

Management of NGU **(Non-gonococcal urethritis)**

Summary

We try to get an objective diagnosis of NGU using Gram-stain microscopy of urethral sample combined with NAAT testing for gonorrhoea, chlamydia and *Mycoplasma genitalium*

Many people presenting with proven urethritis will not have a clear microbiological cause found. At present the specialty does not support further testing for organisms that are not clearly known to be pathogens.

Testing for *M. genitalium* will be requested after microscopy on **all laboratory-proven cases of NGU** and is done at the West of Scotland Specialist Virology Centre. We adopt '**resistance-guided therapy**' if *M. genitalium* detected: see separate guideline

It is reasonable to defer treatment while awaiting results in selected situations.

Investigations in suspected NGU

Gram-stained urethral smear: where there are symptoms or signs suggestive of urethritis (urethral discharge, dysuria, penile irritation).

- Use a 5mm plastic loop (swab within a Connect setting), introduced to at least 1cm, to collect urethral specimen for smear preparation. The result depends on the quality of the smear – do not place a thick clump of discharge in the middle of the slide – evenly spread it across centre of slide.
- Urine should have been held for 2 to 4 hours before urethral sampling to exclude NGU, but all men with symptoms should have samples taken and testing rearranged if needed.
- If loop/swab insertion not possible, then first pass urine can be examined for threads and spun in centrifuge for subsequent microscopy
- Microscopy should only be done by BMS as lab is subject to CPA process of accreditation.

GC culture (plated where possible)

***Chlamydia trachomatis*/ Gonorrhoea NAAT** on first-pass urine. Please place sample in 'suspected M.gen' tray in Central

M. genitalium PCR test will be added on to the Ct/GC sample by the biomedical scientist if NGU confirmed: please explain this to the person when giving the initial results. Please do not request *M genitalium* directly just for symptoms.

MSSU – if urinary tract infection is suspected: haematuria, frequency, urgency. Urine dipstick should be done and recorded in near-patient testing section of NASH.

Dipstick leukocyte tests are of inadequate sensitivity to be of use routinely; however, where clinical suspicion of NGU in symptomatic male but smear negative, leukocyte esterase remains useful when done on remains of first pass urine (if >1+ then a diagnosis of NGU can be made and should prompt a review of slide preparation technique).

In someone presenting as a contact of *Trichomonas vaginalis* then take a first pass urine sample for centrifugation in Sandyford Central satellite lab.

In a **CONNECT** take a:

1. Urethral swab (dry the slide on a hotplate in preparation for transport to Sandyford Central or local lab as per protocol for Gram-stain and microscopy) and send charcoal swab for culture (please send two client labels with specimen so that the culture plates can be labelled accurately at Sandyford Central).
2. First catch urine for Chlamydia/GC NAAT (*M. genitalium* testing will be arranged by the Sandyford lab if needed subsequently)

Who not to test

- Those with no relevant symptoms
- Those with balanitis only unless obvious urethral discharge.
- Those with obvious genital ulcer disease, such as HSV.

What about other tests?

Many private laboratories are now offering multiplex testing for organisms commonly found in the genital tract. These are not clearly associated with urethritis and attempts to eradicate them may cause more harm than good.

If someone presents with symptoms of urethritis having already had private testing then please record carefully where possible the exact name of the organism detected and the laboratory service used.

Typically these may be

- *Ureaplasma urealyticum*
- *Ureaplasma parvum*
- *Mycoplasma hominis*

Please discuss findings with the GUM Doctor of the Day

Management

Diagnosis

- NGU is confirmed when ≥ 5 polys / high-power field (HPF) averaged over 5 most populated fields. (++)/+++ PC).
- In unusual circumstances (after senior discussion) NGU may be diagnosed on strength of leucocyte esterase dipstick, microscopy of centrifuged threads or clinically where microscopy is unavailable.

Immediate antibiotic treatment

- Most people will opt for immediate treatment, but with our NAAT test turn-around times around 48h it is reasonable to await all results if symptoms are mild and follow up assured. This is especially important to consider before blind treatment with Azithromycin.

First line

Doxycycline 100mg orally, twice daily for 7 days

Alternative regimens

Azithromycin 1g orally stat,

then 500mg orally, once daily for 2 days

if unable to use any of these, please discuss with senior GUM clinician

Practice points:

- Doxycycline:
 - $> 95\%$ effective in men with *Chlamydia trachomatis*.
 - $<50\%$ effective for complete *M. genitalium* clearance but reduces bacterial load.
 - No evidence that it induces resistance in relevant organisms, so if fails can then use resistance-guided treatment.
- Azithromycin:
 - Risk *M. genitalium* (if present) developing or already having macrolide resistance.
- QT PROLONGATION: Certain medications including fluconazole, macrolide and quinolone antibiotics cause QT prolongation and should not be prescribed with interacting medications. Please use BNF Interaction Checker to ensure these medications are safe to prescribe for your patient and discuss with a senior colleague if necessary.

In a Connect prior to results

In a Connect, interim management whilst awaiting microscopy results:

1. Add to the relevant 'microscopy' tab on NaSH to ensure results are reviewed
2. If no obvious signs and not in undue discomfort then wait for the microscopy results.
3. Blind treatment with doxycycline or ceftriaxone should be discussed with GUM doctor of the day
4. Please re-check permissions and mobile phone / other contact details
5. If no answer when phoning with results, please give the Connect phone number to arrange treatment

People with symptoms who have negative microscopy results

- Await NAAT test results
- If all tests negative and symptoms persist, please ask the person to return to a booked urgent care appointment on the next convenient morning, having held their urine overnight or for a minimum of 6 hours.

