Review Article

Vulvovaginitis in adolescents

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Abstract: Inflammation of the vulva and vagina, called vulvovaginitis, is one of the more common genitourinary complaints encountered in the general practice setting among adolescent females. Classic symptoms of vulvar pruritus, burning and irritation, with or without the presence of vaginal discharge may be non-specific to causative infectious etiologies that include non-specific vulvovaginitis, bacterial vaginosis (BV), *Trichomonas vaginalis*, and candidiasis. Specific recommended diagnostic and therapeutic interventions are described. While most of the infections may be acquired sexually, treatment of sexual partners may or may not be indicated in all of cases. However, regular and systematic surveillance through universal screening is essential to prevent complications and spread of infection. This article reviews aspects of vulvovaginitis in adolescents that are of direct relevance in medical practice.

Keywords: Vulvovaginitis; bacterial vaginosis (BV); *Trichomonas vaginalis*; *Chlamydia trachomatis*; Neisseria gonorrhea; candidiasis

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Introduction

Vulvovaginitis is a common infection among adolescent and young adult women, characterized clinically by vulvar pruritus, irritation and burning, and vaginal discharge (1). Approximately three fourths of women experience vulvovaginitis during their lifetime and many of them have experienced their first infection during adolescence. There are different etiologic causes of vulvovaginitis but the most common causes in adolescents are yeast, bacterial vaginosis (BV), and trichomonas, especially in the presence of a higher rate of sexual activity in this population (2). The interplay of the vaginal pH, the thickness of the vaginal mucosal layer, and the constituency of the microbiome that inhabit the vaginal wall impact susceptibility of adolescents to vulvovaginitis (3-6). Adolescents with disabilities and pregnant adolescents are at a higher risk for vulvovaginal infections.

Pathophysiology of susceptibility to vulvovaginal infections in adolescent females

Pubertal changes in the vulvovaginal region are heralded by the maturation of the adrenal and gonadal organ system (3). Prior to puberty, the labial walls of the vagina are thin and non-stratified with the absence of vaginal secretions; very little labial fat pads and pubic hair exist, and the normal vaginal flora does not yet include lactobacilli (considered "healthy" bacteria) (1,3). Hence, the prepubertal vagina has hardly any physical protection from external irritants. In addition, the vulvar and vaginal mucosa are tender and more sensitive to chemical irritants and trauma. A combination of these factors, along with the anatomical proximity of the anal canal to the vaginal vault in females, make nonspecific vaginitis a common diagnosis during pre-pubertal years (6). Nonspecific vaginitis occurs due to irritation of un-estrogenized epithelium and vaginal cultures are generally

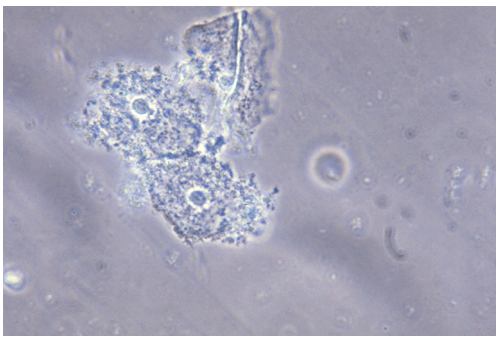

Figure 1 Clue cells. This photomicrograph reveals bacteria that had adhered to vaginal epithelial cells, known as clue cells, obscuring their borders, and displaying a stippled appearance. The presence of these clue cells is one of the signs that the patient has bacterial vaginosis. Credit: Centers for Disease Control and Prevention (https://phil.cdc.gov/Details.aspx?pid=3719).

negative for any pathogen (2).

During puberty, subcutaneous fat is deposited in the labial folds while the vulvar epithelium increases in thickness (3). The accumulation of adipose tissue in the labia majora and mons pubis leads to increased fullness, which then helps protect the vaginal vault from external irritants and fecal contaminants (3). At the same time, pubic hair development on the mons pubis provide an additional layer of protection.

