RANDOX

EDUCATIONAL GUIDE

Vivalytic MG, MH, UP/UU

BOSCH vivalytic

Introduction

Mycoplasma spp. and Ureaplasma spp. belong to a class of bacteria called Mollicutes and are the smallest organisms of the class. These sexually transmitted pathogens can cause both asymptomatic and symptomatic infections, the latter being associated with both acute and chronic infection of the genitourinary tract. These bacterial species are considered commensal but shifts in their prevalence and persistence can cause serious health concerns. The prevalence of these species is higher in women who present with symptoms of genitourinary tract infections than men. Furthermore, these species have been associated with pregnancy complications and infertility in both men and women. Figure 1 shows some examples of the conditions and complications associated with these bacterial pathogens. Additionally, infection by any of these pathogens is associated with increased risk of other sexually transmitted infections.

Diseases and Complications Associated with M. genitalium, M. hominis & Ureaplasma spp.

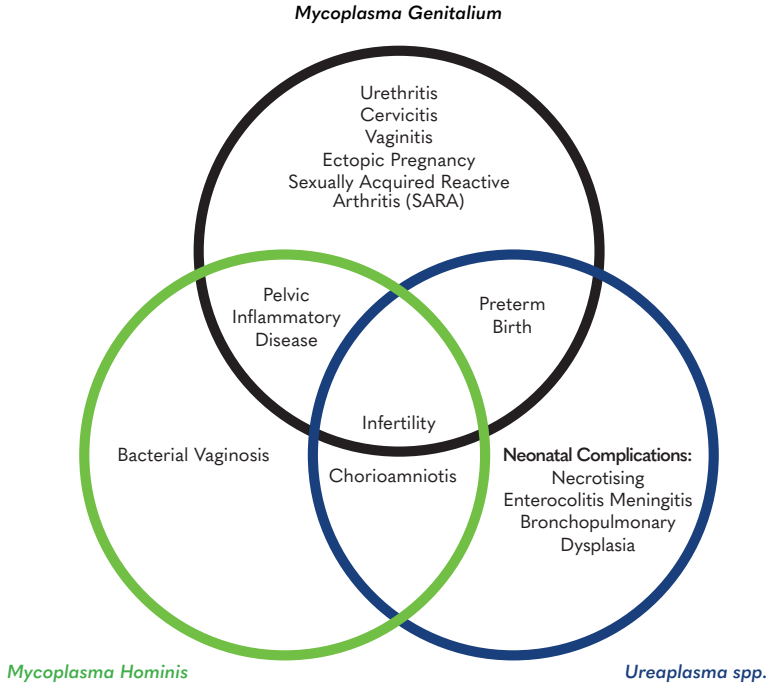

Figure 1. Venn diagram showing conditions and complications associated with M. genitalium, M. hominis and Ureaplasma spp.

These days, antimicrobial resistance (AMR) is a common theme when discussing any bacterial species. Mycoplasma spp. and Ureaplasma spp. are no different. Increasing resistance to primary and secondary treatment strategies for these pathogens is increasing, driving the need for fast, accurate diagnostic and screening methods which can differentiate these species to aid risk-stratification and better inform clinicians to help prescribe the correct therapy.

To this end, the Vivalytic MG, MH, UU/UP Rapid Test aids healthcare professionals to deliver appropriate treatment decisions at the earliest opportunity for improved patient management and prevention of transmission.

Mycoplasma spp

M. genitalium & M. hominis

Mycoplasma spp. are of the bacterial class mollicutes. These species lack a cell wall, and therefore cannot be identified through gram-staining[1] and lack the crucial enzymes for amino acid biosynthesis[2]. Long term exposure to high loads of these species of bacteria has been associated with oncogenic processes known to be related to proliferation, invasiveness, and metastasis of cancerous cells[2]. Mycoplasma genitalium (MG) contains the smallest genome of self-replicating prokaryotes, consisting of around 500 genes. Methods of transmission are generally through direct genital-genital mucosal contact. However, penile-anal contact has also been shown to be responsible for the spread of the pathogen[3]. MG can have serious effects on the female reproductive system and is associated with several risk factors such as Black ethnicity, under 30 years of age, low socio-economic status and more than 2 sexual partners in the last 12 months[2]. Infection by MG is likely to result in inflammation of the reproductive system, causing conditions such as Pelvic Inflammatory Disease (PID), cervicitis, vaginitis, and urethritis[3]. Around 70% of MG infections in men attending STI clinics are symptomatic, presenting with conditions such as acute, persistent, or recurrent urethritis.

The characteristic lack of cell wall makes it impossible for MG to be identified by gram-staining. Additionally, culture of MG is an extremely arduous process, taking up to 6 months. Serological methods have been applied but lack specificity due to high cross-reactivity with other mycoplasma spp.[1] Nucleic Acid Amplification Testing (NAAT) allows the identification of MG-specific nucleic acids and are considered the only diagnostic method with clinical utility[3].

