SUPPLEMENT TO
OBG MANAGEMENT
April 2023
AVAILABLE AT WWW.MDEDGE.COM/OBGYN/ARTICLE/261449/MYCOPLASMA-GENITALIUM-PATHOGEN-WE-CAN-FINALLY-BEGIN-UNDERSTAND
DEVELOPED UNDER THE DIRECTION AND SPONSORSHIP OF HOLOGIC.
THIS CONTENT WAS PEER REVIEWED BY OBG MANAGEMENT.

Mycoplasma genitalium: A Pathogen We Can Finally Begin to Understand

Kyle Bukowski, MD is a double board-certified OB/GYN and Complex Family Planning sub-specialist. He serves as the Chief Medical Officer for Planned Parenthood of Maryland, and in this role, Dr. Bukowski promotes the mission of ensuring Marylanders and anyone traveling to Maryland have broad access to high-quality, affordable sexual and reproductive health services. Dr. Bukowski received his medical degree and completed his residency at the David Geffen School of Medicine at UCLA. Providing evidence-based, high-quality sexual and reproductive health care is his passion and drives his interest in advocacy and health education.

Obstetrician/gynecologists (OB/GYNs) are acutely aware that the rate of sexually transmitted infections (STIs) in the United States remains far too high.[1] And now, in addition to long-established STIs *Neisseria gonorrhea (NG)* and *Chlamydia trachomatis (CT)*, we must contend with an additional STI—*Mycoplasma genitalium* (*M. genitalium*), which presents like other urogenital tract bacterial infections and has a prevalence up to 10% higher than NG and, at times, higher than CT.[1] We must recognize that riding alongside these known STIs, this historically elusive microbe may have often been the underlying cause of cervicitis, pelvic inflammatory disease (PID), preterm delivery, spontaneous abortion, and infertility.[1]

In fact, *M. genitalium* is not a new STI—and it is by no means rare. This small Gram-negative bacterium, containing the smallest genome of any free-living organism, was first isolated in 1981,[2] and although subsequent research produced strong evidence of pathogenicity,[3,4] routine clinical diagnosis of infection remained unfeasible for nearly 40 years. Slow growth in culture (up to 6 months) is not clinically useful, and the lack of a cell wall prevents detection through traditional Gram staining and microscopy.[2] Thus, *M. genitalium* remained undetected and untreated for decades, lurking among better-known STIs, and when other testing was negative, it may have been the only infection.

By 2015, the Centers for Disease Control and Prevention (CDC) had sufficient data to identify the pathogen as an "emerging infection."[5] Reliable testing for *M. genitalium* infection became possible in 2019 when the United States Food and Drug Administration (FDA) cleared the Aptima Mycoplasma genitalium Assay (Hologic) as the first nucleic acid amplification test (NAAT) for detection of *M. genitalium* infection.[6] With the availability of the assay, the CDC published new testing and treatment recommendations for the organism in its 2021 guidelines.[1] These include identifying a twofold increase in serious morbidities associated with *M. genitalium* infection, as well as an association with other STIs, including HIV.[1]

The new CDC guidelines recommend testing patients with persistent or recurrent cervicitis (of which there is a 10–30% prevalence of *M. genitalium*) and recommend considering testing patients with PID (of which there is a 4–22% prevalence of *M. genitalium*).[1] The guidelines also recommend use of NAAT testing for the detection of the infection. For instance, the Aptima Mycoplasma genitalium Assay, which targets rRNA of the bacterium, is up to 100% sensitive when used with vaginal swab samples.[7-11] In comparison, laboratory-developed PCR tests, targeting genomic DNA, can miss approximately 40% of *M. genitalium* infections.[9]

Because the current guidelines are limited to testing a narrow group of symptomatic patients, an effective response to *M. genitalium* begins with more vigilant attention to cervicitis—namely that the condition is properly diagnosed, coded, and documented to ensure that a patient qualifies for testing if her condition becomes persistent or recurrent.

Healthcare providers need to think more holistically about all symptoms typically associated with common vaginal infections. Presentation of *M. genitalium* infection can be similar to infection with NG, CT, *Trichomoniasis vaginalis* (TV), yeast infections, and bacterial vaginosis (BV) (Table),[12,13] but data clearly indicate that *M. genitalium* may, at times, be the sole pathogen causing abnormal discharge, vaginal irritation, or pain during urination or sex.[1]

The overall prevalence of *M. genitalium* infection ranges from 1.3% in the general female population to 15.9% among females considered high-risk for STIs.[14] In addition, in practice settings where patients may see more than one provider,

Dr. Bukowski is a speaker and consultant for Hologic, Inc.

TABLE *M. genitalium* Presents Similarly to Other STIs and Vaginal Infections

	SIMILAR SYMPTOMS					
	Trichomoniasis	Bacterial Vaginosis	Yeast Infection	Chlamydia	Gonorrhea	*M. genitalium*
Abnormal Discharge	✓	✓	✓	✓	✓	✓
Vaginal Odor	✓	✓				
Vaginal Irritation	✓	✓	✓	✓	✓	✓
Pain During Urination/Sex	✓		✓	✓	✓	✓

Adapted from: Kent and Mobley[12,13]

it is essential to develop and maintain systems for flagging charts to avoid overlooking persistent/recurrent symptoms and to encourage patients to return for reassessment when symptoms do not improve with initial treatment or expectant management.