Prior to onset of puberty, the mucosal epithelium of the vagina maintains a neutral or slightly alkaline pH (<4.5), is thin, appears red, and consists of two cell layers—the basal layer and the parabasal layer (3-6). As the estrogen levels increase during puberty, the mucosal layer of the vaginal vestibule increases in thickness (3). With further exposure to estrogen during puberty, the vaginal mucosal epithelium develops intermediate and superficial layers that become stratified, thicker, and appear light pink (4). As the genital mucosa thickens, it becomes colonized by normal flora, which include lactobacilli, diphtheroids and *Staphylococcus epidermidis* (2). Estrogen stimulation of the superficial layer of mucosal epithelium also causes an increase in glycogen concentration. This increased glycogen concentration is essential in allowing lactobacilli to colonize the vaginal mucosa. Lactobacilli metabolize glycogen to produce lactic acid and hydrogen peroxide (H_2O_2), which contributes to the acidity of the vaginal pH (4). The colonization of vagina by lactobacilli protect against overgrowth of other pathogenic organisms and the acidic pH protects against growth of these organisms. The post-pubertal estrogenized vagina, with its thicker stratified epithelia, increased glycogen content, and acidic pH protects against infection (5). During the menstrual cycle, the morphology of the mature vulva, the thickened vaginal epithelium and the production of cervicovaginal secretions maintain the acidic pH of the vagina that further lends resistance to invasion by pathogenic organisms (5,6).

A condition known as adolescent vulvovaginitis commonly manifest as vaginal discharge that is clear to whitish, without odor and can be chronic (2). No bacterial pathogens are typically isolated and vaginal pH may be less than 4.5. No treatment is required other than reassurance and avoidance of usual irritants like harsh soaps, scented feminine products and douches.

BV

BV is common in adolescents with a prevalence rate of 23% between the ages of 14 and 19 years (7). BV develops when multiple different pathogens infect the vagina resulting in a significant decrease in the number of lactobacilli colonizing the mucosal epithelium. With a reduction in lactobacilli, facultative anaerobic organisms colonize the mucosal epithelium. These facultative or invasive anaerobes include gram-negative bacteria, (such as *Prevotella* species, *Mobiluncus* species), *Gardnerella vaginalis*, *Mycoplasma hominis*, Bacteroides species, Peptostreptococcus, Fusobacterium species, *Atopobium vaginae*, and *Ureaplasma* (2). The increase in vaginal pH allows facultative anaerobes, specifically Gardnerella to adhere better to the mucosa and produce a biofilm that further enhances adhesion of other pathogens to the mucosa (8). While BV is not considered a true sexually transmitted infection (STI), it is reported more commonly in sexually active females as supported by the detection of Gardnerella from cultures of the urethra and penile skin of male partners of women with BV and the high rate of vaginal bacterial concordance in women who have sex with women (9,10). Risk factors that predispose to BV include: Black or Hispanic ethnicity, use of douches, smoking, multiple sex partners, non-use of condoms and sex with women (11).

Adolescent females with BV often present with whitish to gray vaginal discharge often with a malodorous "fishy" smell. Visual inspection of the vaginal vault shows none to mild erythema of the mucosa. Diagnosis is made by meeting three out of the four Amsel criteria: (I) pH >4.5, (II) thin homogenous discharge, (III) fishy odor after application of 10% potassium hydroxide

Table 1 CDC recommended treatment for bacterial vaginosis

Primary choices (choose one)
Oral metronidazole. 500 mg twice daily for 7 days
0.75% metronidazole gel, one applicator intravaginally every night for 5 nights
2% clindamycin vaginal cream: one applicator intravaginally every night for 7 nights
Alternate treatments (choose one)
Oral tinidazole, 2 g/day for 2 days
Oral tinidazole, 1 g/day for 5 days
Oral clindamycin 300 mg twice daily for 7 days
Clindamycin 100 mg ovules, intravaginally each night for 3 nights

CDC, Centers for Disease Control and Prevention.

