GONORRHOEA

What's New

- Gender reassignment surgery guidance on swab taking
- Gentamicin first line for treatment when have known antibiotic allergy
- Caution re previous Quinolone side-efects

Key practice notes

Decreasing sensitivity of gonorrhoea to cephalosporins and azithromycin is now a real threat: two cases of extended drug resistance were reported in the UK in Jan 2019

- First line empirical therapy is now **monotherapy** with ceftriaxone **1g** intramuscularly
- Azithromycin co-treatment should **no longer be used** with ceftriaxone. When used with less effective antibiotics the co-treatment dose is now 2g.
- 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
- TEST OF CURE for all patients regardless of anatomical site of infection
- ALTERNATIVE TREATMENTS for antibiotic allergy should be reserved for established cephalosporin or azithromycin allergy or immediate/severe hypersensitivity reaction to penicillin or other beta-lactam

Diagnosis

1. **Microscopy**

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

Gram negative intracellular diplococci (GNDC)

(*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. Borderline positive GC NAAT results are confirmed in a second test in Edinburgh before the result is released. All positive tests are sent to the Edinburgh reference lab for sequencing, and any discrepant tests notified (subject to regular audit)

The aim is to reduce **unnecessary** invasive swabs and examinations. **Culture should still be offered to selected cases only**.

A **positive** result from a GC NAAT should always, with patient consent, have **culture sensitivity testing** attempted by repeat sampling and sending the specimen to the appropriate bacteriology lab where direct plating or rapid swab transport is available. This will enable us to continue to monitor antibiotic sensitivities. Repeat NAAT should only be undertaken if the diagnosis does not fit the clinical picture at all.

There is a small risk of false positives with NAAT testing so information / 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 women as there is a lower sensitivity compared to vulvovaginal swabs.

3. Culture

Culture should be taken in the following cases:

- All **NAAT-positive cases:** strongly recommended to attempt culture isolation. This includes pharyngeal sampling if infection likely acquired in Asia-Pacific region.
- **Contacts** of gonorrhoea
- 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.

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.

Site of tests for **NAAT testing**:

Male	**Female**
Urine	Vulvovaginal swab
*Rectum	
*Pharynx	Pharynx (*if high index of suspicion, e.g.: GC contact **or** sexual assault, or genital gonorrhoea acquired in Asia-Pacific or known ceftriaxone resistance*
** Only in MSM who report receptive anal or oral sex. Proctoscopy if symptoms, otherwise blind swabs*	*NB urine is not ideal sample for GC exclusion in women*

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

Male	**Female**
Urethra	Endocervical
*rectum (+NAAT)	**Urethra (**only** if urethral discharge)
**pharynx	**rectum (+ NAAT)
	**pharynx
msm-receptive anal sex* ***High index of suspicion, e.g.GC contact **or Sexual assault **or** genital gonorrhoea acquired in Asia-Pacific or known ceftriaxone resistance*	

Examples of typical test sets:

A routine **asymptomatic** screen consists of:

Male (non-MSM)	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*
Woman	Vulvovag swab for GC/Ct NAAT *No exam needed*.

Plus opt-out bloods for STS/HIV/HepBcAb

A **symptomatic** screen consists of:

Urethral discharge	Urethral Gram stain and culture† Urine for GC/Ct NAAT
MSM with 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)*
Woman with cervicitis **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

† 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 confirmed positive NAAT test for *N. gonorrhoeae*
4. A recent sexual partner of a confirmed case of gonorrhoea (within last 14 days)

Treatment of uncomplicated ano-genital and pharyngeal infection – antibiotic susceptibilities not known

*NB: Try to establish **antibiotic susceptibility** by checking NaSH Results Reporting if culture already taken in Sandyford, or on NHSGGC or relevant regional Board's Clinical Portal if culture may have been taken in the community.*

Ceftriaxone 1 gram intramuscularly

Alternative if IM injection contra-indicated (eg bleeding disorder) or patient refuses 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.

