



Medical Diagnostic Laboratories, L.L.C.
2439 Kuser Road
Hamilton, NJ 08690

A MEMBER OF GENESIS BIOTECHNOLOGY GROUP

Presorted
First-Class Mail
U.S. Postage
PAID
Trenton, NJ
Permit 348



► **Research & Development**
Lichen Sclerosis
Continued pg 2



► **Test Announcement**
Tests now available in the clinical laboratory
Full Article pg 3



► **Journal Watch**
Summaries of recent topical publications in the medical literature
Full Article pgs 5

The LaboratorianSM

Vaginitis in Pregnancy

Author: Dr. Scott Gyga, Ph.D.
Femeris Women's Health Research Center

Overview

Vaginitis during pregnancy can present with differences in vaginal discharge and inflammation based on the infection. There are a number of infections that cause vaginitis, which include bacterial vaginosis, aerobic vaginitis, vulvovaginal candidiasis, and sexually transmitted infections such as *Trichomonas vaginalis*, herpes simplex viruses (HSV1 and HSV2), *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. These infections can place pregnant women and their fetuses at varying levels of increased risk for morbidity and mortality. These vaginal and cervical infections can induce inflammation, which can lead to pregnancy complications such as amnionitis, still births, preterm labor and delivery (PLD), premature rupture of membranes (PROM), and endometritis (1).

Bacterial Vaginosis

The vaginal microflora is a dynamic ecosystem normally inhabited by lactobacilli. These bacteria support healthy vaginal conditions by maintaining an acidic environment that is inhospitable to other pathogenic microorganisms. *L. crispatus*, *L. gasseri*, *L. jensenii*, and *L. iners* are considered to be the four major vaginal *Lactobacillus* species (2- 4). Usually, the vaginal flora is dominated by one of these bacteria accompanied by less abundant and less frequently detected minor *Lactobacillus* species (5). *L. iners*, however, is different from other vaginal lactobacilli as it is less prone to hydrogen peroxide production and along with *G. vaginalis*, can be detected in both healthy and disturbed vaginal microflora including BV (2, 6-8). Moreover, *L. iners*' dominance, along with the depletion of other *Lactobacillus* species, indicates that the vaginal microflora may be in a transitional stage between abnormal and normal (4, 9-11). The numerical prevalence of the healthy lactobacilli, *L. crispatus*, *L. gasseri*, and *L. jensenii*, in the vagina prevents its colonization by other pathogens. Many important aspects of women's reproductive health rely on the protective role of these lactobacilli in the vaginal environment.

The most common alteration in vaginal microflora is a condition known as bacterial vaginosis (BV) (7, 12). BV is very common in women of reproductive age and is one of the most common reasons that women seek treatment from health care providers (13). BV is a disorder characterized by an overgrowth of anaerobic bacteria in the vagina leading to a replacement of healthy lactobacilli. Bacterial species including *Gardnerella vaginalis*, *Atopobium vaginae*, *Megasphaera* Type 1 and Type 2, BVAB2, *Bacteroides* species, *Mobiluncus* species, *Mycoplasma* species, and *Ureaplasma urealyticum* are described as indicative diagnostic markers of BV (7, 8, 14). The presence of these microorganisms, along with a depletion of the protective lactobacilli, suggests that vaginal microbial conditions are abnormal. Clinical symptoms of BV include an increase in vaginal pH, vaginal discharge and an unpleasant fishy odor. The particular ways a woman acquires an infection remain unknown. Since microorganisms associated with BV are shown to have their natural habitat in the gastrointestinal tract, BV might be an endogenous infection (6). Nevertheless, the prevalence of BV is higher in sexually active women having sexual contacts with new and/or multiple partners. Decreasing the number of unprotected sexual encounters may reduce the overall incidence rate as well as the rate of re-infection (15).

Women with BV have a three- to four-fold higher risk for acquisition of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* and are also at higher risk for HIV infection (16-17). Women with BV who undergo invasive surgery such as a hysterectomy or abortion suffer from post-operative infections two- to three- times more often than women without BV (18). BV is also associated with pelvic inflammatory disease and endometritis (19-20). Accurate diagnosis and appropriate

treatment of BV is especially critical for pregnant women, as the disease is associated with a five-fold increased risk for late miscarriage and pre-term birth (12, 18). Pregnant women with BV, either with or without symptoms, and a history of PLD, PROM, postpartum endometritis, and choriomnionitis are considered high-risk patients (1). Mixed results have been reported from studies that investigated BV treatment for these high risk patients to reduce the rate of preterm delivery: one demonstrated adverse outcome, two demonstrated no effect, and four demonstrated a benefit (21). A few studies that investigated pregnant patients with BV, and in the later studies, both BV and intermediate abnormal vaginal flora have reported significant reductions in spontaneous preterm births and late-term miscarriage with the use of oral clindamycin before 20 weeks of gestation (21, 22). However, the CDC does not have enough evidence to provide a treatment recommendation for these high-risk patients. The CDC does recommend oral metronidazole or clindamycin treatment for symptomatic pregnant women, which can result in cure rates of approximately 70% (21).

Aerobic Vaginitis

Aerobic vaginitis (AV) is a state of abnormal vaginal flora that is distinct from the more common bacterial vaginosis (BV). AV is caused by a displacement of the healthy vaginal *Lactobacillus* species with aerobic pathogens such as *Escherichia coli*, Group B Streptococcus (GBS), *Staphylococcus aureus*, and *Enterococcus faecalis* that trigger a localized vaginal inflammatory immune response. Clinical signs and symptoms include vaginal inflammation, an itching or burning sensation, dyspareunia, a yellowish discharge, an increase in vaginal pH > 4.5, and inflammation with leukocyte infiltration (23). Severe, persistent or chronic forms of AV can also be referred to as desquamative inflammatory vaginitis (DIV) (24-25).

