Mycoplasma hominis and Ureaplasma urealyticum infections

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INTRODUCTION — The term "mycoplasma" is widely used to refer to any organism within the class Mollicutes, which is composed of eight genera (including *Mycoplasma*, *Ureaplasma*, *Acholeplasma*, *Anaeroplasma*, and *Asteroloplasma*). Over 200 named *Mycoplasma* species exist, and 13 *Mycoplasma* species, two *Acholeplasma* species, and two *Ureaplasma* species have been isolated from humans [1]. However, only six species, five of which inhabit the genitourinary tract, are established or presumed human pathogens; *Mycoplasma pneumoniae* is a respiratory tract pathogen [2]:

- *M. pneumoniae*
- *Mycoplasma hominis*
- *Mycoplasma genitalium*
- *Mycoplasma fermentans* (incognitus strain)
- *Ureaplasma*
  - *Ureaplasma urealyticum*
  - *Ureaplasma parvum*

The clinical features and treatment of human infections with *M. hominis* and *Ureaplasma* will be reviewed here. *M. pneumoniae* and *M. genitalium* infections are discussed separately. (See "Mycoplasma pneumoniae infection in adults" and "Mycoplasma genitalium infection in men and women".)

EPIDEMIOLOGY — Although *M. hominis* and, to a lesser extent, *Ureaplasma* have been implicated in a number of conditions related to parturient women and their fetuses and newborns, the precise roles of *Mycoplasma* and *Ureaplasma* spp remain unproven, or even speculative, in many diseases for the following reasons [3]:

- Many healthy asymptomatic adults have genitourinary colonization with *Mycoplasma* and *Ureaplasma* spp.
- Colonization with several mycoplasmas, or with other non-mycoplasmal organisms such as chlamydias, is the rule.
- Published studies on the pathogenicity of these organisms commonly have important design limitations.
- Detection of these organisms is difficult and complex. Although newer nucleic assays increase detection, they do not necessarily contribute to establishing causality.

M. hominis, *M. genitalium*, and *M. fermentans* are part of the normal genital flora of many sexually experienced men and women [4]. The percentage of women with vaginal colonization by *M. hominis*, *M. genitalium*, and *Ureaplasma* spp increases after puberty in proportion to the number of lifetime sexual partners [5]. Genital colonization may also be linked to lower socioeconomic status.

The rate of colonization with *M. hominis* increases more rapidly with increasing sexual experience in women than in men, suggesting that women are more susceptible to colonization [6]. By adulthood, approximately 80 percent of healthy women have *Ureaplasma* spp and 50 percent have *M. hominis* in their cervical or vaginal secretions [3]. Sexually active men are also frequently asymptomatically colonized with *M. hominis* (25 percent in one series of 99 men attending a clinic for sexually transmitted diseases) [7].

Newborns who are colonized with *Mycoplasma* spp are presumed to have been exposed during passage through the birth canal, since colonization is less common in infants born by caesarean section. Neonatal colonization is transient and the proportion of infants colonized decreases proportionately with age [8]. Infants more than three months of age are rarely if ever colonized. *M. hominis* is seldom recovered from prepubertal boys, whereas a small percentage of prepubertal girls have been found to be colonized in some studies.

MICROBIOLOGY AND PATHOGENESIS — Mycoplasmas and ureaplasmas are the smallest free-living organisms. Because they lack a cell wall, neither mycoplasmas nor ureaplasmas can be visualized by Gram stain. In order to culture these organisms, specialized media containing animal serum is required. (See 'Diagnosis' below.)

Most species of *Mycoplasma* undergo similar biochemical reactions in the microbiology laboratory as many other bacterial species. However, there are a few biochemical tests that are useful for species identification. For example, ureaplasmas are unique because of their ability to hydrolyze urea. It is unknown whether there is a difference in pathogenicity between the two named species of *Ureaplasma*, *U. urealyticum* and *U. parvum* [1].

