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Lesson 4 Volume 39

Vaginal Infections of Gynecologic Etiology *

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to identify the etiology, diagnosis and treatment of common vaginal infections of gynecologic etiology, which are often encountered when treating female patients.

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INTRODUCTION

Urologists, as specialists of the genitourinary tract, should be familiar with the diagnosis and treatment of a variety of vaginal infections. Recognizing the differences among common genital infections, including sexually transmitted infections, is critical for proper treatment. The urologist's approach should first include a detailed history to best identify pertinent inciting factors that may place the patient at higher risk for specific vaginal infections, as well as a physical examination. Afterward a differential diagnosis should be established to guide diagnostic testing, followed by treatment with antimicrobials or antivirals if appropriate. In this Update we present the diagnostic and therapeutic approaches to common vaginal infections.

OVERVIEW

Incidence and predisposing factors. Vaginitis is a general term for disorders related to infection, inflammation or changes in the normal vaginal flora. **The vaginal epithelium of premenopausal women is well estrogenized and rich in glycogen. Döderlein lactobacilli, particularly Lactobacillus crispatus, convert glucose into lactic acid to create an acidic vaginal environment (pH 4.0 to 4.5), which maintains normal flora and inhibits growth of pathogenic organisms.** STIs, antibiotics, foreign body (eg retained tampon or condom), irritants and allergens (eg vaginal washes or douches), estrogen level, pregnancy, sexual activity and contraceptive choice are factors that may contribute to the breakdown of the normal vaginal ecosystem, causing increased susceptibility to vaginitis. Risk factors for STIs include a prior or coexisting STI, a new partner, more than 1 partner, concurrent partners or a partner with a STI. Additional risk factors include inconsistent condom use and exchanging sex for money or drugs. In a randomized telephone survey of women in the United States conducted in 1998, 8% of Caucasian women and 18% of African American women reported at least 1 episode of vaginal symptoms of any severity in the previous year.[1] A health care professional was consulted for 55% and 83% of the Caucasian and African American women, respectively, and most women purchased an over-the-counter antifungal preparation to treat the symptoms.

Evaluation. Clinical History: As part of the clinic visit, urologists should first elicit details about symptoms. However, findings from the history may not lead to a definitive diagnosis as there is considerable overlap of symptoms among various types of vaginal infections. Questions should be phrased to characterize vaginal and vulvar symptoms such as discharge, burning, irritation or discomfort, pruritus, vaginal bleeding, pain, dysuria and dyspareunia, as well as timing of symptoms and estrogen status. Information about sexual history should be obtained in a compassionate manner. To maintain effective rapport with patients, it may be helpful to use open-ended questions ("Tell me about any new sexual partners you've had since your last visit."), understandable, non-judgmental language ("Are your sexual partners men, women or both?") and generalized or "normalized" language ("Some of my patients have difficulty using a condom. How is it for you?"). **The Five P's approach to obtain sexual history is recommended for eliciting sensitive information. The 5 P's are 1) Partners (including gender of sexual partners), 2) Practices for sexual intercourse, 3) methods for Prevention of pregnancy or contraception, 4) methods for Protection from STIs and 5) Past history of STIs.** Additional information obtained should include menses, vaginal hygiene practices (eg douching) and medication history (prescriptions and over-the-counter medicine).

A recent federal guideline recommends that providers offer regular screening for several STIs, onsite STI treatment when indicated and risk reduction interventions tailored to the individual.[2] Other prevention methods include pre-exposure vaccination, particularly for human papillomavirus. Counseling patients at history intake may be appropriate and should include discussion of abstinence, reduction in number of sexual partners and/or use of male condoms. Consistent and correct use of latex condoms is known to significantly reduce the risk of HIV,[3] as well as HPV and HPV associated diseases such as genital herpes, hepatitis B, syphilis and chancroid.[4-8] By limiting lower genital tract infections, condoms may also decrease the risk of pelvic inflammatory disease in women.[9]

Physical Examination Findings: All women who are suspected of having vaginitis should undergo a physical examination. A pelvic examination should be performed to assess the degree of vulvovaginal inflammation, characteristics of vaginal discharge and presence of lesions or foreign bodies. The vulva should be examined initially, which can guide further evaluation and diagnostic testing. Normal vulvae are often seen with bacterial vaginosis, while the presence of erythema, edema or fissures may suggest candidiasis or trichomoniasis. Ulcers as seen with STIs can be found in the external or internal genital areas. A speculum examination should also be performed to inspect the vagina, vaginal discharge and cervix. In reproductive age women normal physiological vaginal discharge is characteristically white or transparent, can be thick or thin and is mostly odorless with a volume of 1 to 4 ml per 24 hours. **Various infections have a characteristic vaginal discharge. Trichomoniasis is associated with a greenish-yellow purulent discharge, candidiasis with a thick, white, adherent "cottage cheese-like" discharge and BV with a thin, homogeneous "fish smelling" gray discharge.** Cervical erythema and friability with a mucopurulent discharge in the presence of a normal vagina are suggestive of cervicitis rather than vaginitis. If genital ulcers are visualized, the inguinal lymph nodes should be inspected and palpated. Lastly, bimanual examination should be performed to assess for tenderness and/or abnormal anatomy. Vaginal infections are often classified based on characteristics of vaginal discharge (table 1), and STIs are often described as ulcerative infections (table 2).