AV is associated with an increased vaginal pH (> 4.5), a depletion of vaginal healthy Lactobacilli, and an overgrowth of aerobic or facultative anaerobic bacteria, usually the Gram-negative bacilli *E. coli* or Gram-positive cocci GBS, and occasionally *S. aureus*, and *E. faecalis*. The high concentration of these aerobic bacteria and the absence of the healthy vaginal Lactobacilli results in the triggering of the immune system as evidenced by vaginal inflammation, high levels of proinflammatory cytokine production, recruitment of leukocytes, and the generation of toxic leukocytes and parabasal cells. The patient may present with all or some of the signs and symptoms of AV: yellowish discharge, itching or burning sensation, dyspareunia, no fishy odor (negative amine test) associated with BV, inflammation, toxic leukocyte infiltration, the presence of parabasal cells and naked rounded vaginal epithelial cells (23, 26).

In a study of 631 patients receiving routine prenatal care from a vaginitis clinic, 7.9% had moderate to severe AV signs and symptoms and 6% had 'full-blown' BV (23). In a study of 3,000 women, 4.3% were found to have severe AV, also called DIV. Furthermore, 49.5% of the women with DIV were peri- or postmenopausal. A reported hypothesis is that a drop in estrogen may trigger the development of AV in the aforementioned menopausal women, as well as postpartum nursing women (25). In a more recent study of 215 women, 19.1% were found to have 'common vaginitis' caused by BV, vulvovaginal candidiasis (VVC), or trichomoniasis (TV),

WHAT'S INSIDE >>

- P2 Vaginitis In Pregnancy
- P3 Vaginitis In Pregnancy (References)
- P3 New Tests Announcement
- P4 Q&A
- P4 E-Quiz
- P4 Recent Publications
- P5 Journal Watch



► **Research & Development**
Lichen Sclerosis
Continued pg 2

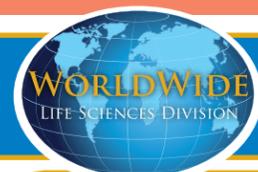


► **Test Announcement**
Tests now available in the clinical laboratory
Full Article pg 3



► **Journal Watch**
Summaries of recent topical publications in the medical literature
Full Article pgs 5

The LaboratorianSM



WORLDWIDE MEDICAL PRODUCTS, INC.

A MEMBER OF GENESIS BIOTECHNOLOGY GROUP



BLOW OUT SALE!!!

(While Supplies Last)

Part No.	Description	Quantity	Price
09049-6	Stretch Gauze Bandage - 4" Roll, N/S	96/case	\$13.95
09075-1	Abdominal Pad - 5 x 9, N/S	576/case	\$37.95

C-FOLD PAPER TOWELS

Part No.	Description	Quantity	Price
11011025	13" x 10"	2400/case	\$39.95



ECO-FRIENDLY

SPECTAINER URINE CONTAINER, TAMPER-EVIDENT - STERILE



Part No.	Description	Quantity	Price
42012656	60 mL	500/case	\$79.95
42012657	90 mL	400/case	\$74.95
42012658	120 mL	300/case	\$59.95

BIOEXCELL® POWDER-FREE LATEX GLOVES



Part No.	Description	Quantity	Price
71011010	Extra-Small	1000/case	\$62.95
71011011	Small	1000/case	\$62.95
71011012	Medium	1000/case	\$62.95
71011013	Large	1000/case	\$62.95
71011014	Extra-Large	1000/case	\$62.95



BIOEXCELL® POWDER-FREE NITRILE GLOVES

Part No.	Description	Quantity	Price
71011000	Extra-Small	1000/case	\$69.95
71011001	Small	1000/case	\$69.95
71011002	Medium	1000/case	\$69.95
71011003	Large	1000/case	\$69.95
71011004	Extra-Large	1000/case	\$69.95

whereas 12.6% were found to have 'inflammatory vaginitis' (IV). Of the IV group, 77.8% were characterized as having DIV (27). In fact, 42.9% of the women with DIV were found to be GBS positive, a 5-fold increase over the healthy patients (17.7% positive) (27). This study was similar to an earlier study that found 43% of DIV patients were GBS positive (24).

Patients with AV present with distinct clinical signs and symptoms of abnormal vaginal flora that can be confused with common vaginitis etiologies such as BV, VVC, and TV. AV is treated with an antibiotic course of therapy characterized by an intrinsic activity against the majority of bacteria of fecal origin, bactericidal, and low effect on healthy vaginal flora, namely Lactobacilli (28). AV treatment is different than the metronidazole (BV, TV) and antifungal (VVC) antimicrobial agents used to treat common vaginitis. In addition to the clinical symptoms of vaginal discharge, dyspareunia, itching and burning sensation, and a strong inflammatory response, AV was shown to have an association with miscarriage and preterm labor and delivery (12, 26, 29). Inflammation derived from the cervical-vaginal environment (vaginitis) and urinary tract infections are known to be associated with triggering labor. Cellular components of GBS such as peptidoglycan and hemolysin and *E. coli* lipopolysaccharide (LPS), known mediators that trigger the inflammatory response, are proposed to be the causative agents that can initiate preterm labor. Additionally, GBS and *E. coli* are also major bacterial species involved in neonatal sepsis (12, 26, 29).

Vulvovaginal Candidiasis

Vulvovaginal Candidiasis (VVC) is a common cause of vaginitis especially in pregnancy. Signs and symptoms associated with VVC include curd-like discharge, pruritus, dysuria, dyspareunia, vaginal soreness, and inflammation of the vulva and vagina. However, these signs and symptoms are not specific for VVC. Although these symptoms can cause patient discomfort and distress, VVC has not been associated with a significant increased risk in pregnancy morbidity. Current recommended treatment for VVC in pregnant women is only topical azole therapies applied for 7 days (21).

