Vulvovaginitis and Cervicitis

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Vulvovaginitis and cervicitis refer to inflammatory and/or infectious disease processes of the female genital tract: vulva, vagina, and cervix. Symptoms can include genital itching, pain or discomfort, edema, dysuria, vaginal discharge, odor, and in more severe cases pelvic pain. Female genital complaints are quite common in a family medicine practice so familiarity with the workup and treatment is important. The symptoms can be nonspecific, and there is considerable overlap of presenting features regardless of the etiology of the process. In many cases the patients have already attempted self-diagnosis and even treatment with home remedies or over-the-counter products and medications. Given the nonspecific nature of the symptoms, those self-diagnoses can often times be incorrect, and the products or measures the patient has employed in their attempt to treat those symptoms can lead to more inflammation and exacerbate the condition. It is imperative, therefore, to take a detailed history, perform a focused but complete physical exam, and utilize laboratory measures, including microscopy, in order to arrive at the correct diagnosis.

The most common etiologies for vulvovaginitis and cervicitis include both sexually and nonsexually transmitted diseases, and coinfections are not uncommon. Depending on the disease process involved, the symptoms may be restricted to just one of the areas of the genitals (e.g., the vulva) but often can include more than one or all and be difficult for the patient to determine exactly. The most common causes of vaginal

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complaints, particularly in reproductive aged women, include bacterial vaginosis, candidal vaginitis, and trichomoniasis. Cervicitis is often one of the sexually transmitted diseases (STDs), such as gonorrhea or chlamydia. The keratinized epithelium of the vulva can be affected by other generalized skin disorders (such as atopic dermatitis or psoriasis) and mycotic infection as well as masses. However, there is considerable overlap and any one of these processes can causes symptoms in any or all of the particular areas of the female genitals. In general, testing for STDs (in particular gonorrhea and chlamydia) should be obtained during the evaluation given considerable overlap in the clinical presentations and the prevalence of coinfections.

The vulva is composed of keratinized stratified squamous epithelium, whereas the vaginal and the ectocervix mucous membrane is nonkeratinized squamous epithelium. There is a transition in the epithelium from the labia to the vestibule. The normal vaginal environment contains lactobacilli that convert the glycogen from these cells into lactic acid and hydrogen peroxide, maintaining the acidic pH (around 4.0) characteristic of the healthy premenopausal woman's vagina. This acidic environment helps to prevent the overgrowth or invasion of pathogenic organisms. Disruption of this normal balance of chemical and biological elements can then lead to infection or inflammation causing vulvovaginitis or cervicitis.

Office Evaluation

Obtaining a good history can be complicated by some patient's reluctance to discuss these issues; often the patients are embarrassed or simply uncomfortable discussing symptoms in the genital area and may not know how to describe their symptoms well. In addition to the usual characteristics of the complaint (their best description of symptoms and their and duration), exacerbating and alleviating factors and any associated symptoms (dysuria, dyspareunia, pelvic pain, fever), it is important to inquire about any previous episodes (and treatments), involvement of any other areas of the body, treatments attempted at home (their success or lack thereof), sexual behaviors (number and gender of partners, as well as if anal, oral, or vaginal penetration is involved), and partner symptoms. Comorbidities can be a complicating factor, as well (diabetes mellitus (DM), human immunodeficiency virus (HIV)).

A complete physical exam should be performed, including a thorough pelvic exam, abdominal or costovertebral tenderness on palpation; close inspection of the skin of the entire area including separation of the labia, noting any atypical findings of the skin or genitals or surrounding structures; and a vaginal speculum examination, noting the presence of any odor, lesions, discharge, or other findings of the vagina and cervix. Document the presence or absence of any discharge and its characteristics, such as color, consistency (thin, thick, frothy, clumpy), origin (if from the cervical os, adherent to the vaginal walls, etc.), or odor; friability or bleeding from the cervix; and any tenderness or masses on the bimanual exam (cervical motion tenderness; tubal, ovarian, uterine, or adnexal tenderness).

Vaginitis

The diagnosis may be narrowed after a thorough history and physical exam described above; however, the identification of the true cause of the patient's symptoms is not possible without performing a simple laboratory evaluation due to the similarities in signs and symptoms. Vaginal specimens can be collected during the speculum exam noted above, including testing for sexually transmitted diseases (STDs) and swabs for preparing a wet mount and KOH specimen. Depending on the method used for the specimen identification (nucleic acid amplification, culture, PCR, etc.), the samples may be taken from the cervical os or the vaginal side walls. There is typically pooling of fluids (mucous and semen) in the posterior fornix, so the best sample is not obtained from this site. The wet mount is prepared using a cotton-tipped swab to collect a specimen from the vaginal side wall. The swab can then be touched directly onto pH paper to determine the pH of the vaginal fluid, then either placed in a test

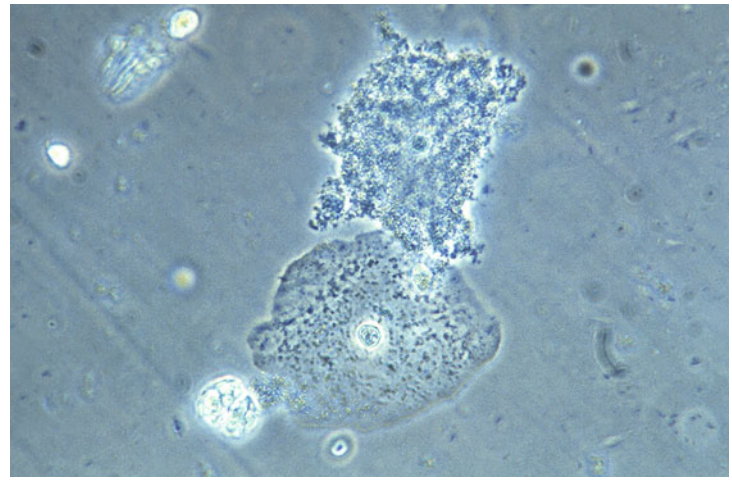

Fig. 1 Two epithelial cells on vaginal wet mount preparation: one normal and the other with the surface studded with coccobacilli, termed clue cell, as seen in bacterial vaginosis (Public Health Image Library from the CDC)

tube with about three drops of saline and a drop is placed on two slides or the swab can directly place the drop of the vaginal specimen on the slides with a drop of saline on one; on the other of these slides a drop of 10 % KOH is placed and then a cover slip is placed over each to examine under the microscope. Before covering the KOH specimen, wafting the aroma from the slide to the nose of the examiner is termed the whiff test and can identify identifying scents associated with certain infections. The best visualization of the elements under investigation would be with the use of the low power (10x) first and then high power (40x) to allow viewing of the smaller elements.

In the case of a healthy vaginal environment, the vaginal discharge is white or transparent, thick, or thin and mostly odorless, and the vaginal pH will be in the normal range (4.0–4.5). Microscopy will show epithelial cells (large, round to somewhat oval cells, sometimes folded, with a relatively small nucleus and clear to somewhat granular cytoplasm) with occasional polymorphonuclear (PMN) cells (or leukocytes; smaller, rounded to oval cells with segmented, larger nuclei), occasional erythrocytes (RBCs: small round cells with no nuclei), and lactobacilli (small rod-shaped bacteria) and even sperm can be seen at times (very small motile organisms with the characteristic tail). When there is an alteration in the healthy vaginal chemical or biological environment, there may be other findings on microscopy: clue cells (epithelial cells that are covered in small, round bacteria, particularly prominent at the edges of the cells) (Fig. 1), fungal elements (buds, hyphae, and pseudohyphae; Fig. 2), a large proportion of PMNs, flagellated trichomonads (Fig. 3), a lack of lactobacilli or PMNs; and higher numbers of basal cells (smaller epithelial cells with a higher nucleus-to-cytoplasm ratio). Identifying these elements on the laboratory evaluation will assist greatly in the accurate diagnosis of the etiology of the patient's complaints.