In Office Testing: Abnormal vaginal discharge may be assessed by determination of the pH of vaginal secretions, a potassium hydroxide test and microscopic examination of the discharge. An elevated pH (>4.5) is common with BV or trichomoniasis and can be determined by narrow range pH paper. However, due to the poor specificity of pH testing,

ABBREVIATIONS: BV (bacterial vaginosis), HIV (human immunodeficiency virus), HSV (herpes simplex virus), KOH (potassium hydroxide), STI (sexually transmitted infection), VVC (vulvovaginal candidiasis)

Table 1. Common vaginal infections characterized by vaginal discharge

Infection	Etiology	Symptoms	Physical Examination Findings	Diagnosis	Treatment	Follow-up
Bacterial vaginosis	Multimicrobial	Homogeneous thin white discharge that coats vaginal walls, fish smelling vaginal discharge (whiff test)	Clue cells identified on microscopy, elevated vaginal fluid pH (>4.5)	Amsel criteria, Gram stain, Affirm VPIII	500 mg Metronidazole orally twice daily × 7 days, 5 gm metronidazole gel 0.75% intravaginally once daily × 5 days, 5 gm clindamycin cream 2% at bedtime × 7 days	Not necessary
Trichomoniasis	T. vaginalis	Diffuse, malodorous or yellow-green vaginal discharge	Elevated vaginal fluid pH (>4.5)	Nucleic acid amplification test, Affirm VPIII, OSOM Trichomonas Rapid Test	2 gm Metronidazole orally as single dose, 2 gm tinidazole orally as single dose, 500 mg metronidazole orally twice daily × 7 days, treat sexual partners	Retest within 3 mos
Vulvovaginal candidiasis	C. albicans	Thick, white, adherent, "cottage cheese-like" discharge	Normal vaginal pH (<4.5)	Presence of budding yeasts, hyphae or pseudohyphae on wet mount preparation; culture	Over-the-counter or prescription azole regimens (uncomplicated)	Not necessary

vaginal discharge should also be examined microscopically. This can be done by preparing 2 separate samples on slides, diluting 1 sample with 1 to 2 drops 0.9% normal saline solution and adding 10% KOH solution to the other sample. The presence of BV or trichomoniasis immediately elicits an amine odor after KOH is applied. With the addition of a coverslip, the slides can be examined under a microscope at low and high power. **Specifically motile "clue cells" in the normal saline specimen are characteristic of BV, whereas the KOH specimen can be used to identify hyphae or blastospores in candidiasis.** However, the sensitivity of microscopy is approximately 50% compared with nucleic acid amplification tests (trichomoniasis) or culture (yeast).[10] Therefore, the absence of trichomonads in saline or fungal elements in KOH samples does not rule out these infections.

In 25% to 40% of patients with genital symptoms a specific cause will not be identified on initial diagnostic evaluation,[11] with symptoms usually having a non-infectious etiology. In such cases less common causes of vaginitis should be considered and secondary evaluation should be performed based on the dominant symptoms (eg inflammation or irritation, pruritus, pain etc).

Special Populations: All pregnant women and their sexual partners should be asked about STIs because of the severe repercussions these infections can have on the fetus. In addition to serological testing for HIV, syphilis and hepatitis B, the CDC (Centers for Disease Control and Prevention) recommends that all pregnant women younger than 25 years and older women at increased risk for infection be screened for Chlamydia trachomatis and Neisseria gonorrhoeae at the first prenatal visit. There is no evidence to support routine screening for BV or Trichomonas vaginalis, or routine herpes simplex virus type 2 serological screening among asymptomatic pregnant women. Other special populations to consider include postmenopausal women with vaginal atrophy, women taking specific medications such as tamoxifen and women with recurrent symptoms.

BACTERIAL VAGINOSIS

Etiology. BV is a polymicrobial infection that occurs when normal vaginal flora, particularly lactobacillus, are replaced with high concentrations of anaerobic bacteria, Gardnerella vaginalis, ureaplasma and mycoplasma. BV is reported as the most prevalent cause of vaginal discharge or malodor, although most affected women are asymptomatic.[12] BV is associated with having multiple partners or a new sexual partner, douching and lack of condom use. Women who have never been sexually active are rarely affected. Studies show that women with BV are at increased risk for acquiring other sexually transmitted infections, including HIV, N. gonorrhoeae, C. trachomatis and HSV-2. Bacterial vaginosis is also associated with increased complications after gynecologic surgery or pregnancy and increased risk of recurrence.[13-16]