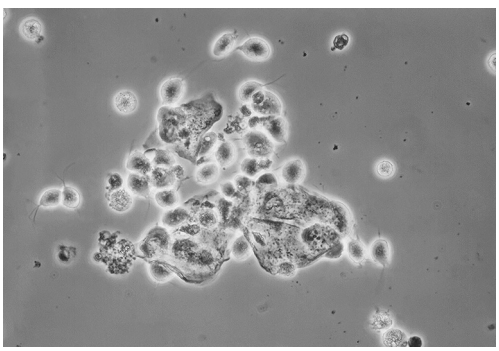

Figure 2 *Trichomonas vaginalis*. This photomicrograph of a wet-mounted vaginal discharge specimen, revealed numbers of *Trichomonas vaginalis* protozoan parasites, leading to a diagnosis of trichomoniasis, which is a very common sexually transmitted disease (STD) caused by the protozoan, *T. vaginalis*. Although symptoms of the disease vary, most women and men, who harbor the parasite, are unaware that they are infected. Credit: Centers for Disease Control and Prevention (https://phil.cdc.gov/Details.aspx?pid=14500).

solution on the slide smeared with vaginal fluid, and (IV) 20% or more "clue cells" on saline microscopy (*Figure 1*) (1,11,12). The standard for diagnosis is a positive finding on Gram stain (1,11,12). Based on the Gram stain the relative concentration of lactobacilli, Gram-negative and Gram-variable rods and cocci, and curved Gram-negative rods, which are characteristic of BV, is determined (1,11-14).

BV can be associated with the development of pelvic inflammatory disease (PID), and predispose adolescents to acquire other STIs (13,14). BV may contribute to preterm labor and late miscarriages in pregnant adolescents by facilitation of other STIs (15). A meta-analysis reported positive correlation between BV and cervical human papillomavirus (HPV) infection, which could raise the question that BV may indirectly increase the risk for development of cervical dysplasia later in life (16).

Current treatment recommendations by the Centers for Disease Control and Prevention (CDC) are listed in *Table 1* (12). Recurrent BV is common with documented rates between 30% and 50% and treatment recommendations are not universal (2,11). The CDC recommends that infrequent recurrences can follow the same treatment guidelines as in *Table 1*. However, longer duration treatment with metronidazole or clindamycin intravaginally for monthly recurrences have been studied with good results (11). Partner treatment has not been shown to have beneficial effect on preventing recurrences (2).

Trichomoniasis

Caused by a flagellated, protozoa, *Trichomonas vaginalis* (*Figure 2*), trichomoniasis has a prevalence rate of about 2.3% in the adolescents but can be as high as 14.4% in certain high-risk female adolescent population (17). It is known to infect the squamous epithelium of the genital tract and transmission is typically through sexual contact (1). Co-infection with BV is reported at 60–80% with a 2–3-fold enhanced acquisition of HIV infection (16). Trichomonas infection is difficult to detect because 70–85% of cases are asymptomatic (1,17,18). Adolescent females with symptoms present with frothy, profuse, malodorous vaginal discharge accompanied by pruritus, with or without abdominal pain and significant irritation. Under vaginal speculum examination, the vaginal mucosa displays a "strawberry-like" appearance of the cervix (*Figure 3*) due to the presence of punctuate intraepithelial hemorrhages (1,12).

The standard for laboratory diagnosis is the nucleic acid amplification test (NAAT) of vaginal, endocervical and urine specimen with sensitivity and specificity in the high 90's range; the turnaround time for NAAT test can be a day or two depending on the laboratory turnaround time (12). A practical method of diagnosis consists of microscopic examination of a saline vaginal wet prep to observe the presence of motile, flagellated trichomonads; however, the accuracy of this method is highly dependent on clinician skill and experience, and absence of trichomonads does not necessarily rule of the diagnosis (17). The use of other

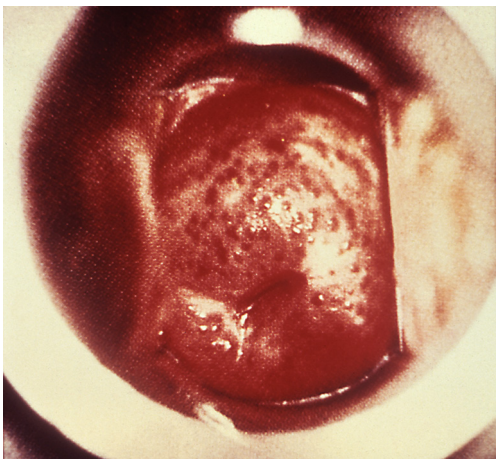

Figure 3 Strawberry like appearance of cervix. This image depicts an intravaginal colposcopic view of a female patient, revealing what is referred to as a strawberry cervix, due to a *Trichomonas vaginalis* infection, or trichomoniasis. The term strawberry cervix is used to describe the appearance of the cervix due to the presence of *T. vaginalis* protozoa. The cervical mucosa reveals punctate hemorrhages, along with accompanying vesicles or papules. Credit: Centers for Disease Control and Prevention (https://phil.cdc.gov/Details.aspx?pid=5240).

