Guidelines

## British Association of Sexual Health and HIV UK National Guideline for the Management of infection with Neisseria gonorrhoeae, 2025



International Journal of STD & AIDS 2025, Vol. 0(0) 1–15 © The Author(s) 2025 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/09564624251345195 journals.sagepub.com/home/std



Helen Fifer<sup>1</sup><sup>®</sup>, Muhammad Azam Ismail<sup>2</sup><sup>®</sup>, Suneeta Soni<sup>3</sup><sup>®</sup>, Uzochi Nwaosu<sup>4</sup><sup>®</sup>, S. Tariq Sadiq<sup>5</sup>, Alice Milligan<sup>1,6</sup>, John Saunders<sup>1</sup> and Nicholas Medland<sup>7</sup>

#### Abstract

This guideline offers recommendations on the diagnosis, treatment and health promotion principles needed for the effective management of gonorrhoea. It is an update of the 2018 guideline.

#### Keywords

Gonorrhea (Neisseria gonorrhoeae), bacterial disease, treatment, diagnosis

## Changes since 2018 guideline

- Pharyngeal testing is recommended for all individuals with urogenital gonorrhoea, and all contacts.
- Updated recommendations for diagnosing disseminated gonococcal infection and managing ocular infection.
- Ciprofloxacin is no longer recommended as first line therapy due to safety concerns but may be used if clinically appropriate.
- Cefixime dose increased from 400 mg single dose to 400 mg as two separate doses 6–12 h apart, due to rising antimicrobial resistance.
- Routine test of cure is not necessary for anogenital infections treated with ceftriaxone 1 g if infection is susceptible to ceftriaxone.

## Scope and purpose

This guideline provides evidence-based recommendations for the diagnosis, treatment regimens and health promotion principles needed for the effective management of gonorrhoea. The guideline is aimed primarily at individuals aged 16 years or older presenting to healthcare professionals working in departments offering specialist level 3 care in sexually transmitted infections (STIs) management within the United Kingdom (UK). However, the principles of the recommendations are applicable across all levels of STI care, and nonspecialist services may need to develop, where appropriate, local referral pathways.

## **Editorial independence**

This guideline was commissioned and edited by the British Association for Sexual Health and HIV (BASHH) Clinical Effectiveness Group (CEG), which provided funding for the literature search and project management. No other funding was obtained.

## **Rigour of development**

This guideline was produced according to specifications set out in the BASHH CEG document 'framework for guideline

University of London, London, UK <sup>6</sup> Moorfields Eye Hospital NHS Foundation Trust, London, UK

 $^{7}\,\rm Kirby$  Institute, University of New South Wales, Sydney, New South Wales, Australia

#### Corresponding author:

 $<sup>^{\</sup>rm I}$  Blood Safety, Hepatitis, STIs and HIV Division, UK Health Security Agency, London, UK

<sup>&</sup>lt;sup>2</sup> Sheffield Teaching Hospitals NHS Trust, Sheffield, UK

<sup>&</sup>lt;sup>3</sup> University Hospitals Sussex NHS Foundation Trust, Brighton, UK

 <sup>&</sup>lt;sup>4</sup> Chelsea & Westminster Hospital NHS Foundation Trust, London, UK
 <sup>5</sup> St George's School of Health and Medical Sciences, City St George's,

Helen Fifer, Blood Safety, Hepatitis, STIs and HIV Division, UK Health Security Agency, 61 Colindale Avenue, London NW9 5EQ, UK. Email: helen.fifer@ukhsa.gov.uk

development and assessment' (2015, updated 2019) accessed at https://www.bashhguidelines.org/media/1229/2015-guidelines-framework-amended-dec-2019.pdf and has been updated by reviewing the previous gonorrhoea guideline (2018) and the medical literature since its publication. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) system was used to assess the evidence and make recommendations.

A search of published articles from January 2018 to October 2023 was conducted in Medline, Embase and the Cochrane Library using the subject headings 'gonorrhoea' OR 'gonorrhea' OR '*Neisseria gonorrhoeae*' AND 'prevalence' OR 'transmission' OR 'sequelae' OR 'diagnosis' OR 'incubation' OR 'therapy' OR 'treatment' OR 'resistance' OR 'antibiotic' OR 'failure' OR 'partner notification'. Articles were limited to those in the English language, humans, randomised controlled trials, systematic reviews, or observational studies.

Article titles and abstracts were reviewed and if relevant the full text article was obtained. Abstracts from meetings in the relevant period were hand-searched and considered. Priority was given to randomised controlled trials and systematic review evidence, and recommendations were made and graded based on best available evidence. The draft guideline was appraised with the AGREE instrument, posted on the BASHH website for a consultation period of two months and any comments received during the consultation period were reviewed by the authors and acted on appropriately. The document was also reviewed by the public panel of BASHH, and their feedback was considered by the authors and used to inform the guideline.

## Aetiology

Gonorrhoea is an infection caused by the gram-negative diplococcus *Neisseria gonorrhoeae*. It is the second most common bacterial sexually transmitted infection in the UK, and disproportionally affects gay, bisexual and other men who have sex with men (GBMSM), young people aged 15–24 years, people of Black Caribbean ethnicity, and people living in deprived areas.<sup>1</sup> Clinical features are determined by the specificity of the organism for certain anatomical sites: the columnar epithelium of the mucous membranes of the urethra, endocervix, rectum, pharynx, and conjunctiva.

Transmission occurs with direct contact between a susceptible mucous membrane and an inoculum containing viable organism, predominantly through penilevaginal, penile-anal and penile-oral sex.<sup>2</sup> Two studies in GBMSM in Australia found a significant association between self-reported kissing and pharyngeal gonorrhoea, after controlling for other types of sexual behaviour, although there were limitations of these studies.<sup>3</sup> Transmission between extragenital sites may possibly occur by oral-anal sex (rimming) or using saliva or other body fluids as sexual lubricants.<sup>4</sup> Secondary infection to other anatomical sites, through systemic or transluminal spread, can also occur.

## Antimicrobial resistance

Antimicrobial resistance (AMR) in *N. gonorrhoeae* is an urgent global concern and varies widely between countries.<sup>5,6</sup> *N. gonorrhoeae* has developed resistance to all drugs used to treat it including ceftriaxone, the most widely recommended first line empiric treatment globally. AMR surveillance is crucial to ensuring that guidelines are appropriate to the local setting and relies on samples for culture and antibiotic susceptibility testing. The prevalence of ceftriaxone resistance is very low in England and Wales, with no cases detected in the sentinel gonococcal resistance to antimicrobials surveillance programme (GRASP).<sup>7</sup> However, ceftriaxone resistant strains are prevalent in the Asia Pacific region and ceftriaxone resistance has been reported in the UK and globally, usually associated with travel to or from this region.<sup>8–10</sup>

## **Clinical features**

Symptoms and signs depend, in part, on the site of infection. Co-infections (e.g., *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Mycoplasma genitalium*, *Candida albicans* and bacterial vaginosis) are not uncommon and should be considered as a cause of symptoms.<sup>11–13</sup>

## Penile urethral infection in people assigned male at birth

Symptoms of discharge and/or dysuria occur in over 90% of individuals appearing two to five days following exposure, with mucopurulent urethral discharge present on examination. Rarely, individuals may complain of testicular and epididymal pain with tenderness and swelling present on examination.

## Urethral infection in people assigned female at birth

Urethral infection may present with dysuria without urinary frequency.

## Endocervical infection

The most common symptom, occurring in about 50% of individuals, is an increased or altered vaginal discharge. In about a quarter of individuals, lower abdominal pain is reported. However, pelvic and lower abdominal tenderness is an uncommon examination finding in the absence of coinfection with *C. trachomatis*. Gonorrhoea rarely causes intermenstrual bleeding and menorrhagia. On examination,

a mucopurulent endocervical discharge may be seen and easily induced endocervical bleeding may be present.

#### Rectal infection

Most cases are asymptomatic, but symptoms may include anal discharge and perianal/anal pain or discomfort. Rectal infection in cis-gender women is seen with and without a recent history of anal sex and is usually associated with urogenital infection, although isolated rectal infection also occurs.<sup>14</sup>

## Pharyngeal infection

This is predominantly asymptomatic, but some individuals may report a sore throat.<sup>15</sup>

## Complications

Transluminal spread of *N. gonorrhoeae* from the urethra or endocervix may occur and cause epididymo-orchitis, prostatitis or pelvic inflammatory disease (PID). In a study of nearly 4000 cis-gender women attending a sexual health clinic in the UK, PID was reported in approximately 14% of those with gonorrhoea.<sup>16</sup> Although gonococcal PID presents in a similar way to non-gonococcal PID, those with gonococcal PID are more often febrile and unwell.

