ONORRHOEA (*NEISSERIA GONORRHOEAE*)

Including NEISSERIA MENINGITIDIS

What's New

Ciprofloxacin now restricted – second-line, senior approval needed – due to MHRA advice

Key practice notes

- Decreasing sensitivity of gonorrhoea to cephalosporins and azithromycin is now a global threat: two cases of extended drug resistance were reported in the UK in Jan 2019.
- First line **empirical** therapy remains **monotherapy** with Ceftriaxone **1g** intramuscularly. If injections are declined then use oral Cefixime 400mg plus azithromycin 2g oral
- **Genotypic ciprofloxacin resistance testing** is available to help antibiotic choice but ciprofloxacin should only be used when other antibiotics are inappropriate and after full discussion with the patient about potential disabling, irreversible side effects.
- **Azithromycin co-treatment** is only used to support **less effective** antibiotic regimens (e.g. gentamicin, oral Cefixime) at a dose of **2g.** It is not needed with ceftriaxone or Ciprofloxacin
- It is more important than ever to take **cultures** before treatment for suspected gonorrhoea.
- **Pharyngeal sampling** (NAAT+ culture) is required in patients with suspected gonorrhoea likely acquired in **Asia-Pacific region** or if proven genital infection with **ceftriaxone-resistant** organism. This is irrespective of gender or sexual risk behaviour.
- Epidemiological treatment should only be considered if contacts present within **14 days** of exposure. Waiting for results before treating may reduce unnecessary antibiotic exposure.
- Undertake **test of cure** for patients regardless of anatomical site of infection, especially in patients with persistent symptoms or those not treated with ceftriaxone.
- Rarely, presumptive gonorrhoea seen on microscopy turns out to be due to **meningococcal** infection: meningococcal cases need senior GUM review to advise on best management

Diagnosis

1. Microscopy (GNDC)

Very useful for acutely symptomatic patients with urethral discharge, proctitis or cervicitis.

Gram negative intracellular diplococci

(*NB Microscopy provides a **provisional diagnosis** – always make this clear. Final diagnosis is the result of the NAAT +/- culture)*

Where on-site microscopy unavailable dry the slide on a hotplate for transport to your slide-reading lab as per protocol for gram-stain and microscopy

2. NAAT

NAAT testing is our primary method of excluding gonorrhoea from all anatomical sites. We use the Abbott RealTime Gonorrhoea/ *Chlamydia trachomatis* PCR test across the whole of NHSGGC. This test *always* tests for both gonorrhoea and chlamydia – do not request just a GC test alone on NaSH.

Pharyngeal GC NAAT Abbott results are confirmed by a second test on a different assay in Glasgow before a final result is released. See below re SpeeDx testing: this can act as an additional confirmatory test for borderline/indeterminate results (see Management section).

There is a small risk of false positives with NAAT testing especially in very low prevalence populations so partner notification should take this into account, especially if the clinical likelihood is low. See the table below on how to manage results from both tests.

Urine samples should not be taken from cis-women as there is a lower sensitivity compared to vulvovaginal swabs.

3. Culture

Culture should be taken in the following situations:

- All **NAAT-positive cases:** strongly recommended to attempt culture isolation and to assess antibiotic sensitivity. This includes pharyngeal sampling if infection likely acquired in Asia-Pacific region.
- **Contacts** of gonorrhoea eligible for empirical treatment
- Any genital or rectal discharge

- Suspected PID / cervicitis

Carefully plate each sample onto a selective plate. Cover one quarter of Petri dish. If you do not have local plating then transfer a charcoal swabs to your local lab as soon as possible.

4. Ciprofloxacin resistance testing (SpeeDx)

This is reported as part of our routine laboratory confirmation workflow. However ciprofloxacin is no longer first line and is currently not being reported by the lab on NaSH or clinical portal

Testing (*consider anatomically appropriate tests with Gender patients)*

Site of tests for **NAAT testing***:

Ensure that the tests on NaSH match precisely what you have ordered from the lab.