Although *Mycoplasma* and *Ureaplasma* spp normally exist in a state of adherence to mucosal epithelial cells of the respiratory or urogenital tracts, they can disseminate to other sites and cause infection when there is a disruption of the mucosa (eg, instrumentation, surgery, trauma) and/or an underlying immaturity in host defenses, such as in the developing fetus or premature infant. *M. hominis* and ureaplasmas have surface proteins that facilitate cytoadherence [3]. Ureaplasmas can attach to erythrocytes, white blood cells, host mucosal cells, and even spermatozoa [1].

While the microbiological burden of the genitourinary mycoplasmas may be higher in HIV-infected individuals, than in the HIV uninfected population, there is no evidence that disease caused by these organisms is more frequent or more severe in the setting of HIV infection [9].

CLINICAL FEATURES AND POSSIBLE DISEASE ASSOCIATIONS — *M. hominis* and *Ureaplasma* have been associated with genitourinary tract and nongenital infections. However, as stated above, evidence that mycoplasmas and ureaplasmas cause most of these conditions is tenuous at best. Assertions on causation are often based on strong associations between the presence of one organism and a disease condition.

Infections that have been linked to *M. hominis* include:

- Pelvic inflammatory disease (PID)
- Chorioamnionitis
- Postpartum and postabortal fever
- Pyelonephritis
- Central nervous system infections
- Septicemia
- Wound infections
- Joint infections
- Upper and lower respiratory tract infections
- Endocarditis
- Neonatal bacteremia and meningitis
- Neonatal abscesses

Ureaplasma spp have been linked to:

- Chorioamnionitis
- Postpartum and postabortal fever
- Congenital pneumonia
- Neonatal bacteremia
- Neonatal abscesses

These manifestations are discussed in greater detail in the following section.

Genitourinary tract infections and complications of pregnancy

Cervicitis and pelvic inflammatory disease — *M. hominis* is commonly found in the genitourinary tract of both males and females. It is more often detected in women. The role of *M. hominis* as a cause of PID remains controversial [2]. In one study, *M. hominis* was isolated from 4 of 50 fluid samples taken directly from the fallopian tubes of women with salpingitis versus none of 50 samples from control woman [10]. In the same study, significant rises or falls in antibody titers to *M. hominis* occurred in 9 of 16 women with salpingitis who had positive lower genital tract cultures for *M. hominis* [10]. The presence of infection in the absence of changes in antibody titers may reflect the localized nature of salpingitis. The significance of these findings is uncertain. *M. hominis* is rarely present in patients with salpingitis who do not also have evidence of concurrent chlamydial or gonococcal infections or bacterial vaginosis. As a result, its role as a primary pathogen in salpingitis is still uncertain. (See "Pelvic inflammatory disease: Pathogenesis, microbiology, and risk factors".)

The association between *M. genitalium* and cervicitis or pelvic inflammatory disease is discussed in detail elsewhere. (See "Mycoplasma genitalium infection in men and women", section on 'Cervicitis' and "Mycoplasma genitalium infection in men and women", section on 'Pelvic inflammatory disease'.)

Non-gonococcal urethritis — *U. urealyticum* has been associated with non-gonococcal urethritis (NGU) in some studies [11], but not others [12,13]. In a meta-analysis of studies involving 1507 NGU patients and 1223 controls, *U. Urealyticum* (but not *U. parvum*) was more common in men with NGU [14]. In another study, *U. urealyticum* was significantly associated with NGU only in men with fewer than 10 lifetime heterosexual partners [15]. The authors postulated that adaptive immunity may

attenuate the clinical manifestations of *U. urealyticum* infection, so that men with more exposure to this organism are less likely to have symptoms of NGU from it. However, this hypothesis is not proven and other explanations are possible. (See "Urethritis in adult men", section on 'Nongonococcal urethritis'.)

