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GUIDELINES

2021 European Guideline on the management of proctitis, proctocolitis and enteritis caused by sexually transmissible pathogens

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Abstract

This guideline intents to offer guidance on the diagnosis and management of patients with gastrointestinal symptoms and a suspected sexually transmitted cause. Proctitis is defined as an inflammatory syndrome of the anal canal and/or the rectum. Infectious proctitis can be sexually transmitted via genital–anal mucosal contact, but some also via digital contact and toys. *Neisseria gonorrhoeae, Chlamydia trachomatis* (including lymphogranuloma venereum), *Treponema pallidum* and herpes simplex virus are the most common sexually transmitted anorectal pathogens. Shigellosis can be transferred via oral–anal contact and may lead to proctocolitis or enteritis. Although most studies on these infections have concentrated on men who have sex with men (MSM), women having anal intercourse may also be at risk. A presumptive clinical diagnosis of proctitis can be made when there are symptoms and signs, and a definitive diagnosis when the results of laboratory tests are available. The symptoms of proctitis include anorectal itching, pain, tenesmus, bleeding, constipation and discharge in and around the anal canal. The majority of rectal chlamydia and gonococcal infections are asymptomatic and can only be detected by laboratory tests. Therefore, especially when there is a history of receptive anal contact, exclusion of anorectal infections is generally indicated as part of standard screening for sexually transmitted infections (STIs). Condom use does not guarantee protection from STIs, which are often spread without penile penetration. New in this updated guideline is: (i) lymphogranuloma venereum proctitis is increasingly found in HIV-negative MSM, (ii) anorectal *Mycoplasma genitalium* infection should be considered in patients with symptomatic proctitis after exclusion of other common causations *such N. gonorrhoeae, C. trachomatis*, syphilis and herpes, (iii) intestinal spirochetosis incidentally found in colonic biopsies should not be confused with syphilis, and (iv) traumatic causes of proctitis should be considered in sexually active patients.

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Conflict of interest

Dr. Ross reports personal fees from GSK Pharma, Mycovia and Nabriva Therapeutics as well as ownership of shares in GSK Pharma and AstraZeneca Pharma; and is author of the UK and European Guidelines on Pelvic Inflammatory Disease; is a Member of the European Sexually Transmitted Infections Guidelines Editorial Board; is a Member of the National Institute for Health Research Funding Committee (Health Technology Assessment programme). He is an NIHR Journals Editor and associate editor of Sexually Transmitted Infections journal. He is an officer of the International Union against Sexually Transmitted Infections (treasurer), and a charity trustee of the Sexually Transmitted Infections Research Foundation. Dr. Kreuter reports personal fees from InfectoPharm, Paul-Ehrlich-Gesellschaft für Chemotherapie e.V., DERFO - Dermatologische Fortbildungs-Gesellschaft, MSD SHARP & DOHME, Böhringer Ingelheim, and MSD SHARP &

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Aetiology and transmission

Anal sexual intercourse is widely practised both among heterosexuals but especially in MSM and transgender women.[1] As a consequence rectal infections should be routinely excluded when MSM are screened for STIs.[2–4] In the absence of receptive anal intercourse, *Neisseria gonorrhoeae* can still be transmitted easily to the anal canal via fingering, and in women via genital infection due to the proximity of the vagina. Intestinal infections can be acquired through oral–anal sexual contact. These infections may lead to symptomatic proctitis, proctocolitis or enteritis, but are most frequently asymptomatic (Table 1).

Clinical features of proctitis, proctocolitis and enteritis

Symptoms

In patients with acute proctitis (inflammation of the rectum):

- Mucopurulent anal discharge.
- Anorectal bleeding.
- Anorectal pain.
- Anorectal itch.
- Constipation.
- Sensation of rectal fullness or incomplete defecation.
- Tenesmus[5].

In patients with mild proctitis (and in those with chronic proctitis):

- History of mucus streaking of the stool.
- Constipation.
- Sensation of incomplete defecation.

In patients with acute proctocolitis (inflammation of rectum and colon):

- Small volume diarrhoea.
- Bloody stool.
- Abdominal pain.
- Anorectal bleeding.
- Sensation of incomplete defecation.
- Tenesmus.

