Mycoplasma genitalium

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Module 2: Self-Study Lessons
Lesson 10: Mycoplasma genitalium

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Introduction

Mycoplasma genitalium has emerged as an important bacterial sexually transmitted infection (STI). Recent data suggest the *M*. *genitalium* prevalence is as high or higher than the *C*. *trachomatis* prevalence in both males and females. The clinical presentation associated with *M*. *genitalium* infection is similar to that with *Chlamydia trachomatis*, and infection with *M*. *genitalium* has been associated with the STI syndromes of urethritis, cervicitis, and pelvic inflammatory disease (PID). In addition, *M*. *genitalium* may cause infertility and preterm delivery in pregnant women. It is frequently detected in the rectum, but whether it causes proctitis is unclear. Antimicrobial resistance in *M*. *genitalium* emerged around 2008 and has been rapidly expanding, making treatment of this infection challenging. Highly sensitive and specific diagnostic assays are available to detect it in clinical practice, and national guidelines outline recommendations for who should be tested and treated.

Epidemiology in the United States

Surveillance Data

Mycoplasma genitalium is not a reportable infection in the United States, and information on the prevalence of this infection is derived from three sources: (1) the 2017-2018 cycle of the National Health and Nutritional Examination Survey (NHANES), (2) a sentinel surveillance system in sexual health clinics, and (3) research studies. Among people of reproductive age (14–59 years of age) participating in NHANES, a population generally at lower risk of STIs, *M. genitalium* prevalence was 1.7%, which is lower than with *C. trachomatis* but higher than *N. gonorrhoeae* in a representative sample of young adults.[1,2,3,4] In contrast, the overall prevalence of *M. genitalium* among 1,743 attendees at 6 urban sexual health clinics in 2020 was 16.6%; among those participating in this surveillance study, 56% had genitourinary symptoms, and 44% were asymptomatic (Figure 2).[5] In those sexual health clinic attendees, *M. genitalium* prevalence was significantly higher among males with symptoms than among males without symptoms, but there was no significant difference in prevalence between females with and without symptoms.[5][Q] Mycoplasma genitalium Epidemiology

- **Sex**: Whether *M. genitalium* prevalence differs by sex depends on the population surveyed. Among people at relatively low risk of STIs participating in the 2017-2018 cycle of NHANES, *M. genitalium* prevalence was similar in males and females (1.8% and 1.7%, respectively).[2] The *M. genitalium* prevalence in the sexual health clinic surveillance study noted above was slightly higher in persons who identified as females (17.8%) than males (16.0%).[5]
- **Age**: Like other bacterial STIs, *M. genitalium* is most common among younger individuals. Among NHANES participants, *M. genitalium* prevalence was 3.9% in people 20–29 years of age, which was more than four times higher than the prevalence in older adults 40–59 years of age (0.9%).[2] In the sexual health clinic surveillance study, the prevalence was higher for younger people; those younger than 19 years of age had a very high prevalence rate (30.4%), but this sample size was very small (only 23 people).[5] The higher prevalence in younger individuals may be due to higher levels of sexual activity in young people or possibly to the development of partial immunity after initial infections, although this latter hypothesis has not been rigorously explored.[6]
- **Race/Ethnicity**: *M. genitalium* infection is more common among people who report Black race and this is consistent in both community and sexual health clinic surveillance settings.[2,5] In 2020, *M. genitalium* prevalence was lowest among Hispanic and non-Hispanic White sexual health clinic attendees (11-12%), whereas it was 21% in people reporting non-Hispanic Black race/ethnicity.[5]
- **Region and State**: *M. genitalium* prevalence varies by geographic location. Among sexual health clinic patients in 2020, the prevalence was lowest in the Pacific Northwest (9.9%) and highest in the South-Central United States (22-24%).[5]

Factors Associated with Acquisition of *M. genitalium*

The rate of new *M. genitalium* infections in women ranges from 0.9 per 100 person-years among university students in Great Britain to 18.2 per 100 person-years among women in the United States who engaged in exchange or survival sex (or were at high risk of STIs for other reasons).[7,8] Although relatively few studies have assessed factors associated with acquiring a new *M. genitalium* infection, bacterial vaginosis may play a role. Kenyan women engaging in exchange or survival sex who had bacterial vaginosis and women in the United States with asymptomatic bacterial vaginosis were more likely to subsequently acquire *M. genitalium* than women who did not have bacterial vaginosis.[7,9,10] Other factors are likely associated with an increased risk of acquiring a new *M. genitalium* infection, but few longitudinal studies have been done to identify them. Incidence in males appears to be somewhat lower than in females but potentially higher than the rate of other new bacterial STIs. Among men who have sex with women only (MSW) seeking sexual health care, the rate of new *M. genitalium* infections was 7 per 100 person-years, slightly higher than the rate of new chlamydial infections (6 per 100 person-years) and more than double the rate of new gonorrhea infections (3 per 100 person-years).[11]

Impact

Between 2017-2018, there were an estimated 3 million people of reproductive age (14–59 years) in the United States with a prevalent *M. genitalium* urogenital infection.[2] To date, no monetary costs for *M. genitalium* infections have been calculated, but these infections have been associated with PID, infertility, and preterm delivery—all conditions associated with high costs.[12]

Microbiology, Pathogenesis, and Transmission

Organism and Classification

Mycoplasma genitalium is a member of the Mollicute Class of bacteria.[13] In 2018, a name change to *Mycoplasmoides genitalium* was proposed, but this has been disputed, and most continue to refer to the organism as *Mycoplasma genitalium*.[13,14] Mycoplasmas are very small (0.5 and 1.5 µm in size) flask-shaped organisms; the protruding terminal (narrow) element contains an attachment organelle that drives gliding motility (Figure 3).[15,16] They are characterized by their absence of a rigid peptidoglycan cell wall and fastidious nature. The latter makes culture challenging, and few strains have been adapted to grow on agar. Tissue culture, requiring weeks to months, is typically used to isolate clinical strains of *M. genitalium*, but this has been accomplished by only a few laboratories globally.[17] Several other *Mycoplasma* species, including *M. pneumoniae*, *M. hominis*, *M. fermentans*, *M. penetrans*, *Ureaplasma urealyticum*, and *U. parvum*, are known to colonize humans, but only *M. pneumoniae* and *M. genitalium* are recognized human pathogens. Although *M. penetrans* has been associated with urethritis among men who have sex with men (MSM), to date, there is insufficient evidence linking *M. hominis*, *U. urealyticum*, *U. parvum*, and *M. fermentans* to disease syndromes.[18,19][Q] Mycoplasma genitalium Microbiology

Transmission

The primary mode of transmission for *M. genitalium* is sexual. The organism is found infrequently in people who have not yet become sexually active.[20,21,22,23] The person-to-person sexual transmission probability with *M. genitalium* has not been clearly defined, but it appears to be lower than with other common bacterial STIs, most likely due to a relatively lower *M. genitalium* organism load. Limited evidence suggests that vertical transmission of *M. genitalium* can occur in some instances. In addition, *Mycoplasma genitalium* has been detected in the trachea of an infant born to an infected birth parent and in conjunctival specimens from infants born to infected birth parents.[24,25] Autoinoculation from the male urethra to the conjunctiva has also been documented.[26]

Natural History

The duration of *M. genitalium* infection varies substantially. Among women engaging in exchange or survival sex, the median duration of infection ranged from 1 to 3 months, but up to 16% of women in one study had infection that persisted for at least 12 months.[20,27] In men treated with incompletely effective antibiotic regimens, the median duration of infection was 4.7 months, but the organism persisted after resolution of symptoms in some men for up to 11 months.[28] In another study, 30% of asymptomatic MSM with HIV who had *M. genitalium* cleared their infection spontaneously over an 18-month time period, with clearance possibly due to the production of *M. genitalium*-specific antibodies that are present in urethral secretions.[29,30] Data on sequelae from asymptomatic infections are fairly limited, and the uncertainty over how often sequelae occur is a major factor in current testing and treatment guidelines.

Antimicrobial Susceptibility in *Mycoplasma genitalium*

Limited antimicrobials are available to treat *M. genitalium* infections. The lack of a rigid cell wall renders cell-wall-mediated antibiotics ineffective, and beta-lactam antibiotics, including penicillins, cephalosporins, and carbapenems, have no activity against *M. genitalium*. Culture is challenging; much of the available data on antimicrobial resistance are derived from pairing clinical treatment failure data with molecular detection of characteristic mutations. Minimum inhibitory concentrations (MICs) are not used in individual treatment decisions and are only performed in select research laboratories. Azithromycin, a macrolide antibiotic, and moxifloxacin, a fluoroquinolone antibiotic, have historically been the primary antimicrobials used to treat *M. genitalium* infections. Shortly after these two antibiotics began being used to treat *M. genitalium* infections (around 2008-2010), there was a rapid expansion of resistance to them. By 2016-2017, macrolide resistance had grown to greater than 50%, quinolone resistance to nearly 8%, and, globally, resistance to both antibiotic classes to approximately 3%.[31] As a result of these resistance trends, M. *genitalium* is one of three bacteria on the Watch List included in the United States Centers for Disease Control and Prevention (CDC) 2019 Report of Antibiotic Resistance Threats.[32] The following summarizes resistance data with antimicrobials that have been used to treat *M. genitalium*. Details regarding treatment recommendations are outlined below in the section on Treatment of *Mycoplasma genitalium* Infection.

