

A Brief Review of Viral and Bacterial Sexually Transmitted Diseases in Colorectal Practice

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Abstract

Context: Sexually transmitted diseases (STDs) are a common source of presentation to colorectal surgeons. Clinicians need to remain mindful of the possibility of STDs when faced with atypical clinical presentations. This article aims to provide surgeons with a synopsis of common pathogens, their clinical presentations, diagnostic investigations and treatment regimens.

Evidence Acquisition: The most common bacterial pathogens include *Chlamydia trachomatis* and *Neisseria gonorrhoea* with synchronous infections at presentation occurring frequently. Patients often present with proctitis. Gonorrhoea patients can also experience bloody purulent perianal discharge. Less common bacterial pathogens include syphilis, chancroid and donovanosis. The commonest STD worldwide remains human papillomavirus. Given its vast array of subtypes its manifestations include benign hyperproliferative lesions like perianal warts and extend to anal intraepithelial neoplasia and squamous cell carcinoma. Other important viral infections of the anorectum include human immunodeficiency virus and subsequent acquired immune deficiency disease as well as herpes simplex virus and molluscum contagiosum.

Results: Debate exists whether the increasing incidence of STDs affecting the anorectum reported in western literature represents a real increase or a reflection of greater patient and clinician recognition and reporting.

Conclusions: Regardless, a broad understanding of common bacterial and viral pathogens remains important part of modern colorectal practice. Remaining mindful of the manifestations of these common pathogens, options for diagnosis and management are important in disease control to limit the impact of these pathogens across the wider community.

Keywords: Sexually Transmitted Diseases, Colorectal Surgery, Proctitis

1. Context

Sexually transmitted diseases (STDs) frequently manifest with symptoms and signs in the anorectum. Sexually transmitted infective organisms (whether viral or bacterial) are typically transmitted via anal intercourse, but can also represent contiguous spread from the genitals.

The majority of organisms responsible for proctocolitis and enteritis are transmitted via direct or indirect faecal-oral transmission. However, these are typically transmitted through waterborne or contaminated food sources rather than sexual contact. Examples include *Campylobacter*, *Shigella*, *Salmonella*, *Entamoeba histolytica* and hepatitis A.

The true incidence of sexually transmitted diseases of the anorectum remains unclear given their associated stigma. Similarly, reports of increasing incidence may represent improvements in patient reporting associated with education campaigns and clinician recognition (1).

2. Evidence Acquisition

Estimating the rates of anoreceptive intercourse across Western populations is likewise difficult. Rates differ be-

tween populations (increased prevalence amongst North and Latin America as well as parts of South Asia and Africa) and most figures are probably under-reported. It is estimated that 2% - 10% of males will engage in homosexual activity over their lifetime, but only 2% of males will practice regular ano-receptive intercourse. Estimates among heterosexual populations are similarly difficult. Between 5 and 10% of females are estimated to engage in anal intercourse with some regularity and it is thought that this is more likely than men to be unprotected (2).

Clinicians need to be mindful of the possibility of STDs in colorectal clinics as they can present in unusual ways and patients often do not volunteer that they engage in anal intercourse for sexual gratification. Symptoms and signs may include rectal bleeding with or without diarrhea, tenesmus, as well as ulcers and lesions of perianal and perineal skin, as well as anal and rectal canals (3).

3. Results

A logical way of classifying ano-rectal STDs is between viral and bacterial pathogens (Table 1).

3.1. Bacterial

3.1.1. *Chlamydia (Chlamydia trachomatis) and Lymphogranuloma venereum (LGV)*

Chlamydia trachomatis remains the most frequently reported bacterial STD in the western world (4). It is an obligate intracellular bacterium whose clinical manifestations resemble those of gonorrhoea (synchronous infections also occurring with relative frequency). Ano-rectal disease is most commonly transmitted with anoreceptive intercourse, but can also occur with oral-anal transmission or as a late presentation of genital infection.

Chlamydia has an incubation period of 5 to 14 days. Different serovars produce varying clinical manifestations. Serovars D to K (non-LGV) produce cervicitis, pelvic inflammatory disease (PID), urethritis and proctitis (manifested with tenesmus, pain and anal discharge). Asymptomatic infections are also common.