Bacterial Vaginosis

Bacterial vaginosis (BV) is the most common cause of vaginal complaints in women [1], though many women can be asymptomatic. There is no true inflammation, hence the term vaginosis, rather than vaginitis, and typically there is no vulvar involvement. BV involves a shift in the normal vaginal flora with a lack of lactobacilli and with an overgrowth of anaerobic organisms such as *Gardnerella vaginalis*, *Haemophilus* species, *Bacteroides*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Mobiluncus*, and others. The exact mechanism of the alteration in the flora is unclear, but the lack of the lactobacilli raises the pH, no longer prohibiting the growth of the offending anaerobic bacteria, and a massive overgrowth occurs. It appears there is a biofilm [2] produced by the *Gardnerella* on the vaginal side walls that other bacteria then adhere. These

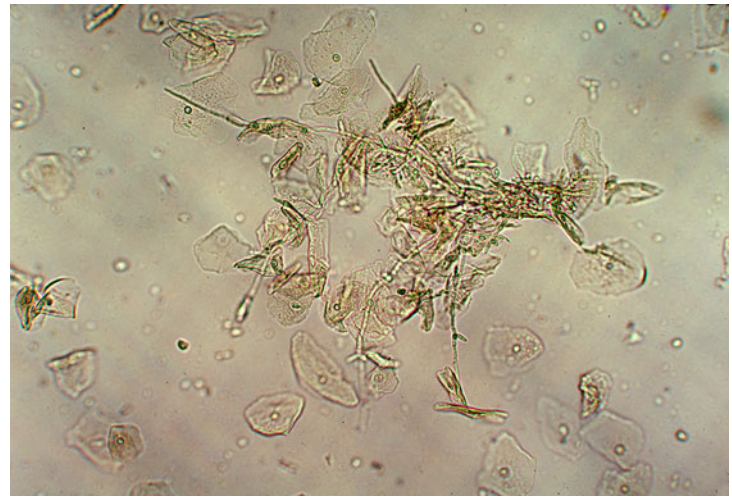

Fig. 2 Vaginal wet mount preparation showing epithelial cells and pseudohyphae of *Candida albicans* (Public Health Image Library of the CDC)

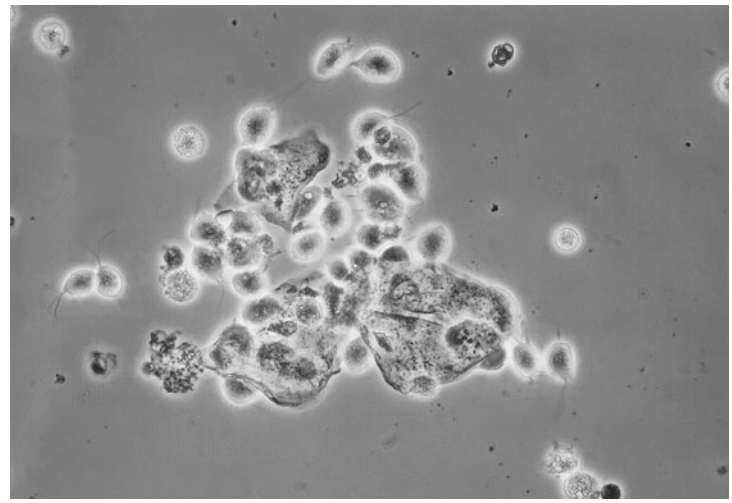

Fig. 3 Vaginal wet mount preparation showing the flagellated trichomonads (Public Health Image Library of the CDC)

organisms produce proteolytic carboxylase enzymes that break down the vaginal peptides and produce amines that give the characteristic "fishy" odor noted during the whiff test. There is desquamation of these cells to produce the classic clue cells (Fig. 1) seen on the wet mount.

BV is not considered a sexually transmitted infection, but sexual activity does seem to be a factor: women with new or multiple sexual partners are at a higher risk, and there is a decrease in risk with the use of condoms and having monogamous sexually active long-term relationships. There is a high prevalence in women who have sex with other women, particularly with new or multiple partners. Other risk factors include douching (which can eliminate the lactobacilli that help to maintain the healthy acidic vaginal environment), smoking, and possibly a genetic component to susceptibility.

The prevalence is hard to determine, as this is not a reportable disease, and can vary considerably based on the population studied [3]. It is commonly found in women of reproductive age, rarely in postmenopause and not in children. There may be no symptoms or just the complaint of an unpleasant odor, worse after intercourse or during menses. A vaginal discharge may be present that is typically thin and off-white (gray or yellow). Dysuria, dyspareunia, and pelvic pain are not usual complaints and, if present, may be a sign

of mixed vaginitis or coinfection. On physical exam a homogenous, thin, sometimes malodorous vaginal discharge may be seen, typically adherent to and smoothly coating the vaginal walls. Acute cervicitis, with a mucopurulent discharge from the cervical os, and even cervical motion tenderness can be seen if there has been assent of the infection into the cervical canal and even to the upper portions of the genital tract, though it is more likely a sign of coinfection.

Diagnosis of BV is made primarily by characteristic laboratory findings, elevated pH, and the characteristic findings seen on microscopy: clue cells with a lack of lactobacilli and PMNs. Amsel's criteria is used when microscopy is available and is considered diagnostic of BV if any three of the following are present: characteristic vaginal discharge (thin, off-white, homogenous, smoothly coating the vaginal walls), elevated pH (>4.5), predominance of the epithelial cells (>20 %) that are clue cells on saline wet mount, and positive whiff test (fishy odor with the addition of 10 % KOH to the vaginal sample). Gram stain is considered the gold standard of diagnosis; however, this requires more time, resources, and expertise. Utilizing Gram stain as the gold standard, Amsel's criteria is >90 % sensitive and 77 % specific [4]. A shift in vaginal flora can be seen on a pap smear specimen; however, the sensitivity is low and should not be relied upon for diagnosis. There is no indication to treat asymptomatic patients with this finding on the pathology report.

There are some serious health consequences as a result of BV: increased risk of preterm delivery in pregnancy, endometrial bacterial colonization and endometritis, pelvic inflammatory disease (PID), postpartum fever, post-hysterectomy vaginal cuff cellulitis, postsurgical abortion infection, and increased risk for acquisition of other STDs (HIV, HSV 2, gonorrhea, chlamydia, and trichomonads). The Centers for Disease Control and Prevention (CDC) does not currently recommend treatment of asymptomatic women, only those with the symptoms and diagnostic criteria above, as there is insufficient evidence of the benefit of treating asymptomatic women at this time [5]. Though this is not considered a sexually transmitted infection, it is a common finding for those women presenting in such a scenario; and the treatment guidelines here are consistent with those of the CDC, in their Treatment Guidelines for Sexually Transmitted Diseases [5].