Azithromycin

During 2008-2013, *M. genitalium* azithromycin cure rates declined substantially, reflecting the emergence and spread of macrolide resistance.[33] Macrolide resistance to *M. genitalium* is due to single-point mutations in the 23S rRNA gene, referred to as macrolide resistance mutations (MRMs).[34] The MRMs are similar to macrolide resistance in other microorganisms, but unlike antimicrobial resistance in *Neisseria gonorrhoeae*, there are no subtle gradations in susceptibility. Macrolide resistance in *M. genitalium* is bimodal, with either near-complete susceptibility (MICs ≤0.004 µg/mL) or total resistance (MICs ≥8 µg/mL) (Figure 4).[35] Macrolide resistance likely arose because of the widespread use of azithromycin. *Mycoplasma genitalium* has a high mutation rate, and bacterial populations naturally include organisms with MRMs that survive and proliferate after azithromycin treatment.[36] Available data suggest that approximately 44-64% of *M. genitalium* isolates in the United States are resistant to azithromycin, with similar, if not higher, rates of resistance in other regions globally.[28,35,37,38] In addition, among baseline azithromycin-susceptible *M. genitalium* isolates, the selection of resistant strains occurs in approximately 10% of those treated with azithromycin alone, but in less than 4% of people treated first with doxycycline followed by high-dose azithromycin.[39,40][Q] Mycoplasma genitalium and Azithromycin Resistance

Doxycycline

Despite relatively good susceptibility in the laboratory (MICs in United States strains range from less than 0.125 to 2.0 µg/mL), doxycycline has consistently low cure rates in clinical settings (Figure 5).[35] The low cure rate with doxycycline does not appear to be due to antimicrobial resistance. The *tetM* resistance determinant has not been identified in *M. genitalium*, and although numerous 16S rRNA mutations that are associated with tetracycline resistance in other organisms have been detected in *M. genitalium*, none have been linked to the efficacy of doxycycline treatment for *M. genitalium*.[41] Attempts to induce doxycycline resistance in the laboratory by passaging strains in sub-inhibitory concentrations have been unsuccessful.[42]

Minocycline

Minocycline is an older and more potent tetracycline than doxycycline and has shown some efficacy when used for *M. genitalium* treatment failures. Among Australian patients in whom moxifloxacin had failed or was contraindicated, 68% experienced microbiologic cure after a 14-day regimen of minocycline.[43] No resistance mutations have been identified for minocycline. Older MICs range from 0.031-0.25 µg/mL, which is lower than doxycycline MICs.[44]

Moxifloxacin

Moxifloxacin has increasingly been used as a component of first-line *M. genitalium* therapy. Other fluoroquinolones, such as ciprofloxacin and levofloxacin, have limited efficacy against *M. genitalium*. Sitafloxacin, a more potent fluoroquinolone that is not available in the United States, is used for treatment failures in countries where it is available to clinicians. Prior to 2010, *M. genitalium* cure rates after moxifloxacin monotherapy treatment were uniformly 100%, but dropped to 89% after 2010 and have continued to decline.[45] Decreased cure rates after moxifloxacin are largely due to the emergence of quinolone resistance, mediated by ParC gene mutations. The ParC S83I has emerged as the mutation most strongly associated with treatment failure, and it was detected in 10% of specimens in the Americas tested between 2011-2017.[31,46,47]The presence or absence of the S83I mutation correlates strongly with fluoroquinolone treatment response. For example, in Australia, among people with *M. genitalium* who did not have the S83I mutation, the cure rate for a 7-day course of moxifloxacin monotherapy was 96.5%.[47] Concurrent mutations in the GyrA gene also increase the likelihood of resistance. When the GyrA mutation M95I was present in combination with the ParC S83I mutation, moxifloxacin treatment failure occurred in nearly 81% of Australian patients between 2019-2020, whereas only 43% failed when S83I alone was present in the absence of M95I.[47]

Pristinamycin

Pristinamycin is manufactured in France and available in some countries outside the United States. It is not been approved by the U.S. Food and Drug Administration (FDA) and is not currently available in the United States. In other settings, it is an important treatment option for people in whom other antimicrobial treatments have failed with a cure rate of 75%, irrespective of whether it is used alone or in combination with doxycycline.[48] Little work has been done to determine resistance determinants for pristinamycin, and only one potential mutation has been identified (A2062T in the 23S rRNA gene).[49]

Other Antibiotics

Omadacycline and tinidazole are FDA-approved antibiotics, with in vitro data suggesting they may be effective against *M. genitalium*. Omadacycline is a newer tetracycline with MICs of 0.063-0.5 µg/ml, the same range as MICs for minocycline and somewhat lower than MICs for doxycycline (0.125-2 µg/mL) and tetracycline (0.5-16 µg/mL).[50] Tinidazole is a nitroimidazole antibiotic, with MICs ranging from 0.8-6.3 µg/mL, lower than MICs for two other nitroimidazoles used to treat bacterial vaginosis in women (metronidazole MIC range=6.3-12.5 µg/mL and secnidazole MIC range=3.1-12.5 µg/mL). Higher MICs for tinidazole may be due to a resistance mutation in the MG-342 gene, but the prevalence of this resistance mutation is currently unknown. In 2025, however, a case report noted that tinidazole effectively cured a man with *M. genitalium* treatment failure and.[51] Treatment studies with tinidazole are ongoing.

Clinical Manifestations

Mycoplasma genitalium has a tropism for urogenital and rectal tissues. Infection with *M. genitalium* has been associated with a range of genitourinary manifestations, including urethritis, cervicitis, pelvic inflammatory disease (PID), and proctitis. In addition, *M. genitalium* may cause preterm delivery in pregnant women and female infertility. No definitive data link *M. genitalium* to epididymitis or male infertility, although studies on this are limited. Rare cases of conjunctivitis have been documented. Although *M. genitalium* has been identified in oropharyngeal specimens, pharyngitis has not been reported in people with *M. genitalium* in the oropharynx.

Urogenital Infections in Women

Urethritis

Mycoplasma genitalium has been detected in a small proportion of women with urethritis (4-9%) and has been linked to urethral inflammation and female urethritis.[52,53] *Mycoplasma genitalium* has also been detected in up to 22% of women reporting dysuria, a frequent complaint among women with urinary tract infections (UTI).[54] Notably, first-line therapies for female UTIs, such as trimethoprim-sulfamethoxazole and nitrofurantoin, have poor efficacy against *M. genitalium*.

Vaginitis

In clinical settings, *M. genitalium* has been detected in 13-21% of women with vaginitis.[5,55] Although some studies have reported a significant association of *M. genitalium* and vaginitis, it is unclear whether the vaginitis results from *M. genitalium* infection of vaginal epithelial cells and/or the cervix—or from other causes.[55] In a study involving 21 sites in the United States, among 1,051 women who sought care for vaginitis symptoms, 8.8% had *M. genitalium* identified.[56] The rates of M. *genitalium* were even higher among women who had bacterial vaginosis diagnosed as the cause of vaginitis.[56] Detection of *M. genitalium* in women with vaginitis may reflect synergy between *M. genitalium* and other bacteria that play a pathogenic role in bacterial vaginosis. The higher incidence and prevalence of *M. genitalium* in women with bacterial vaginosis suggests that bacterial vaginosis may enhance susceptibility to *M. genitalium* infection.[9,10]

Cervicitis

Mycoplasma genitalium has been detected in 10-29% of women with cervicitis (Figure 6).[57,58] Not all studies have shown a consistent association with *M. genitalium* and cervicitis, but those studies that accounted for other known causes of cervicitis (and/or defined cervicitis as 30 polymorphonuclear cells or greater per high-power field in cervical mucus) have shown that women with cervical *M. genitalium* infection are approximately two times more likely to have cervicitis than women without cervical *M. genitalium*.[12]

Pelvic Inflammatory Disease (PID)

Mycoplasma genitalium has been detected by NAAT in 4-18% of women with PID, and women with *M. genitalium* infection are approximately 2.0-2.5 times as likely to have PID as women without *M. genitalium* infection (Figure 7).[12,59,60] Some experts have debated the causal nature of this association, in part because few studies have followed women over time to observe the development of PID after a woman acquires *M. genitalium*. One systematic review and meta-analysis found that women with *M. genitalium* infection had an approximately 67% higher risk of being diagnosed with PID, and among women diagnosed with PID, approximately 1 in 10 had *M. genitalium* detected.[61] There are only two prospective studies that have addressed this issue, and when analyses are limited to these 2 studies, the relationship between *M. genitalium* and PID is less pronounced.[20] Larger and more rigorous longitudinal studies are needed to resolve the controversy. A strong relationship with post-abortal PID and perihepatitis (Fitz-Hugh Curtis

syndrome) has also been reported.[62,63] Women with *M. genitalium*-associated PID have a similar clinical presentation as women with *C. trachomatis*-associated PID, with two exceptions: women with *M. genitalium* infection more frequently had abdominal tenderness on examination and were somewhat less likely to report post-coital bleeding.[64]

Infertility

Mycoplasma genitalium can ascend to the fallopian tubes, and in serologic studies that adjusted for prior chlamydial infection, women with antibodies to *M. genitalium* were 4–5 times more likely to have tubal factor infertility than women without antibodies to *M. genitalium*, suggesting that some women may suffer tubal occlusion after infection (Figure 8).[65,66,67] These data, however, are not consistent, and other studies have shown a more modest relationship with infertility.[12] Fecundability (probability of conception in a single menstrual cycle) may also be impaired during or after an *M. genitalium* infection.[68,69] For example, the per-menstrual cycle probability of pregnancy was 27% lower in Kenyan women with active *M. genitalium* infection, and the time to conception was 24% longer among women in the United States with serologic evidence of a prior *M. genitalium* infection.[69] Notably, delayed time to pregnancy may involve some synergy with *M. genitalium* and bacterial vaginosis. Fecundability among Kenyan women was nearly 50% lower when both *M. genitalium* infection and bacterial vaginosis were present, but there was only a marginal reduction in fecundability with either bacterial vaginosis or *M. genitalium* alone.[68]

Ectopic Pregnancy

There are limited data on *M. genitalium* and ectopic pregnancy, and the few studies that have been published are conflicting. One study demonstrated a modest and non-significant 60% increase in the odds of ectopic pregnancy among women with antibodies to *M. genitalium*, but only among younger women (15–30 years of age). In contrast, *M. genitalium* was detected in Fallopian tube tissue among Saudi Arabian women with ectopic pregnancy more commonly than among women with total hysterectomies or tubal ligation (20.2% versus 3.9%).[70] To date, there is no consensus on whether *M. genitalium* infection can result in ectopic pregnancy.

Preterm Delivery

Pregnant women with *M. genitalium* may be at higher risk of preterm delivery. Two meta-analyses summarizing data published through 2021 demonstrated an approximately two-fold increase in the likelihood of delivery prior to 37 weeks.[12,71] Some evidence also suggests that pregnant women with *M. genitalium* may be at increased risk for spontaneous abortion, but relatively few studies have been conducted and data are conflicting.[12,71] Data are even more limited on whether *M. genitalium* is linked to lower birth weight.[72,73] Given these unclear consequences of asymptomatic infections in pregnancy and limited antimicrobial treatment options for pregnant women, screening asymptomatic pregnant women for *M. genitalium* is not currently recommended.[38]

Urogenital Infections in Men

Urethritis

Mycoplasma genitalium is responsible for 15-30% of nongonococcal urethritis (NGU) and is detected in more than 30% of men with non-chlamydial NGU.[74] *Mycoplasma genitalium* is also sometimes present in persons with gonococcal urethritis; among males from 6 United States cities with urethritis, 21.2% with *M. genitalium* also had *Neisseria gonorrhoeae* infection.[37] Symptoms associated with *M. genitalium* NGU are similar to those observed with *C. trachomatis* infection, although men with *M. genitalium* were more likely to report urethral discharge and to have cloudy or purulent discharge than men with other causes of NGU.[75] In clinical settings, *M. genitalium* has been a common cause of persistent and/or recurrent urethritis and may be present in up to 40% of people who have been treated with doxycycline or azithromycin without success.[74]. In a retrospective review involving men with symptomatic urethritis who were evaluated at an STI clinic,

persistent and/or recurrent urethritis that resulted in a follow-up visit increased by 51% during 2015-2019.[76] The significant increase in follow-up visits occurred in men who were treated with azithromycin but not those treated with doxycycline.[76] Further, similar changes were seen among men with urethritis who tested negative for chlamydia.[76] Taken together, these findings suggest that macrolide-resistant *M. genitalium* may have driven this increase in persistent and/or recurrent urethritis.[76] [Q] Mycoplasma genitalium Urethritis in Males

Epididymitis

It is unclear whether *M. genitalium* causes epididymitis. It has been detected in men with epididymitis, but this appears to occur rarely, and there are no studies comparing detection of *M. genitalium* in men with and without epididymitis.[77,78]

Manifestations in Men or Women

Conjunctivitis

Although *M. genitalium* conjunctivitis has been documented, this is rare. Only one case of a man with *M. genitalium*-associated conjunctivitis has been reported.[26] The organism has also been detected in conjunctival specimens from infants born to infected birth parents, but this was not accompanied by information on whether the infants had conjunctivitis.[24]

Oropharyngeal Infection

Oropharyngeal infection with *M. genitalium* is rare. Using contemporary, highly sensitive NAAT assays, *M. genitalium* has been detected in the oropharynx in 1-5% of people, although it was found more frequently (12.3%) in one study of Italian MSM.[79,80,81] *Mycoplasma genitalium*-associated pharyngitis has not been reported.