#### Disseminated gonococcal infection

Haematogenous dissemination may occur from infected mucous membranes. Historically, this was estimated to occur in between 0.5% and 3% of people with gonorrhoea, with cis-gender women and those who are pregnant being at higher risk. Individuals with terminal complement deficiency or taking eculizumab (which inhibits terminal complement activation) may also be at higher risk.<sup>17–20</sup> Disseminated gonococcal infection (DGI) may result in severe sepsis, morbidity, and death.<sup>21–23</sup>

Two distinct clinical syndromes are classically described in DGI: a triad of tenosynovitis, polyarthralgia and dermatitis, or purulent arthritis with or without additional symptoms.<sup>17–20</sup> However, a case series in Australia of 106 people with DGI observed the classic triad in only one individual, with arthritis the predominant feature (89%), followed by fever (62%).<sup>22</sup> Arthritis affected a single joint in 38% of cases, 2–4 joints in 27% and ≥5 joints in 22%. The knee was the most commonly affected joint (55%), followed by the wrist (35%), ankle (28%), and elbow (15%). Tenosynovitis (4%) and dermatitis (9%) were infrequent. Half of the patients with confirmed DGI had negative tests for gonorrhoea at mucosal sites.

Another series of 149 cases in California between July 2020 and July 2021 found no significant associations with age, gender, or ethnicity.<sup>21</sup> Urogenital, pharyngeal,

or rectal symptoms were present in only 39% of cases. The most common manifestations were septic arthritis (53%), fever (38%), polyarthralgia (35%), bacteraemia (31%), and tenosynovitis (19%). Mucosal testing for gonorrhoea was limited, with urine samples being the most tested (76 samples), and 55% of these yielded positive results.

A number of other rare but serious clinical presentations of DGI have been reported including pericarditis,<sup>24</sup> vasculitis,<sup>25</sup> endocarditis<sup>26</sup> and meningitis.<sup>27</sup>

Reporting diagnoses of DGI is critical for surveillance. Given the variety of clinical presentations, DGI is often diagnosed in non-genitourinary medicine settings. All clinicians in England should report cases to GRASP.enquiries@ukhsa.gov.uk and to local Public Health in Wales and Scotland.

## Ocular infection

Acute gonococcal conjunctivitis can occur following inoculation with infected secretions.<sup>28</sup> Gonococcal conjunctivitis usually presents as unilateral or bilateral red eye(s) with purulent, often hyper-purulent discharge.<sup>29</sup> *N. gonorrhoeae* can penetrate intact corneal epithelium: patients are at risk of rapidly progressive corneal ulceration and thinning leading to possible perforation.<sup>30</sup> Ocular infection can be complicated by periocular inflammation and pain, severe lid oedema (pre-septal cellulitis) and orbital cellulitis. Uveitis, endophthalmitis, dacryoadenitis and symblepharon have been reported.<sup>29</sup>

## Gonorrhoea following gender-affirming surgery

A small number of cases of gonococcal infection of the neovagina following penile inversion and sigmoid vaginoplasty have been reported.<sup>31,32</sup> Where clinical symptoms were present, these included discharge, pain, and bleeding.<sup>33</sup> No reports of gonococcal infection of the neopenis were identified.

#### Diagnosis

This section should be read in conjunction with UK Health Security Agency's (UKHSA) 'Guidance for the detection of gonorrhoea in England' 2021.<sup>34</sup> The diagnosis of gonorrhoea is established by the detection of *N. gonorrhoeae* at an infected site, either by nucleic acid amplification tests (NAAT) or by culture. No test for gonorrhoea offers 100% sensitivity and specificity.<sup>34–37</sup> See Figure 1.

#### Diagnostic tests

*Microscopy*. Microscopy of gram-stained genital specimens allows direct visualisation of *N. gonorrhoeae* as monomorphic gram-negative diplococci within polymorphonuclear leukocytes.

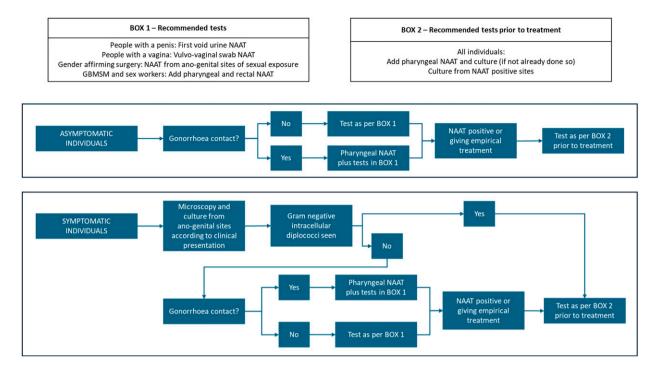


Figure 1. Algorithm for appropriate tests for diagnosing gonorrhoea.

Penile urethra

- Microscopy of urethral or meatal swab smears has good sensitivity (90–95%) in people with discharge from the penile urethra and is recommended to facilitate immediate presumptive diagnosis in these individuals (GRADE 1B).<sup>13,38,39</sup>
- Microscopy of penile urethral smears in those without symptoms is less sensitive (40–60%) therefore, it is not recommended in asymptomatic individuals (GRADE 1B).<sup>13,38</sup>

#### Endocervix

- Microscopy has only 37–50% and 20% sensitivity compared with culture for detecting gonorrhoea from endocervical and urethral smears, respectively.<sup>11</sup>
- The sensitivity of cervical microscopy compared to NAATs in a more recent study was only 16%.<sup>40</sup>
- Cervical microscopy can be considered in symptomatic individuals (GRADE 1C).

#### Rectum and pharynx

- Ano-rectal smears and microscopy can be considered if rectal symptoms are present (GRADE 1C).<sup>41</sup>
- The sensitivity of microscopy for detecting asymptomatic rectal infection is low and is not recommended (GRADE 1C).<sup>42</sup>
- Microscopy of pharyngeal specimens is not recommended due to low sensitivity and specificity (GRADE 1C).

*Nucleic acid amplification tests.* NAATs are more sensitive than culture, particularly for oropharyngeal and rectal sites.<sup>43–45</sup> NAATs show high sensitivity (>95%) in both

symptomatic and asymptomatic infection.<sup>44,46,47</sup> Most platforms show good sensitivity and specificity at detecting *N. gonorrhoeae* in the urine and rectal sites.<sup>48</sup> Although not all NAATs are licensed for use at extra-genital sites, their use is recommended.<sup>34</sup> Commercially available NAATs differ in their cross–reactivity to commensal *Neisseria* species which may be present at significant levels, particularly in the pharynx.<sup>49</sup> It is recommended that laboratories confirm any reactive test with an alternative molecular target if the positive predictive value of the initial test for the population tested is less than 90% (GRADE 1B).<sup>34,37,50</sup> This is particularly important for extra-genital specimens.<sup>48,51</sup>

#### Penile urethra

• NAATs show equivalent sensitivity in urine and urethral swab specimens although a first-pass urine is the pre-ferred sample.<sup>46,52</sup>

#### Endocervix

- Self-collected or clinician-collected vulvovaginal swabs (VVS) perform better than endocervical swabs and significantly better than urine.<sup>34,35,37,53–56</sup> VVS are therefore recommended as the optimal specimen (GRADE 1A).
- For people who have had a hysterectomy, there is no evidence on optimal sampling site. We suggest considering urine and VVS for NAAT with subsequent culture from that site if positive (GRADE 2D).

#### Rectum and pharynx

• Infection can occur at multiple anatomical sites and an individual with gonorrhoea may have more than one

strain of *N. gonorrhoeae*.<sup>57-59</sup> Rectal and pharyngeal sampling should be routine in all sex workers and in GBMSM (GRADE 1A).

- Given the low prevalence of oropharyngeal gonorrhoea in cisgender women in most settings, universal testing is unlikely to be cost-effective.<sup>60</sup>
- Among men who have sex with women who are contacts of gonorrhoea, if only urogenital testing were performed, an estimated 36% of infections would remain unidentified.<sup>61</sup> Pharyngeal sampling should therefore be routine in all sexual contacts of gonorrhoea.<sup>60,61</sup> (GRADE 1B)
- Oropharyngeal infection is more difficult to treat.<sup>62–65</sup> The previous guideline recommended pharyngeal sampling in anyone with genital gonorrhoea who was at risk of ceftriaxone-resistant infection, based on travel history. In practice this is difficult to implement, and resistance is not confined to those with a travel history. Therefore, anyone with genital gonorrhoea (regardless of travel, gender or reported sexual behaviour) should have pharyngeal sampling prior to treatment. (GRADE 1C)
- Extra-genital sampling should otherwise be performed based on an assessment of risk and symptoms in everyone else. <sup>66–68</sup>
- Although self-collected oropharyngeal swabs for NAATs have been shown to be acceptable to patients and show comparable results to clinician–collected swabs, there is a higher likelihood of invalid or equivocal results, and thus it is important to ensure patients understand step-bystep instructions on sample collection.<sup>69–73</sup>

#### Culture

- The primary role of culture is for antimicrobial susceptibility testing, which is of increasing importance as antimicrobial resistance in *N. gonorrhoeae* continues to evolve and spread.
- Specimens for culture (urethral, endocervical, neovaginal, anorectal and pharyngeal swabs) should be taken at the same time as NAATs from people suspected clinically of having gonorrhoea.<sup>34</sup>
- All individuals with gonorrhoea diagnosed by NAAT should have cultures taken from each positive site for susceptibility testing prior to treatment (GRADE 1D). There is evidence from a small study of good concordance between clinician-collected and patient-collected samples for culture from the pharynx; endocervix (clinician collected) and vagina (patient-collected); urethra (clinician-collected) and male urine (patient-collected).<sup>74</sup> More data are needed before patient-collected specimens for culture can be routinely recommended.
- For culture, the sensitivity depends on several factors including time from sample collection to plating. Services should seek to minimise this time whether by direct plating in the clinic or use of transport media with prompt transfer for plating in the laboratory.<sup>75</sup> If there is a delay in plating of more than a few hours, then swabs in non-

nutritive transportation medium (e.g. charcoal swabs) should be refrigerated.