Sexually Transmitted Infections

Trichomonas vaginalis

T. vaginalis is a flagellated, anaerobic protozoan and is the most common non-viral sexually transmitted pathogen. An estimated 7% to 13% of pregnant patients are infected (1). Approximately half of female *T. vaginalis* infections are asymptomatic, as are most male infections (30). Symptomatic infections manifest as Trichomoniasis with symptoms of yellow, green or gray discharge which can at times appear frothy, odor, itching, and pain during urination and/or intercourse. Signs of infection include small red ulcerations on the vagina and/or cervix, positive amine (whiff) test and elevated pH. Wet-mount microscopy of a vaginal swab often reveals white blood cells and rapidly motile trichomonads. However, detection of trichomonads by microscopy has a sensitivity of only 60%-75%; whereas, polymerase chain reaction (PCR) can detect *T. vaginalis* with a sensitivity of 85%-100% (31, 32). Trichomoniasis is associated with a number of serious clinical complications, as pregnant women with Trichomoniasis are at increased risk for pre-term labor and delivery of low birth weight neonates (33, 34). In addition, Trichomoniasis is associated with HIV transmission (35, 36). Trichomoniasis is often presented as a mixed infection with BV in approximately 70% of cases (37). Treatment for asymptomatic pregnant patients has not been shown to have a beneficial outcome; in fact, some studies have shown a possible increase in prematurity and low birth weight (21). Symptomatic pregnant patients are treated at the discretion of the physician with a single 2g oral dose of metronidazole, an antibiotic used to treat infections caused by anaerobic bacteria and parasites (21). Sex partners should be treated regardless (21). Although generally effective, up to 2.4% to 9.6% of *T. vaginalis* strains have been reported to be resistant to metronidazole (38-40). If metronidazole treatment fails, the only other approved treatment for Trichomoniasis is the related drug tinidazole, which is currently not recommended for pregnant patients. Increases in metronidazole concentration and duration have been shown to have successful outcomes, but this has not been demonstrated for pregnant patients (41).

Herpes Simplex Virus type 1 and type 2

HSV-1 and HSV-2 are DNA viruses that infect mucosal layers and proximal skin mostly at oral and genital sites, respectively, even though both viruses have the ability to infect both sites. As of late, this association with sites of infection have been blurred since 30% of primary genital tract infection are due to HSV-1 (21). This may be due to changes in sexual practices. Approximately 1 in 5 adults in the United States are infected with HSV and women (22%) are twice as likely to be infected compared to men (11%). For pregnant women, 22% have been shown to be infected at the beginning of their pregnancies, while 2% acquire infection during pregnancy (42, 43). Recurrent infections that typically last 7 to 10 days and are more common and less severe than primary infections, are usually caused by HSV-2. Primary infections during pregnancy can often lead to more severe presentations, such as vulvovaginitis, gingivostomatitis, and even disseminated herpes, the latter causing up to 50% mortality. Primary infections within >36 weeks gestation have a high risk of vertical transmission (30% to 50%), much higher than primary infections that occur <20 weeks (<1%) and active lesions of recurrent infections at the time of delivery (3%). HSV infections in pregnant patients are treated with acyclovir for primary, recurrent, or suppressive therapy (21, 44).

Chlamydia trachomatis and *Neisseria gonorrhoeae*

C. trachomatis and *N. gonorrhoeae* are commonly reported sexually transmitted infections in women, with an estimated 2.86 and 0.8 million new infections annually in the United States, respectively (45). The greatest number of new infections occur in women under 25 years of age with an estimated prevalence of 6.8% for *C. trachomatis* among sexually active women 14-19 years of age. Up to 40% of *C. trachomatis* infections occur as a coinfection with *N. gonorrhoeae*. Although up to 50% to 70% of infections are asymptomatic, in women it can cause cervicitis, urethritis, proctitis, and increased vaginal discharge (21). *N. gonorrhoeae* infections can have mild symptoms mistaken for a bladder or vaginal infection or more pronounced symptoms including a painful or burning sensation when urinating, increased vaginal discharge, and itching or vaginal bleeding between periods. Vaginitis occurs only rarely. Chlamydial and gonorrheal infections in women can lead to serious consequences including pelvic inflammatory disease (PID), tubal factor infertility, ectopic pregnancy, and chronic pelvic pain (21). Annual screening is recommended for all sexually active women under 25 years of age and for women over 25 years of age categorized as high risk using nucleic acid amplification testing (NAAT) such as PCR. All pregnant women should be screened for *C. trachomatis* and *N. gonorrhoeae* during their first prenatal visit. Women under the age of 25 and those at increased risk for chlamydia and gonorrhea, such as women who have a new or more than one sex partner, should be retested during the third trimester to prevent maternal postnatal complications and chlamydial infection in the infant. Women found to have a chlamydial and gonorrhea infection during the first trimester should be retested within approximately 3-6 months, preferably in the third trimester (21). In pregnant women, untreated Chlamydia has been associated with pre-term delivery, as well as ophthalmia neonatorum (conjunctivitis) and pneumonia in the newborn. Although *N. gonorrhoeae* infections are not as common, they can have more severe risks including spontaneous septic abortion, chorioamnionitis, and postpartum infections (44). Pregnant patients with signs and symptoms of PID (pelvic or lower abdominal pain without identifiable causes and at least one of three presentations: cervical motion, uterine, or adnexal tenderness) should be admitted to the hospital for proper treatment (1, 21).

Table 1: Summary of treatment guidelines.