Proctitis

Rectal *M. genitalium* prevalence in MSM ranges widely, from 1-30%, but was as high as 41.5% in young MSM with HIV (Figure 9).[79] Among women, rectal *M. genitalium* has been detected in 2.6% of South African women and in as many as 22% of females attending sexual health clinics in the United States.[82,83] In a recent study in France involving 365 men with proctitis, among the 315 who underwent testing for *M. genitalium*, 46 (15%) had a positive test for *M. genitalium*.[84] Although *M. genitalium* prevalence is often higher in people with rectal symptoms than without rectal symptoms, data on whether it causes proctitis are conflicting. Some studies have identified an association, while others have not.[85,86,87]

Reactive Arthritis

In rare circumstances, reactive arthritis may occur in people who have had an *M. genitalium* infection. There are case reports of *M. genitalium* (in the absence of chlamydia and gonorrhea) detected in the synovial fluid of a man with Reiter's syndrome, in a man with seronegative rheumatoid arthritis, and in a man with sexually acquired reactive arthritis after *M. genitalium* urethritis.[88,89] There are no larger-scale studies of the relationship between *M. genitalium* and Reiter's syndrome.

Laboratory Diagnostic Tests and Resistance Assays

Mycoplasma genitalium Diagnostic Testing

The preferred method to diagnose *M. genitalium* infections is the use of an Food and Drug Administration (FDA)-cleared nucleic acid amplification test (NAAT).[38] To date, there are no FDA-cleared point-of-care tests for the diagnosis of *M. genitalium*. Serologic assays and culture have been used in research settings but have no practical application in clinical care.

- **Nucleic Acid Amplification Test:** The FDA has cleared multiple NAATs to detect *M. genitalium* in clinical specimens. Most tests are approved for first-void urine and swab samples (urethral, vaginal, endocervical, penile-meatal), although there is some variability in approved sample type by manufacturer. Sensitivity of these assays is high, including 98% for urethral swabs (transcription-mediated amplification [TMA] only), 91-100% for male urine; 92-99% for vaginal swabs; 82-83% for endocervical swabs; and 78-86% for female urine specimens. Specificity is higher, ranging from 87-99%. Assays performed on self-obtained vaginal swab samples often have higher sensitivity than clinician-obtained vaginal swab samples, although this is not uniformly the case. Although none of these assays are FDA-cleared for use in extragenital samples or for home testing, laboratories that have undergone a validation process and obtained Clinical Laboratory Improvement Amendments (CLIA) certification for *M. genitalium* NAATs in oropharyngeal and/or rectal specimens may report results for clinical care.
- **Serology**: Although serology has been used in research efforts, it is not used in clinical practice to diagnose *M. genitalium* infections. Western Blot assays, which are labor-intensive and have an element of subjectivity in their interpretation, are the most common serologic assays and have only been implemented in a few laboratories.[66,67,69] ELISA assays have also been developed and used in studies of infertility, but are not sufficiently sensitive and specific to be used for diagnosing *M. genitalium* infection.[90,91]
- **Culture**: Although it is possible to culture *M. genitalium*, it is a lengthy process that takes several weeks and typically requires tissue culture.[17] Few research laboratories have this capacity and culture is not used to diagnose *M. genitalium* infections in clinical settings.[Q] Diagnostic Testing Methods for Mycoplasma genitalium

Resistance Testing

Mycoplasma genitalium resistance testing has been more widely available in Europe and Australia than in the United States. Macrolide resistance testing assays are commercially available in the United States through several laboratories, but at this time, assays that detect *M. genitalium* fluoroquinolone resistance are not commercially available. Most *M. genitalium* resistance assays are NAATs, but next-generation sequencing approaches are also being explored and may provide greater efficiency.[92]

- **Macrolide Resistance Testing**: Several commercially available NAAT assays incorporate the detection of genetic mutations linked to macrolide resistance. These assays detect both *M. genitalium* and any of five major macrolide resistance mutations (MRM) in the 23S rRNA gene that are associated with high rates of azithromycin treatment failure.[93] The MRM assays are a key component of resistance-guided therapy.[38] Although some of the assays that incorporate the detection of MRM have lower sensitivity overall than the FDA-approved NAATs for detecting *M. genitalium*, their published sensitivity for detecting MRM ranges from 95-100%; specificity ranges from 95-97%.[94] First-generation versions of these assays do not have an internal control that confirms the detection of wild-type *M. genitalium*, making it impossible to differentiate between a truly negative (susceptible) result and a failure to amplify. In the United States, macrolide resistance testing is most often performed using a reflex process whereby samples positive for *M. genitalium* subsequently have resistance testing performed. When using this reflex process, resistance testing can usually be performed on the same clinical specimen as used for the diagnostic test.

- **Fluoroquinolone Resistance Testing**: As quinolone resistance expands, additional assessment for quinolone resistance-associated mutations (QRAMs) may be needed (using a rule-out strategy). Detecting wild-type sequences in the ParC gene effectively rules out the presence of quinolone resistance.[95] To date, in the United States, assays to detect QRAMs are not commercially available, and clinical testing for fluoroquinolone resistance is not recommended. Although the concomitant detection of specific mutations in the GyrA gene more closely correlates with treatment failure, assays to detect these mutations are currently only available in research settings.[47]

Diagnostic Testing and Screening Guidelines

When considering whether to test for *M. genitalium*, it is important to differentiate between screening and diagnostic testing. Screening is performed on asymptomatic people with the goal of identifying a pathogen that is not causing current clinical signs or symptoms but may result in sequelae if not eradicated. Routine screening of asymptomatic persons for *M. genitalium* is not recommended.[38] Diagnostic testing is performed on symptomatic patients with the goal of identifying the pathogen causing the clinical signs or symptoms and providing appropriate treatment. The 2021 STI Treatment Guidelines recommend diagnostic testing for *M. genitalium* in patients who have persistent and/or recurrent genitourinary symptoms and that it be considered in all cases of PID.[38]Table 1.

***Mycoplasma genitalium* Testing Recommendations**

Type of Test		Definition	Recommendat
Screening Test	Testing of asymptomatic people with the goal of preventing disease sequelae and prevent transmission to others		Routine testing of asymptomatic p recommended.
Diagnostic Test	Testing of symptomatic persons to direct treatment decisions		Testing recommended for: • Men with persistent or recu • Women with persistent or Testing should be considered for: • Women with pelvic inflamr

Source:

- Wetmore CM, Manhart LE, Lowens MS, et al. Demographic, behavioral, and clinical characteristics of men with nongonococcal urethritis differ by etiology: a case-comparison study. Sex Transm Dis. 2011;38:180-6. [PubMed Abstract]
- Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *Mycoplasma genitalium*. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Diagnostic Testing

Guidelines on diagnostic testing for *M. genitalium* vary globally, ranging from recommendations in the European Guidelines to test any person with any STI syndrome for *M. genitalium* to recommendations in the 2021 STI Treatment Guidelines to test only men with persistent or recurrent urethritis, women with persistent or recurrent cervicitis, and to consider testing women with PID.[38,96] The 2021 STI Treatment Guidelines recommend using an FDA-cleared NAAT for the testing process, but testing of extragenital sites for *M. genitalium* is not recommended.[38] If resistance testing with the capability to detect MRM is available, this should also be ordered to enable resistance-guided therapy. The following summarizes recommendations in the 2021 STI Treatment Guidelines for *M. genitalium* diagnostic testing for males with NGU, females with cervicitis and PID, persons with proctitis, and extragenital testing.[38]

- **Males with NGU**: For males with acute NGU, routine *M. genitalium* testing is not currently recommended.[38] Instead, testing and organism-directed therapy is only recommended for males with persistent or recurrent urethritis.[76] This recommendation was established prior to documentation of a 60% reduction in the number of cases of persistent or recurrent urethritis after one sexual health clinic implemented routine *M. genitalium* testing and treatment with moxifloxacin for all men with NGU.[97] This finding, coupled with increasing sexual health clinic visits for chlamydia-

negative persistent and/or recurrent NGU from 2015-2019, suggests that there may be a benefit to testing males with acute NGU for *M. genitalium* when they first present with symptoms.[76]

- **Female Cervicitis and PID**: Given associations with cervicitis and PID, *M. genitalium* testing should be considered in females with cervicitis and/or PID; provider judgment should determine whether to test women with cervicitis and/or PID at the time of presentation.[38] For women with persistent or recurrent cervicitis, *M. genitalium* testing is recommended.[38]
- **Proctitis**: Although the prevalence of *M. genitalium* in the rectum can be high (up to 42% of MSM with HIV and up to 22% of women), the association with proctitis is inconsistent, and most rectal infections are asymptomatic.[83,85,86,87] For these reasons, routine testing of people with proctitis for *M. genitalium* is not recommended.[38] However, *M. genitalium* testing may be performed in people with persistent proctitis if *N. gonorrhoeae* and *C. trachomatis* have been ruled out.[38]
- **Extragenital Testing**: Testing for *M. genitalium* at extragenital sites, such as the pharynx, is not recommended, based primarily on the low overall prevalence of pharyngeal infection.[38][Q] Indications for Mycoplasma genitalium Diagnostic Testing

Screening

Asymptomatic people should not be screened for *M. genitalium*.[38] Unlike chlamydia and gonorrhea, screening for *M. genitalium* is not recommended for women under the age of 25 years, nor is screening pregnant women at prenatal care visits recommended.[38] *Mycoplasma genitalium* is not included in the routine STI screening for bacterial STIs that is recommended for people taking HIV preexposure prophylaxis (PrEP). The recommendation against screening is consistent across the globe, reflecting the uncertain consequences of asymptomatic *M. genitalium* infections and the mandate to avoid prescribing antibiotics when they may not be necessary.[98] This is particularly relevant in pregnancy, given the extremely limited number of antimicrobials with efficacy against *M. genitalium* that are not contraindicated in pregnancy.[38] In addition, screening for *M. genitalium* in pregnancy in asymptomatic women is not recommended as the consequences of asymptomatic infection in pregnancy remain unknown, and there are limited antimicrobial options available for the treatment of *M. genitalium* in pregnancy.[38] Nevertheless, if future evidence demonstrates causal relationships with infertility, adverse pregnancy outcomes, or increased transmission or acquisition of HIV, screening may be warranted.[Q] Routine screening for Mycoplasma genitalium

Reporting Requirements

Mycoplasma genitalium is not a reportable infection. Therefore, there are no reporting requirements.