The association between *M. genitalium* and urethritis is discussed in detail elsewhere. (See "Mycoplasma genitalium infection in men and women", section on 'Urethritis in men'.)

Urinary tract infection — *M. hominis* can frequently be recovered from the lower genitourinary tract in men and women, but a causal relationship to cystitis, epididymitis, or prostatitis has not been established. This organism may be responsible for up to 5 percent of cases of acute pyelonephritis, particularly when prior instrumentation has been performed or obstruction is present [2,16]. *Ureaplasma* spp are thought to cause some upper urinary tract infections.

Chorioamnionitis — There is evidence that *M. hominis* and *U. urealyticum* are frequently found in the amniotic fluid of women with preterm labor, preterm premature rupture of membranes, spontaneous labor at term, premature rupture of membranes at term, or chorioamnionitis [17]. Although these observations suggest that intrauterine colonization or infection is common, the role of these organisms in premature labor and chorioamnionitis remains incompletely understood. (See "Intra-amniotic infection (clinical chorioamnionitis or triple I)", section on 'Microbiology'.)

In a study of asymptomatic pregnant women who underwent amniocentesis during the second trimester, those in whom *Ureaplasma* spp was detected by PCR had a higher rate of subsequent preterm labor and preterm delivery [18].

Adverse pregnancy outcomes — *U. urealyticum* and *M. hominis* have increasingly been linked to adverse pregnancy outcomes. Some of these outcomes are the result of obvious infections such as chorioamnionitis mentioned above, but other associations are more tenuous and relate to increased colonization rates and titers of the organism [19,20]. Controversies abound as to whether these organisms are causal or not, since colonization rates of ureaplasmas (35 to 90 percent) and *M. hominis* (5 to 75 percent) are high and variable in the normal pregnant female population and are highest in the sexually active patient. An additional unclear factor is the role that other organisms, such as those that cause bacterial vaginosis, play in concert with the genital mycoplasmas leading to adverse pregnancy outcomes. While PCR-based diagnoses have yielded more information on colonization rates, they have not shed much light on whether these organisms have an etiologic role.

Adverse pregnancy outcomes and fertility issues that are potentially influenced by infection or colonization with *U. urealyticum* and/or *M. hominis* include:

- Spontaneous pre-term labor
- Pre-term premature rupture of fetal membranes
- Miscarriage
- Stillbirth
- Low birth weight

The role of these organisms in female infertility is highly controversial. No causal relationship has convincingly been shown. There appears to be an association between *M. hominis* and *U. urealyticum* colonization rates and male infertility in China [21], but again, no causality has been demonstrated.

Some studies have reported that treatment of pregnant women at risk for pre-term labor with antimicrobials effective against mycoplasmas and ureaplasmas is associated with prolongation of gestation and thus suggest that these organisms are responsible for adverse pregnancy outcomes of pregnancy [22]. However, many of the antimicrobials used have known significant anti-inflammatory effects, and these effects, not the eradication of the organism, may play a role in the improved outcomes with treatment.

Postpartum and postabortal fever and/or bacteremia — It has been estimated that *M. hominis* causes approximately 10 percent of all cases of postpartum and postabortal fever. In one study, *M. hominis* was recovered from blood cultures in 4 of 51 women (8 percent) with fever after abortion; in contrast, blood cultures were negative for *M. hominis* in all control women who had a recent abortion without fever and from all 102 normal pregnant controls [23]. Further evidence in support of *M. hominis* infection was a fourfold rise in antibody titers in approximately one-half of all women who had postabortal fever compared with only 2 of 53 controls who experienced abortion without fever. The higher frequency of antibody production than blood culture recovery suggests that many patients with postabortal fever develop nonbacteremic *M. hominis* infection.

In another series, *M. hominis* was isolated from the blood in 10 of 327 women (3 percent) who had blood cultures taken a few minutes after delivery; none had fever, and all remained well without treatment [24].