In patients with enteritis (inflammation of the small intestine):

- Large volume, watery diarrhoea.
- Bloody stool.
- Mid-abdominal cramps.
- Nausea with or without vomiting.
- Malaise.
- Fever.
- Weight loss.

History

Risk factors for proctitis, proctocolitis and enteritis include:

- HIV seropositive status.
- Other STIs in last 6 months.
- Condomless receptive anal intercourse in the last 6 months.
- A history of traumatic sex in last 3 months (particularly last 4 weeks):
  - Multiple sexual partners/Group sex/Chemsex (sexualized substance use).[6–9]
  - Receptive fisting.
  - Using and sharing sex toys

In HIV-infected patients with low $CD4^+$ T-cell counts (<200 cells/μL), gastrointestinal illness can be caused by opportunistic infections that usually are not sexually transmitted, including CMV[10], *Mycobacterium avium*, *Salmonella* spp., *Campylobacter* spp., *Shigella* spp., *Entamoeba histolytica*[11], *Cryptosporidium* spp., Microsporidia and *Cystoisospora belli*.[12] In addition, enteritis can be directly caused by HIV infection.[13]

Proctoscopic signs

Proctoscopy should be performed in patient with any of the above-mentioned symptoms.

2.1.1. Proctitis Confined to the distal 12–15 cm of the rectum.

- Muco-pus in lumen.
- Loss of normal vascular pattern (although note that the vascular pattern may not be apparent in the distal 10 cm of the normal rectum).
- Mucosal oedema.
- Contact bleeding.
- Sometimes ulceration: lymphogranuloma venereum (LGV) and syphilis may cause an inflammatory, sometimes ulcerated, tumorous infiltrate in the distal rectum or anal canal.[14,15]

Lymphogranuloma venereum should be considered in MSM with suspected chronic inflammatory bowel disease, since the clinical presentation and histopathologic findings of LGV proctitis are similar to some other inflammatory bowel diseases (4,C; see https://iusti.org/treatment-guidelines/ for grading score definitions).[16] Whereas in the past the majority of LGV infections were found in MSM living with HIV, an increasing proportion of LGV proctitis infections are now diagnosed in HIV-negative MSM.[17]

Proctocolitis As for proctitis, but the inflammatory changes extend beyond the rectosigmoid junction.

Enteritis The rectal mucosa appears normal unless there is concurrent infection with organisms causing proctitis.

Diagnostic tests for the pathogens causing proctitis, proctocolitis and enteritis

Rectal gonorrhoea and chlamydia infection

The majority of rectal chlamydia and gonococcal infections are asymptomatic.[18,19] It is therefore important to exclude both infections with a nucleic acid amplification tests (NAAT) in all who report receptive anal sexual contact within the past 6 months, even in the absence of anorectal symptoms. Anorectal LGV is usually a symptomatic infection, although asymptomatic anorectal LGV does occur in 25% of cases (1a, B).[20–23]

Commercially available NAAT are the tests of choice for the detection of chlamydia and gonococcal infections at the rectal site (2a,B).[24] With appropriate instructions, a patient-collected rectal swab to exclude these infections with the use of a dual NAAT is a valid and acceptable alternative for asymptomatic STI clinic attendees (2a,B).[25]

Rectal gonorrhoea

With the emergence of multidrug-resistant *N. gonorrhoeae* (Ng), culture of Ng for surveillance purposes becomes increasingly important.[26] Material for culture of Ng should be obtained either by the passage of a swab through the anal canal into the distal rectum or under direct vision via an proctoscope (3,C).[27]

Table 1 Sexually associated causes of proctitis, proctocolitis and enteritis†

Causes of distal proctitis	Causes of proctocolitis	Causes of enteritis
Neisseria gonorrhoeae	*Shigella* spp.	*Giardia lamblia*, *Cryptosporidium* spp.
Chlamydia trachomatis:	*Campylobacter* spp.	Microsporidia§
Genotypes D-K	*Salmonella* spp.	Hepatitis A virus
Genotypes L_{1-3} (LGV)	*Escherichia coli*	
Treponema pallidum	*Entamoeba histolytica*	
Herpes simplex virus	*Cryptosporidium* spp.	
Mycoplasma genitalium ‡	Cytomegalovirus§	
Traumatic (sex toys, douching)	Intestinal spirochetosis¶	