Treatment of *Mycoplasma genitalium* Infection

Approach to Treatment

It is important to conceptually understand that *M. genitalium* does not have a peptidoglycan cell wall. Thus, antibiotics that work by targeting cell wall synthesis (e.g., penicillins and cephalosporins) do not have activity against *M. genitalium*.[38] Earlier attempts to treat *M. genitalium* used monotherapy with either azithromycin or doxycycline. Unfortunately, these antibiotics, when used alone, have relatively low cure rates, and the cure rates have declined over time with increasing resistance, especially with macrolide resistance (Figure 10).[99,100,101] Due to high rates of resistance to azithromycin and the low efficacy of doxycycline monotherapy, these antimicrobials are now only used as a component of sequential therapy for *M. genitalium*.[38] Moxifloxacin, a fluoroquinolone antibiotic, has also become a key antimicrobial used to treat *M. genitalium* infections. Ideally, the recommended approach for treating *M. genitalium* is to (1) use sequential therapy with two antibiotics and (2) use macrolide resistance testing (with assays that can detect MRM) to guide the specific regimen used. The rationale for using sequential therapy with doxycycline followed by a second antibiotic is to reduce the overall *M. genitalium* organism burden prior to starting moxifloxacin or azithromycin. This approach enhances cure rates and reduces antimicrobial resistance. The detection of MRM correlates highly with azithromycin treatment failure, but macrolide resistance testing is not often available in the United States. Accordingly, the following discussion will include 2021 STI Treatment Guidelines recommendations for when resistance testing is available and when it is not available.[38]

Recommended Treatment if Resistance Testing is Available

Resistance-guided therapy using MRM detection was developed to enhance treatment efficiency and efficacy for persons diagnosed with *M. genitalium*. Since detection of MRM correlates highly with azithromycin treatment failure, the absence of MRM indicates a macrolide-susceptible infection where azithromycin can be prescribed. The use of azithromycin for macrolide-susceptible infection reduces the empiric use of moxifloxacin, which has more significant side effects than azithromycin and should only be used when there are no other safer alternatives. Using a resistance-guided approach, patients diagnosed with *M. genitalium* infection start treatment with a 7-day course of doxycycline (100 mg orally twice daily for 7 days), with the second component of the regimen determined by the results of the resistance testing.[38] Patients with macrolide-sensitive infections follow the initial doxycycline regimen with high-dose azithromycin (1g orally on day one followed by 500 mg orally once daily for three additional days, for a total of 2.5g). Patients with macrolide-resistant infections follow the doxycycline 7-day course with a 7-day course of oral moxifloxacin 400 mg daily.[38] The sequential approach yielded cure rates of 95% for doxycycline followed by high-dose azithromycin and 92% for doxycycline followed by moxifloxacin when first implemented.[40] When moxifloxacin is contraindicated, CDC guidelines recommend sequential therapy with 7 days of doxycycline followed by the high-dose azithromycin course, but with a test-of-cure added at 21 days after completion of the high-dose azithromycin.[38] Minocycline (100 mg orally twice daily for 14 days) may also be an option for patients who cannot take moxifloxacin.

Table 2. 2021 STI Treatment Guidelines: *Mycoplasma genitalium* Recommended Regimens if *M. genitalium* Resistance Testing is Available

Recommended if macrolide sensitive:
Doxycycline followed by Azithromycin *Doxycycline 100 mg orally 2 times/day for 7 days, followed by Azithromycin 1 g orally initial dose, followed by 500 mg orally once daily for 3 additional days (2.5 g total of Azithromycin)*
Recommended if macrolide resistant:

Doxycycline followed by Moxifloxacin *Doxycycline 100 mg orally 2 times/day for 7 days, followed by Moxifloxacin 400 mg orally once daily for 7 days*

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *Mycoplasma genitalium*. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

[Q] M. genitalium Treatment With Resistance Testing

Recommended Treatment if Resistance Testing is Not Available

In most clinical settings in the United States, *M. genitalium* macrolide resistance testing is not available and, therefore, not incorporated into clinic protocols. Thus, most clinicians treat *M. genitalium* infection without information about macrolide resistance.[38] The empiric approach utilizes a two-stage treatment regimen, with the first stage using 7 days of oral doxycycline, followed by a second stage consisting of oral moxifloxacin 400 mg for 7 days, which is exactly the same regimen outlined above when macrolide resistance is identified.[38] The rationale for using this two-stage approach is that doxycycline up front can reduce the overall *M. genitalium* organism burden prior to the course of moxifloxacin, which has the effect of improving clinical cure rates and may reduce the likelihood of moxifloxacin resistance developing.

Table 3. 2021 STI Treatment Guidelines: *Mycoplasma genitalium* Recommended Regimens if *M. genitalium* Resistance Testing is Not Available

Recommended if *M. genitalium* is detected by an FDA-cleared NAAT:
Doxycycline followed by Moxifloxacin *Doxycycline 100 mg orally 2 times/day for 7 days, followed by Moxifloxacin 400 mg orally once daily for 7 days*

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *Mycoplasma genitalium*. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

[Q] M. genitalium Treatment Without Resistance Testing

Treating *M. genitalium* in Women with PID

Nonpregnant women who present with PID and are managed as an outpatient should receive the recommended empiric PID treatment regimen that consists of ceftriaxone 500 mg in a single intramuscular dose plus doxycycline 100 mg orally twice daily for 14 days plus metronidazole 500 mg orally twice daily for 14 days.[102] Women with PID and a positive test for *M. genitalium* should first receive the standard PID treatment, followed by moxifloxacin 400 mg orally once daily for 14 days; the addition of the moxifloxacin to specifically target *M. genitalium*.[38] Although the standard PID regimen is not effective against *M. genitalium*, the doxycycline will reduce the *M. genitalium* organism load prior to treatment with moxifloxacin.[103] In addition, the metronidazole in the PID treatment regimen may have some activity

against *M. genitalium*; women in a randomized trial who received a metronidazole-containing PID regimen were significantly less likely to have a persistent cervical *M. genitalium* infection than women who did not receive metronidazole.[60][Q] Treatment of M. genitalium in Women with PID

Treatment in Pregnancy

Mycoplasma genitalium infection in pregnancy has emerged as a major challenge. Azithromycin is the only antibiotic available in the United States that is recommended for the treatment of *M. genitalium* during pregnancy, but there is a significant chance for treatment failure with azithromycin monotherapy due to high rates of macrolide resistance. Tetracyclines (including doxycycline and minocycline) and fluoroquinolones (including moxifloxacin) are generally contraindicated during pregnancy. There are no controlled human studies of doxycycline during pregnancy, but it is usually not prescribed, given concerns over staining of primary teeth in infants and associations with congenital anomalies.[104,105] Similar concerns about use in pregnancy apply to minocycline. All fluoroquinolones, including moxifloxacin, are considered class C drugs in pregnancy and should not be used unless there is no other safe alternative.[106,107] Pristinamycin is considered safe in pregnancy, but is not available in the United States. In this setting, the treatment risks should be weighed against the potential sequelae of *M. genitalium* infection during pregnancy and discussed with the patient. Given these challenges, expert consultation is generally recommended when treating *M. genitalium* during pregnancy.

Treatment of Neonates and Children

Mycoplasma genitalium has rarely been detected in neonates and children, and there are no specific recommendations for treatment in non-adults.[38] If treatment of *M. genitalium* is required, age- and weight-specific recommendations and safety considerations for each of the recommended antibiotics (doxycycline, azithromycin, moxifloxacin) should be followed. In general, given the potential adverse effects of doxycycline and moxifloxacin in young children, expert consultation is advised.

Post-Treatment Follow-Up and Test-of-Cure

The 2021 STI Treatment Guidelines do not recommend performing a test-of-cure after treatment of *M. genitalium* in people whose symptoms have resolved.[38] The rationale for this approach is twofold. First, the benefit of identifying and treating asymptomatic infections in the absence of definitive evidence that asymptomatic *M. genitalium* infections cause sequelae is unclear. Second, the continued expansion of antimicrobial resistance in *M. genitalium* increases the risk of untreatable infections and highlights the importance of using antibiotics only when there is a clear benefit. The exception to the CDC recommendation against performing a test-of-cure is when high-dose azithromycin must be used instead of moxifloxacin and macrolide resistance data is not available. Because of the uncertain cure with azithromycin-based regimens, a test-of-cure is recommended in this setting, but should be done no sooner than 21 days or more after the treatment regimen has been completed to allow sufficient time to allow for residual nucleic acids from dead organisms to fully clear. Further, in this setting, test-of-cure should be performed even if the patient has experienced resolution of symptoms, since persistent, ongoing infection has been observed after macrolide-based regimens in persons who had resolution of symptoms. Regardless of the treatment regimen used, routine 3-month follow-up testing to check for reinfection with *M. genitalium* infection is not recommended.[38]

Management of Sex Partners

Given the high concordance of infection between sex partners (30-50%), the 2021 STI Treatment Guidelines note that sex partners of people with *M. genitalium* can be tested and, if positive, treated.[20,23,38] Ideally, this approach would focus on people in ongoing partnerships, with the goal of using concomitant treatment to prevent reinfection. If testing of the sex partner is not an option, the partner can be treated empirically with the same antibiotic regimen as used to treat the person diagnosed with *M. genitalium*.[38] Expedited partner

therapy should not be used for sex partners of people with *M*. *genitalium* infections. Its efficacy has not been evaluated for *M*. *genitalium,* and it may contribute to ongoing development and spread of resistance.

Counseling and Education

Counseling and education for patients in whom *M*. *genitalium* is detected should be consistent with that provided to patients with other bacterial STIs. The following summarizes key counseling messages for persons diagnosed with *M*. *genitalium* infection.

