Clinical presentation, diagnosis, and management of *Mycoplasma genitalium*

By Jessica N. Wellette, DNP, APRN, WHNP-BC; Shelza J. Rivas, DNP, APRN, WHNP-BC, AGPCNP-BC; and Melissa G. Davis, DNP, CNM, FNP-BC, FACNM, C-EFM

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In 2015, the Centers for Disease Control and Prevention (CDC) announced that *Mycoplasma genitalium* was a public health threat.[1] Other sources are now calling it a rising sexually transmitted infection (STI) with similar incidence rates to those for chlamydia and gonorrhea.[2–4] Recent population-based studies have found the prevalence of *M. genitalium* to be higher than all other bacterial STIs.[4] The purpose of this article is to provide an update for clinicians on symptoms, associated consequences, screening, diagnostic testing, and treatment for *M. genitalium*.

Associated consequences and risk factors

M. genitalium has been associated with cervicitis, pelvic inflammatory disease (PID), preterm delivery, spontaneous abortion, infertility, and increased risk of infection with human papilloma virus and human immunodeficiency virus (HIV).[1,2,4,5] A meta-analysis found that *M. genitalium* caused a two-fold increase in preterm birth, spontaneous abortion, infertility, cervicitis, and PID.[6] Studies have found *M. genitalium* to be the culprit in 10% to 30% of clinical cervicitis cases.[1] Among men, *M. genitalium* has been linked to asymptomatic urethritis and recurrent urethritis.[1] Further research in men is needed to identify a distinct correlation between *M. genitalium* and epididymitis, prostatitis, and infertility.[1,2] *M. genitalium* is associated with an increased risk for HIV infection among women and men who have sex with men (MSM).[1,2] HIV infection is twice as prevalent in women with *M. genitalium* as compared to those who are negative for it.[4]

Risk factors for *M. genitalium* include African American race, previous pregnancy, current bacterial vaginosis (BV) infection, and being younger than age 21 years.[7] One prospective US study found that 20% of women who had asymptomatic BV were positive for *M. genitalium*.[8] Another study conducted in Kenya found that an active BV infection increased susceptibility to *M. genitalium*.[4] There also is a correlated risk with increasing numbers of sexual partners for both males and females.[4,9] A Denmark correlational study found shorter duration of sexual relationships and first sexual encounter before age 13 years with the increased rates of *M. genitalium* in women.[9] Coinfection with another STI seems to vary across geographic settings in the United States.[4]

Figure. *Mycoplasma genitalium*

Centers for Disease Control and Prevention (2021). Public Health Image Library

Clinical presentation

Patients with *M. genitalium* are often asymptomatic but may present with vaginal odor, discharge, itching, urethritis, dysuria, urinary urgency, intermenstrual cycle bleeding, postcoital bleeding, cervical friability, and lower abdominal pain (*Table 1*).[2–4,10] In men, *M. genitalium* may present as balanoposthitis, chronic prostatitis, and acute epididymitis.[5] Men also demonstrate a strong association between nongonococcal urethritis and *M. genitalium*.[6] *M. genitalium* has been associated with rectal infections in 3% of women and up to 26% of MSM.[1]

Screening and diagnosis

Current guidelines for *M. genitalium* are evolving to identify individuals most appropriate for screening. It is typically found in the cervix or endometrium in women presenting with PID, and it is estimated that about 4% to 22% of women with PID are positive for *M. genitalium*.[1] Women with recurrent cervicitis or PID should be screened with resistance testing if it is available.[2] Even if testing is unavail-

Table 1. Clinical manifestations and symptoms of *M. genitalium*

- Cervical friability
- Discharge
- Dysuria
- Itching
- Intermenstrual cycle bleeding
- Lower abdominal pain
- Postcoital bleeding
- Urinary urgency
- Vaginal odor

able, *M. genitalium* should be suspected and potentially treated in these individuals.[2] Men with persistent urethritis should be screened for *M. genitalium*.[2] Routine screening for asymptomatic patients is currently not recommended.[2]

M. genitalium is an extremely slow-growing organism (*Figure*). Cultures can take up to 6 months to process and are not recommended.[2] Because *M. genitalium* lacks a cell wall, gram staining is ineffective. Serologic testing lacks sensitivity and specificity.[4] The US Food and Drug Administration has approved nucleic acid amplification testing (NAAT) with use of urine or urethral, penile meatal, endocervical, and vaginal swab specimens[1–4] Given that *M. genitalium* is rarely seen in the oropharynx, oropharyngeal testing is not necessary.[1,4]