Do not confuse GC NAAT with GC culture.

GC culture results are available in Results Reporting for sensitivities.

Male anatomy	**Female anatomy**
Urine	Vulvovaginal swab
Rectum (*Only in MSM who report receptive anal or oro-anal sex. Proctoscopy if symptoms, otherwise blind swabs)*	Rectum (*if high index of suspicion, e.g.: GC contact **or** sexual assault)*
Pharynx (*Only in MSM or genital gonorrhoea acquired in Asia-Pacific or known ceftriaxone resistance)*	Pharynx (*if high index of suspicion, e.g.: GC contact **or** sexual assault, or genital gonorrhoea acquired in Asia-Pacific or known ceftriaxone resistance)*
	NB: urine is not ideal sample for GC exclusion in patients presenting with birth sex female anatomy. Consider anatomically appropriate tests with Gender patients

Site of swabs for **culture** *(selected patients)*

Male anatomy	**Female anatomy**
Urethra	Endocervical
*rectum	Urethra (**only** if urethral discharge)
**pharynx	rectum *(if high index of suspicion, e.g.GC contact **or** Sexual assault)*
	pharynx (*if high index of suspicion, e.g.GC contact **or** Sexual assault **or** genital gonorrhoea acquired in Asia-Pacific or known ceftriaxone resistance)*
MSM-receptive anal sex/oro-anal sex* * MSM-receptive oral sex* **	

Examples of typical test sets:

A routine **asymptomatic** screen consists of:

Male anatomy	Urine for GC/Ct NAAT *No exam needed*
MSM	Urine for GC/Ct NAAT *Rectal swab for GC/Ct NAAT *Pharyngeal swab for GC/Ct NAAT **if indicated by sexual history* *No exam needed.* *Separate forms required for samples from different sites*
Female anatomy	Vulvovaginal swab for GC/Ct NAAT *No exam needed*.

Plus opt-out bloods for STS/HIV/Hep BcAb/HCV PCR as appropriate

A **symptomatic** screen consists of:

Urethral discharge	Urethral Gram stain and culture† Urine for GC/Ct NAAT
Rectal discharge / proctitis	Urine for GC/Ct NAAT Rectal swab for GC/Ct NAAT Rectal Gram stain and culture for GC† (*by proctoscopy*) *(plus HSV/syphilis PCR ; consider mpox PCR)*
Cervicitis **if proctitis**	Vulvovaginal swab for GC/Ct NAAT Endocervical Gram stain and culture† Rectal Gram stain (*if proctitis by proctoscopy*) and culture Rectal Chlamydia/GC NAAT

Plus opt-out bloods for STS/HIV/HepBcAb/ HCV PCR as appropriate

† if GC confirmed on microscopy and exposure in Asia-Pacific region then add pharyngeal sampling (NAAT and culture)

Genital swabs after Genital Reconstructive Surgery

With neovagina (sigmoid or penile skin): NAAT neovaginal swab + first pass urine

With neo-penis: first pass urine (plus vaginal swab if vagina still present)

Management

Indications for treatment

1. Presumptive diagnosis following identification of Gram-negative diplococci on microscopy

2. A positive culture for *N. gonorrhoeae*

3. A positive NAAT test for *N. gonorrhoeae*

4. A recent sexual partner of a confirmed case of gonorrhoea (within last 14 days)

STEP ONE: Is treatment required immediately or can it be safely deferred until more information is available?

STEP TWO: Choose your antibiotic regimen carefully

Consider whether this is uncomplicated or complicated infection, allergy history and contraindications (age, renal impairment etc).