- **Resuming Sexual Activity**: When treated for *M*. *genitalium* infection, people should be told to abstain from sexual activity until they have completed both antibiotics in their sequential therapy, their symptoms have resolved, and any ongoing sex partners have either been tested or completed their own antibiotic treatment.
- **Partner Notification**: People with whom a person has an ongoing sexual relationship should be notified and encouraged to get an *M*. *genitalium* test (and treatment if positive) to reduce the risk of reinfection. People with whom the patient does not intend to have sex with again do not need to be notified.
- **Follow-up Testing**: Follow-up testing for *M*. *genitalium* should only be done in people with persistent or recurrent symptoms. People who are asymptomatic after completing their antibiotic treatment do not require a test-of-cure, with one exception—when macrolide resistance testing is not available and the treatment regimen used was doxycycline followed by azithromycin. In this situation, a test-of-cure should be performed 21 days after the antibiotics have been completed. For patients with *M*. *genitalium* infection, routine 3-month follow-up testing is not recommended, regardless of the treatment regimen used.
- **STI Prevention**: At the time a person is receiving treatment for an STI, it is appropriate to provide counseling messages on how to prevent STIs in the future (e.g., limiting the number of sex partners and consistently using condoms).

Summary Points

- *Mycoplasma genitalium* is not a reportable infection, and the estimated number of people infected is based on survey data. Between 2017 and 2018, there were an estimated 3 million people of reproductive age in the United States with an *M. genitalium* infection.
- *Mycoplasma genitalium* is most common among females younger than 25 years of age.
- Asymptomatic *M. genitalium* infection occurs frequently; *M. genitalium* can also cause urethritis in males and is associated with cervicitis, pelvic inflammatory disease, infertility, and preterm delivery in women. *Mycoplasma genitalium* can infect the rectum and may cause proctitis.
- Screening asymptomatic people for *M. genitalium* is not recommended. Diagnostic testing is recommended for people with persistent or recurrent symptoms.
- FDA-cleared NAATs are the preferred method of detecting *M. genitalium*. Validated specimen types include male and female urine and clinician- and self-collected urethral, vaginal, and endocervical swab specimens. Rectal specimens can be tested in laboratories that have validated this procedure. Culture is challenging and is not used in clinical care.
- Treatment of *M. genitalium* is limited to a few antibiotics. Due to the lack of a rigid cell wall, neither beta-lactams, cephalosporins, nor carbapenems have activity against *M. genitalium*. Doxycycline has low cure rates, and antibiotic resistance in *M. genitalium* has rapidly emerged, reaching nearly 60% for azithromycin and up to 10% for moxifloxacin.
- Resistance-guided therapy leverages assays that detect macrolide resistance; it can increase cure rates and reduce selection for resistance. People with macrolide-sensitive infections should receive sequential treatment with doxycycline (100 mg bid for 7 days) followed by high-dose azithromycin (1 g on day 1 followed by 500 mg on days 2-4). Patients (except pregnant women) with macrolide-resistant infections should receive sequential treatment with 7 days of doxycycline followed by 7 days of moxifloxacin (400 mg daily).
- If resistance-guided therapy is not available or not utilized, treatment for patients (except pregnant women) should consist of sequential treatment with doxycycline (100 mg bid for 7 days) followed by 7 days of moxifloxacin (400 mg daily).
- Treatment of *M. genitalium* during pregnancy is challenging, primarily due to the potential toxicity to the fetus with doxycycline and moxifloxacin. If treatment is required, the best option is high-dose azithromycin (1 g on day 1 followed by 500 mg on days 2-4), followed by a test-of-cure 21 days after completing treatment.
- Except for patients treated an azithromycin-based regimen in the absence of resistance testing, a test-of-cure in asymptomatic patients is not recommended.
- Clinicians should seek expert consultation for the treatment of pregnant women, treatment of young children, and in cases of treatment failure after moxifloxacin.
- Ongoing sex partners of people diagnosed with *M. genitalium* infection should be tested and treated with the same regimen their partner received. Presumptive treatment should only be provided when testing is not possible.

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Figures

Figure 1 *Mycoplasma genitalium*

Illustration credit: Cognition Studio, Inc.; Gwendolyn E. Wood, PhD; Lisa E. Manhart, PhD, MPH; and David H. Spach, MD

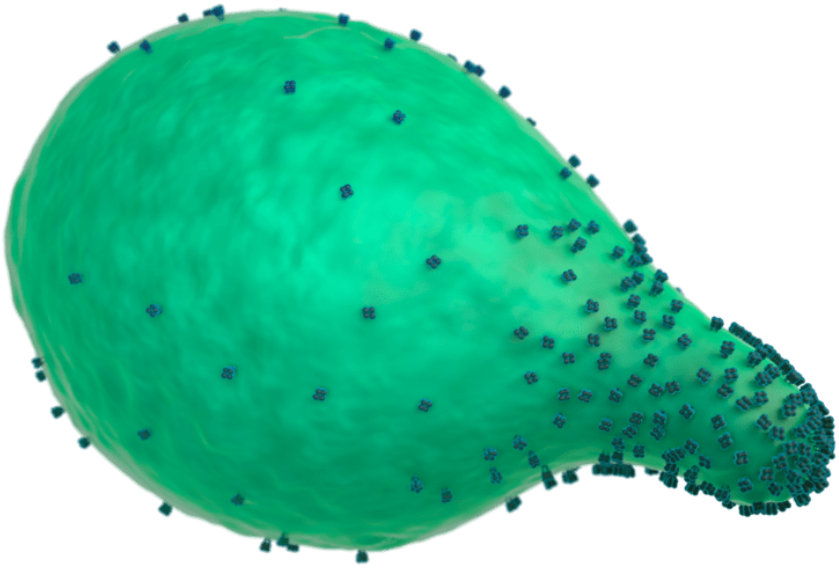

Figure 2 *Mycoplasma genitalium* Prevalence in Sexual Health Clinics in United States

Source: Manhart LE, Leipertz G, Soge OO, et al. *Mycoplasma genitalium* in the US (MyGeniUS): Surveillance Data From Sexual Health Clinics in 4 US Regions. Clin Infect Dis. 2023;77:1449-59.

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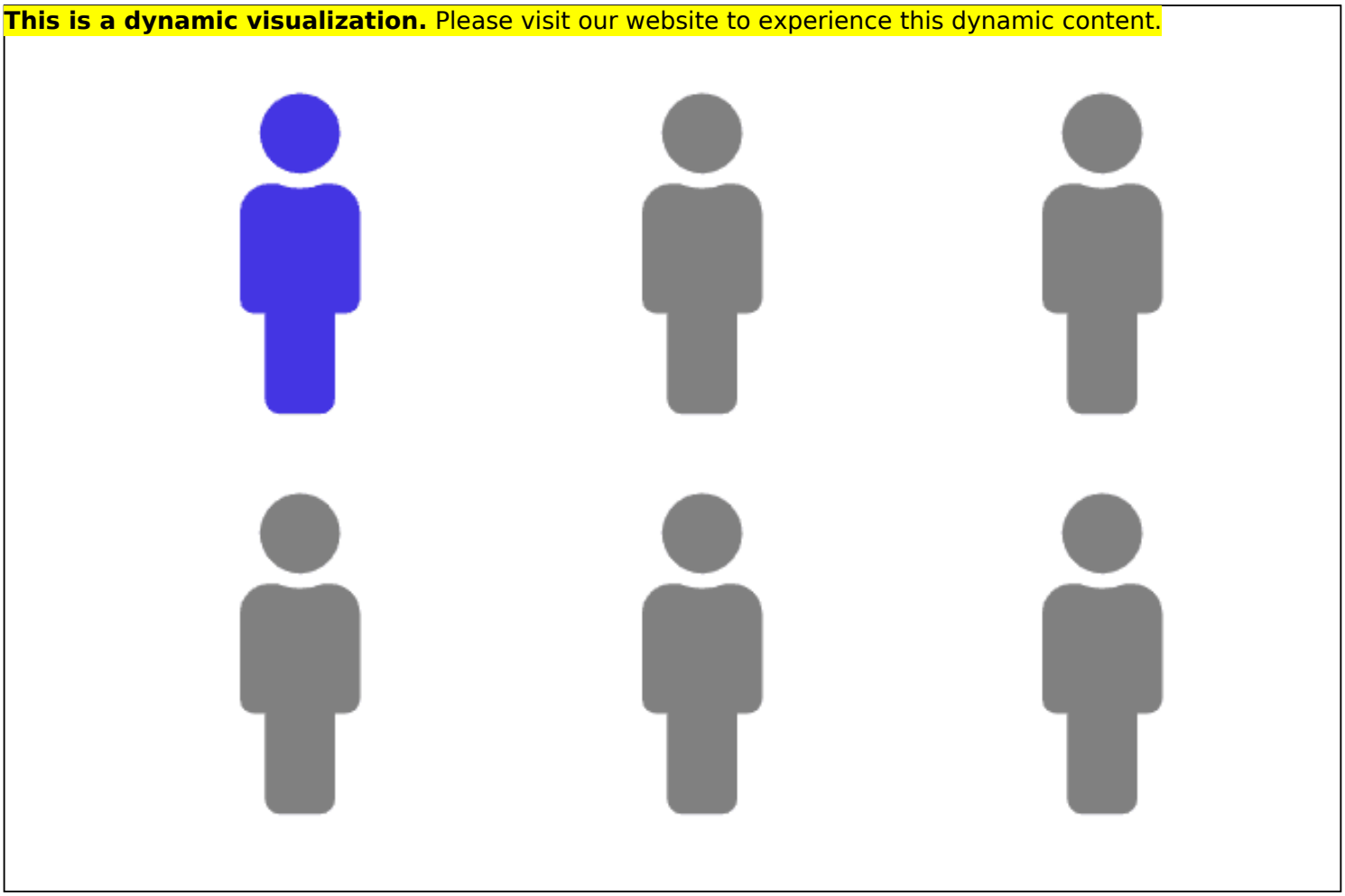

Figure 3 *Mycoplasma genitalium* Structure

Illustration credit: Cognition Studio, Inc.; Gwendolyn E. Wood, PhD; Lisa E. Manhart, PhD, MPH; and David H. Spach, MD