Table 2. Common vaginal infections characterized by genital ulcers

Infection	Etiology	Symptoms	Physical Examination Findings	Diagnosis	Treatment	Follow-up
C. trachomatis	C. trachomatis	Dysuria; urethral pruritis; mucoid, mucopurulent or purulent discharge	Purulent or mucopurulent endocervical exudate visible in endocervical canal	Nucleic acid amplification tests	1 gm Azithromycin orally as single dose, 100 mg doxycycline orally twice daily × 7 days	
N. gonorrhoeae	N. gonorrhoeae	Dysuria; urethral pruritis; mucoid, mucopurulent or purulent discharge	Purulent or mucopurulent endocervical exudate visible in endocervical canal	Nucleic acid amplification tests, gram-neg intracellular diplococci on microscopy	250 mg Ceftriaxone IM as single dose plus 1 gm azithromycin orally as single dose	Retest within 3 mos
HSV	HSV-2, HSV-1	Painful, unilat adenopathy	Multiple, small, round ulcers in clusters with associated erythematous base	Polymerase chain reaction, viral culture	400 mg Acyclovir orally 3 times daily × 7-10 days, 1 gm valacyclovir orally twice daily × 7-10 days, 250 mg famciclovir orally 3 times daily × 7-10 days	Can use episodic or recurrent antiviral therapy for recurrent infections
Chancroid	H. ducreyi	Unilat suppurative adenopathy	Multiple, deep, indurated ulcers with associated yellow-gray purulent base	Special culture media	1 gm Azithromycin orally as single dose, 250 mg ceftriaxone IM as single dose, 500 mg ciprofloxacin orally twice daily × 3 days, 500 mg erythromycin base orally 3 times daily × 7 days	Test for HIV and syphilis coinfection
Genital warts (condyloma acuminatum)	HPV	Occasionally pruritic	Cauliflower-shaped verrucae, single or clusters, 1-5 mm in diameter but can spread into large masses	Physical examination (±3%–5% acetic acid), biopsy	Observation, excision	Pap smears per CDC guidelines

Clinical presentation and diagnosis. BV can be diagnosed clinically using Amsel diagnostic criteria or by Gram stain, which is considered the gold standard laboratory evaluation. A Gram stain deciphers the concentration of lactobacilli, which are identified as long gram-positive rods, compared to gram-negative rods and cocci (G. vaginalis, Prevotella etc) which are characteristic of BV. **Clinical diagnosis of BV requires 3 of 4 symptoms or signs, including 1) homogeneous, thin, white discharge that coats the vaginal walls; 2) clue cells identified on microscopy (eg vaginal epithelial cells studded with adherent coccobacilli, fig. 1); 3) vaginal fluid pH >4.5; and 4) fish smelling vaginal discharge, which can be amplified by the addition of 10% KOH (known as the whiff test).** Other tests include but are not limited to Affirm™ VPIII (Becton Dickinson, Sparks, Maryland), a DNA hybridization probe for high concentrations of G. vaginalis, and OSOM® BVBlue® (Sekisui Diagnostics, Burlington, Massachusetts), which detects vaginal fluid sialidase activity.[17, 18] Culture of G. vaginalis is not recommended as a diagnostic tool because it is not

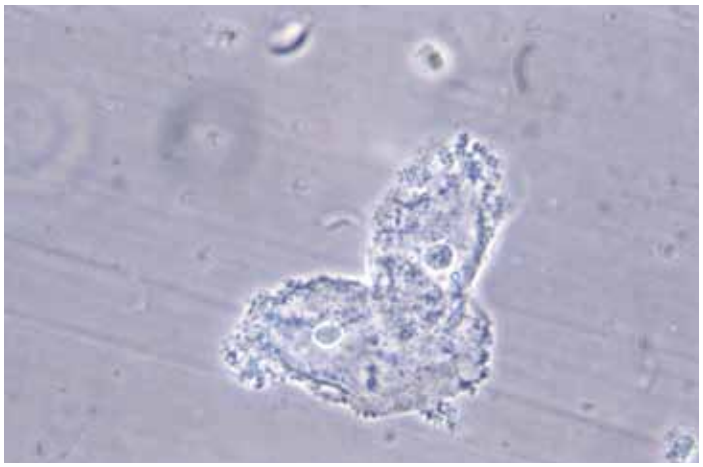

Figure 1. Bacteria that adhere to vaginal epithelial cells, known as clue cells, are indicative of bacterial vaginosis. Reprinted from Centers for Disease Control and Prevention's Public Health Image Library (image No. 3720).

specific.