Lymphogranuloma venereum is caused by infections with LGV serotypes L1, L2, L3 (commonly seen in the tropics and in western populations in homosexual HIV positive men) (5, 6). LGV serovars produce more aggressive infections with perianal, anal and rectal ulcers, perianal abscesses and fistulas as well as strictures- these can be difficult to differentiate from Crohn's disease macroscopically and microscopically (including the presence of granulomas and crypt abscesses). Iliac, perirectal and inguinal lymphadenopathy persisting for several weeks is also common.

Diagnosis is by culture, micro-immunofluorescent antibody titres, polymerase chain reaction (PCR) or more recent nucleic acid amplification tests (NAATs- with sensitivity and specificity of greater than 93%) (7). A presumptive diagnosis of *Chlamydia* proctitis is made and treatment commenced (single dose 1g oral azithromycin or 7 days of oral doxycycline 100mg twice daily) if rectal gram stains show polymorphonuclear leucocytes without visible gonococci. Serotyping is slow, costly and not widely available, meaning that when clinical suspicion of LGV in patients with chlamydia exists treatment with doxycycline is extended to 3 weeks. Sexual contacts need to be traced and index cases need to abstain from sexual activity for a week after treatment.

3.1.2. *Gonorrhoea (Neisseria gonorrhoea)*

Neisseria gonorrhoea is a Gram-negative intracellular diplococcus. It is the second most common STD seen in the western world, but is responsible for the majority of STDs affecting the anorectum. Ano-rectal disease is transmitted by anoreceptive intercourse, oral-anal sex or by contiguous spread from the genitals (35% - 50% of women with rectal infection have concomitant cervical infection) (8).

Neisseria gonorrhoea has an incubation period of 3 to 14

days. Clinical syndromes of infection include urethritis, cervicitis, PID, pharyngitis, conjunctivitis, proctitis and the potential for disseminated gonococcal infection (with transient bacteremia, arthritis, dermatitis, pericarditis, endocarditis, meningitis or perihepatitis).

Symptoms of anorectal gonorrhoea include pruritus ani, tenesmus, bloody or mucopurulent perianal discharge and perianal pain. The majority of people with rectal swabs positive for gonorrhoea are asymptomatic (50% of male carriers and 95% of females). Proctoscopy may reveal non-specific proctitis with mucopurulent discharge that can be expressed from anal glands.

The gold standard for diagnosis is best made with culture of mucopurulent discharge (the use of antibacterial lubricants for proctoscopy can reduce diagnostic yield). Although Gram stains lack sensitivity they are highly specific and provide rapid results. NAATs such as PCR have sensitivities of greater than 95% but do not provide important information about antibiotic sensitivities.

Treatment regimens have changed over time with the prevalence of antibiotic resistance and older regimens including penicillin G or quinolones are largely outdated. Single doses of 250 mg intramuscular ceftriaxone will treat most infections pending sensitivity results. It is advised patients be tested and treated for concomitant *Chlamydia*. Sexual contacts for the past 60 days need to be traced and patients should abstain from sexual activity until symptoms resolve. Routine follow-up is not indicated.

3.1.3. *Syphilis (Treponema pallidum)*

Syphilis is caused by the spirochete *Treponema pallidum*. Known as the "great pretender" syphilis can present with varying clinical manifestations and in different progressive stages: primary (chancre or proctitis), secondary (condyloma lata) or tertiary (with involvement of the nervous and vascular systems).

Ano-rectal disease is transmitted with anoreceptive intercourse- with anal ulcers (chancres) marking the primary stage 2 to 10 weeks after exposure. Chancres are single or multiple. They are present in the anus, perianal skin or distal rectum. They are frequently painful 1 - 2 cm raised lesions with clean bases and no exudate, having progressed from small papules that ulcerate. Untreated chancres typically heal after several weeks. Other clinical manifestations of primary syphilis can include proctitis (with tenesmus, rectal discharge and bleeding) (9).

Untreated, haematogenous spread occurs in 4 - 10 weeks leading to secondary syphilis. This is manifested by fever, malaise, arthralgia, weight loss, sore throat, headaches, a maculopapular rash on the trunk and extremities and condyloma lata (gray/white wart like lesions near the primary chancres). Secondary syphilis resolves after 3 to 12 weeks (approximately one-quarter of untreated patients relapse within the first year- latent syphilis).