#### Specimen pooling

- Pooling of self-collected or clinician-collected rectal, pharyngeal and urine samples from the same individual could provide cost savings. There is a small evidence base with mixed results using different testing platforms, specimen collection and pooling methods.
- The largest study to date has shown that pooling of selftaken swabs has lower sensitivity for detection of *N*. *gonorrhoeae* from pharyngeal sites, when compared with single site testing.<sup>76</sup>
- A recent meta-analysis showed that pooled threeanatomic site testing performed similarly to single anatomic site testing with positive percentage agreements of 93.8% and negative percentage agreements of 99.7%.<sup>77</sup> However, further studies have indicated mixed results. Therefore, we recommend that any service considering the implementation of pooling should perform appropriate clinical evaluation prior to local implementation.

#### Diagnosing DGI and ocular infections

- If DGI is suspected, specimens should be taken from disseminated sites of infection (e.g. synovial fluid) for both culture and NAAT. Blood cultures should be taken from all suspected cases. Laboratories in England should refer isolates from DGI to the UKHSA Sexually Transmitted Reference Laboratory (STIRL). In Wales, isolates should be sent to the Specialist Antimicrobial Chemotherapy Unit, Public Health Wales, Cardiff. In Scotland, all isolates should be sent to the Scottish Bacterial STI Reference Laboratory, Edinburgh. Additionally, specimens should be taken from urogenital and extragenital sites for culture and NAAT (GRADE 1C).
- In suspected gonococcal conjunctivitis, conjunctival swabs should be taken and processed urgently for both culture and NAAT. Although NAATs are not licensed for eye swabs, their use is recommended (GRADE 1C).

**Point-of-care and near-patient tests.** A number of assays have been developed as point-of-care or near-patient tests which have shown high accuracy in detecting *N. gonorrhoeae* from urogenital and rectal sites (96–100% sensitivity, 99% specificity); however, the specificity for pharyngeal samples remains low.<sup>78–80</sup> As these assays become more readily available, it is recommended that local validation is conducted prior to implementation in local departments.

Detecting AMR markers. Commercially available assays have been developed with good sensitivity in detecting genetic markers of resistance to fluoroquinolones<sup>81,82</sup> and can be considered depending on local need. However, it is noted that the Medicines and Healthcare products Regulatory Agency (MHRA) recently recommended against the

use of fluoroquinolones unless there is no alternative (see Treatment section). Testing for mosaic *penA* mutants may predict cephalosporin susceptibility, but these tests are not yet commercially available.<sup>83</sup>

#### Considerations for people following gender-affirming surgery

- The susceptibility of a site to gonococcal infection is likely to be related to the nature of the surgery, with sites constructed from mucosal tissue (e.g., from the vaginal or bowel mucosa) being more susceptible than sites constructed from skin.
- Gonococcal infections of the urethra,<sup>84</sup> sigmoid neovagina<sup>33</sup> and penile skin-lined neovagina<sup>32</sup> have all been reported following gender affirming surgery. Gonococcal infections of the neopenis have not been reported.
- Although the sensitivity of microscopy for infection of the neovagina and neopenis is not known, this may facilitate a presumptive diagnosis of gonorrhoea and could be considered (GRADE 1D).
- We recommend that optimal genital testing in individuals with a neovagina at risk of gonorrhoea should include swabs for NAAT and culture from the neovagina and first -pass urine (GRADE 1D).
- We recommend first -pass urine as the specimen of choice from individuals with a neopenis (GRADE 1D). Where the vagina is still present following gender affirming surgery, a vaginal swab should be considered as directed by the sexual history and symptoms.
- Extragenital testing should be guided by sexual history and symptoms.
- Self-collected sampling has been shown to be highly acceptable and has comparable results to clinician-taken sampling in individuals with a neovagina.<sup>85</sup>

## Testing for other STIs

Approximately 21% of individuals with gonorrhoea have concurrent *C. trachomatis* infection.<sup>7</sup> Testing for other STIs should be undertaken according to BASHH STI testing guidelines.

## Timing of testing

Infection cannot be ruled out in individuals who test within 2 weeks of sexual contact with an individual with gonorrhoea. Therefore, it is recommended that contacts return for repeat testing after this window period if epidemiological treatment is not given (GRADE 1D).

## Management

## General advice

Individuals should be given a detailed explanation of their condition with particular emphasis on the implications for the health of themselves and their partner(s). This should be reinforced, if necessary, with clear and accurate written information (GRADE 1D). Individuals should be advised to abstain from sexual intercourse until 7 days after they and their partner(s) have completed treatment (GRADE 1D).

### Treatment

## Indications for therapy

It is recommended to confirm the presence of *N. gonor-rhoeae* before treatment using the following indications:

- Identification of intracellular gram-negative diplococci on microscopy;
- A positive culture for *N. gonorrhoeae*;
- A confirmed positive NAAT for N. gonorrhoeae.

Treatment of sexual contacts of a person with confirmed gonococcal infection is not routinely recommended, except in some specific circumstances (See Treatment of Contacts).

## Treatment of uncomplicated ano-genital and pharyngeal infections in adults

• Ceftriaxone 1 g intramuscularly (IM) as a single dose (GRADE 1B).<sup>86–90</sup>

Ceftriaxone remains highly effective. Most gonococcal infections with ceftriaxone resistance are still cleared with ceftriaxone 1 g.<sup>9,10</sup> There have been very few treatment failures reported, all associated with extra-genital (usually pharyngeal) infection.<sup>62,63,91</sup>

#### Alternative regimens

Alternative regimens may be given because of allergy, needle phobia or other absolute or relative contraindications. In people with penicillin allergy there is ample evidence to allow the safe use of all but a few early generation cephalosporins (e.g., cephalexin, cefaclor and cefadroxil). Third generation cephalosporins such as cefixime and ceftriaxone show negligible cross-allergy with penicillin.<sup>92,93</sup>

Therefore, in penicillin-allergic people, ceftriaxone and cefixime are suitable treatment options, unless there is a history of severe hypersensitivity (e.g., anaphylactic reaction) to any beta-lactam antibacterial agent (penicillins, cephalosporins, monobactams and carbapenems).

Spectinomycin has been removed as an option in this guideline, as it is no longer available in the UK.

Azithromycin 2 g dose is associated with gastrointestinal side effects; to reduce these, azithromycin may be given as divided doses, with 1 g followed by another 1 g dose 6-12 h later.<sup>94</sup>

- Cefixime 400 mg orally followed by another 400 mg dose 6–12 h later; plus azithromycin 2 g orally (which may be divided as two 1 g doses 6–12 h apart) should also be given (GRADE 1B):
- a. Only advisable if an IM injection is contraindicated and antimicrobial susceptibility results are available;
- b. The dose has been increased from 400 mg as a single dose in the 2018 guideline, due to an increase in the proportion of isolates with reduced cephalosporin susceptibility.<sup>7</sup> In general, the clinical efficacy of betalactam antibiotics relates to the period of time for which the free drug concentration exceeds the minimum inhibitory concentration (MIC) which is best achieved by giving a second dose rather than a higher single dose.<sup>95,96</sup> Ideally cefixime doses should be given 6–8 h apart, and no later than 12 h. If the second dose of cefixime is not taken within 12 h of the first dose, then there is no benefit in taking it at a later time or restarting treatment.
- c. Cefixime has been associated with treatment failure when used as monotherapy for pharyngeal infection, <sup>97–101</sup> therefore it is recommended to use dual therapy with azithromycin where possible.
- Gentamicin 240 mg IM as a single dose plus azithromycin 2 g orally (GRADE 1A):
- a. In one randomised clinical trial (RCT) gentamicin 240 mg IM in combination with azithromycin 1 g cured 94% of urogenital, 90% of rectal and 80% of pharyngeal infections,<sup>102</sup> and another trial using gentamicin 240 mg IM with azithromycin 2 g reported 100% clearance for all sites of infection<sup>103</sup>;
- b. An RCT using gentamicin 5 mg/kg IM monotherapy found 93% cure for anogenital infection but only 26% cure for pharyngeal infection,<sup>88</sup> while another study examining the effectiveness of gentamicin 360 mg IM as monotherapy for treating pharyngeal gonorrhoea was stopped early due to poor efficacy (2/10 cured).<sup>104</sup>
- Azithromycin 2 g as a single oral dose (GRADE 1B):
- a. The clinical efficacy of azithromycin does not always correlate with in vitro susceptibility testing<sup>105,106</sup> and azithromycin resistance is too high for empirical use.
- Ciprofloxacin 500 mg orally as a single dose (GRADE 1B).<sup>107</sup>