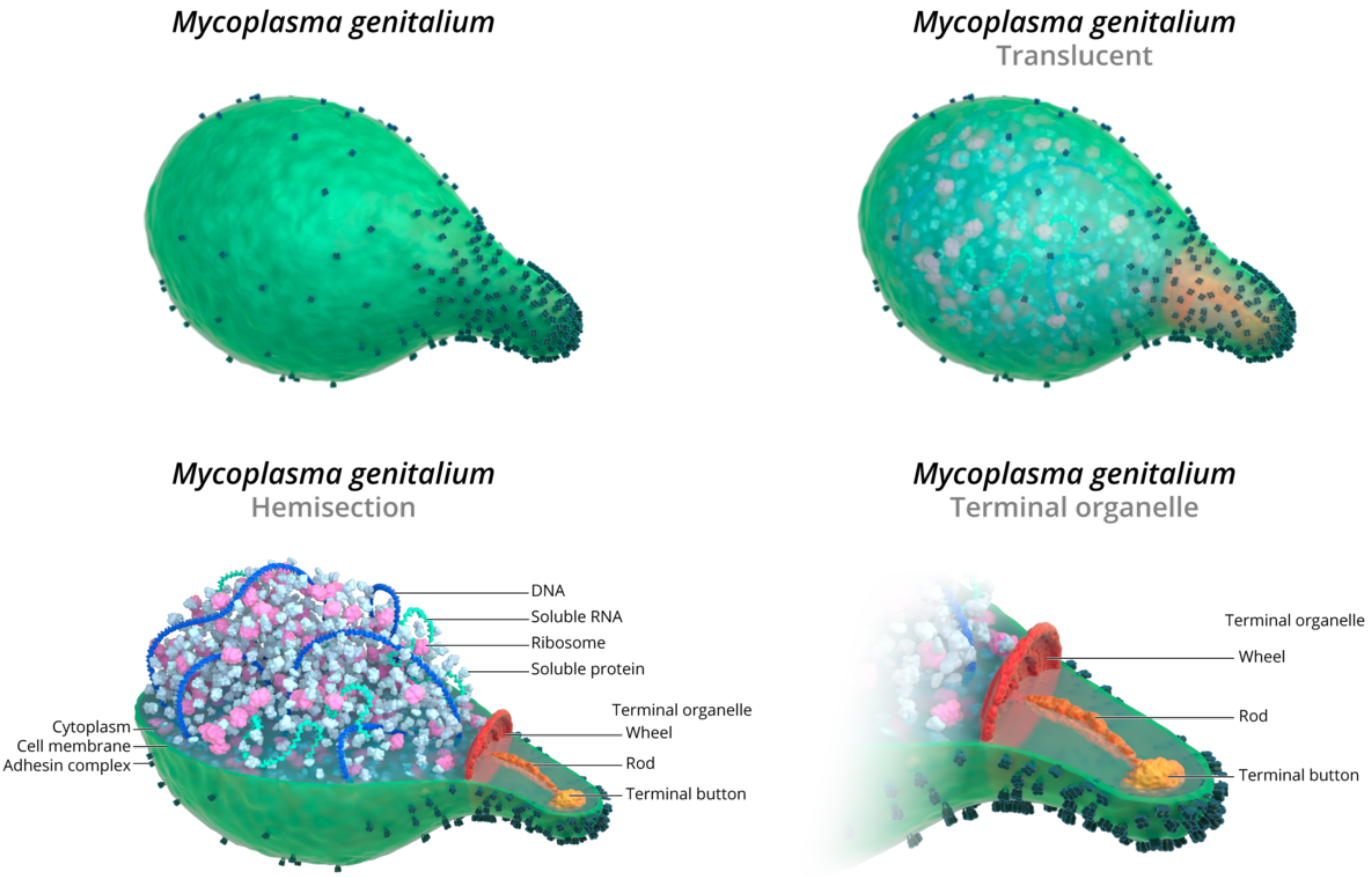

Figure 4 Distribution of Azithromycin MICs Performed on 56 *Mycoplasma genitalium* Clinical Isolates from 2007-2011

Abbreviation: (MICs) = Minimum Inhibitory Concentrations
Isolates with Azithromycin MIC ≥8 m/mL correlated

Source: Wood GE, Jensen NL, Astete S, et al. Azithromycin and Doxycycline Resistance Profiles of U.S. em>Mycoplasma genitalium Strains and Their Association with Treatment Outcomes. J Clin Microbiol. 2021;59:e0081921.

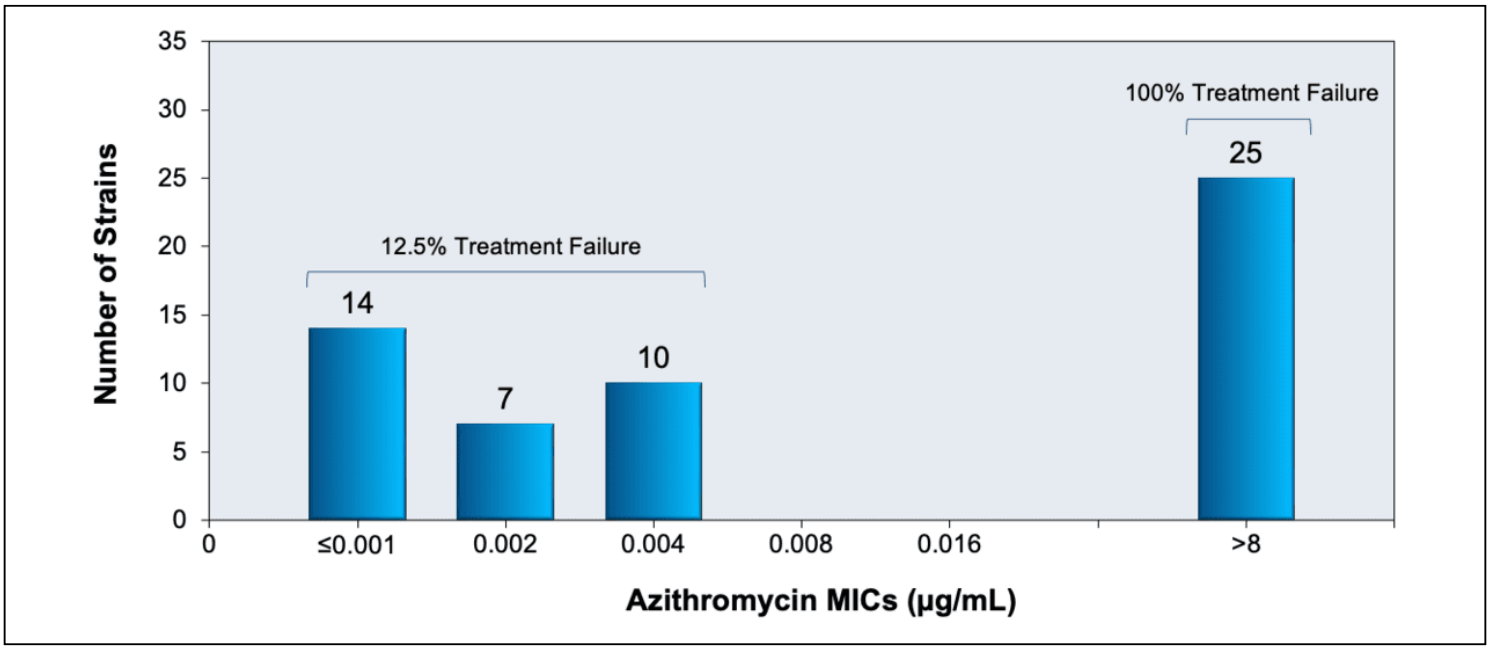

Figure 5 Distribution of Doxycycline MICs Performed on 62 *Mycoplasma genitalium* Strains Cultured

Abbreviation: (MICs) = Minimum Inhibitory Concentrations

Source: Wood GE, Jensen NL, Astete S, et al. Azithromycin and Doxycycline Resistance Profiles of U.S. em>Mycoplasma genitalium Strains and Their Association with Treatment Outcomes. J Clin Microbiol. 2021;59:e0081921.