<i>Chlamydia trachomatis</i>	<ul style="list-style-type: none"> • Azithromycin 1 g orally single dose • Amoxicillin 500 mg orally three times a day for 7 days
<i>Neisseria gonorrhoeae</i> ^b	<ul style="list-style-type: none"> • Ceftriaxone 250 mg IM single dose PLUS Azithromycin 1 g orally single dose • For patients that cannot tolerate a cephalosporin: azithromycin 2 g orally single dose • Either azithromycin or amoxicillin is recommended for treatment of presumptive or diagnosed <i>C. trachomatis</i>
<i>Trichomonas vaginalis</i>	<ul style="list-style-type: none"> • For symptomatic patients: metronidazole 2 g single dose • For asymptomatic patients: clinicians should counsel patients regarding the potential risks and benefits of treatment and communicate the options of therapy deferral until after 37 weeks gestation.
Bacterial Vaginosis	<ul style="list-style-type: none"> • Metronidazole 500 mg orally twice a day for 7 days OR • Metronidazole 250 mg orally three times a day for 7 days OR • Clindamycin 300 mg orally twice a day for 7 days
Vulvovaginal Candidiasis	<ul style="list-style-type: none"> • Only topical azole therapies, applied for 7 days
Herpes Simplex Virus 1 & 2	<ul style="list-style-type: none"> • First outbreak of genital herpes: <ul style="list-style-type: none"> – Acyclovir 400 mg orally three times a day for 7-10 days OR – Acyclovir 200 mg orally 5 times daily for 7-10 days • Suppressing therapy for recurrent herpes: <ul style="list-style-type: none"> – Acyclovir 400 mg orally twice a day • Episodic therapy for recurrent herpes: <ul style="list-style-type: none"> – Acyclovir 400 mg orally three times a day for 5 days OR – Acyclovir 800 mg orally twice a day for 5 days OR – Acyclovir 800 mg orally three times a day for 2 days
Aerobic Vaginitis	<p>No established CDC treatment guidelines for Aerobic Vaginitis.</p> <ul style="list-style-type: none"> • Clindamycin 2% topical cream 4-5 g daily for 4-6 weeks^c • Antibiotic therapy with intrinsic activity against the majority of bacteria of fecal origin with low effect on healthy vaginal flora^d

^a Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. MMWR Recomm Rep 2010; 59(RR-12):1-116.

^b Centers for Disease Control and Prevention. Update to CDC's sexually transmitted diseases treatment guidelines, 2010: Oral cephalosporins no longer recommended for treatment of gonococcal infections. MMWR Aug. 2012; 61(31):590-594 (46).

^c Sobel JD, Reichman O, Misra D, Yoo W. 2011. Prognosis and treatment of desquamate inflammatory vaginitis. *Obstet Gynecol* 117:850-855.

^d Tempera G, Furner PM. 2010. Management of Aerobic Vaginitis. *Gynecol Obstet Invest* 70: 244-249.

Straface G, Selmin A, Zanardo V, De Santis M, Ercoli A, Scambia G.

2012. Herpes simplex virus infection in pregnancy. *Infect Dis Obstet Gynecol* 385697:1-6.

Herpes simplex virus (HSV) is one of the most common sexually transmitted diseases, especially in women of reproductive age. In the United States, approximately 22% of pregnant women are infected with HSV-2, and 2% of women acquire it during pregnancy. Symptoms of genital herpes include blistering and ulceration of the external genitalia and cervix, vaginitis, dysuria, and vaginal discharge. Neonatal herpes infections are rare but can be transmitted through contact with genital lesion secretions during delivery. HSV neonatal infections can lead to eye and skin lesions, meningoencephalitis, disseminated infections, fetal malformations, spontaneous abortion, and preterm labor. Neonates are at greatest risk when mothers contract HSV during the third trimester of pregnancy. Antiviral suppressive therapy from 36 weeks gestation or caesarean section are used in pregnant women with genital lesions to prevent exposure of newborns to the virus through vaginal delivery. Since routine maternal screening for HSV is not yet recommended, most mothers of newborns with HSV infections lack clinical presentation of a genital herpes infection. Research for detection of asymptomatic HSV infections should be pursued, as diagnosis of HSV infection based on clinical presentation alone has a sensitivity of 40%, a specificity of 99% and a false positive rate of 20%.

Bean LM, Jackson MR, Dobak WJ, Beiswenger TR, Thorp JA. 2013. Intra-amniotic fluconazole therapy for *Candida albicans* intra-amniotic infection. *Obstet Gynecol* 121(2.2 suppl.1):452-454.

While vaginal colonization with *C. albicans* can be relatively common during pregnancy (20%-25%), ascending intra-amniotic infections are far rarer (0.80%). These rare cases, however, can have dire consequences, including preterm rupture of membranes, preterm labor, and even death of the fetus. Current treatment guidelines for antifungal therapy in pregnancy include topical, systemic, and vaginal antifungal treatment. The authors identified only one previous intrauterine antifungal treatment, which used amphotericin B. The authors describe two case studies in which aggressive antifungal strategies including intra-amniotic fluconazole treatment were used on patients who were at risk for preterm delivery. The therapies used prolonged patient pregnancies for 6 and 8 weeks, and both neonates survived with normal neurological development. Weekly intra-amniotic fluconazole is proposed to provide better control of available drug concentrations and increased concentrations of drug in fetal blood and tissue, enhancing patient outcomes.

Asemota OA, Nyirjesy P, Fox R, Sobel JD. 2011. *Candida glabrata* complicating in vitro pregnancy: successful management of subsequent pregnancy. *J Fertil Steril* 95:803.e1 – 803.e2.

