Guidance on *Mycoplasma genitalium* testing and management in Ireland, July 2024

Introduction and Background

Mycoplasma genitalium is an emerging STI. The pathophysiology is incompletely understood, in particular the significance (if any) of asymptomatic infection. It has been implicated in urethritis, epididymo-orchitis and proctitis in males and pelvic inflammatory disease (PID), mucopurulent cervicitis in females. It may lead to sexually acquired reactive arthritis (SARA). The prevalence of infection with *Mycoplasma genitalium (M gen)* in Ireland is unknown. Antimicrobial resistance is a particular challenge with this organism, highlighting the need for prudent and judicious use of testing and antimicrobial agents.

In 2020, in response to concerns around the absence of national guidance on testing and management in Ireland and concerns relating to variation in how individuals are being tested and managed a small group came together to develop evidence informed guidance on testing and management of *M gen* in Ireland. The BASHH guidelines[i] were used with additional local information where available. In January 2021, in light of the COVID-19 pandemic and the impact it had on access to STI testing, diagnostics and care some amendments were made to the treatment recommendations.

The group reconvened in June 2023 to review the guidance. The revised draft document has been reviewed by the HSE Antimicrobial Resistance and Infection Control (AMRIC) Clinical Lead and AMRIC General Practitioner team and the National Clinical Advisory Group Lead Primary Care prior to publication.

M gen is not currently a notifiable infection. Given the particular challenge relating to antimicrobial resistance with this organism, it is the view of the working group that steps should be taken to consider making *M gen* a notifiable infection

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Review Date: This guidance will be reviewed 2 years following publication with interim reviews as required in the intervening time period. The SHCPP will ask the working group, via the Chair, Prof Fiona Lyons, to reconvene when this guidance is due for review.

Recommendations	Comment
Who to test	
Asymptomatic testing of individuals (other than contacts of confirmed cases) is NOT recommended	In line with current BASHH guidelines.
All patients presenting with symptoms and signs of Pelvic Inflammatory Disease (PID)	In line with current BASHH guidelines.
All patients presenting with symptoms and signs of urethritis who: are chlamydia and gonorrhea negative and have failed to respond to 7 days doxycycline 100mg PO twice daily OR are chlamydia and gonorrhea negative and have had a recurrence of symptoms following doxycycline 100mg PO twice daily.	BASHH currently recommends testing of all with symptoms and signs of urethritis.
All patients presenting with sexually acquired epididymo-orchitis.	In line with current BASHH guidelines (consider).
All patients presenting with sexually acquired proctitis.	It is recommended that this is done in the specialist STI setting.
Consider in patients presenting with symptoms (particularly post coital bleeding or abnormal vaginal discharge) and signs of muco-purulent cervicitis.	In line with current BASHH guidelines
Current sexual partners (regular and non-regular partners where there is likely to be further sexual contact) of those who are *M gen* positive. It is reasonable to wait for the result in the contact before treating with clear advice on abstaining from unprotected sexual contact during that time.	In line with current BASHH guidelines
How and where to test	
It is recommended that all *M gen* testing is done using accredited tests.	
It is recommended that resistance testing is performed on all positive samples.	As this time, all M gen resistance testing is undertaken at Public Health England, samples with positive results at the NVRL are sent to the UK. Azithromycin resistance is routinely assessed on positive samples. Fluoroquinolone resistance testing is only performed where there is suspected treatment failure with moxifloxacin.
In patients with urethritis and/or sexually acquired epididymo-orchitis, the sample of choice is a first void urine.	
In patients with sexually acquired proctitis the sample of choice is a rectal swab.	Rectal testing in asymptomatic individuals is **not currently recommended.**
In patients with symptoms of PID, muco-purulent cervicitis the sample of choice is a vaginal swab.	
In asymptomatic contacts of *M gen* samples should be taken from the anatomical site of potential exposure.	
Pharyngeal testing is **not** currently recommended	
All patients diagnosed with *M gen* should be offered testing for HIV, HBV, Syphilis, chlamydia and gonorrhea if not already tested	
Management of positive results	
Where to see patients	
It is recommended that all patients testing positive for *M gen* are referred to an STI clinic for management noting that asymptomatic testing (apart from contacts of confirmed cases) is NOT recommended	
Antibiotic recommendations	
Non-specific urethritis (where chlamydia, gonorrhea and *M gen* status are unknown) ➢ Doxycycline 100mg PO twice daily x 7 days	**Single dose azithromycin for treatment of non-specific urethritis (where chlamydia, gonorrhea and *M***