commercially available tests like the OSOM Trichomonas Rapid Antigen test (Sekisui Diagnostics, Framingham, MA, USA) has demonstrated some utility in the emergency room setting for quicker turnaround time (usually 10 minutes) (17). Trichomoniasis can increase the risk of low birth weight and preterm delivery; it is also associated with an enhanced transmission of HIV infection (17,18). Risk factors for trichomonas infection in adolescent females include: marijuana use, sexual partner 5 years or older than her, sex with non-steady partners and delinquency (19).

Treatment of trichomonal infection requires a single oral dose of either metronidazole, 2 grams or tinidazole, 2 grams; alternative therapy includes: metronidazole 500 mg orally twice daily for 7 days (1,12). Partner treatment is highly recommended (2). Metronidazole topical gel is not effective for treatment of trichomonas infection. There is a high rate of reinfection, with trichomonas recurrence rates reported at 17% (2). While antimicrobial resistance is a concern, it is low (18). Recurrent trichomonas infection can be managed with metronidazole 500 mg twice daily for 7 days and if this regimen fails, the use of either metronidazole or tinidazole, 2 g daily for 7 days may be considered (2,12).

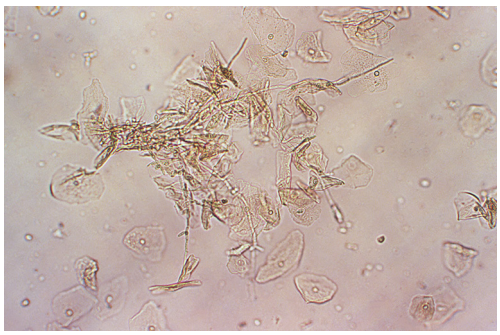

Figure 4 *Candida albicans*. This photomicrograph of a wet mounted vaginal smear specimen, revealed the presence of *Candida albicans* fungal organisms, which had been extracted from a patient with a case of vaginal candidiasis, also known as moniliasis. Credit: Centers for Disease Control and Prevention (https://phil.cdc.gov/Details.aspx?pid=15675).

Vulvovaginal candidiasis

The exact prevalence of vulvovaginal candidiasis is not known but studies have reported prevalence rates between 20% and 75% (20). The overall estimate is that three-fourths of women will experience at least 1 vulvovaginal candidiasis in their lifetime; however, the incidence is likely much higher because many women tend to self-treat vaginal yeast infection and do not seek medical care (2). Most vulvovaginal yeast infections are due to *Candida albicans* but recurrent episodes can be attributed to *Candida glabrata* (19). Risk factors that predispose to yeast infection include: use of broad-spectrum antibiotic therapy, use of feminine hygiene products along with tight-fitting clothing and depressed immunity, especially in adolescents who have HIV or diabetes mellitus (20). Any form of immunodeficiency state can increase the risk for recurrent infections. The pathophysiologic mechanism involved in vulvovaginal candidiasis points to the role of estrogen in enhancing the epithelial adherence of Candida species (2).

Patients with vulvovaginal candidiasis present with complaints of intense itching, maybe dysuria along with the presence of a thick, white "curd-like" vaginal discharge (2). On visual examination of the external genitalia, erythema, edema and excoriations may be evident on the vulva. Vaginal pH is normal and microscopic examination of the vaginal discharge set on a wet prep with potassium hydroxide (KOH) that shows the presence of budding yeast hyphae and pseudohyphae (*Figure 4*). The sensitivity of microscopic examination to detect yeast is about 50% (1,2). Vaginal

culture is not indicated unless recurrent infections (defined as >4 infections within 1 year) are evident (2). Treatment regimen consists of 1 single dose of oral fluconazole 150 mg but topical therapy utilizing over-the-counter vaginal creams from 1 to 7 days can have an efficacy of up to 90% (1,12).

