

## *Mycoplasma genitalium*: The Smallest Pathogen Becoming a Big Concern



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Initially discovered in the 1980s, researchers have been investigating the elusive *Mycoplasma genitalium*, a sexually transmitted infection (STI), through laboratory studies for nearly 30 years.<sup>1</sup> Yet, *M. genitalium* has remained a footnote in the STI literature because it is difficult to detect, limiting sufficient data to provide clinical guidance. The smallest free-living cell, and containing a single copy of DNA, *M. genitalium* evades microscopy because it lacks cellular walls, and its average 6-month culture period is unfeasible for clinical diagnosis.<sup>2</sup>

Now, greater understanding of *M. genitalium* and the availability of US Food and Drug Administration (FDA)-cleared assays have prompted new guidelines from the US Centers for Disease Control and Prevention (CDC), including the first ever guidance of whom to test. Following the 2019 FDA approval of the first nucleic acid amplification test (NAAT) to detect *M. genitalium*, the CDC recommends in its updated 2021 STI Treatment Guidelines testing for the infection in women with recurring cervicitis and in men with persistent or recurring urethritis. The CDC also recommends that testing for *M. genitalium* should be considered for women with pelvic inflammatory disease (PID).<sup>3</sup>

Because presentation of *M. genitalium* is consistent with *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG), and *Trichomonas vaginalis* (TV),<sup>4,5</sup> and because testing for the pathogen has not been commercially available until recently, underdiagnosis of *M. genitalium* infection is likely. Prevalence of about 10% in both women and men is consistently higher than gonorrhea and, at times, greater than chlamydia.<sup>6</sup> *M. genitalium* has, on average, been detected in about 10% to 30% of women with clinical cervicitis, up to 22% of women with PID, and approximately 40% of men with persistent or recurring non-gonococcal urethritis (NGU).<sup>3</sup> Available data also reveal

a significant correlation between the presence of *M. genitalium* and other STI pathologies, including, potentially, human immunodeficiency virus (HIV).<sup>1</sup>

Research conducted to date is “mostly supportive of a causal relationship” with cervicitis and PID in women and confirms a causal relationship with NGU in men. The CDC notes a “2-fold increase” in women's risk of cervicitis, PID, preterm delivery, spontaneous abortion, and infertility when *M. genitalium* is present.<sup>3</sup>

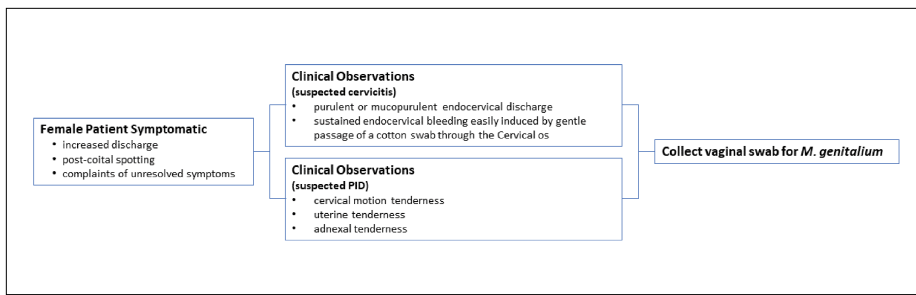
### Recognizing Recurrent Cervicitis and PID Is Essential

Part of recognizing how and when health care providers should test for *M. genitalium* is a need to better understand recurrent cervicitis and PID. Recurrent cervicitis is defined as inflammation of the cervical tissue that has persisted despite attempts at treatment and where re-exposure to an infection did not occur. Although frequently asymptomatic, diagnostic criteria include purulent or mucopurulent endocervical discharge visible in the endocervical canal or on an endocervical swab specimen and/or signs of inflammation such as sustained endocervical bleeding easily brought on by gentle passage of a cotton swab through the cervical os. The etiology of cervicitis is also commonly associated with CT, NG, TV, herpes simplex virus, and *M. genitalium*.<sup>3</sup>