Treatment

Antibiotics that function by targeting the cell-wall biosynthesis such as beta-lactams or penicillins are ineffective for treatment of *M. genitalium*.[1,2] Metronidazole, the recommended treatment for BV, is not effective.[11] The current recommended treatment for PID is not effective against *M. genitalium*.[1]

Over the years, treatment for *M. genitalium* has become more difficult as resistance to microbial therapy is increasing, specifically among macrolides and quinolones.[3] Recommended treatment was previously 1 g azithromycin, but multiple studies have found that *M. genitalium* is showing resistance to azithromycin.[1–3] Therefore, two-stage approaches, ideally using resistance-guided therapy, should be used to treat *M. genitalium* (*Table 2*). However, antimicrobial resistance testing for macrolide or quinolone markers is not currently available in the US.[2] Molecular assays that incorporate detection of mutations associated with macrolide resistance are pending.[2] The CDC recommends that where resistance testing is not available, the macrolide-resistant regimen should be used.[2] If *M. genitalium* is detected in the presence of PID, moxifloxacin 400 mg once daily for 14 days should be added to the treatment regimen.[1] Using resistance-guided treatment for *M. genitalium* can increase cure rates to more than 90%.[2] Once the patient has been treated with the recommended medications, a test of cure is generally not indicated.[1,2]

M. genitalium has been found to affect 1% to 8.5% of pregnancies.[12] Azithromycin without doxycycline is recommended for *M. genitalium* in pregnancy and during lactation. Macrolides have not been shown to have adverse fetal or infant effects.[12,13] Doxycycline may cause

Table 2. Resistance testing and treatment

Testing	Initial medication	Followed by	Followed by
Resistance testing available and macrolide sensitive	Doxycycline 100 mg orally twice a day for 7 days	Azithromycin 1 g orally one time	Azithromycin 500 mg daily x 3 days
Resistance testing available and macrolide resistant	Doxycycline 100 mg orally twice a day for 7 days	Moxifloxacin 400 mg daily for 7 days	
No resistance testing available	Doxycycline 100 mg orally twice a day for 7 days	Moxifloxacin 400 mg daily for 7 days	
Pregnancy	Azithromycin 1 g orally one time	Azithromycin 500 mg daily x 3 days	
Breastfeeding	Azithromycin 1 g orally one time	Azithromycin 500 mg daily x 3 days	

dental enamel staining and growth restriction in the long bones.[13] Moxifloxacin is contraindicated in pregnancy and has not been studied in breastfeeding, although fluoroquinolones are typically avoided due to potential risk to the infant's developing joints.[13]

Partners of patients diagnosed with *M. genitalium* can be tested and treated accordingly.[1] If testing is unavailable, the partner can be treated with the same regimen as the patient. During the time that partners are being treated, they should abstain from sexual intercourse to reduce the risk of reinfection. Further research is needed to accurately determine rates of reinfection.[1]

Patient counseling and education

Because patients with *M. genitalium* may have coinfections, counseling and education should center on discussion of other testing including for HIV, STI prevention, and safer sex practices.[4] Providers should encourage condom use for STI protection. STI testing should be encouraged with each new sexual partner to minimize infection risk, ideally before any sexual encounter has occurred. Providers may also encourage patients to have open and honest conversations about their sexual health with their current partner as long as they feel safe and comfortable in doing so. Providers should also educate patients about possible pregnancy implications from *M. genitalium* including increased risk of infertility, spontaneous abortion, and preterm labor.

Conclusion

M. genitalium is a rising STI that providers should be aware of because it may present as recurrent vaginal infection, intermenstrual bleeding, lower abdominal pain, postcoital bleeding, urinary urgency, and other symptoms similar to vaginitis in women. In males, *M. genitalium* may present as recurrent urethral or testicular infections. Although current guidelines do not recommend routine screening for *M. genitalium*, patients with suspected symptoms should be tested and treated according to CDC guidelines. Providers should remain up to date on the most current screening, diagnosis, and treatment guidelines. ■

Jessica N. Wellette is an Assistant Professor of Nursing at Vanderbilt University School of Nursing and WHNP at VUSN Faculty Nurse-Midwife and Primary Care Practice in Nashville, Tennessee. Shelza J. Rivas is an Assistant Professor of Nursing at Vanderbilt University School of Nursing and WHNP/AGPCNP at VUSN Faculty Nurse-Midwife and Primary Care Practice. Melissa G. Davis is an Associate Professor at Vanderbilt University School of Nursing and the Clinical Director of VUSN Faculty Nurse-Midwife and Primary Care Practice. The authors have no actual or potential conflicts of interest in relation to the contents of this article.

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