



Sexually transmitted infections of the anus and rectum

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Abstract

Sexually transmitted infections (STIs) represent a significant public health concern. Several STIs, once thought to be on the verge of extinction, have recently reemerged. This change is thought to be partially related to an increase in STIs of the anus and rectum. Importantly, the global human immunodeficiency virus and acquired immunodeficiency syndrome (HIV/AIDS) epidemic has contributed to the emergence of particular anorectal lesions that require specialized approaches. In this report, we review common anorectal STIs that are frequently referred to colorectal surgeons in the United States. Epidemiology, clinical presentation, and management are summarized, including the latest treatment recommendations. The particularity of anorectal diseases in HIV/AIDS is addressed, along with recent trends in anal cytology and human papillomavirus vaccination.

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Key words: Sexually transmitted disease; Rectal disease; Sexual behavior; Human papillomavirus; Human immunodeficiency virus; Perianal disease; Highly active antiretroviral therapy; Human papilloma virus vaccines;

Anal cytology

Core tip: Anorectal sexually transmitted infections constitute a group of emerging diseases not well recognized by the medical community. An understanding of recent trends in sexual behavior and the epidemiology of sexually transmitted infections is critical to identifying populations at risk. Our scientific review summarizes important characteristics of the most common sexually transmitted infections of the anus and rectum, in addition to the latest recommendations in diagnosis and management. This review also addresses the particularity of anorectal diseases in human immunodeficiency virus and acquired immunodeficiency syndrome and recent trends in anal cytology and human papillomavirus vaccination.

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INTRODUCTION

Sexually transmitted infections (STIs) are a substantial health concern, with an estimated worldwide incidence of 333 million cases per year^[1]. In the United States (US), the annual incidence reaches approximately 15 million cases^[2]. Anorectal involvement is common, although the exact prevalence remains unknown due to numerous asymptomatic infections and a lack of accurate epidemiologic data. Patients with anorectal symptoms or lesions are often referred to colorectal surgeons for complete evaluation or management. This article reviews STIs of the anus and rectum, examining their epidemiology, presentation, and management.

Anorectal STIs are commonly the result of anal receptive intercourse but may also be due to contiguous spread from a genital infection. The incidence of

anorectal STIs has risen in recent years, a trend primarily attributed to an increase in the practice of anal receptive intercourse^[3]. Although traditionally associated with homosexual men, anal receptive intercourse is in fact more practiced among heterosexual couples in absolute numbers, showing wide geographical, ethnical and cultural variability^[4].

Symptoms of STIs are often nonspecific and latent, making diagnoses challenging. In one study among men who have sex with men (MSM), routine screening found that 85% of rectal infections with chlamydia or gonorrhoea were asymptomatic^[5]. Common complaints of anorectal STIs include anal pain, tenesmus, urgency, purulent drainage, and bleeding. Common lesions include ulcerations, vegetations, and clinical proctitis^[1]. Transmission may occur through a variety of sexual practices, such as receptive anal intercourse and oro-anal sexual contact.

When evaluating a patient with an anorectal STI, it is important to remember that coinfection is common and has been reported to be as high as 41% in some high risk populations^[6]. In addition, human immunodeficiency virus (HIV) transmission is facilitated by virtually any STI, whether in the presence or absence of ulcerative lesions^[7-10]. This fact has major implications since coinfection has been shown to alter the natural history of HIV and the response to treatment^[11]. For example, the presence of gonococcal infection increases the infectiousness of HIV, a pattern that reverses following successful gonorrhoea treatment^[12]. Similarly, syphilis is associated with a decrease in CD4 cell counts and an increase in HIV viral load, which both improve after treatment for syphilis^[13].

Two clinical entities can be distinguished based on anatomical involvement and common causative agents: distal proctitis and proctocolitis. Typical organisms in distal proctitis include *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Treponema pallidum*, and Herpes simplex virus. In proctocolitis, organisms associated with food or water-borne diseases are more common and include *Entamoeba histolytica*, *Campylobacter* spp., *Salmonella* spp., *Shigella* spp., *Cryptosporidium* spp., and Cytomegalovirus (CMV)^[14].