Treatment. All non-pregnant women who are symptomatic and all pregnant women (asymptomatic and symptomatic) should be treated, with the goal of achieving relief of vaginal symptoms and signs of infection, and reducing the risk of acquiring other STIs. **Recommended regimens for treatment of BV are 500 mg metronidazole orally twice daily for 7 days or 5 gm 0.75% metronidazole gel intravaginally once daily for 5 days or 5 gm 2% clindamycin cream at bedtime for 7 days. Alcohol should be avoided while taking metronidazole, and topical clindamycin may weaken latex condoms for up to 5 days after use.** Treatment of male sexual partners has not been shown to be beneficial for prevention of BV recurrence.[19]

VULVOVAGINAL CANDIDIASIS

Etiology. VVC, which is primarily caused by Candida albicans and infrequently by other Candida species or yeasts, is among the most common vaginal infections. Approximately 75% of all women will have at least 1 episode of VVC in their lifetime, of whom two-thirds will have 2 or more episodes.[2] Classification of VVC as either uncomplicated or complicated to help guide treatment is based on clinical presentation, microbiology, host factors and response to therapy. Complicated VVC occurs in 10% to 20% of women, and special diagnostic and therapeutic aspects should be considered.

Clinical presentation and diagnosis. Patients with VVC frequently present with non-specific bothersome symptoms, often with a combination of vulvar pruritus, pain, swelling and redness. Physical examination findings include vulvar edema, fissures, excoriations and thick curdy vaginal discharge (fig. 2). **Candidal vaginitis is associated with a normal vaginal pH (<4.5). VVC is diagnosed in symptomatic women 1) when budding yeasts, hyphae or pseudohyphae are seen in wet mount preparation (using saline, 10% KOH) or Gram stain of vaginal discharge, or 2) by culture. Wet mount preparation is considered first line diagnostic testing, although vaginal cultures should be obtained if a woman exhibits signs or symptoms in the presence of a negative wet mount. However, a positive Candida culture in a woman without symptoms or signs should not be treated, given that Candida species and other yeasts are part of the normal vaginal flora.**

Uncomplicated VVC occurs as infrequent, mild-to-moderate infections, with C. albicans as the likely culprit. Complicated VVC is defined as recurrent or severe infections or non-C. albicans candidiasis, or that which occurs in women with diabetes mellitus, debilitation or immunocompromised conditions (eg HIV infection or corticosteroid use).

Treatment. Uncomplicated VVC can be effectively treated with a short course of topical antifungals (1 to 3-day regimens). The topically applied "azole" drugs are more effective than nystatin and result in relief of symptoms and negative cultures in up to 90% of patients who complete therapy.[2] Several over-the-counter intravaginal regimens exist (5 gm clotrimazole 2% cream intravaginally daily for 3 days or 5 gm miconazole 4% cream intravaginally for 3 days or 200 mg miconazole vaginal suppository for 3 days etc). Examples of prescription options include intravaginal agents (terconazole cream or suppository) and oral agents (150 mg fluconazole orally as a single dose). Uncomplicated VVC is not usually acquired through sexual intercourse and, therefore, treatment of sexual partners is not necessary. Follow-up typically is not required unless symptoms persist or recur. VVC develops in some women after treatment with antibiotics for a urinary tract infection, and may require treatment by the urologist or primary care provider.

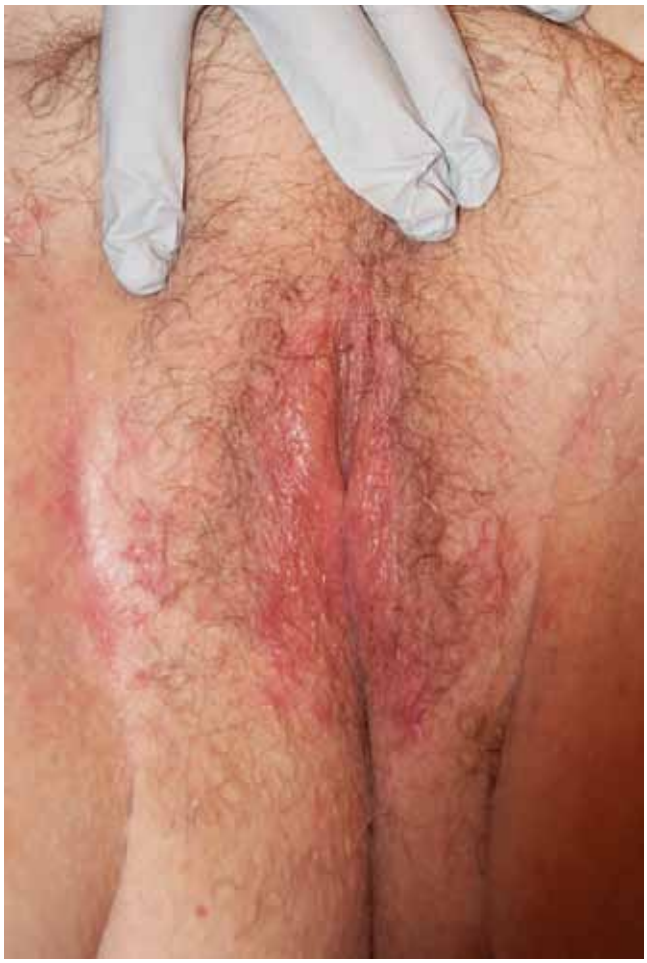

Figure 2. Candidiasis of female external genitalia.