LGV, lymphogranuloma venereum.
†STI coinfections may exist.
‡It is advised to test for Mg, only in patients with persistent symptoms after exclusion of Ct and Ng.
§In severely immunocompromised patients (in the context of HIV infection with low $CD4^+$ T-cell counts (<200 cells/μL).
¶Intestinal spirochetosis is incidentally found in colonic biopsies in immunocompetent patients (especially in relation to inflammatory bowel syndromes).

Direct microscopy of slides of rectal swabs by Gram stain analysis may increase the proportion of men treated for gonorrhoea at their first attendance to an STI outpatient clinic.[28–30] Gram-negative diplococci may be seen within the cytoplasm of polymorphonuclear leucocytes, permitting a presumptive diagnosis of rectal gonorrhoea and syndromic management (Fig. 1). Since the sensitivity is suboptimal, confirmation by additional NAAT and/or culture is required (2b, B).

Rectal chlamydia infection

1 Caused by biovar trachomatis (genotypes D–K): *Chlamydia trachomatis* genotypes D–K infect epithelial cells of mucosal surfaces and the diagnosis of rectal chlamydia is usually made by testing rectal material with a NAAT, collected as for gonorrhoea (see above).[31]
2 Caused by biovar LGV (genotypes L_{1-3}): Rectal specimens from MSM that test positive for *C. trachomatis* (Ct) by NAAT should be characterized further (genotyping for LGV; 2a, B) as described in the European guideline on the management of lymphogranuloma venereum.[20] The lack of chlamydia genotyping capacity across Europe causes significant underreporting of LGV infections among MSM.[32] If molecular LGV characterization is unavailable, a Ct IgA-specific antibody test can be an alternative choice to make a presumptive diagnosis of LGV.[33] LGV is likely in the case of an elevated antibody titre (more than twice the normal ranges) in combination with a confirmed rectal Ct infection.

Rectal *Mycoplasma genitalium* infection

A number of studies have not shown a significant association between Mg and proctitis, although cases of proctitis in which Mg is the sole pathogen detected have occurred. Testing first line for Mg in men with proctitis is therefore not recommended.[34–36] Rectal mono infection with Mg in MSM causes less pronounced symptoms compared to rectal Ct and rectal Ng.[35,36] It is advised to only test for Mg using NAAT in patients with persistent symptoms, after exclusion of other common causes such as Ct, Ng, syphilis and HSV. If available, a positive NAAT diagnosis should be followed with an assay for macrolide resistance (3,B).[37] Any role of microorganisms such as *Mycoplasma hominis*, and *Ureaplasma* species in anorectal pathology is highly speculative. Although a role of *Ureaplasma urealythicum* in HPV-related carcinogenesis has been suggested, it remains unproven.[38]

Anorectal syphilis

Syphilis incidence is increasing, especially in MSM. Its protean clinical manifestations require testing when anorectal symptoms are present. Anorectal syphilis can be diagnosed by the detection of treponemes in exudate from an ulcerating lesion using dark-field microscopy, or an anorectal mucosal or ulcer swab for polymerase chain reaction (PCR) for *Treponema pallidum* DNA