Candida glabrata is the second most common cause of vulvovaginal candidiasis as well as systemic yeast infections typically in immunocompromised hosts. *Candida* infections have also been associated with severe neonatal infections and pregnancy loss in rare cases. In cases of patients receiving *in vitro* fertilization (IVF) embryo transfer, it is presumed that the endometrial cavity can be infected with *C. glabrata* at the same time the embryo is implanted. This report highlights the case of a 30 year old woman with no known health problems that underwent an IVF procedure, resulting in her first pregnancy. She presented 15 weeks later with a dichorionic-diamniotic twin pregnancy and increasing vaginal bleeding over a period of 7 days. Despite indomethacin and broad spectrum antibiotic treatment, she developed preterm premature rupture of membranes and delivered both fetuses at 16 weeks. Autopsy of the fetuses were normal, while examination of the placenta revealed edema with fibrin deposition, severe inflammation and a large amount of *C. glabrata* like fungal organisms. After establishing that *C. glabrata* was the cause of the fetal loss, the patient was treated vaginally with boric acid for three weeks, after which she was culture negative for *C. glabrata*. The patient was also given a 4 week course of nystatin to decrease the chance of recurrence and was once again culture negative at the end of treatment. The patient then repeated the IVF treatment resulting in a second dichorionic-diamniotic twin pregnancy. As a follow-up to the previous *C. glabrata* infection, the patient was monitored with monthly vaginal smears and yeast cultures, which were all negative. The pregnancy was without incident and resulted in the birth of healthy twin boys via cesarean section. Although this is a very rare outcome in the case of IVF embryo transfer with only six known cases, it is important to consider for current pregnancies, as well as for those considering additional embryo transfers when vaginal cultures remain positive for *C. glabrata*. The authors concluded that eradication of vaginal colonization by *C. glabrata* may prevent infection of the next IVF pregnancy. The authors also recommend that due to the growing number of cases of *C. glabrata* chorioamnionitis after IVF, a vaginal culture for yeast should be performed prior to any embryo transfers.

Bodnar L, Krohn M, Simhan H. 2009. Maternal vitamin D deficiency is associated with bacterial vaginosis in the first trimester of pregnancy. *J Nutrition* 139:1157-1161.

Hensel K, Randis T, Gelber S, Ratner A. 2011. Pregnancy-specific association of vitamin D deficiency and bacterial vaginosis. *Am J Obstet Gynecol* 204:e1-e9.

Bacterial vaginosis is a leading cause of vaginitis among women of reproductive age in the United States, affecting approximately 21 million women per year. It is characterized by depletion of the normal lactobacilli flora and the increase of anaerobic bacteria. BV carries several risk factors including an increased risk of acquiring STDs and in pregnant women is associated with endometritis as well as an increased risk of miscarriage and pre-term labor and delivery. A possible link between vitamin D deficiency and BV has been investigated in two studies. The first study concluded that pregnant African-American women diagnosed with BV had a lower vitamin D concentration than women with normal vaginal flora. It also stated that as vitamin D status improved, the prevalence of BV decreased. The second study also found a significant association with vitamin D deficiency and BV among pregnant African-American women. Based on these studies it is concluded that vitamin D deficiency plays a role in BV among pregnant African-American women and should be analyzed during its treatment and prevention during pregnancy.

Coleman JS, Gaydos CA, Witter F. 2013. *Trichomonas vaginalis* vaginitis in obstetrics and gynecology practice: new concepts and controversy. *Obstet Gynecol Surv* 68(1):43-50.

Trichomonas vaginalis is the most common sexually transmitted infection in the United States. *T. vaginalis* infections have been associated with negative pregnancy outcomes, including pre-term delivery, low birth weight, and neonatal conjunctivitis. Symptoms include abdominal pain, vulvovaginal irritation, urethral discharge or dysuria and diagnosis is made by a wet mount or by PCR. Members of the 5-nitroimidazole group of antibiotics, including metronidazole (Flagyl) and tinidazole (Tindamax), are used with a cure rate of 90%-95%. Treatment of infected partners is also recommended to prevent reinfection. Due to the fact that metronidazole crosses the placenta, these medications are prescribed with caution during pregnancy since, although rare, it has been associated with midline facial defects. This article recommends additional screening of *T. vaginalis* during pregnancy, and greater surveillance and testing in clinical practice.

Krivochenitser R, Jones JS, Whalen D, Gardiner C. 2013. Under-recognition of cervical *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections in pregnant patients in the ED. *Am J Emerg Med* 31(4):661-3.

Chlamydia trachomatis (CT) and *Neisseria gonorrhoeae* (GC) are two of the most common bacterial sexually transmitted diseases. The high prevalence of GC or CT infections within the general population has led the United States Preventive Services Task Force, to recommend screening of all sexual active women for GC or CT. Screening is especially important for pregnant women because of the risk of transmission of the infection to the fetus. Other complications associated with GC or CT infections include increased rates of preterm delivery, premature ruptures of membranes, low birth rate and intrauterine growth retardation among others. These risks can be reduced with antibiotic treatment, which is very effective with few and minor complications. In this study, Krivochenitser *et al*, conducted a retrospective cohort study to determine the proportion of pregnant women, testing positive for GC or CT, that were untreated or who were not followed up to provide treatment. The study participants presented to the Emergency Departments (ED) of three academic medical centers in Grand Rapids Michigan. Forty nine percent (49%) of all patients (739) that tested positive for GC or CT were left untreated. There were 179 pregnant patients of the 735 participants and 143 (80%) did not receive treatment in the ED, after a positive GC or CT test. According to the authors, there were no significant variables, such as age or socioeconomic background that differentiated the untreated patients from the treated patients. Follow-up data showed that 114 (80%) of the 143 pregnant patients with an STI were contacted after discharge from the ED by either telephone or email. The authors concluded that in this study, although pregnant patients do receive screening for STIs, most are discharged without treatment. The author suggests one theory for the lack of onsite treatment could be that ED physicians attribute the symptoms presented by these patients to new-onset pregnancy. They further suggested improved point-of contact detections of STIs and revised guidelines to include more liberal policies for treating pregnant patients that are less symptomatic.