Recurrent vulvovaginitis, defined as 4 or more episodes of symptomatic infections within 1 year, affects <5% of women and may require a longer duration of treatment. First line recommendation for a maintenance regimen is oral fluconazole weekly for 6 months. Culture proven non-C. albicans candidiasis can occur but there is a lack of data proven treatment options. Most often patients are treated with a non-fluconazole azole regimen (topical or oral) for a longer duration (7 to 14 days). If recurrence develops 600 mg boric acid in a gelatin capsule vaginally daily for 2 weeks has clinical and mycological eradication rates of approximately 70%.[20]

TRICHOMONAS VAGINITIS

Etiology. Trichomoniasis, the most common non-viral STI in the United States, affected an estimated 3.7 million people in 2008.[21] Disparities exist among those affected, with a prevalence of 13% in African American women vs 1.8% in Caucasian women.[22] T. vaginalis infection is associated with up to a threefold increased risk of HIV infection,[23,24] as well as preterm birth and other adverse pregnancy outcomes. T. vaginalis is a flagellated protozoan that principally infects the squamous epithelium in the urogenital tract (vagina, urethra and paraure-

thral glands). Coexistence of T. vaginalis and BV pathogens is common, with reported coinfection rates of greater than 80%.

Clinical presentation and diagnosis. Infected women may have diffuse, malodorous or yellow-green vaginal discharge with or without vulvar irritation. However, up to 85% of those infected have minimal or no symptoms, and untreated infections may last for months or years.[25, 26] Historically a Giemsa stained specimen from a laboratory culture may reveal ultrastructural details, such as flagella, that are exhibited by the protozoan organism T. vaginalis (fig. 3). **However, the nucleic acid amplification test is highly sensitive compared to wet mount microscopy and is reported to detect 3 to 5 times more infections.[27] Additionally the Aptima® CV/TV assay (Hologic® Gen-Probe, San Diego, California) detects RNA via transcription mediated amplification with a clinical sensitivity of 95% to 100% and specificity of 95% to 100%.[28, 29] This assay is FDA (U.S. Food and Drug Administration) cleared for detection of T. vaginalis from vaginal, endocervical and urine specimens.** Other FDA approved point of care tests using vaginal or endocervical swab collections to detect T. vaginalis include

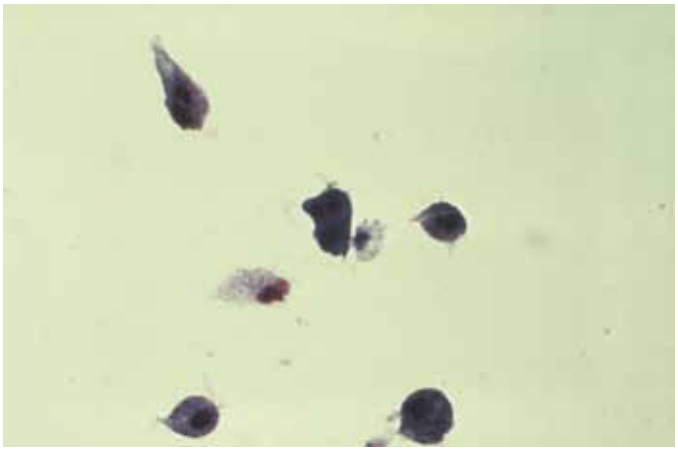

Figure 3. Giemsa stained specimen from laboratory culture demonstrates flagellated protozoa pathognomonic of T. vaginalis. Reprinted from Centers for Disease Control and Prevention's Public Health Image Library (image No. 5237).

OSOM Trichomonas Rapid Test and Affirm VPIII.

Treatment. The best method for prevention of trichomoniasis is consistent and correct use of condoms during all penile-vaginal sexual encounters.[30] Studies have shown that partners of men who have been circumcised may have a reduced risk of T. vaginalis infection.[31, 32]

Recommended treatment regimens for trichomoniasis are 2 gm metronidazole orally as a single dose, 2 gm tinidazole orally as a single dose or 500 mg metronidazole orally twice a day for 7 days. Patients should be advised to abstain from sex until they and their partners are treated (ie when therapy has been completed and any symptoms have resolved), and patients infected with T. vaginalis should also be tested for other sexually transmitted diseases including HIV. It is noteworthy that women can be treated with 2 gm metronidazole in a single dose at any stage of pregnancy. Concurrent treatment of all sexual partners is critical, and partners should be referred for therapy or offered testing.