Uncomplicated infection, presumptive treatment (with or without susceptibility testing)

Ceftriaxone 1 gram intramuscularly

Alternative if IM injection contra-indicated (eg bleeding disorder), patient requires remote treatment, or patient declines injectable therapy.
NB: Higher risk of treatment failure:

Cefixime 400mg po stat

plus

Azithromycin 2g po stat

Antibiotic allergy

Due to emerging resistance, reserve alternative treatments due to drug allergy to the following situations:

- known history of **true allergy** to cephalosporins
- known **immediate/severe hypersensitivity reaction** to penicillin or other beta-lactam

In these circumstances use:

Gentamicin* 240mg IM with **azithromycin 2g** po stat
or

Spectinomycin 2g IM with **azithromycin 2g po stat**
(Second choice, does not cover oropharynx, named pt form needed)

Or only if IM injection refused as a last resort

Azithromycin 2g stat orally

*NB. Please discuss if patient has known renal dysfunction. Only if wt > 50kg. Please see prescribing guidance in BNF.

In the interests of preserving antibiotic susceptibility, where drug reactions or allergies are unclear, attempts should be made to clarify (such as through Clinical Portal or discussion with GP, check ECS as well to verify). Where the penicillin reaction is established to be mild or moderate, ceftriaxone may be used as in non-penicillin-allergic patients.

Antibiotic allergy and decline/unavailable for injection

MHRA strengthened restrictions in January 2024 stating that fluoroquinolones should only be used when other recommended antibiotics are inappropriate. As at Feb 2024 this applies even to single-dose treatments. Until further information and reassurance is provided following these warnings we are restricting use of fluoro-quinolones even for stat doses within Sandyford.

For treatment of gonorrhoea a typical scenario would include

- history of cephalosporin or beta-lactam immediate hypersensitivity excluding cefixime use AND
- contraindication to or decline of gentamicin AND
- susceptibility predicted by NAAT SpeeDx test or culture

Contraindications include risk of pregnancy; previous fluoroquinolone side-effects, aged under 16 or over 60 years, on corticosteroids, known renal impairment, previous organ transplantation, previous convulsions.

If after discussion of the possibility of disabling and irreversible side-effects this remains the best antibiotic please send the patient the following patient information leaflet by SMS.

Complicated infection (suspected PID, epididymitis)

Ciprofloxacin 500mg oral stat monotherapy
(***if culture sensitive)***

Discuss with senior staff first. Admission to the local hospital may need to be considered for parenteral antibiotics (see below for treatment suggestion or contact your local microbiologist for advice):

Gonococcal PID: **Ceftriaxone 1g IM stat** in addition to the regimen chosen for PID

Gonococcal epididymorchitis: **Ceftriaxone 1g IM stat** in addition to the regimen chosen for epididymorchitis

Gonococcal conjunctivitis: **Ceftriaxone 1g IM stat**

Disseminated gonococcal infection: this requires senior GUM or ID advice as patient will require admission. See BASHH guidance for further discussion.

Other good practice points

Gonococcal antibiotic resistance:

The prevalence of ciprofloxacin resistance was 43% in 2021 in Scotland and 44% in England in 2020. Azithromycin alone is inadequate first-line treatment for gonorrhoea as high-level resistance has been seen locally and in the rest of the UK. Doxycycline is also ineffective. The 'drift' of sensitivity to cephalosporins has stablised recently. In Jan 2019 the first UK transmissions of XDR gonorrhoea were reported, resistant to both ceftriaxone and azithromycin..

Usually we treat gonorrhoea before sensitivities are available –"blind" – and we should use a drug that will cure >95% of infections. **Parenteral ceftriaxone monotherapy** is the preferred choice in Sep 2018 recommended by BASHH CEG. Cefixime is a second-line therapy especially for extra-genital sites of infection. Both are considered safe in single dose in pregnancy (WHO data).

Co-treatment with Azithromycin:

BASHH CEG has now concluded that co-treatment with azithromycin is no longer achieving the aims of reducing drift to cephalosporin resistance and that a higher initial dose of ceftriaxone given alone is a better approach. However alternative regimens have a higher rate of failure and azithromycin co-treatment 2g is recommended in these selected cases. Co-treatment with 2g azithromycin will usually cause gastrointestinal side-effects.