Femeris Women's Health Research Center™
Peer-Reviewed Papers:

1. Chadwick SG, Schuyler JA, Vermitsky JP, Adelson ME, Mordechai E, SE. 2013. X-Plate technology: a new method for detecting fluconazole resistance in *Candida* species. *J Med Microbiol* 62(Pt. 5):720-6.
2. Sobel JD, Subramanian C, Foxman B, Fairfax M, Gygax SE. 2013. Mixed vaginitis- more than coinfection and with therapeutic implications. *Curr Infect Dis Rep* 15(2):104-8.
3. Chadwick S, Prasad A, Smith, Mordechai E, Adelson ME, Gygax SE. 2013. The detection of epidemic USA300 community-associated MRSA using single allele-specific PCR targeting a novel polymorphism of *Staphylococcus aureus* pbp3. *J Clin Microbiol* 51(8):2541-50.
4. Ventolini G, Gygax SE, Adelson ME, Cool DR. 2013. Vulvodynia and fungal association: A preliminary report. *Med Hypotheses* 81(2):228-30.

Abstracts:

1. Balashov S. Presentation: xTAG bead sSuspension array for screening *Neisseria gonorrhoeae* antibiotic resistance genetic determinants in noncultured clinical samples. China Luminex xMPA 2013 Meeting, April 12-13, 2013. Shanghai, China.
2. Hilbert DW, Smith WL, Hedges SR, Mordechai E, Adelson ME, Trama JP, Kaunitz AM, Gygax SE. Characterization of cervical and vaginal immune responses in patients with altered vaginal flora. The 40th Annual Meeting of the Infectious Disease Society for Obstetrics and Gynecology (IDSOG), August 8-10, 2013. Santa Ana Pueblo, New Mexico.



Oncoveda Cancer Research Center™
Peer-Reviewed Papers:

1. Pallai R, Bhaskar A, Sodi V, Rice LM. 2012. Ets1 and Elk1 transcription factors regulate cancerous inhibitor of protein phosphatase 2A expression in cervical and endometrial carcinoma cells. *Transcription* 3(6):323-335.



Institute of Metabolic Disorders
Peer-Reviewed Papers:

1. McCourt P, Gallo-Ebert C, Gonghong Y, Jiang Y, Nickels JT Jr. 2013. PP2A (Cdc55) regulates G 1 cyclin stability. *Cell Cycle* 12(8):1201-10.



HUMIGEN, the Institute for Genetic Immunology
Abstracts:

1. Gallagher G. Presentation: Alternative Splicing in the Human IL-23 Receptor. 2nd Novel Immunotherapeutics Summit, January 30-February 1, 2013. San Diego, CA.



Venenum Biodesign
Abstracts:

1. Donigan M, Gallo-Ebert C, Beasley JR. Comparison of the GLP-1 Detection Technologies. Society for Laboratory Automation and Screening (SLAS) 2013 2nd Annual Conference & Exhibition, January 12-16, 2013. Orlando, FL.
2. Stroke IL, Sturzenbecker LJ, Letourneau JL, Quintero JG, Sabalski JE, Marinelli B, Pechik I, Diller D, Paulish-Miller T, Hilbert DW, Gygax SE, Stein P, Webb M. High throughput screening of combinatorial libraries for inhibitors of *Clostridium difficile* toxins. Society for Laboratory Automation and Screening (SLAS) 2013 2nd Annual Conference & Exhibition, January 12-16, 2013. Orlando, FL.

References:

1. Torres M, Moayedi S. 2012. Gynecologic and Other Infections in Pregnancy. *Emerg Med Clin N Am* 30:869-884.
2. Lamont RF, Sobel J D, Akins RA, Hassan SS, Chaiworapongsa T, Kusanovic JP, Romero R. 2011. The vaginal microbiome: new information about genital tract flora using molecular based techniques. *BJOG* 118(5):533-49.
3. Redondo-Lopez V, Cook RL, Sobel JD. 1990. Emerging role of lactobacilli in the control and maintenance of the vaginal bacterial microflora. *Rev Infect Dis* 12:856-872.
4. Tamrakar R, Yamada T, Furuta I, Cho K, Morikawa M, Yamada H, Sakuragi N, Minakami H. 2007. Association between *Lactobacillus* species and bacterial vaginosis-related bacteria, and bacterial vaginosis scores in pregnant Japanese women. *BMC Infect Dis* 7:128.
5. Forsum U, Hallen A, Larsson PG. 2005. Bacterial vaginosis – a laboratory and clinical diagnostics enigma. *APMIS* 113(3):153-61.
6. Forsum U, Holst E, Larsson PG, Vasquez A, Jakobsson T, Mattsby-Baltzer I. 2005. Bacterial vaginosis – a microbiological and immunological enigma. *APMIS* 113(2):81-90.
7. Srinivasan S, Liu C, Mitchell CM, Fiedler TL, Thomas KK, Agnew KJ, Marrazzo JM, Fredricks DN. 2010. Temporal variability of human vaginal bacteria and relationship with bacterial vaginosis. *PLoS One* 15;5(4):e10197.
8. Zozaya-Hinchliffe M, Lillis R, Martin DH, Ferris MJ. 2010. Quantitative PCR assessments of bacterial species in women with and without bacterial vaginosis. *J Clin Microbiol* 48(5):1812-9.
9. Ferris MJ, Norori J, Zozaya-Hinchliffe M, Martin DH. 2007. Cultivation-independent analysis of changes in bacterial vaginosis flora following metronidazole treatment. *J Clin Microbiol* 45(3): 1016-1018.
10. Jakobsson T, Forsum U. 2007. *Lactobacillus iners*: a marker of changes in the vaginal flora? *J Clin Microbiol* 45(9):3145.
11. Verstraelen H, Verhelst R, Claeys G, De Backer E, Temmerman M, Vanechoutte M. 2009. Longitudinal analysis of the vaginal microflora in pregnancy suggests that *L. crispatus* promotes the stability of the normal vaginal microflora and that *L. gasseri* and/or *L. iners* are more conducive to the occurrence of abnormal vaginal microflora. *BMC Microbiol* 9:116.
12. Donati L, Di Vico A, Nucci M, Quaglio L, Spagnuolo T, Labianca A, Bracaglia M, Ianniello F, Caruso A, Paradisi G. 2010. Vaginal microbial flora and outcome of pregnancy. *Arch Gynecol Obstet* 281(4):589-600.
13. Allsworth J, Peipert JF. 2007. Prevalence of bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data. *Obstet Gynecol* 109:114-120.
14. Fredricks DN, Fiedler TL, Thomas KK, Mitchell CM, Marrazzo JM. 2009. Changes in vaginal bacterial concentrations with intravaginal metronidazole therapy for bacterial vaginosis as assessed by quantitative PCR. *J Clin Microbiol* 47:721-726.
15. Fethers KA, Fairley CK, Hocking JS, Gurrin LC, Bradshaw CS. 2008. Sexual risk factors and bacterial vaginosis: a systematic review and meta-analysis. *Clin Infect Dis* 47(11):1426-35.
16. Wiesenfeld HC, Hillier SL, Krohn MA, Landers DV, Sweet RL. 2003. Bacterial vaginosis is a strong predictor of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infection. *Clin Infect Dis* 36:663-668.
17. Atashili J, Poole C, Ndumbe PM, Adimora AA, Smith JS. 2008. Bacterial vaginosis and HIV acquisition: a meta-analysis of published studies. *AIDS* 22:1493-1501.
18. Larsson PG, Bergstrom M, Forsum U, Jacobsson B, Strand A, Wolner-Hanssen P. 2005. Bacterial vaginosis. Transmission, role in genital tract infection and pregnancy outcome: an enigma. *APMIS* 113:233-245.
19. Ness RB, Kip KE, Hillier SL, Soper DE, Stamm CA, Sweet RL, Rice P, Richter HE. 2005. A cluster analysis of bacterial vaginosis-associated microflora and pelvic inflammatory disease. *Am J Epidemiol* 162:585-590.
20. Andrews WW, Hauth JC, Cliver SP, Conner MG, Goldenberg RL, Goepfert AR. 2006. Association of asymptomatic bacterial vaginosis with endometrial microbial colonization and plasma cell endometritis in nonpregnant women. *Am J Obstet Gynecol* 195:1611-1616.
21. Centers for Disease Control and Prevention. 2010. Sexually transmitted diseases treatment guidelines, 2010. *MMWR Recomm Rep* 2010; 59(RR-12):1-116.
22. Brocklehurst P, Gordon A, Heatley E, Milan SJ. 2013. Antibiotics for treating bacterial vaginosis in pregnancy: review. *The Cochrane Collaboration* 1: 1-123.
23. Donders GGG, Vereecken A, Bosmans E, Dekeersmaecker A, Salembier G, Spitz B. 2002. Definition of a type of abnormal vaginal flora that is distinct from bacterial vaginosis: aerobic vaginitis. *Br J Obstet Gynecol* 109: 34-43.
24. Sobel JD. 1994. Desquamative inflammatory vaginitis: a new subgroup of purulent vaginitis responsive to topical 2% clindamycin therapy. *Am J Obstet Gynecol* 171: 1215-1220.
25. Sobel JD, Reichman O, Misra D, Yoo W. 2011. Prognosis and treatment of desquamative inflammatory vaginitis. *Obstet Gynecol* 117(4): 850-855.
26. Donders G, Bellen G, Rezeberga D. 2011. Aerobic vaginitis in pregnancy. *Br J Obstet Gynecol* 118: 1163-1170.
27. Leclair CM, Hart AE, Goetsch MF, Carpentier H, Jensen JT. 2010. Group B Streptococcus: Prevalence in a non-obstetric population. *J Low Genit Tract Dis* 14: 162-166.
28. Tempera G, Furneri PM. 2010. Management of aerobic vaginitis. *Gynecol Obstet Invest* 70: 244-249.
29. Donders G, Van Calsteren K, Bellen G, Reybrouck R, Van den Bosch T, Riphagen I, Van Lierde S. 2009. Predictive value for preterm birth of abnormal vaginal flora, bacterial vaginosis and aerobic vaginitis during the first trimester of pregnancy. *Br J Obstet Gynecol* 116:1315–1324.