Tertiary syphilis -marked by the formation of chronic gummas- is rare. Gummas are soft inflammatory masses of varying size surrounded by granulation tissue, located anywhere in the body (including the rectum).

The diagnosis of syphilis can be made with visualization of spirochetes on dark field microscopy from chancre scrapings or lymph node biopsies or with the use of Warthin-Starry silver staining. Serology is useful- non-treponemal tests (Venereal disease research laboratory VRDL and rapid plasma regain RPR) if positive are confirmed with treponemal test (enzyme immunoassay EIA, T. pallidum particle assay TPPA or fluorescent treponemal antibody absorption test FTA-Abs). HIV co-infection should also be excluded.

Primary and secondary syphilis is best treated with a single intramuscular (IM) injection of 1.8 g benzathine penicillin (if penicillin allergic, doxycycline 100 mg twice daily for 14 days). Serology should be repeated at 6 months to confirm eradication. Patients presenting with late latent syphilis or treatment failure require weekly 1.8 g IM benzathine penicillin for 3 weeks. Advise no sexual contact for 7 days after treatment is administered. Contact tracing is required- for primary syphilis 3 months, secondary 6 months and latent syphilis 1 year (10).

3.1.4. Chancroid (*Haemophilus ducreyi*)

Haemophilus ducreyi is a Gram-negative facultative anaerobic coccobacillus. Chancroid is rare in the western world, but is seen more frequently in developing countries. Transmission is through skin breaks during sexual intercourse. Incubation is 4 to 10 days.

Ulcers (frequently multiple) develop within hours to days of exposure from tender, erythematous papules that progress to pustules and then ulcerate and erode over days to weeks. Lymphadenopathy (frequently unilateral) is common, especially in males. Abscesses can also form necessitating drainage.

Chancroid is diagnosed with gram staining, culture or PCR (most sensitive test) (11). Treatment is with single dose oral 1g azithromycin or 250 mg IM ceftriaxone or 500mg ciprofloxacin twice a day for 3 days. Sexual contacts within the last 10 days should be traced.

3.1.5. Granuloma inguinale/ Donovanosis (*Klebsiella granulomatis*)

Klebsiella granulomatis is a Gram-negative bacterium transmitted by sexual contact, autoinoculation or faecal contamination. It is rare in western countries, being found more commonly in Africa and South America (12).

Donovanosis presents ulcerating infection of the genitals and anus: ulcerogranulomatous type, hypertrophic or verrucous ulcers, necrotic ulcers or cicatricial or sclerotic forms.

Diagnosis is made by tissue smears, revealing Donovan bodies in macrophages. Treatment is with 3 weeks of oral doxycycline, Bactrim or ciprofloxacin.

3.2. Viral

3.2.1. Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS)

HIV is a RNA retrovirus that infects T lymphocytes. Transmission occurs through mucosal contact with body fluids. Latent periods of up to 2 years have been described. HIV produces diminished immunological function- manifested as AIDS. The incidence of HIV infections in the western world has plateaued in recent times and mortality rates have likewise decreased with the introduction of highly active antiretroviral therapy (HAART) (4).

Ano-rectal disease can manifest HIV and AIDS with the presence anal ulceration, anal condyloma, Kaposi sarcoma, lymphoma or wound healing issues related to hemorrhoids, fissures and fistulas. HIV/AIDS related ulcers are characteristically located proximally in the anal canal (often extending to rectal mucosa), are broad based, deeply ulcerating (often invading into sphincters) and may demonstrate mucosal bridging. Surgeons need to manage fistulas cautiously as poor wound healing is common (13). Surgeons need to work in conjunction with physicians as the use of HAART and higher CD4-positive counts can prevent and control of a large number of ano-rectal HIV manifestations (with particular reference to ulcers). Once present, ulcer management can be challenging and treatment is best aimed at debriding necrotic tissue and facilitating drainage of purulent and feculent collections. Concomitant infections should be cultured and treated (14). Intralesional steroid injections have also been described (15).