For example, presentation of BV may suggest running the *M. genitalium* assay as a secondary test if vaginitis symptoms do not clear with initial treatment. At least one study indicates a likelihood that prior BV infection may increase susceptibility to *M. genitalium*,[15] and this is typical of our still nascent understanding of this microbe's effects on patient health. Thus, in addition to the CDC guidelines, when symptoms of otherwise assumed infection do not clear as expected, testing for *M. genitalium* may be considered—especially because the treatment protocol is distinctive from other STIs.

If resistance testing is available, macrolide sensitive *M. genitalium* is treated with 100 mg doxycycline orally twice daily for 7 days followed by an initial dose of azithromycin 1 g orally, and then 500 mg azithromycin orally once daily for an additional 3 days. Macrolide resistant (or unknown resistant) *M. genitalium* is treated with 100 mg doxycycline orally twice daily for 7 days followed by moxifloxacin 400 mg orally once daily for 7 days.[1]

Given the scarcity of macrolide resistance testing—there is no FDA-cleared *M. genitalium* test available in the United States that detects antibiotic resistance—healthcare providers will need to assess and discuss treatment implications with all patients when prescribing the two-stage regimen that includes fluoroquinolones, as there is some risk of tendinopathy and tendon rupture, particularly among patients older than age 60.[16] If healthcare providers educate patients about the potential adverse effects of moxifloxacin and instruct them to stop the medication immediately if they experience joint or tendon pain or swelling, treating *M. genitalium* should be the priority.

Without question, OB/GYNs have been contending with *M. genitalium* for a long time, though we are only now at the leading edge of understanding this tiny microbe and its effects on the sexual and reproductive health of our patients. Broadening awareness and adoption of the CDC testing guidelines will increase prevalence data, which will lead to a better understanding of the causative relationships between *M. genitalium* and morbid conditions.

With superior diagnostic tools, we can meet the challenge presented by this not-so-new microbe while helping foster regular STI testing, and encourage our patients to seek care when symptoms occur. These are all essential strategies to identify infection as early as possible to reduce spread and long-term sequelae.

Learn more about *M. genitalium*

REFERENCES

1. Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. *MMWR Recomm Rep.* 2021;70(4):1–187.
2. Taylor-RobinsonD, Jensen JS. (2011). Mycoplasma genitalium: from Chrysalis to multicolored butterfly. *Clin Microbiol Rev, 2011*;24(3), 498–514.
3. Taylor-Robinson D, Furr PM, Hetherington CM. The pathogenicity of a newly discovered human mycoplasma (strain G37) for the genital tract of marmosets. *J Hyg (Lond).* 1982;89(3):449-55.
4. JensenJS, Orsum R, Dohn B, Uldum S, Worm AM, Lind K. Mycoplasma genitalium: a cause of male urethritis? *Genitourin Med.* 1993;69(4): 265–269.
5. Frieden, TR, Jaffe, HW, Cono, J, et al. Sexually Transmitted Diseases Treatment Guidelines, 2015. June 5, 2015. rr6403.pdf (cdc.gov)
6. United States Food and Drug Administration, New Release; January 23, 2019. FDA permits marketing of first test to aid in the diagnosis of a sexually-transmitted infection known as Mycoplasma genitalium | FDA
7. Chernesky M, Jang D, Martin I, et al. Comparison of Assays for the Diagnosis of Mycoplasma genitalium and Macrolide Resistance Mutations in Self-Collected Vaginal Swabs and Urine. *Sex Transm Dis.* 202047(10):705-711.
8. García-Sánchez E, Martínez-Díaz de Argandoña C, et al. Comparison of the Aptima MG and Cobas TV/MG tests for the detection of Mycoplasma genitalium in urogenital and extragenital samples. *Enferm Infecc Microbiol Clin (Engl Ed). 2021 July; 2468:1-4.*
9. LeRoy C, et al. French prospective clinical evaluation of the Aptima Mycoplasma genitalium CE-IVD Assay and Macrolide Resistance Detection Using Three Distinct Assays. *J Clin Microbiol*. 2017;55(11):3194-3200.
10. Naidu P, et al. Evaluation of 5 commercial assays for the detection of Mycoplasma genitalium and other Urogenital Mycoplasmas. *Med Microbiol Immunol*. 2021;210(1):73–80.
11. Unemo M, et al. Clinical and analytical evaluation of the new Aptima Mycoplasma genitalium assay, with data on M. genitalium prevalence and antimicrobial resistance in M. genitalium in Denmark, Norway and Sweden in 2016. *Clin Microbiol Infect*. 2018;24(5):533-539.
12. Kent H. Epidemiology of vaginitis. Am J Obstet Gynecol. 1991;165(4):1168-1176.
13. Mobley VL, Seña AC. Mycoplasma genitalium infection in men and women. UpToDate. Last updated February 15, 2019. Accessed September 8, 2021.
14. Baumann L, Cina M, Egli-Gany D, Goutaki M, Halbeisen FS, Lohrer GR, Ali H, Scott P, Low N. Prevalence of Mycoplasma genitalium in different population groups: systematic review andmeta-analysis. Sex Transm Infect. 2018 ;94(4):255-262. doi:10.1136/sextrans-2017-053384. Epub 2018 Feb 9.
15. Lokken EM, Balkus JE, Kiarie J, Hughes JP, Jaoko W, Totten PA, McClelland RS,Manhart LE. Association of Recent Bacterial Vaginosis With Acquisition of Mycoplasma genitalium. *Am J Epidemiol*.2017;186(2):194–201.
16. Persson, R, Jick, S. Clinical implications of the association between fluoroquinolones and tendon rupture: The magnitude of the effect with and without corticosteroids. Br J Clin Pharmacol. 2019;85(5), 949–959.