Do NOT use ciprofloxacin blind if you suspect penicillin allergy

Treatment of uncomplicated ano-genital and pharyngeal infection – antibiotic susceptibilities <u>known</u>

Ciprofloxacin 500mg oral stat monotherapy (***if known sensitive on culture)***
(*not if risk of pregnancy; caution if previous quinolone side-effects, aged over 60 years, on corticosteroids, known renal impairment, previous organ transplantation.)*

or

Ceftriaxone 1g IM stat (see appendix 1)

(If ciprofloxacin resistant or risk of pregnancy)

Treatment of complicated ano-genital and pharyngeal infection

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

Gonococcoal 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.

Practice points

Gonoccocal antibiotic resistance:

The prevalence of ciprofloxacin resistance was 33.7% in 2016 in the UK. 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. There is increasing 'drift' of sensitivity to cephalosporins, mostly associated with certain prevalent sequence types. 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.

Co-treatment of chlamydia:

We no longer recommend expectant treatment for possible chlamydia co-infection: await specific testing and treat with doxycycline where possible if chlamydia positive.

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 try to encourage them to send the patient to the Sandyford for cultures/ treatment and partner notification to occur. Pass the details to the Shared Care Helpline (211 8639) for follow up.

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 diagnosed with gonorrhoea should see a sexual health adviser at diagnosis and at each follow up visit, until partner notification is documented as complete.
- Partners should be screened for infection and advised to avoid sex until their infection status is confirmed by NAAT, and (if applicable) their partner has tested negative following treatment.
- Rectal gonorrhoea is a marker for unsafe sex and may indicate further risk reduction work including PrEP is needed.

Treatment of 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 treatment is given check to see if sensitivities from source are available to guide treatment choice, if not follow guidance for blind treatment.
    - If it is **more than two weeks** since exposure treatment should be **withheld** and test results awaited
- Patients **not** treated should re-attend for a repeat GC test within the next two weeks.

Follow-up

Test of cure is recommended in **all** cases after 2 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 to the Sexual Health Adviser or nurse with SHA competencies to check adherence to management of treatment and to complete partner notification and to determine whether further follow up via phone is necessary.

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 (draft) [accessed online 29 Nov 2018].

British Association for Sexual Health and HIV Clinical Effectiveness Group. (2012). United Kingdom National Guideline for Gonorrhoea Testing [accessed online June 2018].

Gonococcal antibiotic surveillance in Scotland (GASS): prevalence, patterns and trends in 2016 http://www.hps.scot.nhs.uk/bbvsti/wrdetail.aspx?id=75728&wrtype=6#images [accessed 22/05/2018]; Jill Shepherd Vol: 51 No: 38 Year: 2017

Public Health England GRASP Steering Committee and BASHH CEG Position Statement on the Treatment of Gonorrhoea [2015]

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British Association for Sexual Health and HIV Guidelines https://www.bashhguidelines.org/current-guidelines/urethritis-and-cervicitis/gonorrhoea-2019/

Medicines information:

Spectinomycin manufacturer's instructions:
http://www.bashh.org/documents/Spectinomycin%20leaflet.pdf [accessed June 2018]

Summary of Product Charachteristics Ceftriaxone 1g powder for injection
https://www.medicines.org.uk/emc/product/1361/smpc

Summary of Product Charachteristics Gentamicin 40mgs/ml injection.
https://www.medicines.org.uk/emc/product/6531/smpc#POSOLOGY

Intramuscular administration:

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Rodger MA , King L. Drawing up and administering intramuscular injections: a review of the literature. *J Adv Nurs.* 2000;31 (3):574-582.

Medication administration and IV therapy. In: White L. *Foundations of Nursing. 2nd ed.* Clifton Park, NY: Delmar Cengage Learning; 2005: 405-434

Wynaden D, Landsborough I, Chapman R, et al. Establishing best practice guidelines for administration of intra muscular injections in the adult: a systematic review of the literature. *Contemp Nurse.*2005;20(2):267-277.

APPENDIX: 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 5 mls volume.

NOTE: Lidocaine must be prescribed 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**.