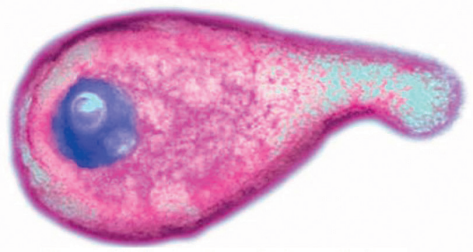

Figure 2. Illustration of M. genitalium

Mycoplasma hominis (MH) is a commensal bacteria found in the genital tract. However, MH is frequently found as a co-infection with Gardnerella Vaginalis, a pathogen responsible for bacterial vaginosis. This suggests MH infection is associated with vaginal flora alterations and ultimately bacterial vaginosis. This is supported by findings that MH load is almost 30% higher in women with bacterial vaginosis than in asymptomatic women[4].

Bacterial vaginosis is a lower genital tract infection associated with the disruption of normal vaginal microbiota caused by under representation of bacteria which produce lactic acid and increases in strict and facultative anaerobes[5]. Bacterial vaginosis can develop into PID. The anaerobes ascend to the upper genital tract causing the manifestation of symptoms such as cervical motion tenderness, uterine tenderness, or adnexal tenderness[5]. The nonspecific nature of these symptoms is part of the driving force for the requirement for highly specific tests to aid in the correct characterisation of members of the Mycoplasma spp. and the subsequent treatment of the conditions they cause. It is also important to note that bacterial vaginosis is thought to be a causal factor in NCNGU (Non-chlamydial non-gonococcal urethritis) in men through sexual transmission[5] and MH is thought to be associated with chorioamnionitis, a condition characterised by inflammation the placental membranes leading to sever infection, brain defects and lung problems[6].

MH shares many characteristics with MG, including the lack of cell wall characteristic of mollicutes. Therefore, the challenges faced in diagnosis of MG infection are also seen MH diagnosis. As gram-staining is not possible and serological techniques lack specificity, NAAT is the only clinically useful diagnostic method for MH.

Ureaplasma spp

U. urealyticum & U. parvum

Ureaplasma spp. are one of the most prevalent bacteria with pathogenic potential. They are thought to have evolved from gram-positive bacteria through degenerative evolution, causing them to lose their peptidoglycan cell wall[7]. These bacteria are insensitive to β-lactam antibiotics and can be transmitted either through sexual contact or from mother to child either during pregnancy or through infected bodily fluids at the time of birth. Ureaplasma spp. bind to mucosal surfaces, facilitated by cytoadherence proteins found on their bacterial surface. The high virulence and persistence displayed by these bacteria is largely influenced by biofilm formation[7].

The 14 serotypes of Ureaplasma spp. are categorised into biovars 1 (U. parvum) and 2 (U. urealyticum). These opportunistic microorganisms are likely to be found in the lower urogenital tract of both healthy and diseased individuals. Ureaplasma spp. are an independent risk factor for chorioamnionitis and preterm birth and are associated with NCNGU, several neonatal conditions, and infertility[7]. In addition, high bacterial load of U. urealyticum is associated with post-partum endometritis[8]. In neonates, Ureaplasma spp. are associated with low birth weight, meningitis, and the onset of various respiratory diseases such as bronchopulmonary dysplasia and chronic lung disease in later life[7].

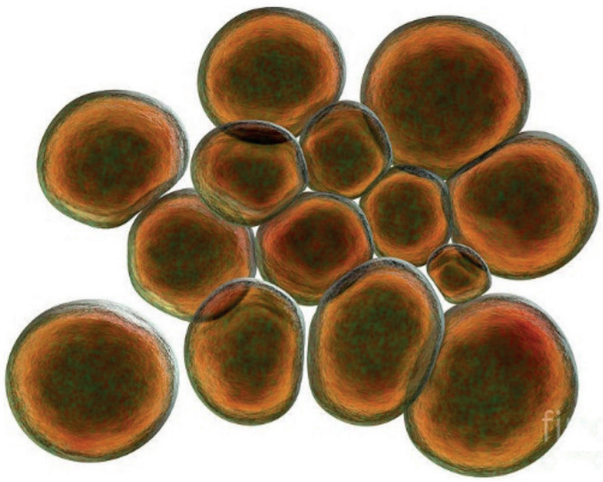

Figure 3. Illustration of U. urealyticum colony

Like Mycoplasma spp., Ureaplasma spp. cannot be identified through gram-staining as they lack a cell wall. Culture is the gold standard method for identification but again, like Mycoplasma spp., this is a long, arduous process, taking around 48 hours and requiring a complex substrate. Serological assays prove insensitive and lack utility due to the commensal nature of Ureaplasma spp[7].