Treatment of BV is recommended in symptomatic women for relief of symptoms and in presurgical patients undergoing gynecologic procedures (hysterectomy and surgical abortion); partner treatment is not recommended. Several oral and topical regimens are acceptable and effective: metronidazole (Flagyl) 500 mg orally twice daily for 7 days; metronidazole gel 0.75 %, one full applicator (5 g) intravaginally once a day for 5 days; or clindamycin cream 2 %, one full applicator (5 g), intravaginally at bedtime for 7 days. Alternative regimens include tinidazole (Tindamax) 2 g orally once daily for 2 days, tinidazole 1 g orally once daily for 5 days, clindamycin (Cleocin) 300 mg orally twice daily for 7 days, or clindamycin ovules 100 mg intravaginally once at bedtime for 3 days. Oral treatment is as effective as topical, but associated with more side effects, such as metallic taste, nausea, neutropenia, peripheral neuropathy, some drug reactions, and a disulfiram-like effect (nausea/vomiting/diarrhea) with concurrent consumption of alcohol. Clindamycin cream can weaken condoms and either route can be associated with the development of pseudomembranous colitis.

Treatment recommendations for women with bacterial vaginosis in pregnancy include oral medications for those who are symptomatic: metronidazole, either 500 mg twice daily or 250 mg three times daily, or clindamycin 300 mg twice daily, all for 7 days. Despite metronidazole crossing the placenta, there has been no good evidence of teratogenic effects in pregnancy. Though pregnant patients with bacterial vaginosis have an increased risk of complications including premature rupture of membranes and preterm delivery, postpartum endometritis, and post-cesarean wound infection, a routine screening and treatment regimen has not been found to effectively decrease these rates. Topical treatments are preferred in breast-feeding women, to decrease concentrations of drugs in breast milk and thus infant

exposure and complications such as diarrhea and candidal infections due to alteration of gut flora or other toxicities.

Follow-up after treatment is unnecessary if symptoms resolve, though recurrence of BV is very common: usually within the first year after treatment and often associated with a new sexual partner. This could be the result of reinfection or persistence of BV-associated organisms or a failure to restore the normal vaginal flora (in particular a lack of lactobacilli recolonization of the vagina). Simply retreating can be sufficient, particularly if compliance with the initial regimen may have been an issue. If the patient has continued recurrences (>3 in 12 months), suppressive therapy may be indicated: twice weekly metronidazole gel for 4–6 months or oral nitroimidazole followed by intravaginal boric acid (600 mg nightly) and suppressive metronidazole gel. Caution: boric acid can cause death if taken orally. Prevention measures include patient education regarding identifying the presence of the infection (recognizing the odor and/or discharge), risk reduction with consistent use of condoms, limiting the number of sexual partners, and avoiding douching. The use of probiotics (supplemental lactobacillus in various forms) has not been shown to be beneficial.

Candidiasis

The second most common cause of vaginal infection is due to candidiasis [6] (commonly called a "yeast infection") or vulvovaginal inflammation in the presence of candidal species. The presence of candidal species is not considered abnormal as they are typically found in the normal flora of the vagina and skin of healthy women. It is thought there is some disruption to this normal environment that allows the organism to overgrow and cause infection. The diagnosis requires the presence of vulvovaginal inflammation with pruritus of the vulva and vagina, a common complaint. The symptoms are the result of overgrowth of *Candida* and penetration of the superficial epithelial cells. *Candida albicans* is responsible for the great majority of these infections, less commonly with other species such as *C. glabrata* and *C. parapsilosis* [6]. All species produce similar vulvovaginal symptoms, though usually less severe with *C. glabrata*.

Sexual activity is not believed to play a role in the transmission of vulvovaginal candidiasis (VVC). Though many patients have no identifiable risk factors or precipitating condition, there are risk factors that appear to increase the likelihood or frequency of infections [7]. Antibiotic use causes inhibition of the normal bacterial flora and can allow the growth of fungal organisms leading to symptomatic infection. Immunosuppression as a result of medical conditions (such as poorly controlled diabetes or HIV) or use of medications (glucocorticoids and other immunosuppressive agents) has been linked to the development of this infection. The condition is so common that routine screening for any of these factors is not necessarily indicated, unless there is persistence of infection. Behavioral factors can play a role as well: douching (which can alter the normal biological and chemical vaginal environment), use of tampons or pads, and wearing tight and/or synthetic clothing and use of certain contraceptives (such as the vaginal sponge) all seem to increase the rate of this infection.

The prevalence of VVC is difficult to determine given that it is not a reportable infection, and there are often self-diagnosis and treatment with readily available and highly utilized over-the-counter medications, though it does appear that most women are affected with this infection at least once in their lifetime [5, 8]. When patients do present for medical attention, they are often treated merely based on symptoms without confirmation by microscopy or culture. The clinical presentation is typically that of vulvovaginal pruritus, with accompanying burning, soreness, and irritation. Dysuria (usually externally rather than internally) and dyspareunia can accompany the symptoms. There may or may not be a reported vaginal discharge, but if so it is typically described as white and thick or "clumpy," usually with no abnormal odor.

The characteristic findings on physical exam consist of erythema of the vulva and vaginal mucosa, with possible edema, vulvar

excoriations, and even fissures. There may be little or no discharge, and if present it is often thick, white, and curd-like (though other cases, it is thin and watery) with no or minimal odor. The cervix typically does not show involvement other than adherence of any discharge that may be present in the vaginal vault. The clinical presentation however can be quite variable and have considerable overlap with other etiologies of vulvovaginitis.

The diagnosis of VVC is made in women with the characteristic findings of vulvovaginal inflammation and confirmed with the presence of *Candida* on the wet mount. The vaginal pH is usually normal, so if abnormally elevated, coinfection or an alternate etiology should be considered. Microscopic findings on wet mount include the presence of budding yeast (oval cells) and pseudohyphae (chains of cells) (Fig. 2). The addition of 10 % KOH to the vaginal sample, which breaks down the epithelial and other cell walls, can allow better visualization of the fungal elements. During inspection of the wet mount, the presence of clue cells or motile trichomonads should be excluded as a concurrent or alternate infection. Routine culture is not typically helpful as it may merely indicate the presence of colonization of *Candida*, not infection. It is more helpful in the setting of resistant or recurrence of candidal infection. There is no other point of care testing that is available or of proven benefit in diagnosing this condition. Pap smear pathology reports may indicate the presence of candidal species; however, again this may merely indicate the colonization of the vagina with this organism and not the presence of infection. There is no indication to treat asymptomatic women in these cases.

Treatment of VVC is for relief of symptoms and based on the classification: complicated or uncomplicated [5]. Uncomplicated candidiasis episodes are sporadic or infrequent with mild to moderate symptoms in women with a normal immune system that is likely to be due to *C. albicans*. Complicated candidiasis involves severe symptoms and recurrent episodes in immunocompromised women and is more likely to be caused by non-*C. albicans* species. Uncomplicated cases typically respond to all azole therapies (oral or topical) within a few days, whereas complicated cases take longer to respond. In either case, partner treatment is not indicated. Over-the-counter topical intravaginal treatments in uncomplicated cases include butoconazole (Gynazole-1) 2 % cream, 5 g daily for 3 days; clotrimazole (Gyne-Lotrimin) 1 % cream, 5 g for 7–14 days; clotrimazole 2 % cream, 5 g for 3 days; miconazole (Monistat) 2 % cream, 5 g for 7 days; miconazole 4 % cream, 5 g for 3 days; miconazole 100 mg, vaginal suppository daily for 7 days; miconazole 200 mg, vaginal suppository daily for 3 days; miconazole 1,200 mg, vaginal suppository for 1 day; or tioconazole (Monistat 1Day) 6.5 % ointment 5 g for 1 day. Prescription intravaginal agents include butoconazole 2 % cream 5 g for 1 day, nystatin 100,000-U vaginal tablet for 14 days, terconazole (Terazol) 0.4 % cream 5 g for 7 days, terconazole 0.8 % cream 5 g for 3 days, or terconazole 80 mg vaginal suppository for 3 days. The only oral agent is fluconazole (Diflucan) 150 mg tablet in a single dose, which maintains therapeutic concentrations in vaginal secretions for at least 72 h. As all are equally as effective, patient preference is often the deciding factor, with the oral medication associated with more side effects and drug interactions, though in the generic form may be less expensive than the over-the-counter treatments.