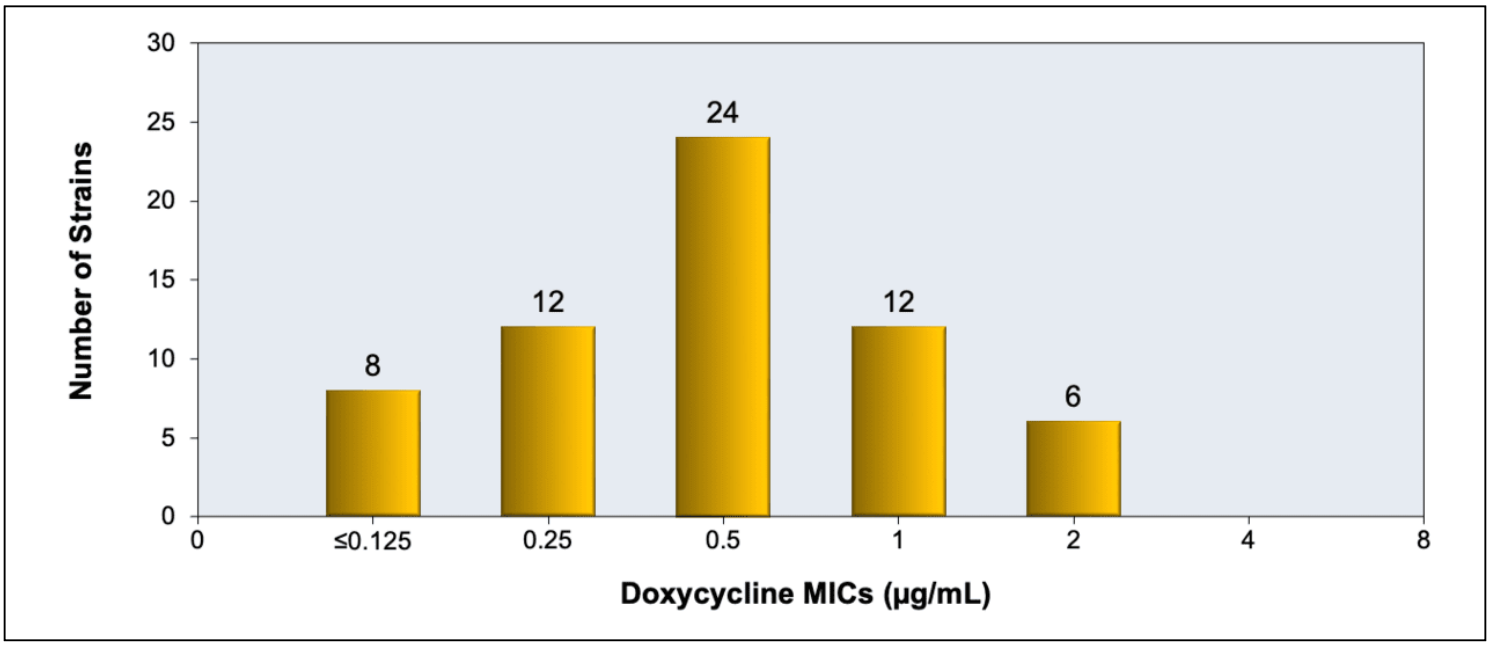

Figure 6 Cervicitis with Purulent Cervical Discharge

Illustration: Cognition Studio, Inc. and David H. Spach, MD

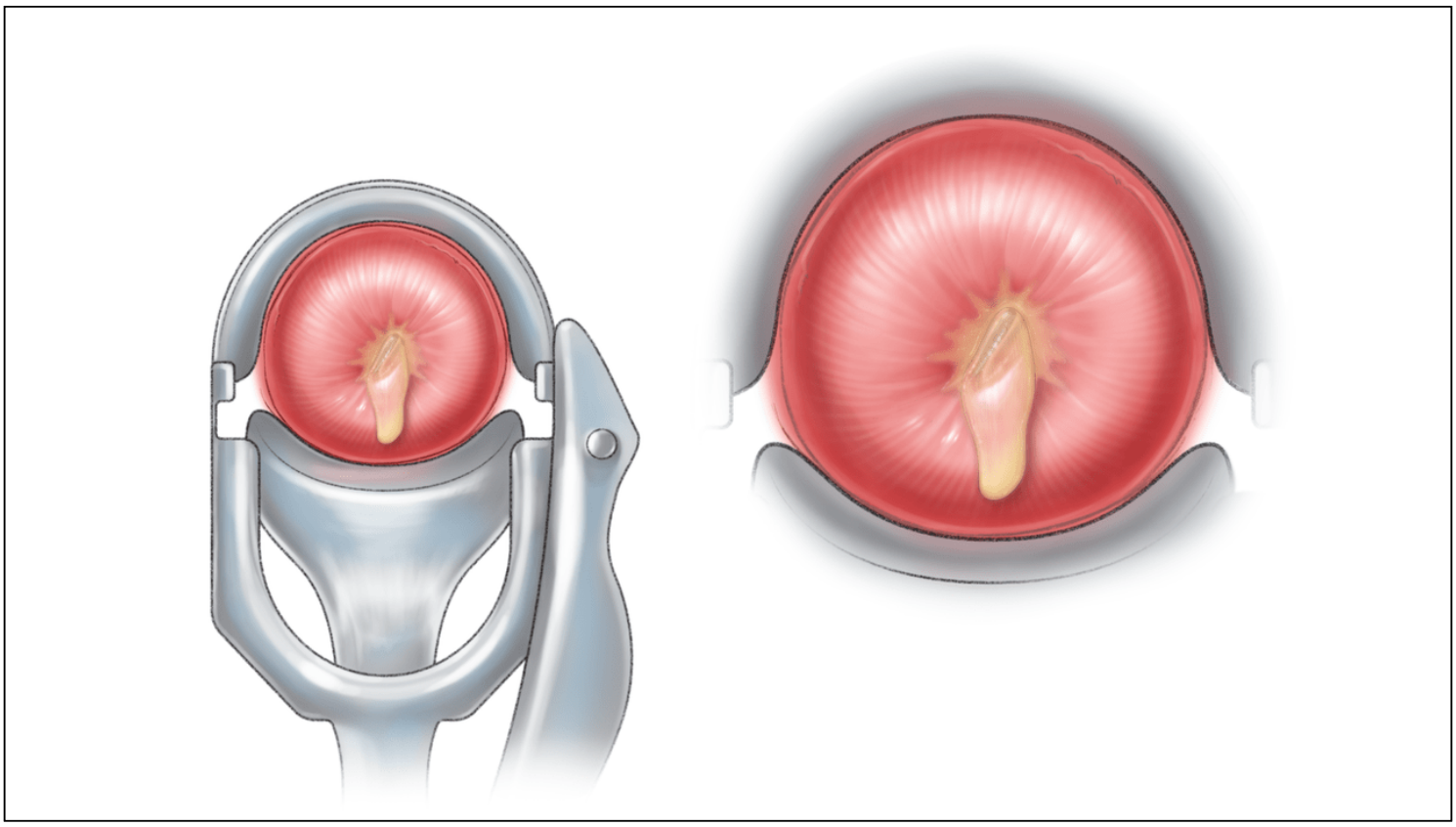

Figure 7 Pelvic Inflammatory Disease

Illustration: Cognition Studio, Inc. and David H. Spach, MD

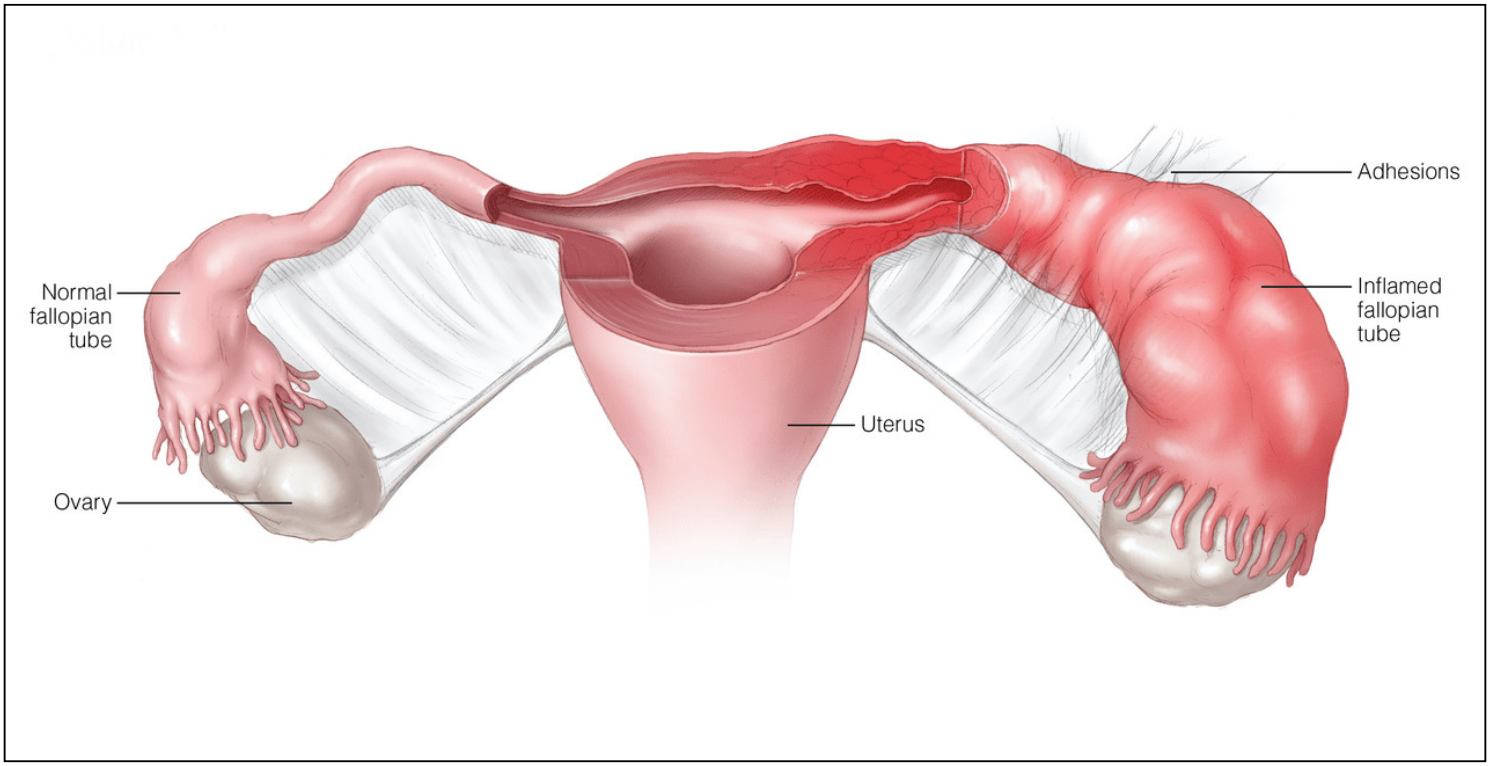

Figure 8 Tubal Occlusion Following Salpingitis

Illustration: Cognition Studio, Inc. and David H. Spach, MD

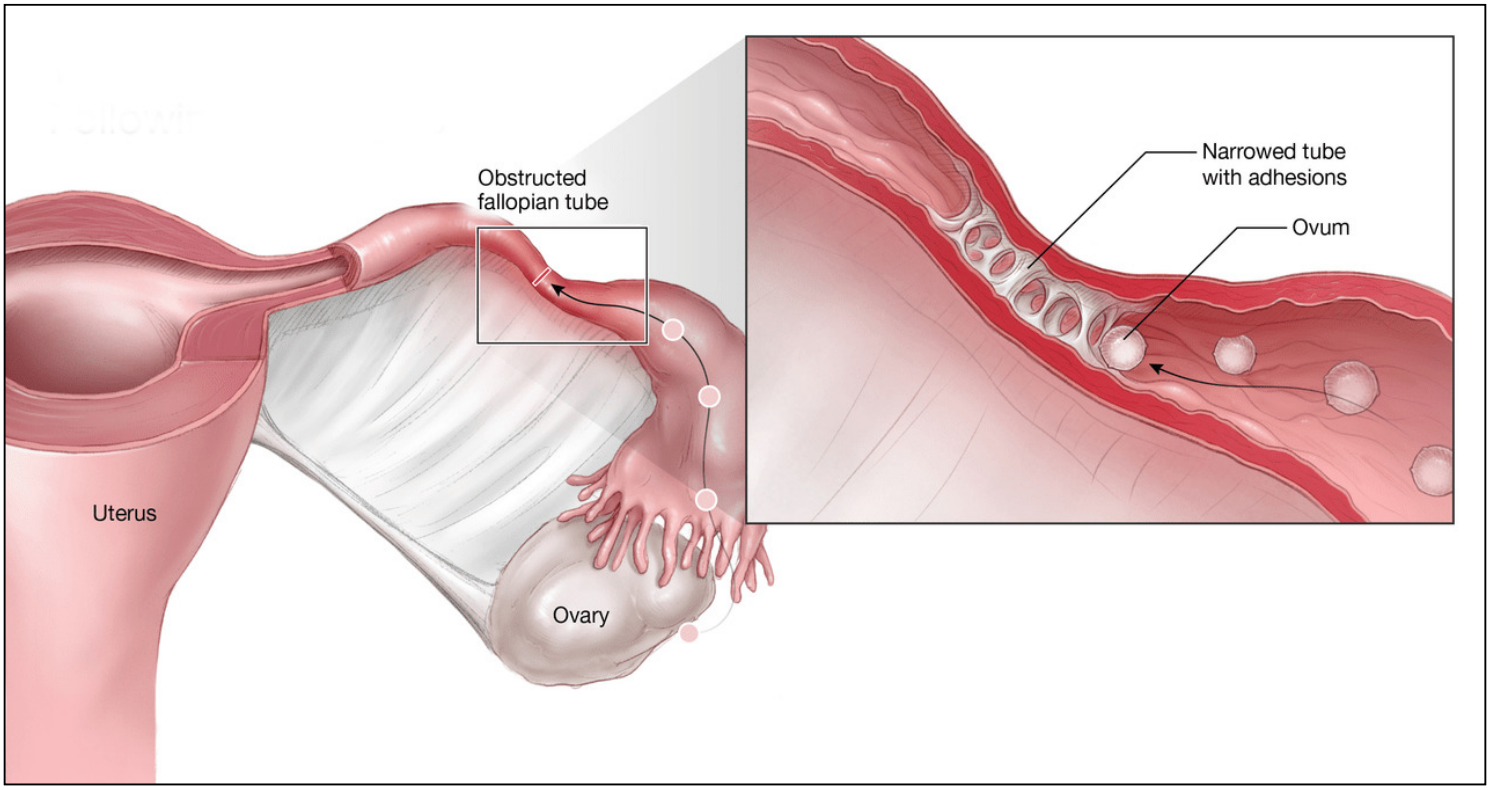

Figure 9 Proctitis

Illustration: Cognition Studio, Inc. and David H. Spach, MD

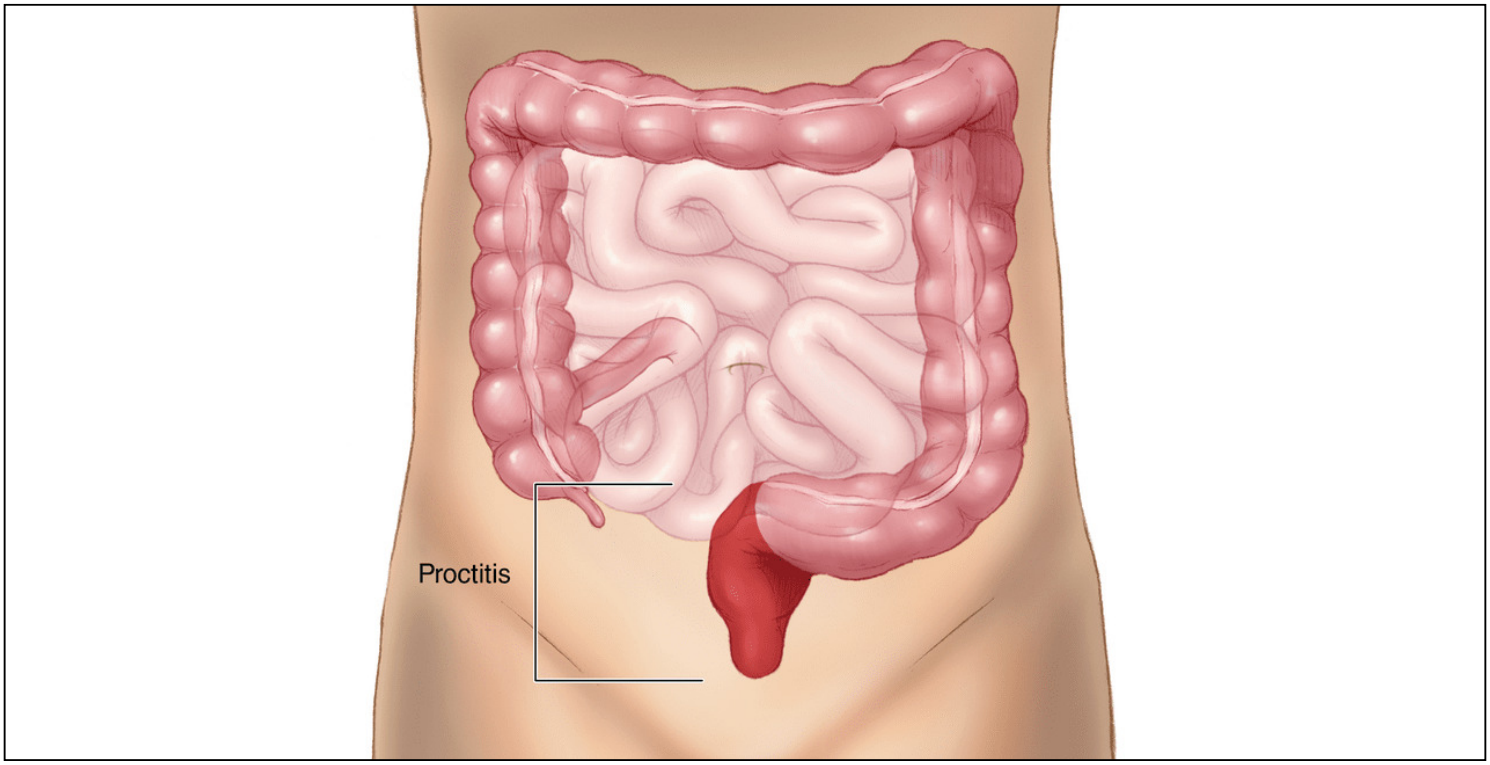

Figure 10 Efficacy of Azithromycin and Doxycycline Monotherapy in the Treatment of *Mycoplasma genitalium* in 3 Randomized Comparative Trials

Source: (1) Mena LA, Mroczkowski TF, Nsuami M, Martin DH. A randomized comparison of azithromycin and doxycycline for the treatment of *Mycoplasma genitalium*-positive urethritis in men. Clin Infect Dis. 2009;48:1649-54. (2) Schwebke JR, Rompalo A, Taylor S, et al. Re-evaluating the treatment of nongonococcal urethritis: emphasizing emerging pathogens--a randomized clinical trial. Clin Infect Dis. 2011;52:163-70. (3) Manhart LE, Gillespie CW, Lowens MS, et al. Standard treatment regimens for nongonococcal urethritis have similar but declining cure rates: a randomized controlled trial. Clin Infect Dis. 2013;56:934-42.

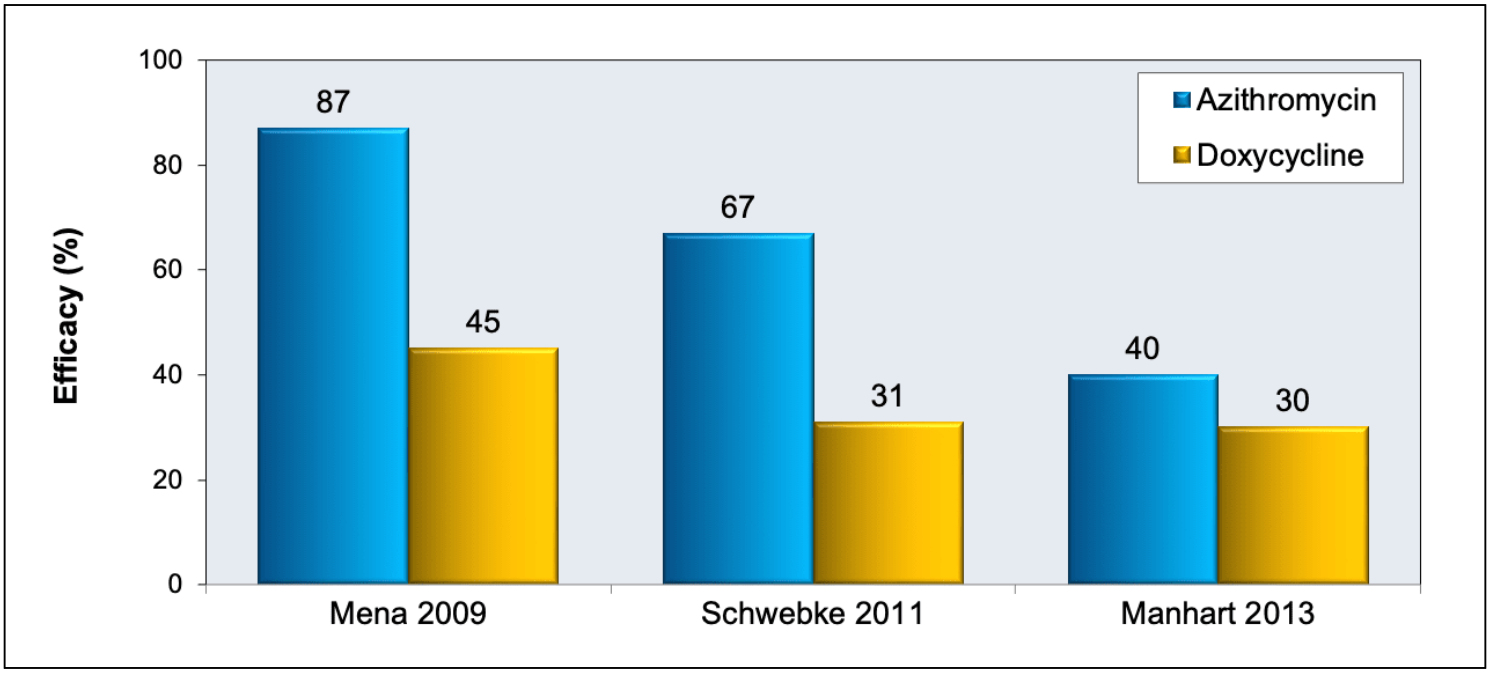

Table 1.

***Mycoplasma genitalium* Testing Recommendations**

Type of Test	Definition	Recommendat
Screening Test	Testing of asymptomatic people with the goal of preventing disease sequelae and prevent transmission to others	Routine testing of asymptomatic p recommended.