***M. genitalium* and sequential resistance-guided therapy**

- If *M. genitalium* is detected please see the separate protocol
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Management of Sexual Contacts:

- People with confirmed NGU, should abstain from sexual contact for SEVEN days from the start of treatment and ideally until all results have returned.
- At initial finding of NGU partner notification remains informal, and a judgement must be made whether to start this process or await more results. The sexual health advisers do not routinely support this initial process.
- Where NGU is likely to have been sexually acquired those affected should consider informing partners with whom they have had sexual contact in the previous **FOUR** weeks. They may prefer to wait for full test information before doing so.
- It is important to document wishes about exact infection disclosure as this makes management of partners far easier when they are identified
- If a specific pathogen is identified, formal partner notification will be arranged via the SHA office – see separate protocols for these conditions.
- Partners who do attend should be evaluated and offered testing for Ct/GC. Testing for *M. genitalium* is only to be done **in an ongoing partner** of someone with proven *M. genitalium* (see *M genitalium* guideline).
- Practitioners can decide to omit partner notification if NGU is not thought to have been sexually acquired. Reasoning for this should be documented.

Partner treatment:

- There is **no direct evidence of treatment benefit** to partners of anyone with chlamydia-negative NGU.
- Ongoing partner treatment may **reduce risk of recurrent and or persistent NGU** in the index person
- Ongoing partners **may wish to be treated epidemiologically** using the same regimen if practical to reduce need to return to the clinic.

Patient Information and follow-up

BASHH Patient Information Leaflet:

https://www.bashhguidelines.org/media/1040/ngu_pil_digital_2015.pdf

- Everyone found to have NGU should have the following discussed and documented:
 1. Explanation of causes of NGU, including that we do not always find a clear-cut cause.
 2. Current antibiotic treatment remains effective and now we have testing for *M. genitalium* very few people go onto develop persistent symptoms
 3. That we may contact them at the end of the week to arrange more treatment if *M. genitalium* is detected.
 4. Information on how to access BASHH NGU patient information leaflet and Sandyford website.
 5. Side-effects of treatment and importance of adherence
 6. Abstain sexual intercourse.
- NGU can cause considerable anxiety in relation to partners and transmission and support may be needed from the SHA team, with support of the GUM complex clinic if needed.
- Patients should be reminded that the results phone line may read out a series of negative reassuring results, but they have still been found to have NGU and should complete the antibiotic course.
- Patients should be advised to contact Sandyford if symptoms have not resolved by the end of **three** weeks.
- There is no reason to have any further checks if symptoms have cleared

Refractory or Relapsing NGU

Recurrent NGU is defined as the recurrence of symptomatic urethritis 30-90 days following treatment of acute NGU.

- Refer into GUM Complex clinic with access to microscopy or consultant-led urgent care session.
- Confirm urethritis on gram stain
- Consider re-infection from previous partner or re-exposure if a new partner
- Aetiology:

- 50%cases – no infectious cause found
- *Mycoplasma genitalium* in 20-40% (where M genitalium testing not done at initial presentation)
- Chlamydia trachomatis in 10-20% when azithromycin has been used.
- T.vaginalis (up to 10% where endemic)

Possible investigations

1. Urethral Gram stain. (important to document objective finding of NGU).
2. Urethral swab in Feinberg's medium for TV culture (Sandyford Lab).
3. First void urine for CT/GC NAAT and for TV centrifugation and culture (Sandyford Lab).
4. Urine sample for *Mycoplasma genitalium* testing if not already excluded. (if NGU confirmed this will be done automatically; but a separate sample and form will be needed if Ct/GC sample not taken)
5. MSSU (red top universal) for C&S.

Management

If no lab evidence of urethritis, strongly reassure.

If persistent microscopic evidence of NGU:

Ideally wait for results of further investigation to guide management.

If treatment required immediately:

If Doxycycline was used first line:

Azithromycin 1g orally stat then 500mg x 2 days*

PLUS

Metronidazole 400mg BD for 5 days

***If azithromycin was used first line:**

Doxycycline 100mg BD for 7 days

PLUS

Metronidazole 400mg BD for 5 days

If third line/ alternative treatment required please discuss with Consultant on call.

Retreatment of partners should be considered with the above regime.

References

2015: BASHH Clinical Effectiveness Group.

UK National Guideline on the Management of Non-gonococcal urethritis

[Horner PJ](#), [Blee K](#), [Falk L](#), [van der Meijden W](#), [Moi H](#).

Available at:

<https://www.bashhguidelines.org/current-guidelines/urethritis-and-cervicitis/ngu-2015/>
[accessed 18/09/2023]

Please ensure the published guideline is read with the Nov 2018 update here:

<https://www.bashhguidelines.org/media/1199/ngu-bashh-update-2018.pdf> [accessed 18/09/2023]

Horner PJ et al should we be testing for urogenital Mycoplasma hominis, Ureaplasma parvum and U. urealyticum in men and women? – a Position Statement from the European STI Guidelines Editorial Board

Available at <https://iusti.org/wp-content/uploads/2019/12/UrogenitalMycoplasmas.pdf>
[accessed 18 Sep 2023]