Pregnancy Complications and Infertility

Pregnancy complications and infertility are commonly associated with many sexually transmitted pathogens including Mycoplasma spp. and Ureaplasma spp.. The table below details the reproductive complications associated with these bacteria:

Pathogen	Infertility	Pregnancy Complications
M. genitalium	Detection of MG in infertile women is significantly higher than in reproductively healthy women suggesting MG is an independent risk factor for infertility – MG is carried by sperm to the uterus where it translocates through the endometrium to the Fallopian tubes where it colonises the Fallopian tube epithelium, destroying the ciliated epithelium, resulting in infertility.	Ectopic pregnancy – pregnancy implanted outside the intrauterine cavity. MG contributes to ectopic pregnancy by altering the structure of the Fallopian tubes. Salpingitis (inflammation of the Fallopian tubes), a condition associated with MG infection, also contributes to ectopic pregnancy. Preterm Birth – MG colonisation is an independent risk factor for spontaneous preterm birth.
M. hominis	MH, frequently found as a co-infection with Gardnerella Vaginalis, a pathogen responsible for bacterial vaginosis (BV). Infertility is linked with Bacterial Vaginosis (BV). BV-associated bacteria are, on average, linked to an over 3x increase in infertility risk – Thought to be due to the alterations caused by inflammation of the endometrium resulting in decreased affinity for embryo implantation. Idiopathic infertility has previously been linked with alterations in vaginal bacterial flora, including those related to BV.	Chorioamnionitis – Inflammation of the foetal membranes (Chorion – outer membrane, Amnion – inner membrane) often resulting in preterm birth. **Neonatal complications:** - Necrotising enterocolitis - Meningitis - Bronchopulmonary dysplasia
Ureaplasma spp.	U. urealyticum (UU) colonisation is associated with infertility – One study9 found 32% of infertile women studied were colonised by UU. Furthermore, UU has been shown to attach to sperm cells, decreasing their mobility, contributing to infertility.	Ureaplasma spp. have been associated with various pregnancy complications including: - Chorioamnionitis - Preterm Birth - Low Birth Weight - Spontaneous abortion - Stillbirth

The identification of MG, MH, UP/UU is crucial in pregnant women to reduce the risk of developing these potentially severe infections, which places both the mother and child in danger of serious adverse complications and in some cases, death.

Antimicrobial Resistance

Much of the antimicrobial resistance (AMR) displayed by these bacteria can be accredited to their ability to form biofilms. These biofilms block antibiotic activity through a variety of mechanisms which reduce binding affinity and, in some cases, excrete enzymes which break down antibiotics, blocking their effectiveness. For example, MG is known to be more than 80% resistant to macrolide administration. Secondary treatment strategies utilise the fluoroquinolones class of antibiotics, however, in the UK the cure rate associated with moxifloxacin has dropped from 96% to 89% since 2010[1].

The characterisation of these species is crucial in clinical practice to ensure the correct therapy is prescribed by the clinician. The species and strain of the infectious agent is of upmost importance when selecting an antibiotic strategy; the class of antibiotic chosen for a particular strain will determine the efficacy of the treatment.

Vivalytic MG, MH, UP/UU Rapid Test

Aiding in the diagnosis and containment of sexually transmitted infections (STIs) in symptomatic and asymptomatic individuals, the MG, MH, UP/UU Rapid Test guides appropriate treatment decisions at the earliest opportunity for improved patient management, prevention of transmission and supporting emerging macrolide resistance.

A recent study[10] compared the Vivalytic MG, MH, UP/UU Rapid Test with a sensitive reference method and was shown to deliver rapid, accurate results. In this investigation, 239 urogenital samples (132 urine and 107 swabs) were tested displaying an overall concordance rate of 97.7% (Positive percent agreement = 96%, Negative percent agreement = 98.7%) for urine samples and 95.6% (Positive percent agreement = 94.6%, Negative percent agreement = 98%) for swab samples[10]. To achieve comparable results, both tests had been conducted within 48 hours. The study concludes that the Vivalytic MG, MH, UP/UU Rapid Test displays excellent correlation and is suitable for use in both hospital and outpatient settings[10]. Providing strong evidence for its utility as a diagnostic tool, the Vivalytic MG, MH, UP/UU Rapid Test can quickly and accurately detect MG, MH, UP and UU bacterial species in both swab and urine samples.

Panel Features

- Detection method: Real-Time PCR.
- Result time: 1 hour.
- Sample volume: 300µl.
- Sample type: Urine or Swab (Urethral, Vaginal, Cervical, Rectal).

The Vivalytic system is a fully automated, cartridge-based platform capable of both Hi-Plex and Lo-Plex infectious disease testing. Each easy-to-use cartridge contains all necessary reagents, is fully sealed to minimise risk, and can be conveniently stored at room temperature.

Vivalytic Features

- Cartridge based platform.
- Fully automated.
- Suitable for both non-laboratory & laboratory settings.
- Small footprint device.
- Rapid turnaround from sample entry to results.

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