In the 2018 guideline, ciprofloxacin was recommended as first line therapy if phenotypic or genotypic antimicrobial susceptibility data indicated susceptibility to ciprofloxacin. The rationale for this was that using alternative antibiotics can reduce the selective pressure which comes from the universal use of ceftriaxone, and this may delay the emergence of ceftriaxone resistance.<sup>108,109</sup>

In 2018 the European Medicines Agency issued an alert following their review of serious side effects associated with the use of fluoroquinolone antibiotics. These include side effects involving muscles, tendons, joints, and the nervous system. It was advised that ciprofloxacin should be avoided in people who have previously had serious side effects with a quinolone antibiotic and used with caution in those over the age of 60 years, those taking a corticosteroid, people with kidney disease and those who have had an organ transplantation. However, following a review (https://www. gov.uk/drug-safety-update/fluoroquinolone-antibiotics-mustnow-only-be-prescribed-when-other-commonly-recommendedantibiotics-are-inappropriate), the MHRA updated this recommendation to state that quinolones should only be used when other antibiotics are inappropriate. Therefore, although known to be an effective treatment when susceptibility data are present, ciprofloxacin is no longer recommended as a first line treatment but may be used if clinically judged appropriate.

#### Treatment of complicated infections

#### Gonococcal pelvic inflammatory disease

• Ceftriaxone 1 g IM as a single dose in addition to the regimen chosen to treat PID. For details, please see BASHH PID guideline.

#### Gonococcal epididymo-orchitis

 Ceftriaxone 1 g IM as a single dose in addition to the regimen chosen to treat epididymo-orchitis. For details, please see BASHH epididymo-orchitis guideline.

**Gonococcal ocular infection.** Gonococcal conjunctivitis may rapidly progress to a potentially blinding keratoconjunctivitis; prompt diagnosis and treatment are essential to reduce the risk of vision loss.<sup>29,110–112</sup> If gonococcal eye infection is suspected, empiric systemic and topical treatment is advised. There are no recent clinical trials on the management of gonococcal conjunctivitis.

Joint management by ophthalmologists and sexual health clinicians is essential and patients should be referred urgently to Ophthalmology and followed closely until resolution of symptoms. Contact lens wearers are advised to stop use until all symptoms are fully resolved.

- Ceftriaxone 1 g IM as a single dose (GRADE 1D):
- a. There is a single study of the treatment of gonococcal conjunctivitis conducted in 12 adults.<sup>113</sup> All were successfully treated with a single dose of ceftriaxone.
- b. In patients with a history of severe hypersensitivity to any beta-lactam antibacterial agent, the alternative systemic regimens outlined above (11.3) should be followed.
- Adjunctive cefuroxime 5% eye drops (GRADE 2D):
- a. Hourly day and night for 48 hours then hourly daytime only for 5 days. Maintain four times daily (QDS) until complete resolution;
- b. In patients with history of severe hypersensitivity to any beta-lactam antibacterial agent, topical azithromycin

hourly day and night for 48 h then hourly daytime only for 5 days is advised. Maintain QDS until complete resolution;

- c. Given the high proportion of patients that develop corneal complications (27–56%) and the potential for irreversible vision loss if they occur, intensive topical antibiotic treatment should be given even in the absence of corneal involvement.
- d. Due to the high prevalence of quinolone resistance, topical quinolones (e.g., moxifloxacin, levofloxacin) should not be used empirically in the management of gonococcal eye disease unless confirmed as susceptible.

Consider additional lavage of the infected eye with saline solution (NaCl 0.9%) if copious discharge is present.

If pre-septal or orbital cellulitis is suspected, IV treatment may be required.

#### Disseminated gonococcal infection

• Ceftriaxone 1 g IM or IV every 24 h (GRADE 1D).

The length of treatment should be determined based on the clinical presentation and response to treatment, and in conjunction with an infection specialist. There are no recent clinical trials of the management of DGI.

For arthritis and arthritis-dermatitis syndrome, therapy should continue for 7 days but may be switched 24– 48 h after symptoms improve to oral cefixime 800 mg twice daily or ciprofloxacin 500 mg twice daily if the isolate is susceptible (note warning above for fluoroquinolones).

For gonococcal meningitis and endocarditis, parenteral therapy with ceftriaxone 1–2 g IV every 12–24 h should be continued for 10–14 days for meningitis and at least 4 weeks for endocarditis.

## Management of ceftriaxone treatment failures

The case definition for treatment failure is adapted from the 2019 European Centre for Disease Prevention and Control Response Plan to control drug resistant gonorrhoea in Europe (See Box 1 below).<sup>114</sup> All cases of probable or confirmed treatment failure in England should be reported to UKHSA via the HIV and STI Data Exchange (https://hivstidataexchange.ukhsa.gov.uk/hivstide), in Wales should be reported to Public Health Wales, in Scotland should be reported to Public Health Scotland at phs.bbvsti@phs.scot, and in Northern Ireland should follow locally agreed pathways with the Public Health Agency.

NAAT-positive specimens two weeks after treatment can be due to persistent nucleic acid (DNA or RNA) and in these cases, a repeat NAAT one week later should be taken, and further treatment considered only if repeatedly positive. Individuals with suspected reinfection should be re-treated with ceftriaxone 1 g IM. Box I. Definition for ceftriaxone treatment failure.

p or al e	Probable case: Points I to 3.	<ol> <li>A person who returns for test of cure or who has persistent symptoms after having received treatment for laboratory confirmed - gonorrhoea with ceftriaxone I g IM. and</li> </ol>
	Confirmed case:	2. Remains positive for one of the
e,	Points I to 4.	following tests:
1)		<ul> <li>Isolation of N. gonorrhoeae by culture</li> </ul>
of		taken at least 72 hours after
e.		completion of treatment;
		or
e		• Positive NAAT taken 2–3 weeks
		after completion of treatment
ıt		<ol> <li>Reinfection is excluded as far as feasible.</li> </ol>
		4. Resistance to ceftriaxone
		(MIC >0.125 mg/L) as confirmed by
		the national reference laboratory.

Most individuals with ceftriaxone-resistant infection will still clear infection with ceftriaxone 1 g IM.<sup>9,10,115</sup> For individuals with confirmed treatment failure due to ceftriaxone resistance, repeat culture and NAAT specimens should be taken from both genital and pharyngeal sites. In England ceftriaxone resistant isolates (or residual positive NAAT specimens if isolates are not available) should be sent to the STIRL, UKHSA Colindale. In Wales and Scotland, isolates should be sent to the devolved region national Public Health laboratory.

Treatment options are limited and should be guided by the results of antimicrobial susceptibility testing where possible, and in conjunction with expert advice. Isolates with ceftriaxone resistance are usually also resistant to most other antimicrobials. Often these multi-drug resistant (MDR) isolates have low gentamicin MICs, however gentamicin has a high failure rate in treating pharyngeal infections.<sup>88,104</sup> Ertapenem and ceftriaxone MICs are usually similar, but for some isolates with raised ceftriaxone MICs, the ertapenem MIC is lower.<sup>116,117</sup> However, this is not universal, particularly in the presence of a penA mosaic allele, and ertapenem MIC testing should be performed.<sup>118</sup> Some infections with MDR N. gonorrhoeae have been successfully treated with ertapenem when ceftriaxone has failed<sup>62,91</sup>; three days of IV ertapenem 1 g was used for these cases, although this was a pragmatic choice and not guided by clinical trial data. In a recent RCT, a single 1 g dose of ertapenem IM was noninferior to ceftriaxone 500 mg IM, although all strains were susceptible to ceftriaxone and had low ertapenem MICs.88

It is recommended to contact the Consultant Microbiologist at UKHSA for treatment advice by emailing GRASP.Enquiries@ukhsa.gov.uk.

See also UKHSA guidance on managing incidents of ceftriaxone-resistant *N. gonorrhoeae* in England: https://www.gov.uk/government/publications/ceftriaxone-resistant-neisseria-gonorrhoeae-incident-management, and specific guidance for Scotland: https://www.publichealthscotland. scot/publications/managing-incidents-of-ceftriaxone-resistant-neisseria-gonorrhoeae/.

## Pregnancy and breast/chest feeding

Pregnancy does not diminish treatment efficacy.<sup>119–121</sup> Pregnant and breast/chest-feeding individuals should not be treated with quinolones. Gentamicin should be avoided in pregnancy.

The manufacturer of azithromycin advises use only if adequate alternatives are not available. In addition, azithromycin should only be used if the isolate is known to be susceptible.

## People living with HIV

Individuals living with human immunodeficiency virus (HIV) should be managed in the same way as HIV-negative individuals.