Nongenitourinary tract disease — The portal of entry for the mycoplasmas and ureaplasmas that cause nongenitourinary manifestations is almost always the genitourinary tract.

Central nervous system disease — *M. hominis* infection has been associated with nonfunctioning CNS shunts [25], brain abscess [26,27], subdural empyema [28], and meningitis [29]. Neonatal meningoencephalitis caused by *M. hominis* or *U. parvum* has also been described. (See 'Meningoencephalitis' below.)

Arthritis — *M. hominis* arthritis can occur in women after childbirth [30], in conjunction with congenital immune defects, such as hypogammaglobulinemia [31], in association with immunosuppression (eg, in solid organ transplant patients) [2] or lymphoma [32], or following joint replacement surgery or trauma [33].

M. hominis arthritis is usually characterized by fever, leukocytosis, and a purulent joint effusion with large numbers of polymorphonuclear cells but a negative Gram stain. In a review of 16 cases of septic arthritis due to *M. hominis*, one-half had undergone manipulation of the urinary tract before the onset of infection [33]. Delays in diagnosis were common, ranging from 5 to 37 days.

Wound infections — *M. hominis* has been associated with infected pelvic hematoma [34,35], infected cesarean wounds, and sternal wound infections [25,36,37]. A minority of sternal wound infections due to *M. hominis* have been anecdotally linked to cardiac and lung transplantation [38]. *M. hominis* wound infections have also been described after maxillofacial, abdominal, vascular, neurosurgical, and plastic surgical procedures [38].

In almost all cases, the clinical features of *Mycoplasma* wound infection are nonspecific. Clues to the presence of *M. hominis* in such cases are indirect. They include the finding of abundant polymorphonuclear leukocytes with a negative Gram stain, negative routine cultures, and a poor response to beta-lactam or aminoglycoside therapy.

Bacteremia — In addition to bacteremia in women with postpartum and postabortal fever, *M. hominis* has also been recovered from blood cultures in patients with recent trauma [34], and obstruction or surgery involving the genitourinary tract or perineal area. In addition, *M. hominis* can cause transient and self-limiting bacteremia in some postpartum women. (See 'Postpartum and postabortal fever and/or bacteremia' above.)

Endocarditis — *M. hominis* is a rare cause of prosthetic and native valve endocarditis with only five cases reported between 1966 and 2004 [39,40]. *M. hominis* endocarditis may also occur rarely in children [41]. Because of difficulties in culturing *M. hominis*, such patients present with culture-negative endocarditis. (See "Epidemiology, microbiology, and diagnosis of culture-negative endocarditis".)

Respiratory tract infection — The significance of *M. hominis* in respiratory secretions must be interpreted with caution. *M. hominis* has been isolated from respiratory secretions in 1 to 3 percent of healthy persons, 8 percent of patients with chronic respiratory complaints, and 14 percent of persons engaging in orogenital sex [42]. *M. hominis* can cause pharyngitis in volunteers whose nasopharynxes were experimentally inoculated with *M. hominis*. However, attempts to implicate *M. hominis* as a cause of naturally-occurring pharyngitis have been unsuccessful [43].

A report described seven patients with ICU-acquired pneumonia during a four-year period who had cultures from bronchoalveolar lavage or pleural fluid that were positive for *M. hominis* [44]. This report and others describing the recovery of *M. hominis* from lower respiratory tract specimens and/or empyema fluid suggest that *M. hominis* is rarely capable of causing lower respiratory tract infection [44-46]. A case report describes a lung transplant recipient with pneumonia and empyema whose bronchial brush specimen and pleural fluid grew *M. hominis* [45]. Another case report documents *M. hominis* as a cause of necrotizing pleuropneumonia in a previously healthy adolescent [47].

Prosthetic joint and bone infection — A few patients with prosthetic joint infections due to *M. hominis* have been described [33,48].