Complicated VVC is involved in approximately 10–20 % of cases; and recurrent infection is usually defined as four or more episodes in a year [5]. Treatment requires longer therapy: 7–14 days of topical therapy or 100, 150, or 200 mg oral fluconazole every third day for a total of three doses followed by maintenance therapy with oral fluconazole once weekly for 6 months or topical therapy intermittently for the same time frame. Severe VVC typically does not respond to shorter treatment regimens so recommendations are for 7–14 days of topical therapy or oral fluconazole 150 mg repeated in 72 h. Resistance is unusual, and when suspected culture should be performed and treatment with a non-fluconazole therapy for 7–14 days first-line or 600 mg boric acid intravaginally daily for 14 days for recurrences. In an immunocompromised host, 7–14 days of topical therapy is recommended.

Candidal vulvovaginitis is not associated with adverse outcomes in pregnancy, so treatment is indicated only for relief of symptoms. Only topical regimens (clotrimazole or miconazole for 7 days) are recommended as there have been case reports of certain birth defects with the use of oral azoles, particularly in the first trimester [9]. In breast-feeding patients, both oral and topical treatments are safe and effective as there appear to be no adverse affects reported.

Follow-up is not necessary if symptoms resolve, and partner treatment is not indicated. There is no good evidence that probiotic (either oral or intravaginal) administration provides any benefit for treatment or prevention of VVC. Prevention involves education of patients and reduction in any risk factors present: avoiding douching, improved control of serum glucose levels, compliance with treatment regimens, and minimizing the use of antibiotics.

Trichomoniasis

The third most common cause of vaginitis is caused by the flagellated single-celled anaerobic protozoan *Trichomonas vaginalis*. The organism primarily infects the squamous epithelium of the urogenital tract including the vagina, urethra and paraurethral glands, cervix, bladder, Bartholin glands, and prostate. The disease is sexually transmitted though not reportable, and women can acquire the disease from other women though men usually do not transmit it to other men. The incubation period is unknown, but in vitro studies indicate 4–28 days in about 50 % of patients, and it can persist for months in epithelial crypts and periglandular areas of women [10].

Since this disease is not reportable, the prevalence is hard to determine, but the best evidence shows an approximate rate of 3 % in the general population of women [11]. This of course varies according to the population studied and the method of diagnosis. Many women can be asymptomatic carriers (often eventually developing symptoms), but the typical vaginitis presentation is that of a thin, frothy gray or yellow-green vaginal discharge with pruritus and vaginal irritation with burning. The discharge may have an odor, and there may be dysuria, urinary frequency, lower abdominal pain, and dyspareunia as a result of involvement of the entire urogenital tract.

Risk factors for trichomoniasis are related to sexual behaviors, such as multiple sex partners, history of an STD, and lack of condom use, as well as related to race and socioeconomic status. It is associated with adverse outcomes in pregnant and nonpregnant patients. In pregnancy trichomoniasis has shown to increase the rates of preterm birth, premature rupture of membranes, and low-birth-weight infants. Other poor outcomes in women include increased shedding of HIV in those infected with HIV, atypical PID, infertility, and post-hysterectomy cellulitis or abscess.

The physical exam can show very few signs or extensive findings including erythema of the vulva and vaginal mucosa; the characteristic thin, frothy, gray or greenish vaginal discharge, possibly malodorous; and petechiae of the vaginal mucosa and cervix may be present, producing the appearance of the "strawberry cervix" on the pelvic speculum exam. The vaginal pH will be elevated and the whiff test can be positive but the diagnosis is actually made based on the laboratory findings. The wet mount will show the presence of the characteristic motile flagellated trichomonad (Fig. 3) with a jerky and spinning motion, best visualized with the high-power lens (40x). The motility is required for the diagnosis so it is imperative to examine the wet mount immediately after preparation as the organism becomes sluggish and dies in 10–20 min after collection. The usually oval protozoan's size is approximately that of the PMNs, and there will typically be a large number of leukocytes present on microscopy. The sensitivity of microscopy is dependent upon the experience of the microscopist and collection technique and is only approximately 60–70 % [12]. Culture is more sensitive than wet mount and is a diagnostic option, particularly in patients with negative or unavailable microscopy, but fixing and staining can change the morphology so is not useful. The use of nucleic acid amplification tests (NAAT) is the most sensitive and specific and can be performed on a self- or clinician-collected vaginal swab or utilizing urine or liquid

cytology specimen. These DNA tests allow for testing of other STDs, as is recommended in this circumstance (since risk of one STD raises the risk of having another) but are more expensive and not yet widely available. In addition, the wet mount should be carefully examined to rule out other causes of vaginitis, such as BV and candidiasis.

Treatment of trichomoniasis is recommended for both asymptomatic and symptomatic patients and their sexual partners for relief of symptoms and to reduce carriage prevalence and the poor outcomes noted above [5]. Treatment regimens include only oral medications: metronidazole (Flagyl) or tinidazole (Tindamax) 2 g in a single dose, with an alternate regimen of metronidazole 500 mg twice daily for 7 days. These medications have a high cure rate (90 %), and the intravaginal metronidazole gel is less effective, so it is not recommended. In the case of allergy, there are no other medications shown to have the effectiveness of the oral nitroimidazoles so the CDC recommends a desensitization protocol. Partners should be treated simultaneously (if possible) and patients advised to avoid intercourse until completion of treatment in both partners with resolution of symptoms or in the case of asymptomatic patients, 7 days. Side effects are dose dependent and include nausea and/or vomiting, metallic taste, headache, dizziness, and a disulfiram-like reaction, so alcohol consumption should be avoided for about 24 h after metronidazole and 72 h after tinidazole treatment.

Treatment in pregnant patients has not been shown to decrease the rates of adverse outcomes, and there have been some studies that have indicated an increase risk [5]. For this reason treatment of pregnant patients is recommended, but the treatment of asymptomatic patients is not straightforward: counseling them on their risks and benefits of treatment and offering delay of treatment until 37 weeks can decrease perinatal transmission without putting them at increased risk. Partner treatment can be accomplished at any time, with the consistent use of condoms or avoidance of intercourse to decrease reinfection. Metronidazole 2 g in a single dose is the drug of choice as there is insufficient evidence of the safety of tinidazole in pregnancy. In this population who often has increased nausea and vomiting during pregnancy, the multidose regimen of 500 mg twice daily for 7 days can be used as an alternate regimen. In breast-feeding patients, the 2 g dose of metronidazole is relatively high for the neonate so advise patients to suspend breast-feeding (pump and discard) for 12–24 h after the dose can eliminate this factor (72 h if tinidazole is used).

Patients positive for HIV can have increased shedding of the virus with infection with *Trichomonas vaginalis* and treatment can decrease this shedding. Routine screening of asymptomatic patients in this population is recommended at entry into care and at least annually, as well as 3 months after treatment even if symptoms have resolved [5]. Some evidence has shown more effectiveness with the longer multidose regimen of metronidazole.