HERPES SIMPLEX VIRUS

Epidemiology and presentation

Herpes simplex virus (HSV) is a highly prevalent STI in the US. Forty-five million Americans are infected with HSV type 2, the causative agent of anogenital herpetic infection, with one million new infections occurring each year^[2]. HSV type 1, the causative agent of oral and ocular lesions, is implicated in up to 30% of anogenital lesions, a proportion that appears to be on the rise, reported at 78% in one study among US college students^[15]. This trend may have important clinical implications, as HSV type 1 produces less symptomatic recurrences and less viral shedding than HSV type 2^[16].

When compared to non-HSV proctitis, HSV proctitis is more commonly associated with the symptoms of anorectal pain, constipation, tenesmus, anal pruritus,

difficulty in initiating micturition, sacral paresthesias, posterior thigh pain, fever, and inguinal adenopathy^[17]. Typical lesions are small vesicles that eventually ulcerate and resolve over a few days. They involve the perianal skin and anal canal but may also extend to the rectum^[18]. Proctoscopy is painful and reveals friable rectal mucosa with multiple erosions or ulcers in the distal rectum. Occasionally, a large solitary ulcer is seen^[14].

Management

Diagnosis is confirmed by cell culture or by the detection of viral DNA with polymerase chain reaction (PCR) (the latter providing greater sensitivity). Cytopathologic tests (*e.g.*, Tzanck preparation, Pap smears) are an insensitive and nonspecific method of diagnosis and therefore should not be relied upon^[19].

Treatment is with acyclovir, famciclovir, or valacyclovir for 7 to 10 d^[19].

HUMAN PAPILLOMAVIRUS

Epidemiology and presentation

Human papillomavirus (HPV) is the most common STI in the US, with estimates indicating 5.5 million new infections occur every year^[2]. The incidence has increased since the mid-1960s, and HPV now accounts for one million patient presentations to colorectal surgeons each year, the highest among STIs^[20]. The typical lesion is the condyloma acuminatum. Over 120 HPV serotypes have been identified^[21]. Serotypes 6 and 11 are found in benign warts, while serotypes 16 and 18 are more commonly seen in dysplasia and malignancies^[22]. Anal HPV disease is linked to the immunosuppression caused by HIV infection and is associated with the practice of anal-receptive intercourse. Of note, infection may also result from autoinoculation of vulvar warts to the perianal skin^[23]. The use of condoms lowers the risk of sexual transmission, although infection remains possible due to skin beyond the area covered by a condom^[24].

Symptoms include the presence of raised lesions, rectal bleeding or discharge, pain, pruritus ani, and difficulty maintaining hygiene. Diagnosis centers on physical examination and the presence of gray or pink fleshy cauliflower-like growths in the perianal region^[25]. Anoscopy can reveal extension of the disease into the anal canal. Buschke-Lewenstein disease is a tumorous form of the disease that results in a giant condyloma^[26].

Management

Diagnosis can be confirmed histologically from a biopsy sample. Clinicians should maintain a high index of suspicion for malignancy in certain groups: immunocompromised patients, patients older than 40 year, those exhibiting large, atypical or pigmented lesions, and patients with lesions that are refractory to treatment^[21].

Various treatment approaches exist for condyloma removal. Tangential excision, cryotherapy, and fulguration of small lesions can be performed in an outpatient set-

ting under local anesthesia. Larger or multiple lesions may necessitate regional or general anesthesia. Overall condyloma clearance rates for surgical techniques range from 60%-90%, with recurrence rates of 20%-30%^[25]. Alternatively, patients can apply a variety of topical agents to the perianal area (not approved for use in the anal canal). Podophyllin application does not require anesthesia but is irritating, associated with potential systemic toxicity, and may not lead to complete resolution. Dichloroacetic acid application is less irritating than podophyllin, but recurrence rates, as with podophyllin, remain higher than surgery. Imiquimod, an immune response modifier that increases the local production of interferon, is used with electrodesiccation for patients who have incomplete responses or following destructive treatment and epithelial healing in the treatment of remaining disease or decrease recurrence. Intramuscular or intralesional interferon-beta injections have been used with mixed results and have been associated with a systemic flu-like syndrome^[20,25].