Fulminant bacteremia and systemic infection — *M. fermentans*, incognitus strain, a commensal in the genitourinary tract, has been shown to rarely cause fulminant and overwhelming infection in immunocompetent individuals and in people with AIDS, the patient population from which it was first isolated [49,50].

Post-transplant hyperammonemia — Hyperammonemia syndrome is a rare but potentially fatal post-transplant complication. The cause is not definitively known, but emerging evidence suggests that it is associated with *Ureaplasma* spp and possibly *M. hominis* infection [51,52]. This is discussed in further detail elsewhere. (See "Noninfectious complications following lung transplantation", section on 'Hyperammonemia'.)

Neonatal disease — One study found that 23 percent of 457 consecutive neonates who were born between 23 and 32 weeks of gestation had positive umbilical blood cultures for *M. hominis* and/or *U. urealyticum* [53]. Neonates with positive cultures more often had evidence of inflammatory response syndrome and their placentas more often had changes compatible with chorioamnionitis than babies with negative blood cultures. Reviews of this topic link maternal *U. urealyticum* colonization to low birth weight, neonatal bronchopulmonary dysplasia, intraventricular hemorrhage, and necrotizing enterocolitis, all of which are associated with prematurity [20,54].

Lung disease — *Ureaplasma* spp are thought to cause congenital pneumonia in neonates [3].

There is controversy about whether colonization with *Ureaplasma* spp results in bronchopulmonary dysplasia in neonates. In a meta-analysis of 23 studies examining the possible relationship between *Ureaplasma* colonization and neonatal bronchopulmonary dysplasia, *Ureaplasma* colonization was associated with chronic lung infection manifesting as long-term oxygen requirements and radiographic changes typical of bronchopulmonary dysplasia [55]. However, the studies included in

the meta-analysis were small and substantial differences between them make the results unreliable. (See "Neonatal pneumonia", section on 'Possible link of Ureaplasma urealyticum to chronic lung disease'.)

Meningoencephalitis — Neonatal meningoencephalitis caused by *M. hominis* or *U. parvum* has been described; infection was presumed to have been acquired in utero or via passage through the birth canal [3,56]. The frequency of neonatal infections may be higher than is generally appreciated. In one study, *Mycoplasma* cultures were performed on 100 preterm infants who underwent lumbar puncture for suspected sepsis or meningitis: *M. hominis* was isolated from the cerebrospinal fluid in five [57].

Bacteremia — *Ureaplasma* spp are thought to be potential causes of bacteremia in neonates, especially in association with meningitis or pneumonia [3].

Abscesses — Subcutaneous abscesses have been described in neonates in case reports [58,59].

DIAGNOSIS — The options for diagnosing infections caused by *M. hominis* and *Ureaplasma* spp are limited due to the shortcomings of both culture and PCR-based techniques. When available, specimens should be sent for both culture and PCR. Given the difficulty in obtaining a diagnosis, patients are often treated empirically. (See 'Treatment' below.)

Culture — Sophisticated methods are required to detect mycoplasmas or ureaplasmas by culture; most hospital microbiology laboratories are not prepared to culture them. Clinical specimens should be inoculated immediately onto specialized broth culture media containing animal serum before they are allowed to dry. Antibiotics, such as penicillin (to which mycoplasmas are not susceptible), are routinely added to this medium to reduce the growth of contaminating organisms.

Media used for culturing these organisms have pH–sensitive dye indicators that help distinguish the urea splitters (ureaplasmas) and ammonia metabolizers (*M. hominis*) that turn media alkaline, from glucose metabolizers (*M. pneumoniae*) that turn media acidic. Organisms should be subcultured onto blood agar plates for definitive identification. On agar, the genital mycoplasmas grow suboptimally under atmospheric conditions and colonies develop best in an atmosphere of 95 percent nitrogen and 5 percent CO_2 [6]. Ureaplasmas form tiny pinpoint colonies and were previously called T (for tiny) strains. *M. hominis* does not produce hemolysis and its colonies look like a "fried egg", having a denser center and paler outer zone. These characteristics can be used to differentiate these mycoplasmas from *M. pneumoniae*, which grows as a spherical "mulberry" colony and does produce beta-hemolysis through elaboration of hydrogen peroxide. Ureaplasmas may grow in one to two days and *M. hominis* may grow in a week. *M. hominis* will escape detection using automated blood culture detection systems, such as BacT/ALERT [60], unless cultures are routinely incubated for three to five days using special media and/or blind subcultures are made from blood cultures [6].