➢ Where it is not possible to use doxycycline, azithromycin 1g PO stat followed by 500mg PO once daily for 2 days	***gen* status are unknown) is <u>NOT</u> recommended.**
Positive *M gen*: resistance unknown **Uncomplicated infection (NSU, non-severe proctitis, mucopurulent cervicitis)** ➢ Doxycyline 100mg PO twice daily x 7 days followed by azithromycin 1g PO stat and 500mg PO once daily for 2 days OR ➢ Moxifloxacin 400mg PO once daily x 7 days **Complicated infection (PID, EO, severe proctitis, SARA)** ➢ Moxifloxacin 400mg PO once daily x 14 days **Positive M gen: markers of macrolide resistance absent** **Uncomplicated infection (NSU, non-severe proctitis, mucopurulent cervicitis)** ➢ Doxycyline 100mg BD PO x 7 days followed by azithromycin 1g PO stat and 500mg PO once daily for 2 days ➢ Where it is not possible to use doxycycline, azithromycin 1g PO stat followed by 500mg PO once daily for 2 days **Complicated infection (PID, epididymo-orchitis, SARA)** ➢ Moxifloxacin 400mg orally once daily x 14 days OR ➢ Minocycline 100mg PO twice daily for 14 days **Positive *M gen*: markers of macrolide resistance <u>present</u>** **Uncomplicated infection (NSU, non-severe proctitis, mucopurulent cervicitis)** ➢ Moxifloxacin 400mg PO once daily x 7 days OR ➢ Minocycline 100mg PO twice daily for 14 days **Complicated infection (PID, epididymo-orchitis, SARA)** ➢ Moxifloxacin 400mg orally once daily x 14 days OR ➢ Minocycline 100mg PO twice daily for 14 days	A study from the Gay Men's Health Service in collaboration with the Virology Department at St James's Hospital[ii] found evidence of macrolide resistance in 75% of isolates. Macrolide resistance mutations are present in almost half of all isolates in Ireland that had resistance testing performed from January 2020 to September 2022[iii]. Where an individual has already received a course of doxycycline prior to starting azithromycin, this does not need to be repeated where the interval is up to 2 weeks since completion of the doxycycline. **Fluoroquinolones exposure can lead to prolonged, disabling and potentially irreversible adverse reactions. This risk is greater in older patients, those with renal impairment and in those on concomitant corticosteroids therapy. The risk of QT prolongation is greater with moxifloxacin than other quinolones. All patients should be assessed for other medication or conditions that may prolong the QT interval. These risks should be discussed with all patients and they should be provided with written information[iv] [v].** Use of single dose macrolide monotherapy is NOT recommended. Where treatment failure with doxycycline/azithromycin is suspected in an isolate initially found to be macrolide susceptible, retreatment with doxycycline/azithromycin is NOT recommended given that the isolate may have become macrolide resistant.
Positive *M gen*: markers of macrolide and quinolone resistance present or failed treatment with moxifloxacin In cases of apparent failed treatment ensure not reinfected since treatment Treatment options include Pristinamycin or Sitofloxacin. Doxycycline can reduce bacterial burden in advance of using these medicines which may needto be imported. In cases where it is proving challenging to get a microbiological cure and there has been resolution of symptoms consider no further treatment.	Such cases may call for collaboration with international colleagues. **Should only be done in a service with experience and expertise in managing *M gen* resistant cases.**
Pregnancy Data on *M gen* and its association with adverse pregnancy outcomes are limited, however it has been associated with asmall increased risk of preterm delivery and spontaneous abortion.	In line with current BASHH guidelines

Azithromycin use during pregnancy is unlikely to increase the risk of birth defects or adverse pregnancy outcomes. A three-day course of azithromycin (1g PO stat followed by 500mg PO once daily for 2 days) can be used for uncomplicated *M. gen* infection detected in pregnancy. The use of moxifloxacin in pregnancy is **contra-indicated**. In women with likely macrolide resistance, or with upper genitaltract infection in pregnancy, options are limited. The FDA recommends avoiding doxycycline in the 2nd and 3rd trimester due to permanent teeth discoloration or inhibition of bone growth. No evidence of substantial teratogenic risk if used in 1st TM but data insufficient to conclude no risk. The BNF advises against its use in all trimesters. There are no data regarding the use of pristinamycin in pregnancy. An informed discussion should be had with the patient around the known and unknown risks associated with the use of these medicines in pregnancy and the known and unknown risks of adverse outcomes associated with *M. gen* infection in pregnancy. Where possible treatment should be delayed until after pregnancy, guided by resistance results.	
Test of Cure	
All patients should attend for a **test-of-cure five weeks** after the start of treatment.	
Management of contacts	
Current sexual partners (regular and non-regular partners where there is likely to be further sexual contact) of those who are *M gen* positive should be offered testing for *M gen*.	
Current sexual partners (regular and non-regular partners where there is likely to be further sexual contact) of those who are *M gen* positive can be offered (once there is no contraindication) the same treatment as their partner and guided by partner resistance results. It is reasonable to wait for the result (including resistance result) in the contact before treating with clear advice on abstaining from unprotected sexual contact during that time.	
Surveillance	
M gen is not currently a notifiable infection. This may change in the future. In the meantime, it is recommended that laboratories and STI services monitor the number of tests, positive results and patient outcomes in line with local audit practices.	

Membership of working group

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[i] BASHH, British Association for Sexual Health and HIV national guideline for the management of infection with Mycoplasma genitalium (2018), https://www.bashhguidelines.org/media/1198/mg-2018.pdf

[ii] Prevalence, Macrolide Resistance, and Fluoroquinolone Resistance in *Mycoplasma genitalium* in Men Who Have Sex With Men Attending an Sexually Transmitted Disease Clinic in Dublin, Ireland in 2017-2018. Mulligan V et al. Sex Transm Dis. 2019 Apr;46(4):e35-e37

[iii] Sutton-Fitzpatrick, Ú. Brennan, C., De Gascun, C. *Mycoplasma genitalium* resistance in Ireland 2020-2022. ISCM, 2023

[iv] http://www.hpra.ie/docs/default-source/publications-forms/newsletters/hpra-drug-safety-newsletter-edition-91.pdf?sfvrsn=7

[v] https://www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/drug-interactions/fluoroquinolone-warning-2019.html