Retesting for trichomoniasis is recommended within 3 months following initial therapy, regardless of whether sexual partners were treated, due to the high rate of reinfection among treated women (17% within 3 months).[33] Most recurrent infections are thought to be caused by antimicrobial resistance. Metronidazole resistance has been documented in 4% to 10% of cases,[34] and tinidazole resistance in 1%.[35] **If symptoms are suspicious for recurrent trichomoniasis, single dose treatment should be avoided and the patient and partner(s) should be treated with 500 mg metronidazole orally twice daily for 7 days. If this regimen fails, 2 mg metronidazole or tinidazole orally for 7 days should be prescribed.**

SEXUALLY TRANSMITTED INFECTIONS

Etiology. C. trachomatis: Chlamydia is the most frequently reported infectious disease in the United States, often affecting men and women younger than 25 years.[36] Most affected women are asymptomatic and, therefore, serve as an ongoing reservoir for infection of their partners. **In women C. trachomatis infection can result in scarring of the fallopian tubes, ovaries and endometrial lining, which increases the risk of future ectopic pregnancy and tubal infertility. C. trachomatis is a small obligate intracellular gram-negative bacterium with a distinct life cycle consisting of phase 1 when the small elementary bodies attach and penetrate into cells, followed by phase 2 when the cells are transformed into the metabolically active form known as the reticulate body.** In high risk populations reported rates of coinfection with C. trachomatis and N. gonorrhoeae have been as high as 50%, although rates are much lower in the general population.

N. gonorrhoeae: **In the United States N. gonorrhoeae is the second most prevalent STI. Symptomatic gonorrhea results in cervicitis and pelvic inflammatory disease, which can lead to serious sequelae in females, such as infertility, ectopic pregnancy and chronic pelvic pain. N. gonorrhoeae is a gram-negative diplococci bacteria that possesses a high number of virulence factors including outer membrane adhesins used for attachment, local invasion, dissemination and adaptation to evade host defense mechanisms.**

Chancroid: Chancroid accounts for 20% to 60% of infections in parts of Africa, Asia and Latin America.[37] Similar to genital herpes and syphilis, chancroid is a risk factor in the transmission of HIV infection in these regions and the United States.[36, 38] **Haemophilus ducreyi is a fastidious gram-negative coccobacillus that cannot survive for long outside the human host, hindering diagnostic culture methods.**

Genital Herpes: The 2 types of herpes simplex virus that can cause genital herpes are HSV-1 and HSV-2. Most cases of recurrent genital herpes are caused by HSV-2, which has been reported to affect up to 50 million people in the United States,[39] although there has been a recent increase in HSV-1 infections.[40-42]

Human Papillomavirus: More than 100 types of infectious HPV have been identified, with at least 40 known to infect the genital area.[43] Most sexually active persons become infected with HPV at least once in their lifetime,[21, 44] yet most HPV infections are self-limited and asymptomatic or unrecognized. Oncogenic, high risk HPV infection (eg types 16 and 18) causes most cervical, vulvar, vaginal, anal and oropharyngeal cancers in females,[45] whereas non-oncogenic, low risk HPV infection (eg types 6 and 11) causes genital warts. **HPV types 16 and 18 account for 66% of all cervical cancers, and types 6 and 11 cause approximately 90% of genital warts.** In 2009 an estimated

34,788 new cancers and approximately 355,000 new cases of anogenital warts were associated with HPV infection.[46-48]

Clinical presentation and diagnosis. C. trachomatis and N. gonorrhoeae: Symptomatic women with C. trachomatis often present with dysuria, urethral pruritis and mucoid, mucopurulent or purulent discharge. **Annual screening is recommended for sexually active women younger than 25 years and older women with increased risk factors (eg new sexual partner, more than 1 partner, a partner with concurrent partners and a partner with a STI).[49]** Screening for Chlamydia in women has been shown to reduce rates of pelvic inflammatory disease.[50,51] However, data do not support routinely screening sexually active men.[52, 53]

Nucleic acid amplification tests are preferred for detection of C. trachomatis and N. gonorrhoeae, and allow for a wide range of specimen types, including endocervical swabs, vaginal swabs and urinalysis in women.[54] Women with N. gonorrhoeae also present with urethritis symptoms similar to those seen with C. trachomatis.[55] **A urethral smear showing gram-negative intracellular diplococci is indicative of gonorrheal infection, which is often accompanied by chlamydial infection. Women found to have gonococcal infection should be treated immediately and retested within 3 months. Pregnant women who remain at high risk for gonococcal infection should also be retested during the third trimester to prevent postpartum complications in the mother and gonococcal infection in the neonate.**

A more severe vaginal infection often caused by C. trachomatis or N. gonorrhoeae is cervicitis, which is characterized by purulent or mucopurulent endocervical exudate visible in the endocervical canal or on a swab specimen. C. trachomatis is the most common cause of non-gonococcal urethritis, although Mycoplasma genitalium accounts for 15% to 25% of non-gonococcal urethritis cases in the United States.[56-59] There are currently no FDA cleared diagnostic tests for M. genitalium.