Nucleic acid-based tests (including PCR) — A limited number of small studies have demonstrated that polymerase chain reaction (PCR) is superior to traditional culture methods for detecting *M. hominis* in genital secretions [61,62]. Although emphasis is often placed on the promise of nucleic acid amplification tests, such as real-time PCR-based assays, these are still not available in most hospital diagnostic laboratories and differ in sensitivity and specificity from one laboratory to another [63]. In addition, sensitivity and specificity vary according to the site from which material was obtained.

A DNA chip assay is capable of identifying 13 targeted urinary tract pathogens including *M. hominis* and *U. urealyticum,* with relatively high sensitivity and specificity compared to PCR tests [64]. It is not commercially available at this time.

Nucleic acid-based assays will help in assigning causality when material from sites not ordinarily colonized (eg, joint fluid or tissue, heart valve tissue, cerebrospinal fluid) are tested. However, results of these tests will probably not contribute much clarity when sites that are frequently colonized with multiple organisms are the focus of testing.

IN VITRO SUSCEPTIBILITY — In vitro susceptibility testing has not been standardized for mycoplasmas or ureaplasmas and in vitro susceptibility test results have not been well correlated with clinical outcomes.

Mycoplasma hominis — The following antibiotic susceptibility patterns have been observed for *M. hominis*:

- *M. hominis* is generally susceptible in vitro to tetracyclines (eg, doxycycline) and clindamycin [65-67]. However, one study suggested up to 13 percent resistance on in vitro testing [66].
- Fluoroquinolones, such as ciprofloxacin and moxifloxacin, are usually active in vitro against *M. hominis*, but resistance can be induced in vitro by increasing concentrations of fluoroquinolones [68,69].
- Chloramphenicol minimum inhibitory concentrations are relatively high for *M. hominis* (2 to 25 mcg/ml), indicating that in vivo resistance will be encountered [70].
- *M. hominis* is generally resistant to the macrolides (erythromycin, azithromycin, clarithromycin), aminoglycosides, sulfonamides, and trimethoprim [25,65,70].
- Limited information suggests that *M. hominis* is susceptible in vitro to linezolid and quinupristin-dalfopristin, although to our knowledge no clinical trials have been undertaken using these agents in patients with *M. hominis* infections [71].

The molecular basis for antimicrobial resistance in *M. hominis* strains is not well understood. Some studies in which introduction of resistance occurred via serial in vitro passages have shown that the presence or absence of resistance was related to specific ribosomal mutations [72,73].

Ureaplasma urealyticum — *Ureaplasma* spp are typically susceptible in vitro to the tetracyclines (eg, doxycycline) [65]. They are also susceptible to clarithromycin, azithromycin, moxifloxacin, and ofloxacin. *Ureaplasma* spp have higher minimum inhibitory concentrations for ciprofloxacin and erythromycin than the other agents listed above.

TREATMENT — Patients with disease thought to be caused by a *Mycoplasma* or *Ureaplasma* spp should be treated. In contrast, patients who are found to be colonized with one of these organisms, but who do not have clinical disease, do not require treatment. Given the difficulty in obtaining a diagnosis, patients are often treated empirically. The treatment of choice is based upon the expected in vitro susceptibility pattern of the organism. As mentioned above, most mycoplasmas and ureaplasmas are susceptible in vitro to macrolides, tetracyclines, and fluoroquinolones. An exception is *M. hominis*, which is **not** susceptible to macrolides. (See 'In vitro susceptibility' above.)