GONORRHEA

Epidemiology and presentation

Gonorrhea, caused by the gram-negative diplococcus *Neisseria gonorrhoea*, has seen resurgence in recent years. Between 1997 and 1999, cases of gonorrhea increased by more than 9% after a 72% decline from 1975 to 1997. An increase in drug-resistant gonorrhea has been seen in Hawaii and in small clusters in other states^[27]. Anorectal transmission is by anal receptive intercourse with an infected partner. Thirty-five to fifty percent of women with gonococcal cervicitis will have a concomitant rectal infection, which is believed to result from contiguous spread from the genital infection^[25].

Rectal gonorrhea is often latent. In a study of MSM who were found to have rectal gonorrhea on routine screening, 84% were asymptomatic^[5]. The incubation period lasts 5 to 10 d, after which symptoms may include pruritus ani, constipation, mucopurulent or bloody anal discharge, pain, and tenesmus^[18]. On physical examination, rectal mucosa can range from normal-appearing to erythematous and friable with pus^[14].

Management

A diagnosis on smear is positive when gram-negative diplococci are identified within the cytoplasm of neutrophilic granulocytes. The gold standard for diagnosis, however, remains culture from a swab through the anal canal^[14]. PCR technique is licensed for the detection of urogenital disease but not for rectal (or pharyngeal) disease^[28].

Treatment is directed towards both gonorrhea and chlamydia, even if chlamydia testing returns negative. The recommended regimen is ceftriaxone 250 mg in a single intramuscular dose plus azithromycin 1 g orally in a single dose, or doxycycline 100 mg orally twice daily for 7 d^[19]. Of note, oral cephalosporins are no longer recommended due to a recently observed decreased susceptibility in the US and Europe^[29].

CHLAMYDIA

Epidemiology and presentation

Chlamydia has an estimated annual incidence in the US of 3 million cases^[2]. In a study of MSM who underwent routine screening, 53.5% of chlamydial infections were limited to the rectum^[5]. Both anal receptive intercourse and oro-anal intercourse have been implicated as causative behaviors.

Chlamydia trachomatis (*C. trachomatis*), an obligate intracellular bacterium, is the causative agent of two clinical entities caused by different serotypes. *C. trachomatis* serotypes D-K [non-lymphogranuloma venereum (LGV) strains] can cause a mild form of proctitis with minimal symptoms (tenesmus, pain, discharge) following an incubation period of 5 to 14 d; however, infections are more commonly asymptomatic. On physical examination, the rectal mucosa can range from normal-appearing to erythematous and friable^[14,25]. *C. trachomatis* serotypes L1, L2, and L3 are responsible for a different clinical entity, LGV. In contrast to serotypes D-K, LGV produces a more aggressive proctitis with anal, perianal or rectal ulcerations, purulent or sanguineous anal discharge, tenesmus, and lower abdominal cramping or pain^[14,25]. Patients may also present with perirectal abscesses, anal fissures, and fistula formation^[30]. This clinical entity can mimic Crohn's disease because of the occurrence of chronic diarrhea and perianal fistula formation^[31].

Management

A rectal swab can be obtained and tested with PCR techniques (although not yet Food and Drug Administration-approved) with better sensitivity and specificity than culture^[19]. Positive serologic testing can support the diagnosis^[14]. For LGV strains, rectal biopsy reveals crypt abscesses, granulomas, and giant cells, mimicking Crohn's disease^[32]. Unlike non-LGV types, no asymptomatic carriers of LGV exist in male homosexuals^[33].