30. Fouts AC, Kraus SJ. 1980. *Trichomonas vaginalis*: reevaluation of its clinical presentation and laboratory diagnosis. *J Infect Dis* 141:137-143.
31. Krieger JN, Tam MR, Stevens CE, Nielsen IO, Hale J, Kiviat NB, Holmes KK. 1988. Diagnosis of trichomoniasis. Comparison of conventional wet-mount examination with cytologic studies, cultures, and monoclonal antibody staining of direct specimens. *JAMA* 259:1223-7.
32. Schwebke JR, Burgess D. 2004. Trichomoniasis. *Clin Microbiol Rev* 17:794-803.
33. Cotch MF, Pastorek JG, Nugent RP, Hillier SL, Gibbs RS, Martin DH, Eschenbach DA, Edelman R, Carey JC, Regan JA, Krohn MA, Klebanoff MA, Rao AV, Rhoads GG. 1997. *Trichomonas vaginalis* associated with low birth weight and preterm delivery. The vaginal infections and prematurity study group. *Sex Transm Dis* 24:353-60.
34. Minkoff HA, Grunebaum N, Schwarz RH, Feldman J, Cummings M, Crombleholme W, Clark L, Pringle G, McCormack WM. 1984. Risk factors for prematurity and premature rupture of membranes: a prospective study of the vaginal flora in pregnancy. *Am J Obstet Gynecol* 150:965-72.
35. Laga M, Manoka A, Kivuvu M, Malele B, Tuliza N, Nzila N, Goeman J, Behets F, Batter V, Alary M. 1993. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: results from a cohort study. *AIDS* 7:95-102.
36. Wang CC, McClelland RS, Reilly M, Overbaugh J, Emery SR, Mandalia K, Chohan B, Ndinya-Achola J, Bwayo J, Kreiss JK. 2001. The effect of treatment of vaginal infections on shedding of human immunodeficiency virus type 1. *J Infect Dis* 183:1017-22.
37. Sobel JD, Subramanian C, Foxman B, Fairfax M, Gygax SE. 2013. Mixed vaginitis-more than coinfection and the therapeutic implications. *Curr Infect Dis Rep* 15(2):104-108.
38. Krashin JW, Koumans EH, Bradshaw-Sydnor AC, Braxton JR, Secor WE, Sawyer MK, Markowitz LE. 2010. *Trichomonas vaginalis* prevalence, incidence, risk factors and antibiotic-resistance in an adolescent population. *Sex Transm Dis* 37(7): 440-447.
39. Schwebke JR and Barrientes FJ. 2006. Prevalence of *Trichomonas vaginalis* isolates with resistance to metronidazole and tinidazole. *Antimicrob Agents Chemother* 50(12): 4209-4210.
40. Schmid G, Narcisi E, Mosure D, Secor WE, Higgins J, Moreno H. 2001. Prevalence of metronidazole-resistant *Trichomonas vaginalis* in a gynecology clinic. *J Reprod Med* 46(6): 545-549.
41. Bosserman EA, Helms DJ, Mosure DJ, Secor WE, Workowski KA. 2011. Utility of antimicrobial susceptibility testing in *Trichomonas vaginalis*-infected women with clinical treatment failure. *Sex Trans Dis* 38(10): 983-987.
42. Cusini M and Ghislanzoni M. 2001. The importance of diagnosing genital herpes. *J Antimicrob Chemother* 47(1): 9-16.
43. Anzivino E, Fioriti D, Michitelli M, Bellizzi A, Barucca V, Chiarini F, Pietropaolo V. 2009. Herpes simplex virus infections in pregnancy and in neonate: status of art of epidemiology, diagnosis, therapy and prevention. *Virology* 6:40.
44. Hollier LM, Workowski K. 2008. Treatment of sexually transmitted infections in women. *Infect Dis Clin North Am* 22: 665-691.
45. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Surveillance, 2011. Atlanta, GA: Department of Health and Human Services; December 2012.
46. Centers for Disease Control and Prevention. Update to CDC's sexually transmitted diseases treatment guidelines, 2010: Oral cephalosporins no longer recommended for treatment of gonococcal infections. *MMWR* Aug. 2012; 61(31):590-594.

Quality Assurance Q&A

Question:

We occasionally need to send in a specimen for a patient that is also an employee of our office. Due to the sensitive nature of this type of situation, I do not want those results to be faxed, mailed or made available via LabTest in the same way our regular patient results are released. I need to be sure that their results remain confidential and cannot be viewed by other employees. I only want them to be released verbally to me as the ordering physician or my Practice Manager Jane when we call directly into your Call Center. Is this possible? How would I go about making these types of arrangements? Thanks for your help.

Answer:

In these sensitive situations we understand the need for special handling of your result reports. Please reach out to a member of our Call Center toll free at 877.269.0090 to request accommodations for a “Confidential Release Requests”. We will need the patient's name, date of birth, and the date of service. We can customize your result release options in a number of ways including:

- Fax to an alternate private fax number
- Mail to an alternate address
- Directly contacting you via cell phone or other private line with a verbal result

If the specimen is still in your possession, it is also very important to indicate your need for a “Confidential Release Request” with specific notification instructions directly on the test requisition form that accompanies the specimen to our facility. This will enable our staff to immediately identify the need for special accommodations.

If you have a question you would like addressed in future issues, please email your question(s) to QAQ&A@mdlab.com



1. **True of False.** Primary infections within the first 20 weeks of gestation have the highest risk of vertical transmission (30% to 50%).
2. Women with Bacterial Vaginosis (BV) have higher risk for acquisition of which of the following infections:
 - a. *Chlamydia trachomatis*
 - b. *Neisseria gonorrhoeae*
 - c. HIV
 - d. All of the above
3. Up to ____% of *C. trachomatis* infections occur as a coinfection with *N. gonorrhoeae*.
4. **True of False.** Since the treatment for is basically the same for vaginitis causing conditions such as Bacterial Vaginosis (BV), Vulvovaginal Candidiasis, and *Trichomonas vaginalis* infection it is not important to distinguish them from Aerobic Vaginitis (AV).
5. Trichomoniasis often presents as a mixed infection with _____ in approximately 70% of cases.
 - a. *Chlamydia trachomatis*
 - b. *Neisseria gonorrhoeae*
 - c. HIV
 - d. Bacterial Vaginosis (BV)

For results to the electronic Epidemiology Quiz, please visit www.mdlab.com and click on the e-Quiz link.

Medical Diagnostic Laboratories, L.L.C.

New Tests Announcement



Now Available on the **OneSwab®**

Test Number	Test Name	Validation	Date
372	<i>Entamoeba histolytica</i> by Real-Time PCR	Validated on OneSwab® for intestinal pathogens	8/7/13
709	<i>Staphylococcus epidermidis</i> by Real-Time PCR	Validated on OneSwab® for Skin and Soft Tissue Infections	6/18/13
368	<i>Fusobacterium species</i> by Real-Time PCR	Validated on OneSwab® for Skin and Soft Tissue Infections	6/18/13
371	<i>Cryptosporidium parvum</i> by Real-Time PCR	Validated on OneSwab® for intestinal pathogens	1/28/2013