Mycoplasma hominis — As mentioned above, *M. hominis*, unlike other mycoplasmas and ureaplasmas, is **not** susceptible to macrolides [65]. Therefore, a tetracycline (eg, doxycycline) is the treatment of choice for infections caused by this organism. Virtually all treatment recommendations in humans are based upon anecdotal observations rather than clinical studies. Few comparative data from prospective treatment trials exist, nor are such data likely to appear since *M. hominis* infections are relatively infrequent and difficult to confirm prior to the institution of empiric therapy.

Adults

Genitourinary tract disease — For adults with genitourinary tract disease caused by *M. hominis*, doxycycline is the drug of choice. For outpatients diagnosed with urethritis, cervicitis, or PID, the United States Centers for Disease Control and Prevention guidelines recommend a regimen that includes doxycycline. Specific treatment recommendations for urethritis, cervicitis, and PID are presented separately. (See "Urethritis in adult men", section on 'Management' and "Pelvic inflammatory disease: Treatment" and "Acute cervicitis", section on 'Recurrent or persistent disease'.)

Nongenitourinary tract disease — Despite rare reports of tetracycline-resistant strains of *M. hominis* [3,74], in adults, we generally use doxycycline (100 mg twice daily) either intravenously or orally. In patients who are unable to take or fail to respond to doxycycline, clindamycin or a fluoroquinolone, such as moxifloxacin, are suitable alternatives [29,69,75].

Some cases of osteomyelitis caused by *M. hominis* have been successfully managed with debridement followed by long courses (six weeks or longer) of therapy with oral doxycycline or clindamycin [33,48]. For *M. hominis* sternal wound infections, resolution may require many months of antibiotic treatment with doxycycline and a fluoroquinolone in addition to debridement and drainage followed by omental or pectoral flap grafting [76]. (See "Postoperative mediastinitis after cardiac surgery".)

The duration of therapy is a matter of clinical judgment. We advise treatment until all clinical signs of infection have resolved.

Neonates — Treatment of *M. hominis* infections in neonates is particularly challenging, since doxycycline and fluoroquinolones are generally avoided due to concerns about toxicities. We favor clindamycin since it has activity in vitro, it has been reported to be successful in the treatment of neonatal infections due to *M. hominis*, and it is not contraindicated in this age group. Chloramphenicol has been reported to be successful in some cases of neonatal *M. hominis* meningitis, but not others [3]. *M. hominis* is relatively resistant to chloramphenicol as discussed above. (See 'Mycoplasma hominis' above.)

Ureaplasma spp — We suggest doxycycline for infections caused by *Ureaplasma* spp in adults [3]. Macrolides (eg, azithromycin) and fluoroquinolones (eg, moxifloxacin) are appropriate alternatives. Clindamycin is not active against ureaplasmas. (See 'Ureaplasma urealyticum' above.)

For neonates with infections caused by *Ureaplasma* spp, erythromycin has been used most commonly [3]. However, we avoid erythromycin in neonates due to an association with pyloric stenosis. We suggest azithromycin or clarithromycin for neonates with disease caused by *Ureaplasma* spp. (See "Infantile hypertrophic pyloric stenosis", section on 'Macrolide antibiotics'.)

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Sexually transmitted infections".)

SUMMARY AND RECOMMENDATIONS

- The term "mycoplasma" is widely used to refer to any organism within the class Mollicutes, which is composed of eight genera. Over 200 named *Mycoplasma* species exist. However, only about six species, five of which inhabit the genitourinary tract, are established or presumed human pathogens; *Mycoplasma pneumoniae* is a respiratory tract pathogen. Mycoplasmas that are thought to cause disease in humans include *M. pneumoniae*, *Mycoplasma hominis*, *Mycoplasma genitalium*, *Mycoplasma fermentans* (incognitus strain), *Ureaplasma urealyticum*, and *Ureaplasma parvum*. (See 'Introduction' above.)

