clinical and laboratory aspects. Lancet 1978; **i:** 761-764.

4. Lewis DA, Bond M, Butt KD, Smith CP, Shafi MS, Murphy SM. A one-year survey of gonococcal infection seen in the genitourinary medicine department of a London district general hospital. Int J STD AIDS 1999; **10**: 588-594.

5. HPA / British Association for Sexual Health and HIV. Guidance for gonorrhoea testing in England and Wales. Downloadable from BASHH website at: http://www.bashh.org/news/478_2010-hpa-guidance-on-gonorrhoea-testing
6. Health Protection Scotland: Guidance on the use of molecular testing for *Neisseria gonorrhoeae* in Diagnostic Laboratories 2011

7. Van Dyck E, Ieven M, Pattyn S, Van Damme L, Laga M. Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by enzyme immunoassay, culture and three nucleic acid amplification tests. J Clin Microbiol 2001; **39**: 1751-1756.

8. Cook RL, Hutchison SL, Østergaard L, Braithwaite RS, Ness RB. Systematic Review: Non-invasive testing for *Chlamydia trachomatis* and *Neisseria goorrhoeaea.* Ann Intern Med 2005; **142**: 914-925.

9. Martin DH, Cammarata C, Van der Pol B, Jones RB, Quinn TC, Gaydos CA, et al. Multicenter evaluation of AMPLICOR and Automated COBAS AMPLICOR CT/NG tests for *Neiserria gonorrhoeae*. J Clin Microbiol 2000; **38**: 3544-3549.

10. Moncada J, Schachter J, Hook EW, Ferrero D, Gaydos C, Quinn T, et al. The effect of urine testing in evaluations of the sensitivity of the Gen-Probe APTIMA Combo 2 Assay on endocervical swabs for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Sex Trans Dis 2004; **31**: 273-277.

11. Van der Pol B, Ferrero DV, Buck-Barrington L. Hook EIII, Lenderman C, Quinn TC, et al. Multicenter evaluation of the BDProbeTec ET system for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in urine specimens, female endocervical and male urethral swabs. J Clin Microbiol 2001; **39**: 1008-1016.

12. Chernesky MA, Martin DH, Hook EW, Willis D, Jordan J, Wang S, et al. Ability of new APTIMA CT and APTIMA GC Assays to detect *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in male urine and urethral swabs. J Clin Microbiol 2005; **43**: 127-131.

13. Schachter J, Chernesky MA, Willis DE, Fine PM, Martin DH, Fuller D,et al. Vaginal swabs are the specimens of choice when screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: results from a multicenter evaluation of the APTIMA assays for both infections. Sex Trans Dis 2005; **32**: 725-728.

14. Association of Public Health Laboratories. Laboratory diagnostic testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Expert Consultation Meeting Summary Report; January 13-15, 2009; Atlanta, GA. Silver Spring, MD: Association of Public Health Laboratories; 2009. Available at

http://www.aphl.org/aphlprograms/infectious/std/documents/ctgclabguidelinesmeetingreport.pdf.

15. Schachter J, Moncada J, Liska S, Shayevich C, Klausner JD. Nucleic Acid Amplification Tests in the Diagnosis of Chlamydial and Gonococcal Infections in the Oropharynx and Rectum in Men Who Have Sex With Men. Sex Trans Dis 2008; **35**: 637-642.

16. Ota KV, Tamari IE, Smieja M, Jamieson F, Jones KE, Towns L, et al. Detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in pharyngeal and rectal specimens using the BD Probetec ET system, the Gen-Probe Aptima Combo 2 assay and culture. Sex Trans Infect 2009; **85**: 182-186.

17. Benn PD, Rooney G, Carder C, Brown M, Stevenson SR, Copas A, et al. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection and the sexual behaviour of men who have sex with men. Sex Trans Infect 2007; **83**: 106-112.

18. Page-Shafer K, Graves A, Kent C, Bals JE, Zapitz VM, Klausner JD. Increased sensitivity of DNA amplification testing for the detection of pharyngeal gonrrhoea in men who have sex with men. Clinical Infectious Diseases 2002; **34**: 173-176.

19. Alexander S. The challenges of detecting gonorrhoea and chlamydia in rectal and pharyngeal sites: could we, should we, be doing more? Sex Trans Infect 2009; **85**: 159-160.

20. Palmer H, 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**: 835-837.

21. Whiley DM, Garland SM, Harnett G, Lum G, Smith DW, Tabrizi SN, et al. Exploring 'best practice' for nucleic acid detection of *Neisseria gonorrhoeae*. Sexual Health 2008; **5**: 17-23.

22. Moncada J, Donegan E, Schachter J. Evaluation of CDC – recommended approaches for confirmatory testing of positive Neisseria gonorrhoeaenucleia acid amplification tets results. J Clin Microbiol 2008; **46**: 1614-9.

23. Katz AR, Effler PV, Ohye RG, et al. False-positive gonorrhoea test results with a nucleic acid amplification test: the impact of low prevalence on positive predictive value. Clin Infect Dis 2004; **38**: 814-819.

24. McNally LP, Templeton DJ, Jin F, Grulich AE, Donovan B, Whiley DM, et al. Low positive predictive value of a nucleic acid amplification test for nongenital *Neisseria gonorrhoeae* infection in homosexual men. Clin Infect Dis 2008 Jul 15;**47**(2):e25-e27.

25. FitzGerald M, Bedford C. National standards for the management of gonorrhoea. Int J STD & AIDS 1996;**7**:298-300

26. Jephcott AE. Microbiological diagnosis of gonorrhoea. Genitourin Med 1997; **73**: 245-252.

27. Hook EW III, Handsfield HH. Gonococcal infections in the adult. In Holmes KK, Sparling PF, et al eds. Sexually Transmitted Diseases 4th ed. New York, NY. McGraw Hill 2008; 627-645.