Recommended treatment for non-LGV disease is with azithromycin 1 g orally in a single dose or doxycycline 100 mg orally twice a day for 7 d. Recommended treatment for LGV disease is doxycycline 100 mg orally twice a day for 21 d^[19].

SYPHILIS

Epidemiology and presentation

In the year 2000, the incidence of syphilis in the US reached an all-time low. However, between 2006 and 2007, the rate of primary and secondary syphilis increased by 15.2%. This rise has been more closely tied to men than women (a male to female ratio of 6 compared to 1 a decade before), suggesting that increases in men have largely been among MSM^[34]. Since 2009, the overall rate of syphilis decreased for the first time in a decade, and was down 1.6% in 2010^[35].

The disease is classically divided into 3 stages: primary (associated with a chancre or proctitis), secondary (associ-

ated with condyloma lata, skin rashes, or lymphadenopathy), or tertiary (associated with cardiac or gummatous lesions). The primary stage of anorectal syphilis appears within 2-10 wk of exposure *via* anal intercourse. Infections can be asymptomatic or manifest with proctitis, ulcers, and pseudotumours. Anal ulcers are frequently painful, in contrast to genital ulcers. Untreated lesions usually heal within several weeks^[14,19,25]. Secondary syphilis may present with a rectal mass, condylomata lata and mucous patches, generalized rash, fever and/or lymphadenopathy. Symptoms will typically resolve without treatment after 3-12 wk^[25]. Tertiary syphilis presents many years later, commonly with debilitating ulcerating gummas^[14].

Management

Diagnosis is based on direct visualization of *Treponema pallidum* spirochetes on dark-field microscopy. This test is of notable value in HIV-positive patients, as serologic tests are more likely to yield false negative results^[1]. A presumptive diagnosis of syphilis is possible with the use of two types of serologic tests: nontreponemal tests (*e.g.*, Venereal Disease Research Laboratory and Rapid Plasma Reagin) and treponemal tests [*e.g.*, fluorescent treponemal antibody absorbed tests, the *T. pallidum* passive particle agglutination assay, various enzyme immunoassays, and chemiluminescence immunoassays]^[19]. DNA PCR identification is possible from biopsies or ulcer exudates^[14].

Recommended treatment in adults with primary or secondary syphilis is with benzathine penicillin G 2.4 million units administered intramuscularly in a single dose. Doxycycline, tetracycline, and possibly ceftriaxone can be used in patients with penicillin allergy. Pregnant women should be treated only with penicillin (allergic patients should first be desensitized)^[19].

PERIANAL DISEASE IN HIV-POSITIVE PATIENTS

Common perianal disease

Anorectal disease is the most frequent reason for surgical referral of HIV-positive patients^[36]. In one retrospective review of HIV-positive/acquired immunodeficiency syndrome (AIDS) patients prior to the advent of highly active antiretroviral therapy (HAART), anorectal disease was found in 34% of patients^[37]. The most common symptoms are anorectal pain, the presence of a mass, and blood in the stool. Risk factors include homosexuality and prior history of STI^[38]. Characteristic lesions include condylomas, ulcers, hemorrhoids, fistulas, fissures, abscesses, and neoplasms. Except for hemorrhoids and fissures, these lesions are more common among HIV-positive patients than HIV-negative patients^[39]. Two or more disorders are found in 16.7% to 66% of patients^[38,39], with an average reported number of disorders per patient of 2.9^[38]. It has been established that AIDS status and CD4⁺ cell count affect post-surgical wound healing. In a prospective study of post-hemorrhoidecto-

my wound healing, all HIV-negative patients were healed at 14 wk, compared to only 66% of HIV-positive patients at that time. Furthermore, at 32 wk, while all HIV-positive patients were healed, half of AIDS patients still suffered from incompletely healed wounds. Complication rates were also higher among HIV-positive and AIDS patients^[40]. With the widespread use of HAART, it is believed that compensated HIV-positive patients are no longer at a significantly elevated risk of complications from anorectal surgery^[25].

HIV-related anorectal infections

In contrast to the common perianal disease described above, certain disorders are specifically associated with HIV.

