Current Clinical Approach to Mycoplasma Genitalium

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Background

Mycoplasma refers to any organism belonging to the Mollicutes class. Although over 200 named Mycoplasma species exist, only six are established human pathogens. Of these six species, five inhabit the genitourinary tract: *M. hominis*; *M. genitalium*; *M. fermentans*; *ureaplasma urealyticum*; and, *ureaplasma parvum*. Mycoplasmas are the smallest free-living organisms and because they lack a cell wall, they are not visible post Gram staining.[1] Since mycoplasmas lack a cell wall, antibiotics that target cell wall synthesis such as penicillin, cephalosporins and other beta-lactams are ineffective.[2,3]

Although *M. hominis* and *ureaplasma* have been associated with genitourinary disease, their pathogenic roles are unclear due to the following: genitourinary colonization with these species is common among healthy asymptomatic adults; significant design limitations of published studies; traditionally these organisms have been difficult to detect; and, mycoplasmas are rarely the only organism isolated from a specimen making it difficult to determine whether they are causative pathogens or simply co-isolates.[1] Unlike *M. hominis* and *ureaplasma*, *M. genitalium* is recognized as "an emerging sexually transmitted pathogen" that is a "significant cause of genital tract infections".[4,5]

Globally, *M. genitalium* prevalence estimates range between 1 and 4 percent of males and 1 and 6 percent among females.[3,4] However, higher prevalence rates have been found among sexually transmitted infection (STI) clinic clients with prevalence as high as 38% among those at risk of a STI.[3,4] Locally, a study conducted on clients at Hassle Free clinic in Toronto between September and December of 2013 found that the overall prevalence of *M. genitalium* was 4.2%, somewhat higher for men at 4.5% compared to women at 3.2%.[6] Another Canadian study that examined clients at two STI clinics in Alberta from January to April of 2016 found an overall *M. genitalium* prevalence of 6.2% with a male prevalence of 5.3% and a female prevalence of 7.2%.[7]

Mycoplasma genitalium is sexually transmitted via genital to genital mucosal contact.[5,8] It has also been found in low rates in anorectal samples and penile-anal transmission has been established.[5,8] Oral-genital transmission is unlikely.[3] Risk factors for *M. genitalium* infection include: young age, smoking, non-Caucasian ethnicity, increasing number of sexual partners and recent sexual intercourse.[3,9] Co-infection with *M. genitalium* and other bacterial STI's has been found among high-risk individuals with *M. genitalium* and chlamydia co-infection being the most common.[3] Although no causal relationship has been established, individuals with *M. genitalium* were two times as likely to be HIV infected.[5]

Similar to bacterial STI's, *M. genitalium* can either be symptomatic or asymptomatic. In fact, the majority of individuals with *M. genitalium* in the genitourinary tract do not develop disease.[9] In males with symptoms, *M. genitalium* causes urethritis and is the cause of 15-20% of non-gonococcal urethritis (NGU), 20-25% of non-chlamydial urethritis NGU and 40% of persistent or recurrent urethritis.[2] Symptoms of urethritis caused by *M. genitalium* typically include dysuria, urethral discharge and urethral pruritis.[3] Males infected with *M. genitalium* may also experience proctitis and balanoposthitis (inflammation of the glans penis and foreskin).[8,9] Among females, symptoms of infection with *M. genitalium* can include: dysuria; cervicitis (including purulent or mucopurulent cervical discharge and cervical friability; vaginal discharge; vaginal itching; lower abdominal pain; menorrhagia; inter-menstrual bleeding; and, post-coital bleeding.[2,3,8,9] Complications that have been found to be associated with *M. genitalium* infection in women include: pelvic inflammatory disease (PID); adverse pregnancy outcomes such as spontaneous abortion and preterm delivery; and, tubal factor infertility.[2,3,8,9] In both males and females, sexually acquired reactive arthritis may occur.[9]

Testing

Routine screening is not recommended. Testing is only recommended in cases of persistent or recurrent urethritis, cervicitis or PID when both chlamydia and gonorrhea have been ruled out.[4]

In Canada, access to testing for *M. Genitalium* is limited as it is only available via the National Microbiology Laboratory (NML) in Winnepeg.[7,10] In order for a sample to be forwarded for testing for *M. genitalium* at the NML, Public Health Ontario (PHO) requires that the following criteria be met: client is symptomatic with persistent or recurrent urethritis, cervicitis or PID; client has negative chlamydia and gonorrhea test results; and, approval by the PHO laboratory microbiologist is granted.[10] The NML which uses a nucleic acid amplification test will test samples positive for *M. genitalium* for mutations associated with antimicrobial resistance.[5]

Testing for *Mycoplasma* (not including *M. genitalium*) and *ureaplasma* is done by culture at the Ontario public health lab and turnaround time can take up to 17 days.[10]

Further testing information can be found at Public Health Ontario: Ureaplasma/Mycoplasma – Culture and Reference Identification | Public Health Ontario.

Treatment

Due to limited test availability, most infections will be managed and treated by syndromic management of urethritis, cervicitis or PID.[4]

The recommended treatment for suspected or confirmed *M. genitalium* that was not previously treated with Azithromycin is:

- Azithromycin 500 mg PO on day one, followed by 250 mg PO on days 2 to 5.[4]

Treatment with Azithromycin 1 g PO in a single dose has been reported to select for macrolide resistance and thus individuals who have not responded to this regimen may not benefit from being re-treated with the 5 day regimen.[2,4] When an individual with suspected or confirmed *M. genitalium*-associated cervicitis or urethritis has previously been treated with azithromycin, the recommended treatment is:

- Moxifloxacin 400 mg PO once daily for 7 days[4]

For suspected or confirmed *M. genitalium*-associated PID, the recommended treatment is:

- Moxifloxacin 400 mg PO once daily for 14 days in addition to a PID standard treatment regimen[4]

Health Canada (2021) advises that test of cure should be done at a minimum of 3 weeks post treatment for those that continue to experience symptoms or live in areas with high antibiotic resistance.[4] It is important to note that a study conducted at a STI clinic in Toronto in 2013 found high resistance rates among study participants with 58% demonstrating macrolide resistance and 20% showing fluoroquinolone resistance.[6]

In cases where treatment is warranted for an uncomplicated genitourinary infection caused by *Ureaplasma* or *M. hominis*, the recommended treatment is:

- Doxycycline 100 mg PO twice daily for 7 days in lower urogenital tract infection

Or

- Doxycycline 100 mg PO twice daily for 14 days in the instance of more extensive infection such as PID[1]

Flouoroquinolones can be used in cases of treatment failure or resistance.[1]

Management

In addition to patient education on *M. genitalium* and its sequelae, patients should be told to abstain from sexual intercourse for 14 days after the start of treatment and until all symptoms have resolved.[9]

Current partners of cases should also be treated to prevent reinfection of the index case.[4] They should be treated whether or not they have symptoms and do not require testing before treatment.[11]

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