Chancroid: Women with chancroid infections often present with a combination of painful genital ulcers and unilateral tender suppurative inguinal adenopathy. It is crucial to rule out syphilis and HSV to make a diagnosis of chancroid. Identification of H. ducreyi on special culture media using 1) vancomycin supplemented with 2% bovine hemoglobin and 5% fetal calf serum or 2) Müller-Hinton agar supplemented with 5% chocolatized horse blood is deemed the gold standard for a definitive diagnosis of chancroid. However, these culture media are not widely available from commercial sources, and even when these media are used, sensitivity is <80%.[60]

Genital Herpes: Although most individuals affected by genital herpes have mild or unrecognized symptoms, the virus can still be shed intermittently from anogenital areas.[61, 62] Clinical diagnosis of genital herpes can be difficult to make because the painful multiple vesicular or ulcerative lesions with an erythematous base typically associated with HSV are absent in many infected persons. Some patients may have painful unilateral inguinal adenopathy. Prognosis and type of counseling differ for the 2 types of genital herpes (HSV-1 and HSV-2) causing the infection and, therefore, type specific laboratory testing should be performed.[42, 63] **Cell culture and polymerase chain reaction are the preferred methods for diagnosing HSV.** However, sensitivity of viral culture is low, especially for recurrent lesions and lesions that are beginning to heal. Nucleic acid amplification tests, including polymerase chain reaction assays for HSV DNA, are more sensitive and readily available.[64-66] Type specific serological testing based on assays of glycoproteins G1 (HSV-1) and G2 (HSV-2) and detection of specific antibodies[67-69] can be performed using the HerpeSelect® 2 ELISA (Focus Diagnostics, Cypress, California).[70] Nearly all HSV-2 infections are sexually acquired, while HSV-1 may be found in oral, cutaneous or anogenital lesions. Therefore, the presence of HSV-1 antibody may be a remnant of a past oral HSV infection from childhood. Those diagnosed with HSV infection should be tested for HIV.

Human Papillomavirus: HPV types that affect the anogenital epithelium and mucous membranes typically have a predilection for women; occur in the perineum, perianal region, vaginal introitus, vulva and cervix; and invade the basal layer of the epidermis through microabrasions. Genital warts, or condyloma acuminatum, are benign anogenital cauliflower-shaped verrucae 1 to 5 mm in diameter that can be single or found in clusters, although they can also grow or spread into large masses in the genital or anal area. The growths are usually asymptomatic but may be pruritic. Warts are not required for transmission but are highly infectious due to the high viral load.

In most cases HPV is diagnosed by characteristic findings on physical examination but if there is uncertainty, a biopsy can be performed to confirm the diagnosis. Applying 3% to 5% acetic acid may cause a white color transformation in the area infected with HPV. Tests are available to detect oncogenic types of HPV infection and are used in the context of cervical cancer screening and management or follow-up of abnormal cervical cytology or histology. These tests should not be used for male partners of women with HPV or in women younger than age 25 years, for diagnosis of genital warts or as a general test for sexually transmitted disease.

Treatment. C. trachomatis and N. gonorrhoeae: **For non-gonococcal cases 1 gm azithromycin orally in a single dose or 100 mg doxycycline orally twice daily for 7 days is highly effective for chlamydial urethritis.** A meta-analysis of 12 randomized clinical trials of azithromycin vs doxycycline for the treatment of urogenital chlamydial infection revealed equivocal efficacy.[71] Treatment of gonorrhea is sometimes challenging due to the ability of N. gonorrhoeae to develop resistance to antimicrobials.[72] **The increased burden of fluoroquinolone resistant N. gonorrhoeae in the United States prompted the CDC in 2007 to discontinue fluoroquinolones for gonorrhea, leaving cephalosporins as the only remaining class of antimicrobials available for its treatment.[73, 74]** Due to the growing concern of antimicrobial resistance, a combination of 2 antimicrobials with different mechanisms of action is administered in an effort to slow down the spread of resistance to cephalosporins. **The recommended regimen for uncomplicated gonococcal infections should include 250 mg ceftriaxone IM in a single dose plus 1 gm azithromycin orally in a single dose, which should be administered on the same day and preferably simultaneously under direct supervision.** Chlamydia and gonorrhea are reportable to health departments. Patient delivered partner therapy, which involves treating the sexual partners of a person who receives a diagnosis of chlamydia or gonorrhea, is associated with a decline in the reinfection rate.[75-77]

Chancroid: **Recommended treatment regimens for chancroid typically include 1 gm azithromycin orally in a single dose or 250 mg ceftriaxone IM in a single dose.** Furthermore, patients should be tested for HIV infection and syphilis when chancroid is diagnosed, with repeat testing at 3 months after

diagnosis if initial tests are negative. **All sexual partners of those infected with H. ducreyi should be treated.**