PID can be difficult to diagnose due to subtle or nonspecific symptoms, but criteria include one or more of the following presentations during pelvic examination: cervical motion tenderness, uterine tenderness, or adnexal tenderness. PID is also commonly associated with CT, NG, TV, and again, *M. genitalium*.<sup>3</sup>

Given the significant prevalence of *M. genitalium* with cervicitis and PID, testing for this pathogen in women with these conditions, per the new CDC guidelines, is necessary because *M. genitalium* can present similarly to other STIs, but the treatment protocol is distinctive (**Figure 1**).<sup>3</sup>

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**FIGURE 1** *M. genitalium* testing algorithm<sup>3</sup>

### Available Testing for *M. genitalium* Answers a Long Unmet Need

The new CDC guidelines correspond directly with development of the newly available NAAT assays using transcription-mediated amplification, which are the only reliable method of detection<sup>7</sup> and the only method recommended by the CDC.<sup>3</sup>

With the advent of these new FDA-approved assays, *M. genitalium* can be detected during annual well-woman visits or any sexual health visit where symptoms of STIs, recurrent cervicitis, or PID could be a concern. Although the assay may be used with both swabs and urine collection, vaginal swabs have been shown to be superior to urine testing for detection of STIs.<sup>8</sup> Turnaround time for *M. genitalium* results varies by lab and the lab's respective workload; however, vaginal swabs offer a streamlined approach that expedites results as labs have the flexibility to run multiple tests on a single patient sample. Cost of the *M. genitalium* assay will depend on patient insurance coverage.

### *M. genitalium* Presumed Harmful and Should Be Treated

The CDC-recommended treatment for *M. genitalium* is doxycycline 100 mg orally twice daily for 7 days, followed by moxifloxacin 400 mg orally once daily for 7 days.<sup>3</sup> Both microbial regimens are contraindicated during pregnancy, and although some studies indicate pristinamycin may be a treatment option for pregnant women, considerably more research is needed in this area given that there is no recommended alternative treatment for *M. genitalium* during pregnancy.<sup>3,9</sup> Pregnant women who test positive for an *M. genitalium* infection should be referred to a specialist to help manage care.

Although the data are insufficient to show whether reinfection will be reduced with treatment of sex partners, the CDC advises that sex partners of anyone who tests positive for *M. genitalium* can be treated with the same microbial regimen, even if testing is not possible.<sup>3</sup>

### *M. genitalium* Is too Prevalent in Women to Be Overlooked

Women with adverse outcomes and other conditions associated with STIs deserve to know whether, or how, this smallest of pathogens is affecting their health.

As more clinicians learn about the importance of *M. genitalium* testing and treatment for women with recurrent cervicitis, they may find themselves with a patient who is pregnant or planning pregnancy, and be uncertain as to how to proceed with treatment. As ObGyns, it is a challenge to counsel pregnant patients in whom *M. genitalium* infection may be a concern that they may be harboring an STI associated

with female genital tract pathology and preterm birth yet cannot not be offered testing and treatment given the lack of clinical guidelines for pregnant individuals.

Clearly, more *M. genitalium* research is essential to understand better the influence of this pathogen on a host of conditions affecting gynecologic and obstetric health overall. In our study conducted at Baylor College of Medicine, the prevalence of *M. genitalium* in pregnant women coming in for routine care was found to be 5.7% and, consistent with other studies, we found associations with premature birth, premature rupture of membranes, spontaneous abortion, cervicitis, and infertility. Also consistent with historical data, *M. genitalium* was found to be more prevalent among women at higher risk for STIs, especially Black and Hispanic women ages 15 to 25.<sup>9</sup>

While research into the effects of *M. genitalium* since its discovery 40 years ago has been handicapped by difficulty in detection, access to testing is no longer an obstacle. On the contrary, more inclusive clinical testing for *M. genitalium* will not only lead to more effective treatment of patients today but will add essential information to our understanding about the effects of this organism on the long-term health of current and future female patients.

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