3.2.2. Human Papillomavirus (HPV)

HPVs are small DNA viruses that can cause benign and malignant changes in the epithelium of the anorectum and genitalia. They are the commonest worldwide STD. Over 120 subtypes have been described. Benign hyperproliferative lesions -such as warts, papillomas or condylomata- are commonly caused by HPV-6 and -11. Anal intraepithelial neoplasia (AIN) and anal squamous cell carcinoma (SCC) and caused by high risk (oncogenic) types like HPV-16, -18, -51, -53, -31, -33. HPV is most commonly transmitted via sexual contact, although perianal and genital HPV transmission can occur via skin-to-skin or skin-to-mucosa contact.

Perianal or anal condyloma accuminata can present with the presence of gray or pink fleshy, cauliflower like growths of varying size in the anal canal or perianal region, pruritus ani, bleeding, discharge, pain or difficulties with post-defecation hygiene. Extension into the rectum is rare. Concomitant genital, perineal and groin

fold infections are common and vaginal speculum exam and Pap smear are mandatory in women. Anoscopy with 5% aqueous acetic acid (areas of active HPV mucosal infection briefly turn cloudy white) and Lugol's iodine (assessing for dysplasia) can be used but their effect on overall clinical outcomes is unproven.

Topical treatment regimen, such as imiquimod (Aldara), can be applied to perianal skin to eradicate HPV from mucocutaneous surfaces following excision of gross lesions. 5% imiquimod is applied nightly three times a week (and washed off after 8 hours) for up to 16 weeks. Complete resolution of external lesions has been reported in over 50% of compliant patients (16) (but be mindful as local skin reactions are common). Recurrence rates of 19% to 23% at 3 to 6 months have been reported (17). Imiquimod is an immune response modifier that induces cytokines, such as alpha-interferon and tumour necrosis factor-alpha. Alternative topical treatments include trichloroacetic acid 60% - 90% which can also be used for lesions in anal canal (causes destruction by protein coagulation), podophyllotoxin (cytotoxin) and cidofovir (broad spectrum antiviral activity).

Surgical excision has the greatest success in terms of clearance rates (71% - 93%) and recurrence rates (4% - 29%) (18, 19). Alternative treatment options include cryotherapy (for anal warts), laser destruction, electrodesiccation for larger lesions (superficial layer of condyloma is fulgurated with cautery and then curetted). Intralesional interferon-alpha injections (blocks viral reproduction) when combined with surgical excision has been shown to reduce recurrence rates, and may be useful with recurrent *condylomata accuminata* (20).

AIN and SCC: A clear understanding of the relationship between HPV, AIN and anal SCC is still in evolution. Intensive surveillance programs with anal cytology, anoscopy with acetic acid and Lugol's iodine and anal mapping have not altered outcomes significantly when compared to regular clinical surveillance and excision and biopsy of suspicious lesions. As such, clinical practice varies when following up and managing patients with AIN I, II and III with respect to local destruction (topical agents, cryotherapy or fulguration), R0 surgical excision or observation and biopsies of clinical changes.

Once detected most patients with anal SCC can be effectively managed with definitive chemoradiotherapy (Nigro protocol)- with abdominoperineal resections being reserved for uncommon treatment failures and patients with poor sphincter function resulting from radiotherapy (21, 22).

3.2.3. Herpes Simplex Virus (HSV)

HSV is a DNA virus of the Herpesviridae family. It is the most prevalent STD in many western countries (affecting 20% of the general population in the United States seropositive for HSV-2) (23).

Two serotypes exist:

- HSV-1 accounts for approximately 13% of ano-rectal herpes infections and is more commonly associated with oral, labial or ocular infections.

- HSV-2 accounts for almost 90% of ano-rectal infections (23) having been transmitted through ano-genital contact.

Affected individuals shed virus that is transmitted by penetrating the mucosa or skin breaks in contacts. HSV infection increases the risk of acquiring and transmitting HIV (24). Perianal symptoms typically develop 4 to 21 days after inoculation and are frequently preceded by systemic symptoms (fever, headache, malaise). Small painful vesicles of the perianal skin and anus cause burning, pruritus ani, tenesmus and may be associated with inguinal lymphadenopathy. Lesions eventually ulcerate and coalesce and persist for 2 to 3 weeks. A chronic relapsing course then ensues with prodromal symptoms of itching, tingling or burning followed by the appearance of lesions. HSV remains latent in the sensory ganglia of nerves innervating the infected site (therefore sacral paraesthesia and perianal pain can also precede the appearance of vesicles and sacral radiculitis can persist after their resolution). Rectal involvement can result in painful proctitis (the second most common STD causing proctitis behind gonorrhoea in the west)- friable mucosa, diffuse ulcers, intact vesicles or pustules on proctoscopy.