Follow-up is not recommended if symptoms have resolved, and routine screening has not been shown to be of benefit. Resistance levels to metronidazole have been found to be low, so in the case of recurrences or persistence of symptoms, explore compliance with treatment in both the patient and her sexual partners as this is thought to be the most common contributing factor. If the 2 g metronidazole dose fails, the use of the 500 mg metronidazole twice daily for 7 days or the tinidazole 2 g single dose is recommended. If this regimen fails, the use of either metronidazole or tinidazole 2 g daily for 5 days is recommended. If continued failure occurs after these regimens, consultation with a specialist is recommended to include sensitivity testing of *T. vaginalis* to both metronidazole and tinidazole.

Prevention is managed with patient and partner treatment as well as patient education regarding the frequency of asymptomatic infections, the sexual nature of transmission, an increased risk for HIV acquisition and transmission, and the importance of both patient and partner compliance with prescription treatment regimens. A discussion regarding changing sexual behaviors through the consistent use of condoms or abstinence, maintaining a mutually monogamous relationship with a noninfected partner, or limiting the number of sexual partners is indicated.

Cervicitis

Inflammation of the uterine cervix can be effected by many of the already noted conditions and can be due to infectious or noninfectious etiologies, with acute typically the former and chronic the latter. The most common infectious etiologies are the STDs chlamydia, *Neisseria gonorrheae*, as well as herpes simplex viruses, *Trichomonas vaginalis*, and BV (discussed elsewhere). Noninfectious causes can be from mechanical or chemical irritation, radiation therapy, and systemic inflammatory diseases. A significant proportion of patients are asymptomatic and detected incidentally on exam, but when present symptoms typically can include varying degrees of vaginal discharge, postcoital bleeding, dysuria, urinary frequency, dyspareunia, or vulvovaginal irritation. The appearance of the cervix on exam will vary depending on the severity and etiology and can include mucopurulent cervical discharge, cervical friability, vesicular or ulcerative lesions, punctuate hemorrhages of the "strawberry cervix," and cervical motion tenderness with palpation. Treatment is directed at the offending etiology and relief of symptoms. When an etiology cannot be found, there is no recommendation for treatment beyond empiric coverage for STDs, particularly in those patients at high risk. Histologic or cytologic cervicitis in asymptomatic women does not require treatment as it is a very nonspecific finding.

Other STDs: GC, Chlamydia, HPV, Pediculosis, HSV, and Syphilis

There is considerable overlap of the symptoms of these conditions and other STDs, and for this reason, all STDs should be entertained when evaluating patients with vulvovaginal complaints and coinfection may be present. STDs are covered in detail elsewhere in this text but a brief description is given here of some of the similar common presentations. The presentation of vulvovaginitis in herpes simplex virus types 1 and 2 can vary widely based on a number of factors but can have the signs and symptoms of vulvovaginal inflammation with edema, pruritus, dysuria, dyspareunia, local pain and itching, and even vaginal discharge. Typically there are characteristic ulcers present on the labia, vagina, and/or cervix to indicate the etiology. Gonorrhea and chlamydia, if symptomatic, typically appear as mucopurulent cervicitis that when wiped away quickly reappears. HPV is discussed later with genital warts. Pediculosis pubis (pubic lice) typically presents with vulvar pruritus, and lice or nits in the pubic hair will be observed on the exam of the genitals. Primary syphilis can present with painful ulcers and secondary syphilis with condyloma lata: flat, moist papules on plaques that can be white, pink, or yellow and can mimic genital warts.

Atrophic Vaginitis

Atrophic vaginitis is an alteration of the normal premenopausal vaginal biological and chemical environment and inflammation that occurs in the mucous membranes of the female genitalia due to the lack of or decreased levels of estrogen. This often occurs in menopausal women but can also occur during other hypoestrogenic states such as postpartum and lactation and when taking antiestrogenic medications. The lack of estrogen stimulation of the cells of the female genital tract results in less glycogen and thinning of the epithelial cells. The decrease in glycogen then results in the loss of lactobacilli with a resultant decrease in lactic acid and hydrogen peroxide, raising the vaginal pH (>5), thus altering the normal premenopausal flora, and making the likelihood of overgrowth or invasion of pathogenic organisms more likely.

Atrophic changes seen as a result of this process include loss of elasticity and thinning of the vaginal epithelium with shortening and narrowing of the vaginal canal and introitus with loss of rugae as well as decreased vaginal secretions. Together, these make the area more susceptible to even minor trauma producing bleeding, petechiae, and even ulceration. There are estrogen receptors in the structures of the urinary tract

derived from the same embryologic origin, including the bladder, urethra, and pelvic floor musculature, that are affected by this same hypoestrogenic state and produce the symptoms of dysuria, urinary frequency, and hematuria. Abstinence can exacerbate the conditions and sexual activity can actually help to preserve the vaginal epithelium and reduce these symptoms by encouraging increased vaginal blood flow and elasticity [13].

The clinical presentation is varying degrees of vaginal dryness, with burning or irritation, sometimes a yellow malodorous vaginal discharge, dyspareunia, dysuria, and urinary frequency and even vulvar or vaginal bleeding and hematuria (not necessarily related to intercourse). The pelvic exam will show the effects of the hypoestrogenic state with sparse pubic hair, decreased vaginal secretions, introital narrowing, fusion or resporption of the labia minora, and pale, dry vaginal epithelium that appears smooth and even shiny with a loss of rugae. There is loss of labial fat that can make the clitoris or urethral meatus look more prominent or even cause urethral prolapse. The vagina can be shortened, narrowed, and poorly distensible. In fact, in severe cases, the cervix can become nearly flush with the vaginal walls as the fornices are obliterated. The vaginal and cervical tissues may show inflammation, have more prominent blood vessels visible through the thinned epithelial tissue, and can show patchy erythema, petechiae, or ulcers with friability of the cervix and easy bleeding of other structures, and there may be a yellow, malodorous discharge present.

The diagnosis is made based on the clinical findings, though laboratory testing is performed in order to rule out any other coexisting conditions. Measuring serum estrogen levels is not usually necessary or beneficial unless there are questionable findings. The laboratory evaluation will show an elevated pH (>5) and lack of lactobacilli on wet mount with a predominance of parabasal cells and may show many PMNs and the presence of other mixed flora. BV and trichomoniasis should be ruled out by the lack of clue cells or motile trichomonads. Parabasal cells are immature squamous epithelial cells that are rounded with a large nucleus to cytoplasm ratio. The maturation index quantifies the proportions of the types of epithelial cells based on their maturity. The superficial and intermediate epithelial cells dominate the wet mount in premenopausal women, whereas in post menopause, there is an increase in parabasal cells, even to the point that no other types are seen.

First-line treatment of atrophic vaginitis is the use of vaginal lubricants and moisturizing agents. The vaginal moisturizing agents should be used on a regular basis, at least one to two times weekly. And water-soluble lubricants should be used generously during intercourse to decrease discomfort. Though these agents do not reverse the atrophic changes, they can be quite useful, particularly in cases of only mild symptoms. Mechanical measures with intercourse itself, dildos, or mechanical vaginal dilators can be used (with lubrication) by a partner or the patient herself to stretch the vaginal tissue, though little is known about the ideal type and frequency that results in the best outcomes.

