

National Guideline on the Diagnosis and Treatment of Gonorrhoea in Adults 2005

Commissioned by: Clinical Effectiveness Group, BASHH (British Association for Sexual Health and HIV).

Aetiology.

Gonorrhoea is the clinical disease resulting from infection with the Gram-negative diplococcus *Neisseria gonorrhoeae*. The primary sites of infection are the mucous membranes of the urethra, endocervix, rectum, pharynx and conjunctiva. Transmission is by direct inoculation of infected secretions from one mucous membrane to another.

Clinical features.

Symptoms. ¹⁻⁴

Men:

- urethral infection commonly causes urethral discharge (>80%) and/or dysuria (>50%).
- urethral infection can be asymptomatic (<10%).
- rectal infection in homosexual men is usually asymptomatic but may cause anal discharge (12%) or perianal/anal pain or discomfort (7%).
- pharyngeal infection is usually asymptomatic (>90%).

Women:

- infection at the endocervix is frequently asymptomatic (up to 50%).
- increased or altered vaginal discharge is the most common symptom (up to 50%).
- lower abdominal pain may be present (up to 25%).
- urethral infection may cause dysuria (12%) but not frequency.
- gonorrhoea is a rare cause of intermenstrual bleeding or menorrhagia.
- rectal infection more frequently develops by transmucosal spread of infected genital secretions than from anal intercourse and is usually asymptomatic.
- pharyngeal infection is usually asymptomatic (>90%).

Neisseria gonorrhoeae may co-exist with other genital mucosal pathogens, notably *Trichomonas vaginalis*, *Candida albicans* and *Chlamydia trachomatis*. If symptoms are present, they may be attributable to the co-infecting pathogen.

Signs. ^{1,2}

Men:

- a mucopurulent or purulent urethral discharge is commonly evident.
- rarely, epididymal tenderness/swelling or balanitis may be present.

Women:

- mucopurulent endocervical discharge and easily induced endocervical bleeding (<50%).
[Note: mucopurulent endocervical discharge is not a sensitive predictor of cervical infection (<50%).]
- pelvic/lower abdominal tenderness (<5%).
- commonly, no abnormal findings are present on examination.

Complications.

Transluminal spread of *N. gonorrhoeae* may occur from the urethra or endocervix to involve the epididymis and prostate in men (1% or less) and the endometrium and pelvic organs in women (probably <10%). Haematogenous dissemination may also occur from infected mucous membranes, resulting in skin lesions, arthralgia, arthritis and tenosynovitis. Disseminated gonococcal infection is uncommon (<1%).

Diagnosis.

- The diagnosis is established by the identification of *N. gonorrhoeae* at an infected site.
- Culture offers a readily available, specific, sensitive and cheap diagnostic test that readily allows confirmatory identification and antimicrobial susceptibility testing. It is currently the method of first choice for use in genitourinary medicine clinics in the UK. Selective culture media containing antimicrobials are recommended to reduce contamination⁵ (recommendation level B).
- Alternative tests include nucleic amplification tests (NAATs) and nucleic acid hybridization tests. NAATs are more sensitive than culture and can also be used as diagnostic/screening tests on non-invasively collected specimens (urine and self-taken vaginal swabs). Comparisons between NAATs and culture suggest the sensitivity of NAATs exceeds 90% for genital sites, whilst the sensitivity of culture may be less than 75% for endocervical swabs⁶. This probably indicates that NAATs are less affected than culture by inadequacies in collection and transport of specimens. The TMA assay (APTIMA Combo 2) and SDA assay (BD ProbeTec-SDA) are more sensitive in women than the PCR assay⁷. There are currently no NAATs which are licensed for use with rectal or pharyngeal samples, although studies suggest that the sensitivity of NAATs at non-genital sites exceeds 90%⁸ whereas the sensitivity of culture can be less than 60% for rectal swabs⁸ and less than 50% for pharyngeal swabs^{8,9}. Caution is required in interpretation of positive results as the specificity of NAATs is not 100%^{10,11}. Confirmation of a NAAT positive result by culture is advisable (recommendation level C).
- Rapid diagnostic tests can be performed to facilitate immediate diagnosis and treatment. Microscopy (x1000) of gram stained genital specimens allows direct visualization of *N. gonorrhoeae* as monomorphic gram negative diplococci within polymorphonuclear leukocytes. In men, microscopy of urethral smears is more sensitive in symptomatic (90-95%) than in asymptomatic (50-75%) patients¹. In women, microscopy of gram stained endocervical smears is more sensitive than urethral smears (37-50% vs 20%)². Microscopy is not appropriate for pharyngeal specimens.

Specimen collection.

Men: routinely from the urethra; rectal and/or oropharyngeal tests when symptomatic at these sites and as indicated by sexual activity. A first pass urine provides an alternative urethral specimen for testing with a NAAT.