#### Chlamydia trachomatis coinfection

- Treatment for confirmed or suspected chlamydia coinfection should follow the current BASHH guideline for the management of chlamydia.
- If an individual has already received azithromycin 2 g for the treatment of gonorrhoea, then this should be sufficient to treat chlamydia and no further chlamydia treatment is required.

#### Adjunctive therapies

In clinical trials, antiseptic mouthwash was not effective in either preventing or treating pharyngeal gonorrhoea in GBMSM.<sup>122–124</sup>

## Follow-up

Test of cure (TOC) practice should be underpinned by confidence in the effectiveness of treatment regimens, including rates of treatment failure and resistance to recommended regimens.

There have been no reported cases of treatment failure when ceftriaxone has been used to treat a ceftriaxonesusceptible genital infection. When antimicrobial susceptibility is known, routine TOC is not necessary for individuals with anogenital infection who have received ceftriaxone 1 g IM (GRADE 2D).

Routine TOC remains recommended for the following people:

- (1) With persistent symptoms or signs;
- (2) With pharyngeal infection;
- (3) Antimicrobial susceptibility is unknown;
- (4) Treated with anything other than ceftriaxone; and
- (5) Who are pregnant.

Assessment after treatment may be helpful to detect treatment failure and emerging resistance, confirm adherence to treatment, ensure resolution of symptoms, explore the possibility of reinfection, and confirm partner notification and health promotion.

## Method and timing of test-of-cure

A positive TOC could be due to treatment failure, reinfection or residual non-viable organism and should be interpreted in the clinical context. Where TOC is considered, we recommend the following approach:

- Culture, performed at least 72 h after completion of therapy, should be used if symptoms or signs are present at time of TOC<sup>125</sup>;
- NAAT should be used if asymptomatic, followed by culture if NAAT-positive.

The time to a negative TOC using NAATs is variable and there are limited studies, all in GBMSM. When an RNA NAAT is used, most individuals with anogenital infection should be negative 7 days following treatment,<sup>126</sup> whilst those with pharyngeal infection should be negative 12 days following treatment.<sup>127</sup> When using a DNA NAAT, most individuals with anogenital infection should be negative 14 days following treatment.<sup>126</sup>

• We recommend TOC using NAAT should be performed at least two weeks after treatment (GRADE 1B).

### Tracing and treatment of contacts

Contact tracing for specific STIs should be performed according to BASHH guidelines (https://www.bashh.org/ guidelines), with reference to look-back periods. People should be informed of the importance of partner notification and supported to do this by appropriately trained professionals.

Partner notification should be pursued in all people identified with gonococcal infection. There are limited data on look-back periods when attempting to ascertain sexual partners potentially at risk of infection. The following partners should be notified, if possible:

- All partners since, and in the 2 weeks (or the last partner if longer than 2 weeks ago) preceding the onset of symptoms in individuals with symptomatic penile urethral infection;
- All partners in the preceding 3 months of individuals with infection at other sites or asymptomatic infection.

## Treatment of contacts

Epidemiological treatment is not needed for all sexual contacts, and ideally treatment should only be given to those partners who test positive for gonorrhoea. All contacts should have pharyngeal testing (see Section 9). However, an infection may be missed if a test is performed too soon after a potential exposure. The time between exposure and a positive test result may vary depending on a number of host, pathogen and diagnostic factors. There is a lack of evidence to support recommendations for the optimal time for testing. Therefore, in order to reduce the unnecessary use of antibiotics, we recommend the following as a pragmatic approach:

- For those presenting after 14 days of exposure we recommend treatment only following a positive test for gonorrhoea<sup>128</sup>;
- For those presenting within 14 days of exposure we recommend considering epidemiological treatment based on a clinical and psychosocial risk assessment and following a discussion with the individual. In particular, the following individuals should be considered for epidemiological treatment:
- a. Individuals who are pregnant;
- b. Contacts of individuals who are pregnant;
- c. Individuals living in geographically remote regions with limited access to clinics;
- d. Individuals experiencing psychosocial barriers which include but are not limited to those who: are homeless, sell sex, are experiencing mental ill-health, misuse substances, are employed on zero-hour contracts, are unable to access childcare or are currently victims or survivors of domestic abuse.

For all other individuals and asymptomatic individuals, it may be appropriate to not give epidemiological treatment, and to repeat testing 2 weeks after exposure.

# Management of contacts using doxycycline as post-exposure prophylaxis

The use of doxycycline as prophylaxis is unlikely to be effective in preventing gonorrhoea infection due to high rates of tetracycline resistance in *N. gonorrhoeae*.<sup>129</sup> Consequently, contacts of gonorrhoea using doxycycline post-exposure prophylaxis (doxyPEP) should be managed in the same way to those not using doxyPEP.

## Auditable outcome measures

- All individuals with gonorrhoea should have cultures taken for susceptibility testing prior to treatment (performance standard 97%).
- All individuals treated for gonorrhoea and requiring a test of cure according to criteria in this guideline are offered a test of cure (performance standard 97%).

- Individuals diagnosed with gonorrhoea should be tested for chlamydia, syphilis, and HIV (unless previously diagnosed with HIV) (performance standard 97%).
- Individuals diagnosed with gonorrhoea should have partner notification carried out in accordance with the BASHH statement on partner notification (performance standard 97%).
- Individuals diagnosed with gonorrhoea should be offered information (written or digital) about their diagnosis and management (performance standard 97%).
- Individuals diagnosed with gonorrhoea should receive first-line treatment or the reasons for not doing so documented (performance standard 97%).
- Cases of possible treatment failures with ceftriaxone should be reported to UKHSA (performance standard 97%).

## **Qualifying statement**

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on professional clinical judgement, consideration of individual circumstances and available resources.

All possible care has been undertaken to ensure specification of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

## **Review** arrangements

An author group will be invited by the BASHH CEG to review and revise the guideline in 2029 using the BASHH framework for guideline development. However, addenda may be issued sooner than 2029, particularly if relevant new data are available relating to testing or treatment options.

#### Acknowledgements

This guideline is dedicated to our wonderful colleague and coauthor, Professor Nick Medland who died in February 2025. Nick played a pivotal role in the development of several BASHH guidelines and we will miss him deeply. We thank members of the BASHH CEG, BASHH National Audit Group, UKHSA GRASP Advisory Group, BASHH Public Panel and BASHH Gender & Sexual Minority Special Interest Group for their valuable contributions to this guideline, and Gökçe Ayan (Veristat) who provided project management. We would also like to thank everyone who provided comments as part of the consultation process.

#### **Declaration of conflicting interests**

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All members of the guideline writing committee completed the BASHH conflict of interest declaration and submitted it to the CEG. No authors had any relevant conflicts of interest to declare, and the content of the guideline is not attributed to any organisation they are associated with.

#### Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

#### **ORCID** iDs

Helen Fifer b https://orcid.org/0000-0001-7756-403X Muhammad Azam Ismail b https://orcid.org/0000-0002-1450-2568

Suneeta Soni b https://orcid.org/0000-0002-8957-8233 Uzochi Nwaosu b https://orcid.org/0000-0002-5500-379X

#### References

- Migchelsen SJ, Edney J, O'Brien N, et al. Sexually transmitted infections and screening for chlamydia in England, 2023. London: UK Health Security Agency, 2024.
- Handsfield HH. Gonorrhea and uncomplicated gonococcal infection. In: Holmes KK, Mardh PA, Sparling PF, et al. (eds). *Sexually transmitted diseases*. New York: McGraw– Hill Co, 1984, pp. 205–219.
- 3. Charleson F, Tran J, Kolobaric A, et al. A systematic review of kissing as a risk factor for oropharyngeal gonorrhea or chlamydia. *Sex Transm Dis* 2023; 50(7): 395–401.
- Chow EPF, Cornelisse VJ, Read TRH, et al. Saliva use as a lubricant for anal sex is a risk factor for rectal gonorrhoea among men who have sex with men, a new public health message: a cross-sectional survey. *Sex Transm Infect* 2016; 92(7): 532–536.
- Unemo M, Lahra MM, Escher M, et al. WHO global antimicrobial resistance surveillance for *Neisseria gonorrhoeae* 2017-18: a retrospective observational study. *Lancet Microbe* 2021; 2(11): e627–e636.
- Lahra MM, Martin I, Demczuk W, et al. Cooperative recognition of internationally disseminated ceftriaxone-resistant *Neisseria gonorrhoeae* strain. *Emerg Infect Dis* 2018; 24(4): 735–740.
- 7. UKHSA. GRASP report: data to August 2024: UK Health Security Agency, 2024.
- Ouk V, Pham CD, Wi T, et al. The enhanced gonococcal surveillance programme, Cambodia. *Lancet Infect Dis* 2023; 23(9): e332–e333.
- Day M, Pitt R, Mody N, et al. Detection of 10 cases of ceftriaxone-resistant *Neisseria gonorrhoeae* in the United Kingdom, december 2021 to June 2022. *Euro Surveill* 2022; 27(46): 2200803.
- Fifer H, Doumith M, Rubinstein L, et al. Ceftriaxoneresistant Neisseria gonorrhoeae detected in England, 2015-24: an observational analysis. *J Antimicrob Chemother* 2024; 79: 3332–3339.
- Barlow D and Phillips I. Gonorrhoea in women. Diagnostic, clinical, and laboratory aspects. *Lancet* 1978; 1(8067): 761–764.
- 12. Lewis DA, Bond M, Butt KD, et al. 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(9): 588–594.