For moderate to severe symptoms of atrophic vaginitis, local vaginal estrogen therapy is more effective and actually reverses the changes seen by the lack of serum estrogen [14]. The doses used for this condition (7.5–25 mcg weekly) are lower than that used for control of the vasomotor symptoms of menopause and avoid or minimize the systemic estrogenic effects of increased risk for breast cancer and thrombosis as there is little systemic absorption [15]. Local vaginal estrogen is often more effective in treating the vulvovaginal symptoms of atrophy than oral estrogen therapy. In the USA, these agents are available as conjugated estrogen creams and estradiol in the form of cream (though there is increased systemic absorption), tablet, or ring and appear to be equally effective in relieving symptoms, though the dose and duration to achieve this affect can vary across patients. With all of these forms, the typical dosing regimen is to use daily for the first 2 weeks and then decrease to approximately twice weekly or the dose that is effective in controlling symptoms. In women with an intact uterus, consideration should be given to adding progesterone, either cyclical or continuous, to decrease the risk of

endometrial malignancy, though the very low doses used do not appear to stimulate the endometrium [15].

Selective estrogen receptor modulators (SERMs) can be used in this setting and are approved to treat the symptoms of vulvovaginal atrophy [16]. This medication selectively binds to estrogen receptors acting as an estrogen agonist, inducing changes in the vaginal epithelium and decreasing the vaginal pH, and appears to have no detrimental effects on endometrial tissue. This is a daily systemic medication, and side effects are more common than with topical meds, the most common being hot flashes.

There is insufficient evidence to support the use of alternative or complementary therapies such as oral or vaginal vitamin D or E. The safety of hormonal use in women either at high risk or with a history of breast cancer or thromboembolism has not yet been established, so these therapies are not recommended for these populations.

Vulvodynia

Vulvodynia is vulvar discomfort (typically burning or pain) of unknown etiology with no visible findings or other medical explanation; therefore, it is a diagnosis of exclusion. Vestibulitis is no longer used to describe this condition, as it implies the presence of inflammation which is not part of the condition [17]. The presentation is that of provoked (with penetration or pressure to the vulva) or unprovoked burning or discomfort of the vulva or particular areas of the vulva (clitoris, vestibule), infrequently with pruritus. The physical exam reveals normal or mild inflammatory changes with hyperalgesia of this area; pain with separation of the labia is common. The pathogenesis is unknown and can vary for each individual, but is most likely a combination of factors, including changes in estrogen concentrations, neuropathic pain, pelvic floor dysfunction, and psychological factors [18]. These factors are then thought to precipitate the mind-brain-body cycle seen in other chronic pain syndromes.

There is paucity of data available, and there is no agreement in diagnosis and treatment strategies [18]. Avoidance of any products (dyes, perfumes, other chemicals) or behaviors (use of tight-fitting clothing, horseback or bike riding, daily use of sanitary pads) that can irritate the area is recommended as well as avoidance of constipation. Use of the application of ice packs wrapped in a soft cloth periodically throughout the day or sitz baths in warm water 10–15 min with subsequent application of a thin layer of petrolatum gel can offer some relief. Pelvic floor rehabilitation or physical therapy by those experienced in this disorder has been utilized. Important is addressing the psychosocial and sexual issues with couples and/or sexual therapy, including cognitive behavioral and mindfulness therapy.

Pharmacologic therapy utilizes medications often used in other types of neuropathic and chronic pain: topical lidocaine, tricyclic antidepressants (desipramine, nortriptyline, amitriptyline), gabapentin, pregabalin, venlafaxine, duloxetine, and estrogen cream. Nerve blocks may be beneficial and require referral to either an anesthesiologist or pain specialist.

Allergens and Irritants

Allergic reactions or inflammation of the vulvovaginal area can occur as a result of exposure to various substances, such as spermicides, soaps, deodorants, detergents, dyes, perfumes, pads or panty liners, latex, douching agents, urine, and more chemicals. There can also be mechanical irritation caused by foreign bodies (dildos/vibrators/personal massagers) particularly if prolonged exposure, as in the case of a retained tampon. Symptoms can include pruritus, stinging, soreness, burning, or even a vaginal discharge. It is important to specifically ask patients regarding the use of any feminine hygiene or other products and the frequency as excessive washing can cause dryness and irritation. Exam will reveal local inflammation and possibly excoriation and often discharge and odor in the case of a retained foreign body. Contact dermatitis can be seen on the vulva with the typical findings of erythematous maculopapular rash. Coinfection can be present so complete exam including microscopy is

warranted. Treatment is avoidance of the offending agents and, in the case of a retained foreign body, removal and treatment of any coinfection (routine use of antibiotics in this setting is not necessary).

Dermatoses

There are a number of generalized skin conditions that can include vulvar symptoms ranging from mild to severe, though these uncommonly affect only the vulva. The symptoms, if present, are typically pruritus and/or irritation/soreness. The exam will often reveal the characteristic findings of the respective conditions: seborrheic dermatitis with pink macular area with scale; atopic or contact dermatitis with erythematous papules; molluscum contagiosum with small pearly, umbilicated papules; folliculitis with inflammation and/or infection of the hair follicles; skin tags that are flesh colored or pigmented and usually pedunculated; and lichen simplex chronicus with thickening or lichenification of the skin. The area may show the results of either acute or chronic changes of redness, excoriations, or even fissures. Aphthous ulcers can present on the mucous membranes of the genital area and are similar to the much more common oral form. Treatment would be directed at the particular skin condition in question, covered elsewhere in this text.

Generalized skin conditions can present with primary genital lesions or can present with a different appearance in the genital area, often related to the presence on mucous membranes and the presence of more moisture. Psoriasis affects the genitals in approx 30–40 % of patients with the disease [19]. On the mucous membranes of the vulva, the lesions tend to have less scale, may appear red, and even have exudate present. Typically the lesions do not involve the vagina, and in some cases, the genitals can be the sole presenting location. Tinea can involve the groin and vulva showing sharply marginated, erythematous dusky red, moist plaques or patches with slight scaling and often with satellite lesions and pustules present. When found in the groin, it is termed tinea cruris. Hidradenitis suppurativa when involving the vulva is typically found in the inguinal and labiocrural folds, mons pubis, and perianal area. Typically there are old scars from previous lesions, and frequently edema is present.

Lichen sclerosis is a primary skin condition of unknown etiology that can occur in genital and extragenital locations. Initially the symptoms can be very subjective with itching, dyspareunia, and dysuria, though the typical presentation is that of pruritus, with the appearance of white papules that coalesce into white plaques: the skin becomes thin and slightly wrinkled ("cigarette paper"). On the vulva it can lead to obliteration or alteration of the normal architecture of the labia minora and stenosis of the introitus or can appear as a figure 8 pattern when involving the perineum and perianal areas. There is an increase in the risk of squamous cell carcinoma so biopsy may be indicated for any suspicious lesion or failure to respond to therapy.

Lichen planus also has an unknown etiology involving the mucocutaneous areas of the body and often has simultaneous oral and genital presentations. Lesions can be papulosquamous with flat white plaques or erosive with red or violaceous, sharply marginated, flat-topped papules or plaques with a thin white lacy network of white or gray lines usually on the labia minora and introitus (sometimes on the vaginal wall). Papulosquamous may be asymptomatic or with some pruritus, whereas erosive are often painful and can even have bleeding.