Diagnosis is made by viral culture or PCR (more sensitive and specific) (25) of ulcer swabs or HSV serology tests (with sensitivity and specificity rates of greater than 90% reported, but beware as seroconversion may take several weeks from initial infection) (4).

Antiviral therapy (oral acyclovir 400 mg taken five times a day for 10 days) shortens the duration of symptoms and the period of viral shedding (26). Recurrent episodes should be treated with oral antivirals and patients experiencing several recurrences per year should be considered for suppressive treatment. Suppressive therapy does not eliminate latent infection or viral shedding and therefore patients need to abstain from sexual contact while lesions are present or prodromal symptoms are noticed as even condoms do not provide complete protection. Secondary bacterial infections also need to also be recognized and treated. No effective HSV-1 or HSV-2 vaccines are currently available, despite ongoing research.

3.2.4. Molluscum contagiosum (Pox Virus)

Molluscum contagiosum is caused by a member of the poxvirus family, being transmitted by direct contact (with the immunosuppressed at higher risk). It causes largely asymptomatic painless 2 - 6 mm flesh colored papules. The incubation period is 1 to 6 months.

The diagnosis is confirmed with biopsies revealing enlarged epithelial cells with intracytoplasmic molluscum bodies. Treatment regimens include curettage, cryotherapy, electrodesiccation, or trichloroacetic acid.

Table 1. Sexually Transmitted Diseases of the Anorectum

Species	Clinical Manifestations	Diagnosis	Treatment
Bacteria			
<i>Chlamydia trachomatis</i>	Proctitis (LGV- anorectal ulcer, abscesses and fistulas)	Culture, nucleic acid amplification, serological antibody titres	Azithromycin 1 g PO single dose or doxycycline 100 mg PO BD for 7 days
<i>Neisseria gonorrhoea</i>	Proctitis, mucopurulent discharge and potential for disseminated infection	Culture of mucopurulent discharge	Ceftriaxone 250 mg IM single doses
<i>Treponema pallidum</i> (syphilis)	10- anorectal chancres, proctitis, 20- condylomata lata, 30- gummas	Dark field microscopy, serology	Benzathine penicillin 1.8 g IM single dose
<i>Haemophilus ducreyi</i> (chancroid)	Ulcers, lymphadenopathy (often unilateral), abscesses	Gram staining, culture, PCR	Azithromycin 1 g PO, or ceftriaxone 250 mg IM single dose or ciprofloxacin 500 mg PO BD for 3 days
<i>Klebsiella granulomatis</i> (donovanosis)	Ulcers	Tissue smears	3 weeks PO doxycycline, Bactrim or ciprofloxacin
Virus			
HIV and AIDS	Anal ulceration, anal condyloma, Kaposi sarcoma, lymphoma or wound healing issues	Serology	HAART, debridement, intral- esional steroid injections
Human papillomavirus HPV	Warts, condylomata accuminata, AIN, SCC	Excisional biopsy	Topical agents (e.g. Imiquimod), surgical excision or destruction
Herpes simplex virus HSV	Small painful vesicles that eventually ulcerate and coalesce, inguinal lymphadenopathy	Viral culture, PCR, serology	Acyclovir 400 mg PO 5/day for 10 days
Pox virus (Molluscum contagiosum)	Flesh colored papules	Biopsy	Curettage, cryotherapy, surgical excision/ destruction, or trichoracetic acid

4. Conclusions

The clinical presentations of sexually transmitted diseases of the anorectum are wide and varied. Clinicians need to remain mindful of common pathogens and the differing nuances associated with their manifestations, diagnoses and treatments. Although high-risk populations should heighten clinician's awareness, these pathogens can affect almost all members of the general population. This article has highlighted the most common bacterial and viral sexually transmitted pathogens implication in anorectal disease. By summarizing common modes of clinical presentation, up to date methods of diagnosis and management it is hoped clinicians in clinical practice and better able to identify and treat such pathogens.

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