- Sherrard J and Barlow D. Gonorrhoea in men: clinical and diagnostic aspects. *Genitourin Med* 1996; 72(6): 422–426.
- Lau A, Kong FYS, Huston W, et al. Factors associated with anorectal Chlamydia trachomatis or Neisseria gonorrhoeae test positivity in women: a systematic review and metaanalysis. Sex Transm Infect 2019; 95(5): 361–367.
- Richardson D, Pickering A, Trotman D, et al. Pharyngeal gonorrhoea in men who have sex with men. *Int J STD AIDS* 2021; 32(5): 449–452.
- 16. Morris GC, Stewart CM, Schoeman SA, et al. A crosssectional study showing differences in the clinical diagnosis of pelvic inflammatory disease according to the experience of clinicians: implications for training and audit. *Sex Transm Infect* 2014; 90(6): 445–451.
- Bleich AT, Sheffield JS, Wendel GD Jr., et al. Disseminated gonococcal infection in women. *Obstet Gynecol* 2012; 119(3): 597–602.
- Lee MH, Byun J, Jung M, et al. Disseminated gonococcal infection presenting as bacteremia and liver abscesses in a healthy adult. *Infect Chemother* 2015; 47(1): 60–63.
- Rice PA. Gonococcal arthritis (disseminated gonococcal infection). Infect Dis Clin North Am 2005; 19(4): 853–861.
- Workowski KA and Bolan GA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015; 64(RR-03): 1–137.
- Tang EC, Johnson KA, Alvarado L, et al. Characterizing the rise of disseminated gonococcal infections in California, July 2020-July 2021. *Clin Infect Dis* 2023; 76(2): 194–200.
- 22. Moussiegt A, François C, Belmonte O, et al. Gonococcal arthritis: case series of 58 hospital cases. *Clin Rheumatol* 2022; 41(9): 2855–2862.
- Birrell JM, Gunathilake M, Singleton S, et al. Characteristics and impact of disseminated gonococcal infection in the "Top End" of Australia. *Am J Trop Med Hyg* 2019; 101(4): 753–760.
- Bristowe H, Day M, Fifer H, et al. Gonococcal pericarditis with tamponade - use of molecular technology to improve diagnosis and management. *Int J Infect Dis* 2023; 134: 150–152.
- Jain S, Win HN, Chalam V, et al. Disseminated gonococcal infection presenting as vasculitis: a case report. *J Clin Pathol* 2007; 60(1): 90–91.
- Belkacem A, Caumes E, Ouanich J, et al. Changing patterns of disseminated gonococcal infection in France: crosssectional data 2009-2011. *Sex Transm Infect* 2013; 89(8): 613–615.
- Edwards JL and Apicella MA. The molecular mechanisms used by *Neisseria gonorrhoeae* to initiate infection differ between men and women. *Clin Microbiol Rev* 2004; 17(4): 965–981.
- Belga S, Gratrix J, Smyczek P, et al. Gonococcal conjunctivitis in adults: case report and retrospective review of cases in Alberta, Canada, 2000-2016. *Sex Transm Dis* 2019; 46(1): 47–51.
- Cuesta Chasco G, Carreras-Castaner X, Zboromyrska Y, et al. Adult gonococcal conjunctivitis: prevalence, clinical features and complications. *J Med Microbiol* 2021; 70(9). doi:10.1099/jmm.0.001416.

- Kawashima M, Kawakita T, Den S, et al. Surgical management of corneal perforation secondary to gonococcal keratoconjunctivitis. *Eye (Lond)* 2009; 23(2): 339–344.
- Badash A, Grennan D and Albrecht J. Sexually transmitted diseases and HIV in transgender patients. *Clin Dermatol* 2024; 42(2): 180–191.
- Bodsworth NJ, Price R and Davies SC. Gonococcal infection of the neovagina in a male-to-female transsexual. *Sex Transm Dis* 1994; 21(4): 211–212.
- Van der Sluis WB, Bouman MB, Gijs L, et al. Gonorrhoea of the sigmoid neovagina in a male-to-female transgender. *Int J STD AIDS* 2015; 26(8): 595–598.
- 34. PHE. Guidance for the detection of gonorrhoea in England: Public Health England, 2021.
- Cook RL, Hutchison SL, Østergaard L, et al. Systematic review: noninvasive testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Ann Intern Med 2005; 142(11): 914–925.
- Van Dyck E, Ieven M, Pattyn S, et al. Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by enzyme immunoassay, culture, and three nucleic acid amplification tests. *J Clin Microbiol* 2001; 39(5): 1751–1756.
- Whiley DM, Garland SM, Harnett G, et al. Exploring 'best practice' for nucleic acid detection of *Neisseria gonorrhoeae*. Sex Health 2008; 5(1): 17–23.
- Mallik A, Das N, Mukherjee S, et al. A systematic review and meta-analysis of different diagnostic procedures to detect gonococcus infection in resource-limited scenario. *Indian J Med Microbiol* 2020; 38(3 & 4): 299–306.
- Mensforth S, Thorley N and Radcliffe K. Auditing the use and assessing the clinical utility of microscopy as a point-ofcare test for *Neisseria gonorrhoeae* in a sexual health clinic. *Int J STD AIDS* 2018; 29(2): 157–163.
- 40. Thorley N and Radcliffe K. The performance and clinical utility of cervical microscopy for the diagnosis of gonorrhoea in women in the era of the NAAT. *Int J STD AIDS* 2015; 26(9): 656–660.
- Grover D, Prime KP, Prince MV, et al. Rectal gonorrhoea in men – is microscopy still a useful tool? *Int J STD AIDS* 2006; 17(4): 277–279.
- Forni J, Miles K and Hamill M. Microscopy detection of rectal gonorrhoea in asymptomatic men. *Int J STD AIDS* 2009; 20(11): 797–798.
- 43. Cornelisse VJ, Chow EP, Huffam S, et al. Increased detection of pharyngeal and rectal gonorrhea in men who have sex with men after transition from culture to nucleic acid amplification testing. *Sex Transm Dis* 2017; 44(2): 114–117.
- 44. Gaydos CA, Van Der Pol B, Jett-Goheen M, et al. Performance of the Cepheid CT/NG Xpert rapid PCR test for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae. J Clin Microbiol* 2013; 51(6): 1666–1672.
- 45. Levy V, Blackmore CS and Klausner JD. Self-collection of specimens for nucleic acid-based diagnosis of pharyngeal, cervicovaginal, urethral, and rectal *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections. *Methods Mol Biol* 2012; 903: 407–418.
- 46. Geelen TH, Rossen JW, Beerens AM, et al. Performance of cobas(R) 4800 and m2000 real-time assays for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in rectal

and self-collected vaginal specimen. *Diagn Microbiol Infect Dis* 2013; 77(2): 101–105.

- 47. Van Der Pol B, Hook EW 3rd, Williams JA, et al. Performance of the BD CTQx and GCQx amplified assays on the BD Viper LT compared with the BD Viper XTR system. *Sex Transm Dis* 2015; 42(9): 521–523.
- 48. Footman A, Dionne-Odom J, Aaron KJ, et al. Performance of 4 molecular assays for detection of chlamydia and gonorrhea in a sample of human immunodeficiency virus-positive men who have sex with men. *Sex Transm Dis* 2020; 47(3): 158–161.
- Palmer HM, Mallinson H, Wood RL, et al. Evaluation of the specificities of five DNA amplification methods for the detection of *Neisseria gonorrhoeae*. J Clin Microbiol 2003; 41(2): 835–837.
- 50. Pope CF, Hay P, Alexander S, et al. Positive predictive value of the Becton Dickinson VIPER system and the ProbeTec GC Q x assay, in extracted mode, for detection of *Neisseria* gonorrhoeae. Sex Transm Infect 2010; 86(6): 465–469.
- Doernberg SB, Komarow L, Tran TTT, et al. Simultaneous evaluation of diagnostic assays for pharyngeal and rectal *Neisseria gonorrhoeae* and *Chlamydia trachomatis* using a master protocol. *Clin Infect Dis* 2020; 71(9): 2314–2322.
- 52. Chernesky MA, Martin DH, Hook EW, 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(1): 127–131.
- Aaron KJ, Griner S, Footman A, et al. Vaginal swab vs urine for detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*: a meta-analysis. *Ann Fam Med* 2023; 21(2): 172–179.
- 54. Schachter J, Chernesky MA, Willis DE, 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 Transm Dis* 2005; 32(12): 725–728.
- 55. Stewart CM, Schoeman SA, Booth RA, et al. Assessment of self taken swabs versus clinician taken swab cultures for diagnosing gonorrhoea in women: single centre, diagnostic accuracy study. *BMJ*2012; 345: e8107.
- 56. Van Der Pol B, Taylor SN, Liesenfeld O, et al. Vaginal swabs are the optimal specimen for detection of genital *Chlamydia trachomatis* or *Neisseria gonorrhoeae* using the Cobas 4800 CT/NG test. *Sex Transm Dis* 2013; 40(3): 247–250.
- Benn PD, Rooney G, Carder C, et al. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infection and the sexual behaviour of men who have sex with men. *Sex Transm Infect* 2007; 83(2): 106–112.
- Lavelle SJ, Jones KE, Mallinson H, et al. Finding, confirming, and managing gonorrhoea in a population screened for chlamydia using the Gen-Probe Aptima Combo2 assay. *Sex Transm Infect* 2006; 82(3): 221–224.
- Pond MJ, Hall CL, Miari VF, et al. Accurate detection of Neisseria gonorrhoeae ciprofloxacin susceptibility directly from genital and extragenital clinical samples: towards genotype-guided antimicrobial therapy. J Antimicrob Chemother 2016; 71(4): 897–902.
- 60. van Liere G, Dukers-Muijrers N, Kuizenga-Wessel S, et al. Routine universal testing versus selective or incidental

testing for oropharyngeal *Neisseria gonorrhoeae* in women in The Netherlands: a retrospective cohort study. *Lancet Infect Dis* 2021; 21(6): 858–867.