- Mycoplasmas and ureaplasmas are the smallest free-living organisms. Because they lack a cell wall, neither mycoplasmas nor ureaplasmas can be visualized by Gram stain. In order to culture these organisms, specialized media containing animal serum is required. (See 'Microbiology and pathogenesis' above.)
- Although *M. hominis* and, to a lesser extent, *Ureaplasma* have been implicated in a number of conditions related to parturient women and their fetuses and newborns, the precise roles of *Mycoplasma* and *Ureaplasma* spp remain unproven, or even speculative in many diseases for the following reasons:
  - Many healthy asymptomatic adults have genitourinary colonization with *Mycoplasma* and *Ureaplasma* spp.
  - Published studies on the pathogenicity of these organisms commonly have important design limitations.
  - Detection of these organisms is difficult and complex. (See 'Microbiology and pathogenesis' above.)
- Although *Mycoplasma* and *Ureaplasma* spp normally exist in a state of adherence to mucosal epithelial cells of the respiratory or urogenital tracts, they can disseminate to other sites and cause infection when there is a disruption of the mucosa and/or an underlying defect in host defenses, such as in the developing fetus or premature infant. (See 'Microbiology and pathogenesis' above.)
- *M. hominis* has been associated with chorioamnionitis. A possible association with pelvic inflammatory disease (PID) is less well established. Nongenitourinary tract infections that have been reported include upper and lower respiratory infections, central nervous system infections, neonatal bacteremia and meningoencephalitis, and others. (See 'Clinical features and possible disease associations' above.)
- *Ureaplasma* spp have been linked to chorioamnionitis, postpartum and postabortal fever, and pneumonia, bacteremia, and abscesses in neonates. There is controversy about a possible association between *Ureaplasma* spp and bronchopulmonary dysplasia. (See 'Clinical features and possible disease associations' above.)
- The options for diagnosing infections caused by *M. hominis* and *Ureaplasma* spp are limited due to the shortcomings of both culture and polymerase chain reaction (PCR)-based techniques. When available, specimens should be sent for both culture and PCR. Sophisticated methods are required to detect mycoplasmas or ureaplasmas by culture; most hospital microbiology laboratories are not prepared to culture them. PCR-based assays are becoming increasingly available in multiplex kits for the diagnosis of respiratory and genitourinary tract pathogens. They will soon replace culture as the diagnostic test of choice, although they do not allow for antimicrobial sensitivity testing. (See 'Diagnosis' above.)
- In vitro susceptibility testing has not been standardized for mycoplasmas or ureaplasmas and in vitro susceptibility test results have not been well correlated with clinical outcomes. Most mycoplasmas and ureaplasmas are susceptible in vitro to macrolides, tetracyclines, and fluoroquinolones. An exception is *M. hominis*, which is **not** susceptible to macrolides. Azithromycin has the greatest activity against *M. genitalium* compared with other antibiotics. (See 'In vitro susceptibility' above.)
- Patients with disease caused by a *Mycoplasma* or *Ureaplasma* spp should be treated. In contrast, patients who are found to be colonized with one of these organisms, but who do not have clinical disease, do not require treatment. Given the difficulty in obtaining a diagnosis, patients are often treated empirically. (See 'Treatment' above.)
  - For nonpregnant adults with disease caused by *M. hominis*, we recommend doxycycline (**Grade 1C**). (See 'Adults' above.)
  - For infants with disease caused by *M. hominis*, we suggest clindamycin (**Grade 2C**). (See 'Neonates' above.)
  - For nonpregnant adults with disease caused by *Ureaplasma* spp, we suggest doxycycline (**Grade 2C**). (See 'Ureaplasma spp' above.)
  - For neonates with disease caused by *Ureaplasma* spp, we suggest azithromycin or clarithromycin (**Grade 2C**). (See 'Ureaplasma spp' above.)

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