28. Ghanem M, Radcliffe K, Allan P. The role of urethral samples in the diagnosis of gonorrhoea in women. Int T STD & AIDS 2004;**15**: 45-47.

29. Raychaudhuri M, Birley HDL. Audit of routine rectal swabs for gonorrhoea culture in women. Int J STD AIDS 2010; **21**: 143-144.

30. Kozakis L, Vuddamalay J, Munday P. Plastic specula: can we ease the passage? Sex Trans Infect 2006; **82**: 263-264.

31. Kolator B, Rodin P. Comparison of anal and rectal swabs in the diagnosis of anorectal gonorrhoea in women. Br J Vener Dis 1979;**55**:186-187.

32. Deheragoda P. Diagnosis of rectal gonorrhoea by blind anorectal swabs compared with direct vision swabs taken via a proctoscope. Br J Vener Dis 1977; **53**: 311-313 .

33. Akduman D, Ehret JM, Messina K, Ragsdale S, Judson FN. Evaluation of a strand displacement amplification (BD Probtec-SDA) for detection of *Neisseria gonorrhoeae* in urine specimens. J Clin Microbiol. 2002; **40**:281-283.

34. Wise CM, Wasilauskas BL, Salzer WL. Gonococcal Arthritis in an Era of Increasing Penicillin Resistance. Ach Intern Med 1994; **154**: 2690-2695.

35. Holmes KK, Counts GW, Beaty HN. Disseminated Gonococcal Infection. Ann Intern Med 1971; 74: 979-993.

36. Peters RP, Nijsten N, Mutsaers J, Jansen CL, Morré SA, van Leeuwen AP Screening of oropharynx and anorectum increases prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae infection in female STD clinic visitors. Sex Transm Dis. **2011** Sep;38(9):783-7

37. McMillan A, Young H, Moyes A. Rectal gonorrhoea in homosexual men: source of infection. Int J STD & AIDS 2000; **11**:284-287.

38. Judson FN, Ruder MA. Effect of hysterectomy on genital infections. Br J Vener Dis 1979; **55**:434-438.

39. Chen M, Ghani AC. Populations and partnerships: insights from metapopulation and pair models into the epidemiology of gonorrhoea and other sexually transmitted infections. Sex Transm Infect 2010; **86**: 433-439.

40. Fung M, Scott KC, Kent CK, Klausner JD. Chlamydial and gonococcal reinfection among men: a systematic review of data to evaluate the need for retesting. Sex Transm Infect 2007; **83**: 304-309.

41. Fowler T, Caley M, Johal R, Brown R, Ross JDC. Previous history of gonococcal infection as a risk factor in patients presenting with gonorrhoea. Int J STD AIDS 2010; **21**: 277-278.

42. Health Protection Agency. GRASP Annual Report 2008. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1245914959952

43. Wilson DP, Heymer K-J, Anderson J, O'Connor J, Harcourt C, Donovan B. Sex workers can be screened too often: a cost-effectiveness analysis in Victoria, Australia. Sex Transm Infect 2010; **86**: 117-125.

44. Chisholm SA, Mouton JW, Lewis DA, Nichols T, Ison CA, Livermore DM. Cephalosporin MIC creep among gonococci: time for a pharmacodynamic rethink? J Antimicrob Chemother 2010; **65**: 2141-2148.

45. Ison CA, Hussey J, Sankar KN, Evans J, Alexander S. Gonorrhoea treatment failures to cefixime and azithromycin in England, 2010. Euro Surveill. 2011;**16**(14):p11=19833. Available online http://www.eurosurveillance.org/ViewArticle.aspx?ArticleID-19833

46. Unemo M, Golparian D, Syversen G, Vestrheim DF, Moi H. Two cases of verified clinical failures using internationally recommended first-line cefixime for gonorrhoea treatment, Norway, 2010. Euro Surveill. 2010; 15(47): pii=19721. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?Articleld-197921

47. Forsyth S, Penney P, Rooney G. Cefixime-resistant Neisseria gonorrhoeae in the UK: a time to reflect on practice and recommendations.Int J STD AIDS. 2011 May;**22**(5):296-7.

48. Tapsall J, et al. Two cases of failed ceftriaxone treatment in pharyngeal gonorrhoea verified by molecular microbiological methods. J Med Microbiology 2009; **58**: 683-687.

49. Unemo M, Golparian D, Hestner A. Ceftriaxone treatment failure of pharyngeal gonorrhoea verified by international treatment recommendations, Sweden, July 2010. Euro Surveill. 2011; **16**(6): pii=19792. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?Articleld-19792

50. Moran JS. Treating uncomplicated Neisseria gonorrhoeae infections: is the anatomic site of infection important? Sex Trans Dis 1995; **22:** 39-47.

51. Bachmann LH, Desmond RA, Stephens J, Hughes A, Hook EW 3rd. Duration of persistence of gonococcal DNA detected by ligase chain reaction in men and women following recommended therapy for uncomplicated gonorrhoea. J Clin Microbiol 2002; **40**: 3596-601.

Appendix I

Levels of evidence and grading of recommendations

Level of evidence
Ia Meta-analysis of randomised controlled trials
Ib At least one randomised controlled trial
IIa At least one well designed controlled study without randomisation
IIb At least one other type of well designed quasi-experimental study
III Well designed non-experimental descriptive studies
IV Expert committee reports or opinions of respected authorities

Grading of recommendation
A Evidence at level Ia or Ib
B Evidence at level IIa, IIb or III
C Evidence at level IV