- McLaughlin SE, Golden MR, Soge OO, et al. Pharyngeal gonorrhea in heterosexual male and female sex partners of persons with gonorrhea. *Sex Transm Dis* 2023; 50(4): 203–208.
- 62. Eyre DW, Sanderson ND, Lord E, et al. Gonorrhoea treatment failure caused by a *Neisseria gonorrhoeae* strain with combined ceftriaxone and high-level azithromycin resistance, England, February 2018. *Euro Surveill* 2018; 23(27): 1800323.
- Fifer H, Natarajan U, Jones L, et al. Failure of dual antimicrobial therapy in treatment of gonorrhea. *N Engl J Med* 2016; 374(25): 2504–2506.
- Moran JS. Treating uncomplicated *Neisseria gonorrhoeae* infections: is the anatomic site of infection important? *Sex Transm Dis* 1995; 22(1): 39–47.
- Moran JS and Levine WC. Drugs of choice for the treatment of uncomplicated gonococcal infections. *Clin Infect Dis* 1995; 20(Suppl 1): S47–S65.
- 66. Huxta RA, Soniyi O, Halbritter A, et al. Extragenital screening of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* among women in the college health setting. Sex *Transm Dis* 2021; 48(9): 643–647.
- 67. van Liere G, Dukers-Muijrers N, Levels L, et al. High proportion of anorectal *Chlamydia trachomatis* and *Neisseria gonorrhoeae* after routine universal urogenital and anorectal screening in women visiting the sexually transmitted infection clinic. *Clin Infect Dis* 2017; 64(12): 1705–1710.
- 68. van Liere G, Hoebe CJ, Niekamp AM, et al. Standard symptom- and sexual history-based testing misses anorectal *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections in swingers and men who have sex with men. *Sex Transm Dis* 2013; 40(4): 285–289.
- Chow EPF, Bradshaw CS, Williamson DA, et al. Changing from Clinician-collected to self-collected throat swabs for oropharyngeal gonorrhea and chlamydia screening among men who have sex with men. *J Clin Microbiol* 2020; 58(9): e01215.
- Dangerfield Ii DT, Farley JE, Holden J, et al. Acceptability of self-collecting oropharyngeal swabs for sexually transmissible infection testing among men and women. *Sex Health* 2019; 16(3): 296–298.
- Freeman AH, Bernstein KT, Kohn RP, et al. Evaluation of self-collected versus clinician-collected swabs for the detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* pharyngeal infection among men who have sex with men. *Sex Transm Dis* 2011; 38(11): 1036–1039.
- Pittman E, Purcell H, Dize L, et al. Acceptability and feasibility of self-sampling for the screening of sexually transmitted infections in cabana privacy shelters. *Int J STD AIDS* 2018; 29(5): 461–465.
- Wayal S, Llewellyn C, Smith H, et al. Self-sampling for oropharyngeal and rectal specimens to screen for sexually transmitted infections: acceptability among men who have sex with men. *Sex Transm Infect* 2009; 85(1): 60–64.
- Barbee LA, Golden MR, Thibault CS, et al. Performance of patient-collected specimens for *Neisseria gonorrhoeae* culture. *Clin Infect Dis* 2021; 73(9): e3196–e3200.

- 75. Brendefur Corwin LM, Campbell P, Jakobsen K, et al. Improvement in *Neisseria gonorrhoeae* culture rates by bedside inoculation and incubation at a clinic for sexually transmitted infections. *Ann Clin Microbiol Antimicrob* 2023; 22(1): 27.
- 76. Sultan B, White JA, Fish R, et al. The "3 in 1" study: pooling self-taken pharyngeal, urethral, and rectal samples into a single sample for analysis for detection of *Neisseria* gonorrhoeae and *Chlamydia trachomatis* in men who have sex with men. J Clin Microbiol 2016; 54(3): 650–656.
- Almeria J, Pham J, Paris KS, et al. Pooled 3-anatomic-site testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*: a systematic review and meta-analysis. *Sex Transm Dis* 2021; 48(12): e215–e222.
- Bristow CC, Morris SR, Little SJ, et al. Meta-analysis of the Cepheid Xpert((R)) CT/NG assay for extragenital detection of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) infections. *Sex Health* 2019; 16(4): 314–319.
- Morris SR, Bristow CC, Wierzbicki MR, et al. Performance of a single-use, rapid, point-of-care PCR device for the detection of *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*: a cross-sectional study. *Lancet Infect Dis* 2021; 21(5): 668–676.
- Van Der Pol B and Gaydos CA. A profile of the binx health io® molecular point-of-care test for chlamydia and gonorrhea in women and men. *Expert Rev Mol Diagn* 2021; 21(9): 861–868.
- Ebeyan S, Windsor M, Bordin A, et al. Evaluation of the ResistancePlus GC (beta) assay: a commercial diagnostic test for the direct detection of ciprofloxacin susceptibility or resistance in *Neisseria gonorrhoeae*. J Antimicrob Chemother 2019; 74(7): 1820–1824.
- Lee DYJ, Ashcroft MM, Chow EPF, et al. Reflex detection of ciprofloxacin resistance in *Neisseria gonorrhoeae* by use of the SpeeDx resistancePlus GC assay. *J Clin Microbiol* 2021; 59(5): e00089.
- Shimuta K, Takahashi H, Akeda Y, et al. Loop-mediated isothermal amplification assay for identifying *Neisseria gonorrhoeae* nonmosaic penA-targeting strains potentially eradicable by cefixime. *Microbiol Spectr* 2022; 10(5): e0233522.
- Fiumara NJ and Asvadi S. Asymptomatic gonococcal urethritis in a male transsexual female. *Br J Vener Dis* 1978; 54(2): 130–131.
- 85. Hiransuthikul A, Janamnuaysook R, Himma L, et al. Acceptability and satisfaction towards self-collection for chlamydia and gonorrhoea testing among transgender women in Tangerine Clinic, Thailand: shifting towards the new normal. *J Int AIDS Soc* 2021; 24(9): e25801.
- 86. Aoki T, Mizushima D, Takano M, et al. Efficacy of 1 g ceftriaxone monotherapy compared to dual therapy with azithromycin or doxycycline for treating extragenital gonorrhea among men who have sex with men. *Clin Infect Dis* 2021; 73(8): 1452–1458.
- Belakebi D, Godreuil S, Picot MC, et al. Response rate to intramuscular ceftriaxone 1 g in patients with gonococcal infection: a French monocentric prospective study. *J Eur Acad Dermatol Venereol* 2023; 37(10): e1229–e1231.
- 88. de Vries HJC, de Laat M, Jongen VW, et al. Efficacy of ertapenem, gentamicin, fosfomycin, and ceftriaxone for the

treatment of anogenital gonorrhoea (NABOGO): a randomised, non-inferiority trial. *Lancet Infect Dis* 2022; 22(5): 706–717.