Idiopathic anal ulcers constitute a diagnosis of exclusion after ruling out HSV, CMV, *Mycobacterium Avium* Complex (MAC), gonorrhea, chlamydia, syphilis, fungus, and cancer on repeated biopsies^[23]. Clinical characteristics include a broad base appearance, localization to the posterior midline and more proximally in the anal canal, erosion into the submucosa and sphincters, and diminished anal sphincter tone. Treatment centers on intralesional steroid injection or surgical debridement^[41], with the latter allowing for appropriate culture specimens for diagnosis. Interestingly, among all perianal ulcers in HIV-positive patients, poor healing is most closely associated with idiopathic ulcers or ulcers with a positive culture for HIV^[42].

CMV serology is found in more than 95% of HIV-positive patients, compared to 34% in the general population. Infection becomes clinically significant when the CD4⁺ cell count falls below 100 cells/mm³. Common presentations include ileocolitis and toxic megacolon. Antiviral treatment is recommended and often required for the patient's lifespan^[23].

MAC infection, very common among AIDS patients and associated with poor survival, can manifest with colorectal involvement and resultant watery diarrhea and dehydration^[15]. Recommended treatment is with at least two pharmaceuticals, usually clarithromycin and ethambutol^[43].

Anal intraepithelial neoplasia (AIN) is associated with HPV serotypes 16, 18, and 31. The neoplastic progression of the disease is believed to be similar to that of cervical cancer secondary to HPV. The absence of a history of anal receptive intercourse does not preclude AIN, and a high prevalence exists among HIV-positive males with CD4⁺ cell counts below 500 cells/mm³^[44]. Also, it is important to note that immune restoration with HAART has not been shown to decrease the risk of AIN^[45]. Anal cytology may provide screening benefits. Previous cost-effective analyses have demonstrated that anal cytology screening for AIN lesions every 2 or 3 years in HIV-negative MSM and yearly in HIV-positive MSM can enhance life-expectancy outcomes relative to other preventive health measures^[46,47]. Recently, quadrivalent HPV vaccination has been recommended in boys for the prevention of external genital lesions^[48], as well as among

homosexual men for the prevention of AIN^[49].

Kaposi sarcoma

Kaposi sarcoma (KS) is a rare disease associated with infection with human herpes virus 8. In HIV patients, KS is considered an AIDS-defining illness^[50]. Prior to the widespread use of HAART, AIDS patients were 20000 times more likely to develop KS than the general population, and up to 21% of HIV positive MSM had KS^[51]. Contemporary epidemiologic reports show that the incidence of KS has markedly decreased since the introduction of HAART^[52,53]. Anorectal KS presents with characteristic small, round, purple lesions; however, early disease can be easily mistaken for hemorrhoids or other benign lesions^[54]. Diagnosis should be confirmed with biopsy. All patients should be started on HAART, as this can induce rapid regression of the disease. Local therapies are available for localized symptomatic disease or for cosmetic considerations. Intralesional chemotherapy and radiation are associated with lesion regression and effective cosmetic and palliation in the majority of patients^[55-57]. Systemic chemotherapy is reserved for patients with advanced or rapidly progressing disease^[58].

CONCLUSION

STIs of the anorectum are increasingly prevalent in the developed world. Changes in trends include the reemergence of several historical diseases. Anorectal STIs are not isolated to homosexual males, and providers should remain abreast of recent trends in sexual behavior. The early recognition of infection or risk-elevating behavior is critical for the initiation of appropriate screening tests and treatment. Since the introduction of HAART, the survival of HIV-positive patients has significantly improved, but management of anorectal lesions in HIV-positive patients remains problematic. Successful treatment relies on specific medical therapies in addition to surgical interventions for both diagnostic and treatment purposes. Prevention strategies encompass a wide array of interventions, from awareness campaigns to validation of new screening methods and vaccines. Finally, clinicians should always remember that no treatment plan is complete unless it involves both the patient and his or her sexual partners.

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