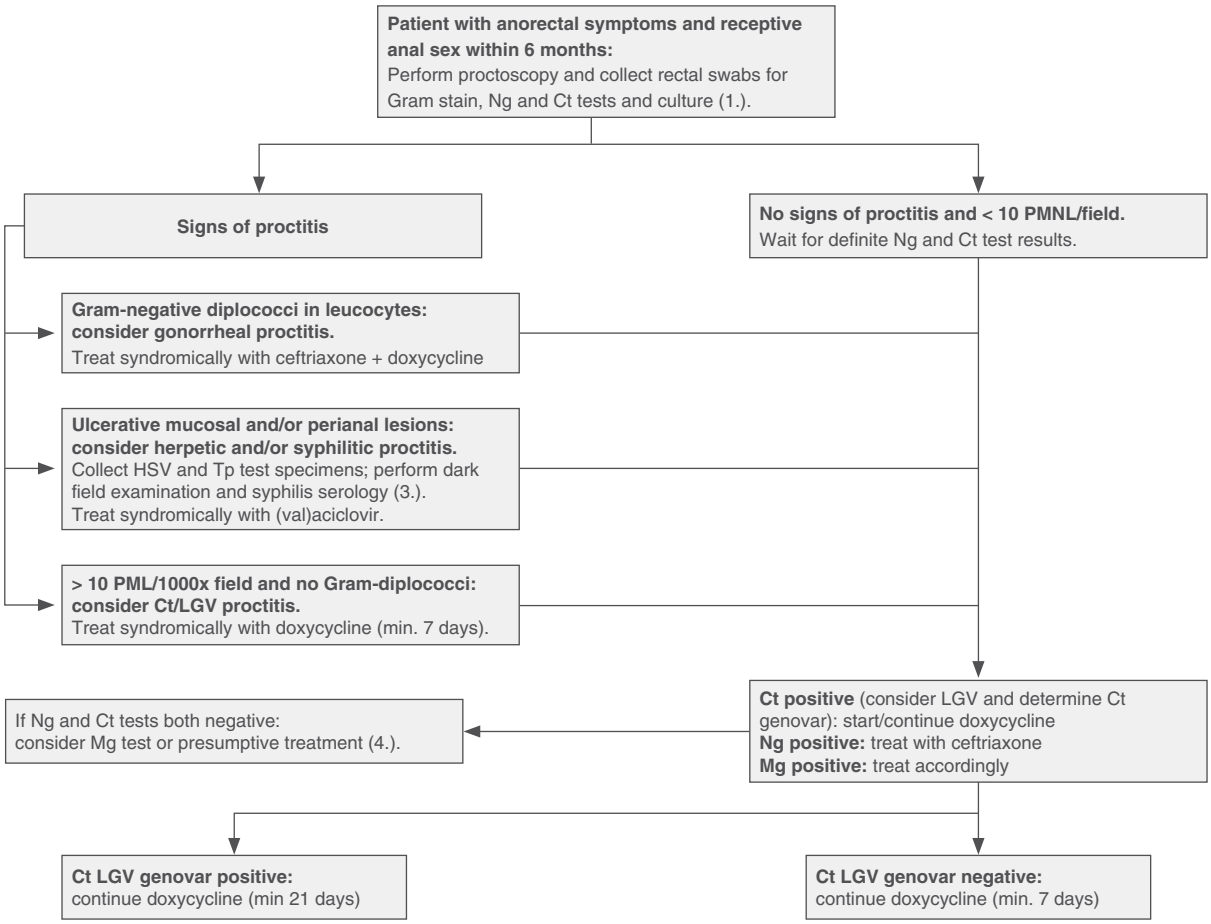

Figure 1 Syndromic management flow chart for patients in whom an anorectal sexually transmissible infection is suspected. (1) Perform a full HIV/STI screening (including hepatitis B and C testing and Ng culture if gonorrhoea suspected. (2) See text for further considerations regarding syndromic treatment of Ng/Ct. (3) Treat with penicillin G benzathine if dark field positive. (4) See IUSTI Mg treatment guideline. Ct, *Chlamydia trachomatis*; HSV, herpes simplex virus; LGV, lymphogranuloma venereum; Mg, *Mycoplasma genitalium*; Ng, *Neisseria gonorrhoeae*; PMNL, polymorphonuclear leucocytes; Tp, *Treponema pallidum*.