Fistulas and Crohn's Disease

Rectovaginal, anovaginal, and less commonly vesicovaginal fistulas can cause symptoms of vulvovaginitis, including malodorous vaginal discharge, pruritus, inflammation, and dyspareunia. In some cases stool or gas is passed from the vagina, making the diagnosis much easier. Often these lesions are palpable on rectal exam, usually located in the midline, lower third of the vagina, along the posterior vaginal wall, and on vaginal exam may be just inside the introitus or hymen. On exam the appearance is that of a red velvety, indurated area. Fistulas can result as a complication of pelvic surgery, vaginal delivery, radiation

therapy, more rarely spontaneously, or due to other pathologies such as inflammatory bowel disease. Crohn's disease can also be present on the vulva as knifelike linear ulcers, particularly in the skin folds. Initial presentation can be only vulvar edema or abscesses that break down to form chronic ulcers (which can mimic hidradenitis suppurativa) and/or large vulvar skin tags.

Bartholin Glands and Duct Disorders

Bartholin glands are mucous-secreting glands that begin functioning to provide moisture to the vestibule of the perineum at puberty and typically involute with age, particularly with menopause. They are small (approximately 0.5 cm) and are connected to the vestibule with a short duct (approx 2–2.5 cm) that opens at the 4 and 8 o'clock positions on either side of the vaginal orifice between the hymenal ring and labia. Cysts and abscesses are formed when there is obstruction of the opening of the duct, with resultant accumulation of the mucous secretions proximal to the obstruction, or cystic dilation of the duct and can become infected (though abscesses can occur without the formation of a cyst). They should be differentiated from other masses found on the vulva and perineum such as lipomas, folliculitis, hidradenitis suppurativa, sebaceous cysts, hematomas, Skene gland cysts (located more anteriorly on either side of urethral openings), other vulvar abscesses, hernias, or even extensions of perianal abscesses.

Both cysts and abscesses are typically unilateral and found in the area of the Bartholin gland and should not be fixed to any underlying tissues: this can be suspicious for malignancy. The cysts are typically smaller than abscesses (approx 1–3 cm) and may be asymptomatic though if large can cause some discomfort. Abscesses, which are more common, are typically larger and quite painful, often to the point the patient is barely able to sit or ambulate normally. On clinical exam cysts are usually soft and non-tender, whereas abscesses are soft, painful masses that protrude into the posterior vaginal introitus and often extend into the labia. There can be associated cellulitis with increased warmth, erythema, fluctuance, induration, and edema. The presence of any palpable solid or irregular mass can be an indication of the presence of malignancy, though this is rare, particularly in premenopausal women. If there is any suspicion of malignancy in postmenopausal women with their first occurrence, biopsy should be obtained [20].

Cysts may require no management, unless large and uncomfortable. Abscesses should be treated at the least with incision and drainage (I&D), though some may spontaneously rupture and drain. The risk of recurrence due to healing of the edges of the incision and reaccumulation of the gland secretions is quite high [21], so further management is recommended with either placement of a Word catheter, marsupialization, silver nitrate stick ablation, laser vaporization, or complete excision. I&D involves sterile prep of the area, administration of a local anesthetic with an incision into the protruding mass in the area of the duct opening external to the hymenal ring to drain the contents. Irrigation and hemostats can be used to break up any loculations present within the cyst or abscess. With all of these procedures, there is a risk of labial or perineal edema, hematoma formation, bleeding, cellulitis, scarring, and dyspareunia.

Antibiotics are typically not necessary unless there is accompanying cellulitis or high risk for complicated infection such as recurrence, immunocompromised patients, pregnancy, risk for MRSA, systemic signs of infection, or suspicion of gonorrhea or chlamydia infection. The infection is typically polymicrobial with the most common aerobic pathogens of staph, strep, and E coli and anaerobic bacteroides with sexually transmitted infections (such as gonorrhea, chlamydia, and trichomonads) decreasing in incidence [22]. When indicated, empiric treatment is started before results of any cultures are received and includes amoxicillin-clavulanate (Augmentin) 875 mg BID to cover E coli and strep, with clindamycin (Cleocin) 300 mg four times a day for staph and bacteroides, both for 7 days. If culture results reveal an STD, it should be treated accordingly.

Word catheter placement involves the placement of a small (stem is approximately 1 in. and diameter is similar to that of a 10 French Foley catheter) balloon-tipped catheter into the incision immediately after the performance of I&D, with inflation of the balloon with 2–3 cm^3 of saline in order to keep it in place and the end tucked into the vagina. If the incision is too large, the catheter will fall out, so it is recommended only about 5 mm incision in this case. The catheter is left in 4–6 weeks to allow epithelialization of a new tract for drainage of the gland secretions; therefore, it is important to ensure the tip is placed within the cyst wall so as to avoid the development of a false tract. At this time the balloon can be deflated and the catheter removed without anesthesia. This procedure is easily accomplished in the office with local anesthesia and is relatively quick and easy, though the patient may experience post-procedure discomfort or the catheter can migrate or become dislodged and fall out before epithelialization, increasing the risk for recurrence. Daily sitz baths after the procedure can help with discomfort.

Marsupialization involves a larger incision over the cyst or abscess or even an excision of an ellipse of the roof of the mass, with the length dependent on the size of the cyst (usually 1–3 cm). Drainage is followed by suturing with eversion of the edge of the cyst wall onto the epithelial surface of the vestibule with interrupted absorbable sutures allowing for the formation of a new ductal orifice for drainage of gland secretions. This procedure is as effective as placement of a Word catheter and also can be accomplished easily in the office setting with local anesthesia, though is somewhat more complicated and time consuming [21]. Again, daily sitz baths are typically recommended.

The placement of a silver nitrate stick (approx 0.5 cm in size) deep within the cyst/abscess after I&D can also be done in the office setting with local anesthesia. The wound is then dressed with gauze and the patient instructed to return in 48 h for debridement of the wound of silver nitrate particles and necrotic tissue. This procedure has been found to be as effective as complete excision [21]. There is significantly more post-procedure discomfort than the previous procedures described and risks of chemical burns to nearby tissue, though there is less healing time, expense, and risk than that of complete excision. Carbon dioxide laser ablation can be accomplished with the use of local anesthesia as well and is effective in treating this condition, though it requires expertise and training in the use of very expensive equipment not typically available in the office setting of family medicine. Complete excision of the gland and duct is definitive treatment though it requires surgical excision in the operating room, with all of the increase in cost and risks inherent to these more involved invasive procedures. For these reasons complete excision is usually used only when recurrent disease fails numerous other attempts at treatment, or malignancy is suspected (though biopsy is the first-line approach). The loss of gland function can rarely cause vaginal dryness and dyspareunia.

Genital Warts

Genital warts are one of the clinical manifestations of infection with the sexually transmitted human papillomavirus (HPV), most commonly types 6 and 11 with low oncogenic potential. Transmission is through direct skin contact during sexual activity, so increased risk exists for patients with increased numbers of sexual partners and history of other STDs, including HIV. Those patients infected with HIV are more likely to develop genital warts than those without [23], and the lesions are more recalcitrant to treatment due to the depressed cell-mediated immunity. The infection itself and the warts are asymptomatic, though there can be pruritus, pain, or discomfort in some patients. The lesions appear as flesh colored or pink, flat, papular, or verrucous papilliform growths on the genital mucosa. They commonly occur around the introitus, but can occur in and around the anogenital epithelium including the cervix, vagina, urethra, perineum, and perianal skin. Large exophytic masses can cause obstruction of the perianal orifices and interfere with urination, defecation, and vaginal delivery.