Diagnostic Test	Testing of symptomatic persons to direct treatment decisions	Testing recommended for: • Men with persistent or recu • Women with persistent or Testing should be considered for: • Women with pelvic inflamn

Source:

- Wetmore CM, Manhart LE, Lowens MS, et al. Demographic, behavioral, and clinical characteristics of men with nongonococcal urethritis differ by etiology: a case-comparison study. Sex Transm Dis. 2011;38:180-6. [PubMed Abstract]
- Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *Mycoplasma genitalium*. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 2. 2021 STI Treatment Guidelines: *Mycoplasma genitalium* Recommended Regimens if *M. genitalium* Resistance Testing is Available

Recommended if macrolide sensitive:
Doxycycline followed by Azithromycin *Doxycycline 100 mg orally 2 times/day for 7 days, followed by Azithromycin 1 g orally initial dose, followed by 500 mg orally once daily for 3 additional days (2.5 g total of Azithromycin)*

Recommended if macrolide resistant:
Doxycycline followed by Moxifloxacin *Doxycycline 100 mg orally 2 times/day for 7 days, followed by Moxifloxacin 400 mg orally once daily for 7 days*

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *Mycoplasma genitalium*. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]

Table 3. 2021 STI Treatment Guidelines: *Mycoplasma genitalium*
Recommended Regimens if *M. genitalium* Resistance Testing is Not Available

Recommended if *M. genitalium* is detected by an FDA-cleared NAAT:
Doxycycline followed by Moxifloxacin *Doxycycline 100 mg orally 2 times/day for 7 days, followed by Moxifloxacin 400 mg orally once daily for 7 days*

Source: Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. *Mycoplasma genitalium*. MMWR Recomm Rep. 2021;70(No. RR-4):1-187. [2021 STI Treatment Guidelines]