- Lo FWY, Kong FYS and Hocking JS. Treatment efficacy for rectal *Neisseria gonorrhoeae*: a systematic review and metaanalysis of randomized controlled trials. *J Antimicrob Chemother* 2021; 76(12): 3111–3124.
- Kong FYS, Hatzis CL, Lau A, et al. Treatment efficacy for pharyngeal *Neisseria gonorrhoeae*: a systematic review and meta-analysis of randomized controlled trials. *J Antimicrob Chemother* 2020; 75(11): 3109–3119.
- 91. Eyre DW, Town K, Street T, et al. Detection in the United Kingdom of the *Neisseria gonorrhoeae* FC428 clone, with ceftriaxone resistance and intermediate resistance to azithromycin, October to December 2018. *Euro Surveill* 2019; 24(10): 1900147.
- Pichichero ME and Casey JR. Safe use of selected cephalosporins in penicillin-allergic patients: a meta-analysis. *Otolaryngol Head Neck Surg* 2007; 136(3): 340–347.
- Zagursky RJ and Pichichero ME. Cross-reactivity in beta-lactam allergy. J Allergy Clin Immunol Pract 2018; 6(1): 72–81.e1.
- Ong JJ, Aguirre I, Unemo M, et al. Comparison of gastrointestinal side effects from different doses of azithromycin for the treatment of gonorrhoea. *J Antimicrob Chemother* 2022; 77(7): 2011–2016.
- Deguchi T, Yasuda M, Yokoi S, et al. Treatment of uncomplicated gonococcal urethritis by double-dosing of 200 mg cefixime at a 6-h interval. *J Infect Chemother* 2003; 9(1): 35–39.
- Chisholm SA, Mouton JW, Lewis DA, et al. Cephalosporin MIC creep among gonococci: time for a pharmacodynamic rethink? *J Antimicrob Chemother* 2010; 65(10): 2141–2148.
- Barbee LA, Kerani RP, Dombrowski JC, et al. A retrospective comparative study of 2-drug oral and intramuscular cephalosporin treatment regimens for pharyngeal gonorrhea. *Clin Infect Dis* 2013; 56(11): 1539–1545.
- 98. Bizova B, Prochazka P, Nycova E, et al. Single-dose cefixime 800 mg plus doxycycline 100 mg twice a day for 7 days compared with single-dose ceftriaxone 1 g plus single-dose azithromycin 2 g for treatment of urogenital, rectal, and pharyngeal gonorrhoea: a randomised clinical trial. *Clin Microbiol Infect* 2024; 30(2): 211–215.
- Ison CA, Hussey J, Sankar KN, et al. Gonorrhoea treatment failures to cefixime and azithromycin in England, 2010. *Euro Surveill* 2011; 16(14): 19833.
- 100. Unemo M, Golparian D, Syversen G, et al. Two cases of verified clinical failures using internationally recommended first-line cefixime for gonorrhoea treatment, Norway, 2010. *Euro Surveill* 2010; 15(47): 19721.
- 101. Yang KJ, Kojima N, Bristow CC, et al. Effectiveness of cefixime for the treatment of *Neisseria gonorrhoeae* infection at 3 anatomic sites: a systematic review and metaanalysis. *Sex Transm Dis* 2023; 50(3): 131–137.
- 102. Ross JDC, Brittain C, Cole M, et al. Gentamicin compared with ceftriaxone for the treatment of gonorrhoea (G-ToG): a randomised non-inferiority trial. *Lancet* 2019; 393(10190): 2511–2520.
- 103. Rob F, Klubalová B, Nyčová E, et al. Gentamicin 240 mg plus azithromycin 2 g vs. ceftriaxone 500 mg plus

azithromycin 2 g for treatment of rectal and pharyngeal gonorrhoea: a randomized controlled trial. *Clin Microbiol Infect* 2020; 26(2): 207–212.

- 104. Barbee LA, Soge OO, Morgan J, et al. Gentamicin alone is inadequate to eradicate *Neisseria gonorrhoeae* from the pharynx. *Clin Infect Dis* 2020; 71(8): 1877–1882.
- 105. Cole MJ, Tan W, Fifer H, et al. Gentamicin, azithromycin and ceftriaxone in the treatment of gonorrhoea: the relationship between antibiotic MIC and clinical outcome. *J Antimicrob Chemother* 2020; 75(2): 449–457.
- 106. Tapsall JW, Shultz TR, Limnios EA, et al. Failure of azithromycin therapy in gonorrhea and discorrelation with laboratory test parameters. *Sex Transm Dis* 1998; 25(10): 505–508.
- 107. Klausner JD, Bristow CC, Soge OO, et al. Resistance-guided treatment of gonorrhea: a prospective clinical study. *Clin Infect Dis* 2021; 73(2): 298–303.
- 108. Allan-Blitz LT, Humphries RM, Hemarajata P, et al. Implementation of a rapid genotypic assay to promote targeted ciprofloxacin therapy of *Neisseria gonorrhoeae* in a large health system. *Clin Infect Dis* 2017; 64(9): 1268–1270.
- 109. Buono SA, Watson TD, Borenstein LA, et al. Stemming the tide of drug-resistant *Neisseria gonorrhoeae*: the need for an individualized approach to treatment. *J Antimicrob Chemother* 2015; 70(2): 374–381.
- 110. Milligan AL, Randag AC, Lekkerkerk S, et al. Increased incidence of adult gonococcal keratoconjunctivitis at two tertiary eye hospitals in Western Europe: clinical features, complications and antimicrobial susceptibility. *Br J Ophthalmol* 2024; 108: 788–792.
- 111. Schwab L and Tizazu T. Destructive epidemic Neisseria gonorrheae keratoconjunctivitis in African adults. Br J Ophthalmol 1985; 69(7): 525–528.
- Ullman S, Roussel TJ, Culbertson WW, et al. *Neisseria* gonorrhoeae keratoconjunctivitis. *Ophthalmology* 1987; 94(5): 525–531.
- 113. Haimovici R and Roussel TJ. Treatment of gonococcal conjunctivitis with single-dose intramuscular ceftriaxone. *Am J Ophthalmol* 1989; 107(5): 511–514.
- 114. ECDC. Response plan to control and manage the threat of multi- and extensively drug-resistant gonorrhoea in Europe – 2019 update. Stockholm: European Centre for Disease Prevention and Control, 2019.
- 115. Poncin T, Merimeche M, Braille A, et al. Two cases of multidrug-resistant *Neisseria gonorrhoeae* related to travel in south-eastern Asia, France, June 2019. *Euro Surveill* 2019; 24(36): 1900528.
- 116. Unemo M, Golparian D, Nicholas R, et al. High-level cefixime- and ceftriaxone-resistant *Neisseria gonorrhoeae* in France: novel *penA* mosaic allele in a successful international clone causes treatment failure. *Antimicrob Agents Chemother* 2012; 56(3): 1273–1280.
- 117. Xu WQ, Zheng XL, Liu JW, et al. Antimicrobial susceptibility of ertapenem in *Neisseria gonorrhoeae* isolates collected within the China Gonococcal Resistance Surveillance Programme (China-GRSP) 2018. *Infect Drug Resist* 2021; 14: 4183–4189.
- 118. Li X, Le W, Lou X, et al. In vitro activity of ertapenem against *Neisseria gonorrhoeae* clinical isolates with

decreased susceptibility or resistance to extended-spectrum cephalosporins in Nanjing, China (2013 to 2019). *Antimicrob Agents Chemother* 2022; 66(5): e0010922.

- Cavenee MR, Farris JR, Spalding TR, et al. Treatment of gonorrhea in pregnancy. Obstet Gynecol 1993; 81(1): 33–38.
- 120. Comunian-Carrasco G, Pena-Marti GE and Marti-Carvajal AJ. Antibiotics for treating gonorrhoea in pregnancy. *Co-chrane Database Syst Rev* 2018; 2(2): CD011167.
- 121. Ramus RM, Sheffield JS, Mayfield JA, et al. A randomized trial that compared oral cefixime and intramuscular ceftriaxone for the treatment of gonorrhea in pregnancy. *Am J Obstet Gynecol* 2001; 185(3): 629–632.
- 122. Chow EPF, Maddaford K, Hocking JS, et al. An open-label, parallel-group, randomised controlled trial of antiseptic mouthwash versus antibiotics for oropharyngeal gonorrhoea treatment (OMEGA2). *Sci Rep* 2020; 10(1): 19386.
- 123. Van Dijck C, Tsoumanis A, De Hondt A, et al. Chlorhexidine mouthwash fails to eradicate oropharyngeal gonorrhea in a clinical pilot trial (MoNg). *Sex Transm Dis* 2022; 49(2): e38–e41.

- 124. Chow EPF, Williamson DA, Hocking JS, et al. Antiseptic mouthwash for gonorrhoea prevention (OMEGA): a randomised, double-blind, parallel-group, multicentre trial. *Lancet Infect Dis* 2021; 21(5): 647–656.
- 125. Jephcott AE. Microbiological diagnosis of gonorrhoea. *Genitourin Med* 1997; 73(4): 245–252.
- 126. Wind CM, Schim van der Loeff MF, Unemo M, et al. Test of cure for anogenital gonorrhoea using modern RNA-based and DNA-based nucleic acid amplification tests: a prospective cohort study. *Clin Infect Dis* 2016; 62(11): 1348–1355.
- 127. Barbee LA, Soge OO, Khosropour CM, et al. Time to clearance of *Neisseria gonorrhoeae* RNA at the pharynx following treatment. *J Clin Microbiol* 2022; 60(6): e0039922.
- Mensforth S and Radcliffe K. Is it time to reconsider epidemiological treatment for gonorrhoea? *Int J STD AIDS* 2018; 29(10): 1043–1044.
- Kohli M, Medland N, Fifer H, et al. BASHH updated position statement on doxycycline as prophylaxis for sexually transmitted infections. *Sex Transm Infect* 2022; 98(3): 235–236.