If immediate microscopy not available.

Purulent urethral discharge does not guarantee a diagnosis of gonorrhoea. Practitioners will need to make individual judgements about need for syndromic treatment before results of microscopy and / or NAAT testing are available, based on risk, likelihood and ease of the patient returning for treatment. With increasing antibiotic resistance try wherever possible to await microscopy confirmation before treating. There is little harm starting doxycyline for urethritis while awaiting results.

Community tests which are positive

All positive NAAT and culture tests are copied to our Shared Care service. If a GP/ hospital clinician contacts you about a NAAT positive GC result in the community the patient may need management at Sandyford.

GC NAAT positive but cultures not yet taken

- Take swab/s from same site as GC NAAT positive sample from and send for GC culture (if not already antibiotic treated). If Asia-Pacific exposure also take pharyngeal culture
- Highlight on form that GC NAAT positive. **SEND TO BACTERIOLOGY**
- Treat for gonorrhoea as above
- Partner notification as per protocol

Partner Notification

- All patients found to have gonorrhoea should have partner notification documented at diagnosis and at each follow up visit, until partner notification is documented as complete.
- Established/occasional partners should attend an urgent care appointment for testing and consideration of immediate treatment. They should be advised to avoid sex until their infection status is confirmed by NAAT, and (if applicable) their partner has tested negative following treatment.
- Previous/one-off partners should attend a Grab appt testing **TWO** weeks after last exposure.
- Look back period is 2 weeks for symptomatic penile infection, 3 months or to last partner for everyone else
- Rectal gonorrhoea is an indicator to discuss and likely recommend PrEP.

Treatment of established/occasional sexual partners

- Around 50% of contacts who report exposure to gonorrhoea are found to have gonorrhoea themselves.
- **Epidemiological treatment** has the advantage of immediate reassurance and prevents onward transmission and additional morbidity should they be infected.

- Patients who later default will have been securely treated. However, as gonorrhoea may be missed on a first screen the chance to extend partner notification may be lost. Half of these patients will have been given antibiotics unnecessarily.
- The decision to treat epidemiologically must be carefully discussed with the patient and these advantages and disadvantages outlined.
    - If it is **less than two weeks** since exposure treatment may be **considered** depending on assessment of risk and patient preference.
    - If it is **more than two weeks** since exposure treatment should be **withheld** and test results awaited
- Partners with recent contact who are not treated should re-attend for a repeat test after at least two weeks have elapsed since exposure.

Follow-up

Test of cure is recommended in **all** cases after 3 weeks

- If symptoms have not cleared within 48h especially if urethral discharge persists, in which case repeat culture is needed to recheck antibiotic sensitivity.
- Review **antibiotic sensitivities** if available, in Results Reporting section of NaSH. Check carefully the date of **specimen collection** on all reports – several laboratory reports may be sent on a single isolate. Be careful on NASH as sensitivities may relate to more than one organism if multiple pathogens identified.
- Offer final review at 3 months for repeat STS ± HIV test.
- **Sequence types** are now imported into NaSH about a month behind: they can be useful e.g. in multiple anatomic sites (same or different infection?) and resolving issues about which partners are linked (should be same ST). Patients can have more than one strain of GC at the same time.
- Referral should be made to the Sexual Health Advisers to check adherence to management of treatment, to complete partner notification and to determine whether further follow up via phone is necessary. All patients should be added to SC SHA Virtual Diary at 3 weeks after treatment.
- If <25yrs encourage re-testing at three months (as 10-30% of young people are re-infected with Chlamydia within 3 months). Patients should be added to SC SHA Re-Test for an automated text reminder at 3 months.