Women: routinely from endocervix if speculum examination performed and from the urethra; rectal and oropharyngeal tests when symptomatic at these sites, when a sexual partner has gonorrhoea and when indicated by the sexual history. Urine or a self-taken vaginal swab provide suitable alternative specimens as screening tests using a NAAT (note: the PCR assay has poor sensitivity on female urine⁷).

- Direct plating of genital samples and use of transport media with prompt laboratory plating both give acceptable results^{5,12} (evidence level IV).

- The use of endocervical samples alone will identify 90-95 % of women with gonococcal infection ^{2, 13}.
- Data is lacking on the sensitivity of a single set of tests from anogenital sites to identify infection with *N. gonorrhoeae*. To confidently exclude infection in patients who attend within three days of sexual contact with a confirmed case of gonorrhoea, a second set of tests should be considered if epidemiological treatment with effective antimicrobial therapy is not given ¹² (evidence level IV, recommendation level C).

Management.

General Advice.

- Referral to a GU Medicine Department for management is strongly encouraged.
- Patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s). This should be reinforced with clear and accurate written information.
- Patients should be advised to avoid unprotected sexual intercourse until they and their partner(s) have completed treatment.

Further Investigation.

- Screening for coincident sexually transmitted infections should routinely be performed in patients with or at risk of gonorrhoea (evidence level III, recommendation level C).

Treatment.

Indications for therapy:

- a positive rapid diagnostic test,
- a positive culture for *N. gonorrhoeae*,
- a positive nucleic acid test - confirmation of the diagnosis by culture is recommended prior to or at the time of treatment ¹¹ (recommendation grade C).
- on epidemiological grounds, if a recent sexual partner has confirmed gonococcal infection,

Recommended treatments ^{3, 14-20}.

Uncomplicated anogenital infection in adults:

- Ceftriaxone 250mg IM as a single dose. (grade A recommendation)
or
 - Cefixime 400mg oral as a single dose. (grade A recommendation)
or
 - Spectinomycin* 2g IM as a single dose. (grade A recommendation)
- *N. gonorrhoeae* has shown the capacity to develop reduced sensitivity and resistance to many classes of antimicrobials. Published trials of gonorrhoea treatment reflect clinical efficacy in a past era of antimicrobial sensitivity. Surveillance data for 2004 shows significant levels of *N. gonorrhoeae* resistance to penicillin (11.2%), tetracyclines (44.5%) and ciprofloxacin (14.1%) in the UK ²¹⁻²³. Most resistant infections are acquired in the UK.
 - Antimicrobial therapy should take account of local patterns of antimicrobial sensitivity to *N. gonorrhoeae*. The chosen regimen should eliminate infection in at least 95% of those presenting in the local community ¹².

Alternative regimens - may be used when an infection is known to be sensitive to these antimicrobials or where the regional prevalence of resistance to them is less than 5%:

- Ciprofloxacin 500mg orally as a single dose. (grade A recommendation)
or
- Ofloxacin 400mg orally as a single dose. (grade A recommendation).
or
- Ampicillin 2g or 3g plus probenecid* 1g orally as a single dose, (grade B recommendation),
- Other single dose cephalosporin regimes, notably Cefotaxime 500mg IM as a single dose. (grade A recommendation)
or Cefoxitin 2g IM as a single dose plus probenecid* 1g oral.
- Cefpodoxime is an alternative oral third generation cephalosporin that as a single dose of 200mg is licensed for the treatment of uncomplicated gonorrhoea²⁴. Published trial data is limited, but in view of its short half-life, less favourable pharmacokinetics than cefixime and suboptimal efficacy against pharyngeal infection, it cannot be recommended (recommendation C).
- Clinicians using alternative regimens are recommended to regularly review local antimicrobial sensitivity testing with microbiology colleagues.
- The alternative treatment regimens listed do not comprise all effective treatment regimens, but reflect clinical practice in the UK.
- High dose azithromycin (2.0g as a single dose) has shown acceptable efficacy in clinical trials, but is associated with a high gastrointestinal intolerance²⁵. The emergence of azithromycin resistant *N. gonorrhoeae* has been reported and clinical efficacy does not always correlate with *in-vitro* sensitivity testing²⁶⁻²⁷. Azithromycin is not a recommended treatment for gonorrhoea.

β lactam allergy.

- Spectinomycin* 2g IM as a single dose.
or
- Ciprofloxacin 500mg orally as a single dose when the infection is known or anticipated to be quinolone sensitive.

Pregnancy and Breastfeeding.

- Pregnant women should not be treated with quinolone or tetracycline antimicrobials.

Recommended Regimes²⁸⁻³⁰

- Ceftriaxone 250mg IM as a single dose. (grade A recommendation)
or
- Cefixime 400mg oral as a single dose. (grade A recommendation)
or
- Spectinomycin* 2g IM as a single dose. (grade A recommendation).

or

- Amoxicillin 3g or Ampicillin 2g or 3g plus probenecid* 1g orally as a single dose, where regional prevalence of penicillin resistant *N. gonorrhoeae* is $\leq 5\%$. (grade B recommendation).