Diagnosis is usually clinical, based on visual inspection and can be confirmed with biopsy, though not necessary. The application of 5 % acetic acid solution causes the lesion to turn white and can aid in diagnosis, with or without the use of colposcopy. A similar-looking normal variant of vulvar anatomy is vestibular papillomatosis with monomorphous, symmetrical, soft, closely set projections usually the same color as the mucous membrane of the vestibule (or sometimes more red), whereas warts are firmer, flesh colored, cauliflower-like (multiple projections from a single base). The indication for biopsy prior to treatment is to rule out any malignant or premalignant lesions as squamous cell carcinoma can coexist. Biopsy is recommended when the diagnosis is uncertain; lesions do not respond to standard therapy; the disease worsens during therapy; the lesion appears atypical, particularly if pigmented, asymmetrical, or irregular border, fixed, bleeding, or ulcerated; or the patient is immunocompromised. Colposcopy and biopsy are recommended for any cervical exophytic lesions. Testing for HPV type is not indicated as it does not change management strategies.

Treatment is only indicated for the relief of symptoms, including cosmetic or psychological concerns, as it does not eliminate all cells infected with the virus and it is unknown if it reduces risk of transmission. Spontaneous resolution does occur at varying rates reported (approximately 20–40 %), so expectant management is an acceptable option, though the patient should be counseled that the lesions may spontaneously regress, increase in number or size, or remain unchanged over time. No one treatment option has been shown to be superior to others [5], and not one treatment is right for all patients and every type of wart. Choice of treatment is based on location and size of lesions, patient characteristics (pregnant or immunocompromised), available resources, and clinical expertise, as well as patient preference, including side effects, cost, and convenience. Options include patient- or provider-applied solutions for ablative or immune-mediated destruction of the lesions or surgical techniques. Intra-anal lesions should be referred to a specialist for surgical treatment.

Patient-applied regimens require the patient to be able to identify and reach all of the lesions to be treated. These regimens include podofilox (Condylox) 0.5 % solution or gel, applied to the wart with a swab or finger for 3 days and then no treatment for the other 4 days of the week, up to four cycles; imiquimod (Aldara) 5 % cream applied daily before bed and then washed off 6–10 h after application, three times per week up to 16 weeks; and sinecatechins (Veregen) 15 % ointment, apply 0.5 cm strand and spread with the finger into a thin layer covering the wart three times per day (do not wash off) for up to 16 weeks. Provider-applied regimens include cryotherapy with liquid nitrogen or a cryoprobe every 1–2 weeks; podophyllin resin 10–25 % in a compound tincture of benzoin applied and allowed to dry before patient sits, stands, or dresses and washed off 1–4 h later, weekly, with a limit of <0.5 ml or treating a total area <10 cm^2 with no open or ulcerated lesions; and tri- or bichloroacetic acid 80–90 % apply a small amount to only the wart tissue and allow the white frosting to develop with drying before allowing the patient to move (in order to avoid irritation to surrounding areas), weekly. If pain is too severe or an excess amount is applied, the area can be treated with soap or sodium bicarbonate solution. Surgical excision techniques are recommended for those with larger or greater number of lesions and are typically more expensive and invasive, with more risk associated but do have the advantage of removal of the warts in one visit.

Warts can proliferate and become friable in pregnancy and imiquimod, sinecatechins, podophyllin, or podofilox should not be used. Rarely types 6 and 11 can cause respiratory papillomatosis and laryngeal warts in children, though the route of transmission is unknown, and it is not clear if cesarean delivery prevents this risk [5]. Cesarean delivery may be indicated in the case of large exophytic lesions that may obstruct the birth canal or increase risk of excessive bleeding.

Most lesions respond to treatment within 3 months. A change in treatment modality is indicated if the lesions do not respond to a full course of therapy or if side effects are too severe.

Recurrence is common, particularly in the first 3 months after treatment. Complications are less common if treatment is administered properly, but side effects are quite common. Hypo- or hyperpigmentation is common with the ablative and immune-modulating therapies. Depressed or hypertrophic scarring risk is greater if insufficient time is taken for healing between treatments. Rarely disabling chronic pain syndromes (vulvodynia, hyperesthesia), painful defecation, or systemic effects (due to podophyllin resin) can occur. Local irritation with discomfort and inflammation, pruritus, erosions, and blistering are the most common side effects.

There are vaccines available for the prevention of HPV, at least one of which (the quadrivalent) encompasses types 6 and 11 and is currently recommended for both boys and girls at the age of 11–12 and up to age 26 if not already immunized. The best time for vaccination is prior to sexual activity, but can be given even after the presence of HPV has been diagnosed, as it may confer immunity to other types. Other prevention measures include decreasing the number of sexual partners and use of condoms; although correct and consistent use can decrease the risk of HPV infection, since they do not cover all areas of skin contact with sexual activity, they not eliminate the risk.

The diagnosis of any STD can precipitate many questions and concerns about sexual fidelity of either the patient or her partner. There is a social stigma that is associated with genital warts that may discourage patients from initiating these conversations with their family doctor, so offering counseling and initiating this discussion by the clinician can be very beneficial and is advised. Some of the issues particular to genital warts and HPV can be as follows: the types of HPV that cause most genital warts do not cause the other types of anogenital cancers; diagnosis with HPV of one partner in a relationship does not indicate infidelity in either partner as the virus is usually asymptomatic and there is a considerable lag time between the time of infection and the time of wart formation; it is impossible to determine at what point and from whom the patient acquired the HPV; it is not life-threatening and only in rare and unusual cases leads to cancer; it does not affect a woman's fertility or ability to carry a pregnancy to term; the treatments available can eliminate the wart, but not the virus itself; and it is unknown how long a person remains contagious.

Malignancies

Pruritus can be a presenting symptom of vulvar intraepithelial neoplasia (VIN), which can be HPV or non-HPV associated. They can appear as raised white papules or plaques, but can be red, pink brown, or gray. Typically they are asymptomatic and a biopsy of the lesion is recommended to rule out any high-grade lesions. Advanced cervical intraepithelial lesions can present with vaginal discharge and can mimic cervicitis with friability. A serosanguinous vaginal discharge with or without odor can be present with malignancies in the upper genital tract, such as the endometrium and fallopian tubes. In these cases the usual workup with history, physical, and laboratory evaluation above will rule out these common conditions and often suggests an alternate diagnosis.

Social Issues

Approximately 25–40 % of patients with vulvovaginal complaints will have no identifiable cause after the initial office evaluation, including the history and physical and laboratory studies described above. Getting more detail of history including sexual practices, use of hygienic products, and the timing of or associated symptoms or having the patient refrain from any use of products in the genital area and return for another full exam can be helpful. All of these patients should have cultures or NAAT specimens sent for STDs, including trichomoniasis and possibly *Candida* (if the history and exam support this diagnosis) as not all of these cases will be identified with the use of microscopy.

Vulvovaginitis and cervicitis can be a very sensitive subject for many patients not only because of the vulnerable nature of the examination but can bring up many personal relationship

issues: How did they get this condition? And from whom? Is their partner to blame or at risk? What did they do to contribute to the acquisition and how can they avoid it in the future? The physician should understand the sensitive nature of these concerns and anticipate these questions or concerns, realizing some patients may be too uncomfortable to raise the questions at the office visit. Explanations should be given regarding the nature of transmission, any contributing factors, and the importance of compliance and partner treatment when applicable. Patients should be discouraged from douching as this alters the vaginal flora and can contribute to the condition and the patient's symptoms. Use of condoms and limiting the number of sexual partners through monogamous long-term relationships can reduce the patient's exposure to and risk of acquiring these types of conditions. Providing written information or resources for the patient to access is very beneficial in directing them to reliable sites for further information.

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