GENITAL INFECTION DUE TO *NEISSERIA MENINGITIDIS*

Introduction

Neisseria meningitidis (known as the meningococcus) is an obligate human commensal bacterium which frequently colonises the upper respiratory tract. Invasive variants are responsible for mengingococcal sepsis and meningococcal meningititis, outbreaks of which been well described in MSM in the last 20 years. Variants of this lineage are now known to have acquired some determinants of genital infection from *Nesseria gonorrhoeae* leading to increased incidence of genital meningococcal infection. As it is clinically and microscopically indistinguishable from *Neisseria gonorrhoeae,* patients have often been treated for gonorrhoea presumptively before the culture results reveal the true cause. The likely route of infection is oro-genital sex from asymptomatic pharyngeal carriage.

Symptoms

People with symptoms can present with:

- Vaginal discharge
- Acute cervicitis
- Salpingitis
- Purulent urethral discharge at the penis
- Dysuria at the penile urethra

Diagnosis

Neisseria meningitidis is diagnosed by a series of speciation tests from colonies grown on agar cultures intended for gonococcal isolation. It is deliberately not detected on the GC NAAT tests. You do not need to do any additional tests to look for meningococcal infection: the lab do this if the culture shows *Neisseria* species.

Management

Discuss all meningococcal cases with a consultant

It is not clear whether people without symptoms need treatment, this decision should be based on individual patient factors and the reason a culture swab was taken.

For symptomatic cases, treatment should be offered. Antibiotic susceptibility should have been reported along with the culture result. Ceftriaxone is effective; oral ciprofloxacin is now restricted..

There is no need for any general public health action such as notification and chemoprophylaxis for household contacts as genital tract infection is not thought to lead to invasive disease. However treating current sexual contacts may reduce the chance of symptomatic reinfection.

References

Gonorrhoea management:

British Association for Sexual Health and HIV Clinical Effectiveness Group. (2018). 2018 UK National Guideline for management of infection with *Neisseria gonorrhoeae.* Available at https://www.bashhguidelines.org/current-guidelines/urethritis-and-cervicitis/gonorrhoea-2018/ [accessed online 08/02/2024

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Medicines information:

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Spectinomycin manufacturer's instructions:

http://www.bashh.org/documents/Spectinomycin%20leaflet.pdf[accessed 08/02/2024]

Summary of Product Characteristics Ceftriaxone 1g powder for injection https://www.medicines.org.uk/emc/product/1361/smpc [accessed 08/02/2024]

Summary of Product Characteristics Gentamicin 40mgs/ml injection. Gentamicin 40mg/ml Solution for Injection or Infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) [accessed 08/02/2024]

APPENDIX 1: PREPARATION OF PARENTERAL ANTIBIOTICS

Preparation and Administration of Ceftriaxone 1g deep intramuscular Injection

To reduce the pain experienced by patients receiving intramuscular ceftriaxone the drug is administered with 1% lidocaine (lignocaine)

1. Take **1 gram** vial of ceftriaxone powder

2. Draw up **3.5mls Lidocaine 1%** into a syringe.

3. Reconstitute the 1gm vial of ceftriaxone with 3.5mls of lidocaine 1%.

4. Draw up the reconstituted ceftriaxone solution from the vial into one syringe. This makes a total of **4.1mls**.

5. Administer the **4.1mls** solution of ceftriaxone 1gm by deep intramuscular injection. Well-developed muscles e.g. ventrogluteal, vastus lateralis and dorsogluteal can take up to 5mls volume.

NOTE: Lidocaine must be prescribed (or documented under PGD) on NaSH.

Preparation and Administration of Spectinomycin 2g Intramuscular Injection

Spectinomycin 2g reconstituted with **3.2ml bacteriostatic water** (supplied) and to shake vigorously. Once dissolved to be drawn up as **5ml.**

The solution should be administered by a single deep intramuscular injection.

Preparation and Administration of Gentamicin 240mg Intramuscular Injection

Due to volume this dose requires to be split

Open up **3** vials of **80mgs/2mls gentamicin**, totalling **6mls (=240mg)**.

Take two 5ml syringes and draw **3ml solution** into each syringe.

Give by deep intramuscular injection, **3 mls per side**.