Pharyngeal infection.

Recommended treatments^{15, 31}

- Ceftriaxone 250mg IM as a single dose (grade B recommendation)

or

- Ciprofloxacin 500mg orally as a single dose if *N. gonorrhoeae* known to be quinolone sensitive (grade B recommendation)

or

- Ofloxacin 400mg orally as a single dose if *N. gonorrhoeae* known to be quinolone sensitive. (grade B recommendation).

- Single dose treatments using ampicillin or spectinomycin have a poor efficacy in eradicating gonococcal infection of the pharynx¹⁵ (evidence level II).

*There may be problems with the availability of these drugs in the UK.

Co-infection with *Chlamydia trachomatis*

Genital infection with *C. trachomatis* commonly accompanies genital gonococcal infection (up to 20% of men and 40% of women with gonorrhoea). Screening for *C. trachomatis* should routinely be performed on adults with gonorrhoea or treatment given to eradicate possible co-infection^{3, 12, 14}. Combining effective antimicrobial therapy against *C. trachomatis* with single dose therapy for gonococcal infection is particularly appropriate when there is doubt that a patient will return for follow up evaluation.

Sexual partners.

Partner notification should be pursued in all patients identified with gonococcal infection, preferably by a trained health adviser in GU Medicine. Action and outcomes should be documented³². Male patients with symptomatic urethral infection should notify all partners with whom they had sexual contact within the preceding 2 weeks or their last partner if longer ago. Patients with infection at other sites or asymptomatic infection should notify all partners within the preceding 3 months. Sexual partners should be treated for gonorrhoea preferably after evaluation for sexually acquired infection. (recommendation level C)

Follow up.

Patients should be assessed after treatment (recommendation C):

- to confirm compliance with treatment,
- to ensure resolution of symptoms,
- to enquire about adverse reactions,
- to re-take the sexual history to explore the possibility of re-infection,
- to pursue partner notification and health promotion.

A microbiological test of cure is not routinely necessary when the infection has been treated with a recommended directly observed therapy, the infection is fully

sensitive to the antimicrobial administered, symptoms have resolved and there is no risk of re-infection. (evidence level III, recommendation C) ³³⁻³⁴. If a patient is symptomatic after treatment, has received a suboptimal treatment, a resistant strain is identified or there is a possibility of reinfection, test of cure with culture is recommended (recommendation C). Pregnancy does not diminish treatment efficacy. All treatments are less effective at eradicating pharyngeal infection ³¹ and test of cure is recommended following treatment of infection at this site (recommendation C). If a test of cure is performed, culture tests should be performed at least 72 hours after completion of antimicrobial therapy ⁵ and NAATs tests two weeks after therapy ³⁵. Infection identified after treatment more commonly indicates reinfection rather than treatment failure ^{4,34}.

Auditable Outcome Measures.

- At least 95% of cases of genital gonorrhoea should be cured by first line therapy ¹².
- All patients with gonorrhoea should be screened for genital infection with *Chlamydia trachomatis* or receive presumptive treatment for this infection.
- All patients identified with genital gonorrhoea should have at least one documented interview with a health adviser in GU Medicine or other health professional trained in partner notification and their action documented.
- All patients identified with gonorrhoea should receive written information about sexually transmitted infections and their prevention.
- For every case of gonorrhoea, at least 0.6 sexual partners should be verified as having been satisfactorily managed within four weeks. This rate of management of sexual partners may be unachievable in departments in some large cities and a lower rate may need to be locally determined ³⁶.

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Author and Centre.

Chris Bignell
Nottingham City Hospital NHS Trust

Membership of the CEG.

Clinical Effectiveness Group: Chairman, Keith Radcliffe; Imtyaz Ahmed-Jushuf; David Daniels (Chairman, BASHH National Audit Group); Mark FitzGerald; Guy Rooney (Royal College of Physicians representative); Jan Welch.

Conflict of Interest.

None.

Evidence Base.

Cochrane Library

The Cochrane Library 2004 Issue 2 (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness, and Cochrane Controlled Trials Register) was searched using the textword 'gonorrhoea' and all entries considered.

MEDLINE

A MEDLINE search of published articles in any language for the years 1990-2004 (August) using the subject headings 'gonorrhea' and 'Neisseria gonorrhoeae'. The sub-headings focused on were: clinical trials, drug therapy, diagnosis, epidemiology, prevention and control, and therapy. All entries in the English language or with abstracts in English were viewed because of the paucity of 'clinical trials' or 'reviews'. Comprehensive reviews of therapy for gonorrhoea that have employed MEDLINE search strategies are published and include trials up to 1993.

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