Genital Herpes: Genital herpes is a chronic, lifelong viral infection that should be addressed at diagnosis along with treatment of acute episodes of genital lesions. Newly acquired genital herpes can result in prolonged genital ulcerations and neurological involvement, making antiviral therapy crucial as first line management. **Recommended regimens for treatment of genital herpes are 400 mg acyclovir orally 3 times daily for 7 to 10 days, 1 mg valacyclovir orally twice daily for 7 to 10 days or 250 mg famciclovir orally 3 times daily for 7 to 10 days. Antivirals for recurrent genital herpes can be used as suppressive therapy to reduce the frequency or episodically to ameliorate or shorten the duration of lesions.[78, 79]**

Quality of life is improved in many patients with frequent recurrences who receive suppressive rather than episodic therapy.[80] Options for suppressive therapy are 400 mg acyclovir orally twice a day or 250 mg famciclovir orally twice a day. For individuals with frequent recurrences (≥10 episodes a year) 500 mg rather than 1 gm valacyclovir orally once a day may be less effective. Episodic therapy for recurrent genital herpes should be initiated within 1 day of onset of herpetic lesions or during the prodrome phase that precedes some outbreaks and continued for 3 to 5 days. Patient counseling is critical in the management of genital herpes, with discussions including effectiveness of suppressive vs episodic therapy, importance of informing sexual partners of infection, potential of transmission during asymptomatic periods, risk of neonatal HSV infection etc. Symptomatic sexual partners should be treated, and asymptomatic sexual partners should be counseled on the signs and symptoms of genital herpes infection.

Human Papillomavirus: **Most HPV genital warts resolve spontaneously, and antiviral therapy is not endorsed to treat HPV infections. However, if lesions are painful or recurrent, treatment is directed toward macroscopic excision or removal of the lesions. Administration of vaccines to protect against cancers caused by HPV is recommended routinely for boys and girls at age 11 or 12 years and can be administered beginning at age 9 years.[81]** Preexposure vaccination is recommended through age 26 years for all females and through age 21 years for all males who have not received any or all of the vaccine doses. The CDC now recommends that 11 to 12-year-old children receive 2 doses of HPV vaccine 6 to 12 months apart instead of the previously recommended 3-dose regimen.[82]

SUMMARY

Urologists should possess a solid understanding of the differential diagnosis and treatment of gynecologic infections, which are common and may present in urological clinical scenarios where a broad differential diagnosis is needed. Many infections are sexually transmitted, and it is imperative to obtain a thorough history of sexual practices, supplemented by a discussion of methods of risk reduction. Other common infections are attributable to an overgrowth of the normally present bacteria or yeast in the vagina. Presenting symptoms and signs are helpful in determining the source of infection, although the appropriate diagnostic tools are crucial to make a definitive diagnosis. If in office diagnostic tests are unavailable, clinical suspicion and judgment may warrant empiric treatment for common uncomplicated vaginal infections. Multiple regimens are available to treat vaginal infections, and up-to-date knowledge is crucial.

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Study Questions Volume 39 Lesson 4

1. The characteristic finding(s) of bacterial vaginosis are
   a. thick, white, adherent, "cottage cheese-like" discharge, hyphae or blastospores on microscopy, normal vaginal pH (<4.5)
   b. greenish-yellow purulent discharge, elevated vaginal pH (>4.5), amine odor on KOH prep
   c. thick, white, adherent, "cottage cheese-like" discharge, motile trichomonads or "clue cells" on microscopy, elevated vaginal pH (>4.5)
   d. thin, homogeneous, "fish smelling" gray discharge, motile trichomonads or "clue cells" on microscopy, elevated vaginal pH (>4.5), amine odor on KOH prep

2. Retesting within 3 months is indicated following initial treatment of
   a. Candida albicans
   b. bacterial vaginosis
   c. Haemophilus ducreyi and genital herpes
   d. Neisseria gonorrhoeae and Trichomonas vaginalis

3. The recommended treatment for non-penicillin allergic patients infected with N. gonorrhoeae is
   a. single doses of 250 mg ceftriaxone IM and 1 gm azithromycin orally
   b. single dose 400 mg cefixime orally
   c. 500 mg ciprofloxacin orally once daily for 5 days
   d. 100 mg doxycycline orally twice daily for 7 days

4. A 33-year-old woman complains of vaginal itching, and a 4 mm wart is seen on examination of the vulva. There is no associated inflammation and vaginal mucus is normal in appearance. She reports multiple male sexual partners in the last month. The next step is
   a. observation
   b. 400 mg acyclovir orally 3 times a day for 7 to 10 days
   c. laser fulguration of the wart
   d. excision of the wart

5. A 28-year-old woman has had 5 episodes of symptomatic vulvovaginal candidiasis in the last year. The next step is
   a. 5 gm clotrimazole 2% cream intravaginally daily for 3 days
   b. 600 mg boric acid in a gelatin capsule vaginally daily for 2 weeks
   c. 150 mg fluconazole orally twice daily for 7 days
   d. 150 mg fluconazole orally weekly for 6 months

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