Vulvovaginal candidiasis can recur, and if the culture show *Candida albicans* as the primary organism, initial intensive therapy for 1–2 weeks followed by weekly fluconazole for 6 months may be considered (1). However, non-*Candida albicans* species are shown to be resistant to fluconazole and may require treatment of these cases with topical imidazole or vaginal boric acid capsules or topical amphotericin B (1,2). In adolescents with recurrent infections, it is prudent to consider further diagnostic evaluation to rule out HIV infection, diabetes mellitus and other states of immune deficiencies for refractory vulvovaginal candidiasis. Sexual partners of patients with recurrent disease should be examined for active infection and treated when indicated. Empiric treatment of partners is not recommended since vulvovaginal candidiasis is not considered a STI (1).

Special vulnerable adolescents

Pregnant adolescents

In the United States, each year, 50% of new cases of STIs are reported in adolescent females 15–24 years of age (21,22). In a population study done by Akoh and Pressman (2017), the three most prevalent infections identified as recto-vaginal colonization of pregnant adolescents were *Group B Streptococcus* (GBS), BV and candida (22). These maternal infections during pregnancy with neonatal transmission during labor and delivery have been associated with adverse health outcomes for the neonates such as prematurity, low birth weight, pulmonary and eye infections (22). CDC has recommended universal screening of all pregnant females for chlamydia, hepatitis B, HIV, and syphilis and those who meet criteria for high risk should also be screened for gonorrhea and hepatitis C (12). Rectovaginal screening for GBS colonization is also indicated for all pregnant women between 35 and37 weeks of gestation (22).

The overall prevalence of STIs is higher among young women including teens. The Akoh and Pressman study (2017) identified younger maternal age as a risk factor for *Neisseria gonorrhea* and trichomonas infections, which they attributed to high-risk sexual behaviors at much younger ages among pregnant adolescent females (22). Other risk factors for infections and inflammatory conditions across pregnancy included African-American race, higher pre-pregnancy body mass index (BMI), younger age at diagnosis and low dietary intake of fat-soluble vitamins A and D (22).

Bacterial vulvovaginitis, of which GBS is a primary causative organism in pregnant adolescents may be asymptomatic; symptomatic females present with vaginal discharge accompanied by erythema, discomfort and burning of the vulvar area (1). Management entails the use of antibiotics based on antibiotic susceptibilities. When there is a high index of suspicion for a GBS infection while awaiting culture results, a broad-spectrum antibiotic with aerobic and anaerobic coverage may be started (1). Women are not routinely screened for BV during pregnancy in spite of the growing evidence linking BV to adverse birth outcomes (15).

Adolescents with cognitive limitations and behavioral concerns

There are subsets of adolescent youth that are known to be at high risk to develop sexual behaviors that range from having unprotected sex with a single partner to engaging with multiple partners to trading sex are often neglected in generalized population studies. These adolescents include those who come from foster care, are victims of maltreatment, runaways, or homeless who have experienced sexual abuse, substance abuse or engaged in delinquent activities (23). Likewise, investigational research on adolescents with developmental or learning disabilities and STIs is limited; one study has shown that adolescents with learning disabilities are at similar or even greater risk for contracting STIs as other youth (24). Majority of the studies are on adolescent females who are sex trade workers, which show the predominance of trichomonas infection, which can be a gateway for other STIs (25,26). It is therefore recommended to evaluate this subset of adolescents for other STIs.

Conclusions

Vulvovaginitis in the adolescent population is a prevalent condition that stems from multiple etiologies. Vulvovaginal infections are generally characterized by vaginal discharge and the most common infections are BV, trichomoniasis, and candidiasis. Since STIs are common and can lead to complications of miscarriage, premature birth, low

birthweight and infertility if untreated, universal annual screening of asymptomatic adolescent females in primary care medical practices is strongly advocated. The treatment of sexual partners is found to be beneficial in cases of STIs, and trichomonas infections but unequivocal for cases of BV and candidiasis. Research on STIs in general and vulvovaginitis in particular in more vulnerable adolescents (such as pregnant adolescents and adolescents who have cognitive limitations) is limited.

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Footnote

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