(2a, B).[39] Positive syphilis serological tests results support the diagnosis.[40]

Intestinal spirochetosis

Human intestinal spirochetosis is incidentally found in colonic biopsies in immunocompetent patients (especially in relation to inflammatory bowel syndromes) colonized by the *Brachyspira* species: *Brachyspira aalborgi* and *Brachyspira pilosicoli*. It affects mainly MSM and people living with HIV. Diagnosis is based on colon biopsy, where spirochetes can be observed on the luminal surface, especially with Warthin–Starry stain or similar silver stains. It is debated if colonization by these spirochetes is associated with gastrointestinal symptoms like chronic diarrhoea.[41,42]

Anorectal herpes simplex virus infection

Anorectal herpes simplex virus (HSV) infection is diagnosed by PCR (2,B).[43] Multiplex PCR may allow detection of unsuspected cases incidentally. A small case series study in Brighton, UK carried out between 2015 and 2018 found a high number of pathogen-associated symptomatic proctitis in MSM with high rates of HSV, particularly HSV-1.[44] Thus, empirical treatment of herpes in MSM with proctitis should be considered especially in cases with severe pain and among people living with HIV (4b, B).

Anorectal human papilloma virus infection and anal cancer

HIV-related morbidity and mortality have considerably decreased since the introduction of antiretroviral therapy (ART).[45] As a result of the significantly prolonged life span of

patients living with HIV in the ART-era, non-AIDS defining malignancies, such as anal carcinoma, are observed in excess in MSM living with HIV. High-risk human papillomavirus (HPV) causes anal carcinoma and its precursor lesions, anal high grade squamous intraepithelial lesion, (HSIL). MSM, especially MSM living with HIV, have a significantly increased risk for anal HPV infection, anogenital warts, HSIL and anal cancer.[46] Moreover, anal HPV is associated with an increased risk for HIV acquisition in MSM.[47] HPV-related disease is not discussed further in this guideline. For recommendations please consult specific guidelines.[48]

Bacterial, viral and parasitic infections causing proctocolitis

Consider testing for enteric pathogens in patients with diarrhoea and fever or diarrhoea for more than 7 days. Test for *Shigella* spp., *Salmonella* spp., *Yersinia* spp., *Campylobacter* spp., *E. histolytica*, *Giardia lamblia*, *Cryptosporidium* spp., Microsporidia, *C. belli*, *Balantidium coli* and *Trichuris trichiura* from faecal samples using microscopy, culture and PCR.[49] Consult a medical microbiologist/parasitologist for clinical management in cases where non-pathogenic protozoa (e.g. *Entamoeba* sp., *Endolimax nana*, *Iodamoeba bütschlii*, *Pentatrichomonas hominis* and *Chilomastix mesnili*) or when protozoa with unclear pathogenic potential (e.g. *Dientamoeba fragilis* and/or *Blastocystis*) are detected.

Bacterial culture is an alternative in situations where PCR is unavailable. Moreover, culture is required in cases suspected to have antimicrobial resistance that could influence clinical management. Sometimes repeated faecal stool analyses are necessary before a diagnosis is made. The number of repeat stool analyses recommended is according to local laboratory protocols.

Amoebiasis

Microscopic examination for the trophozoites of *E. histolytica* in diarrhoeal stool specimens, rectal exudate or scrapings from rectal ulcers should be attempted. Direct wet stool examination/microscopy of freshly obtained (bloody) samples stained with eosin, iodine or trichrome may reveal trophozoites with ingested erythrocytes which is pathognomonic for *E. histolytica* infection.

Cysts of the protozoan may be found in diarrhoeal stools or in formed faeces. It is important to differentiate between *E. histolytica* and the non-pathogenic amoeba *Entamoeba dispar* with PCR because they are morphologically indistinguishable.

Cytomegalovirus infection

The triad of mononucleosis-like illness with rectal symptoms days to weeks after condomless anal intercourse is pathognomonic for sexually transmitted cytomegalovirus (CMV) proctitis.[50] Suggestive findings on proctoscopy or sigmoidoscopy include rectal mucositis and ulceration. Moreover, CMV colitis is an HIV indicator disease and should be considered in late presenters for HIV. CMV serology, CMV-PCR and CMV immunohistochemistry from biopsies and blood samples are supportive of the diagnosis.[51,52] The finding of typical intranuclear inclusion bodies in rectal or colonic biopsies is considered diagnostic.

Giardiasis

Fluid stool samples or duodenal biopsies should be microscopically examined for the trophozoites and cysts of *G. lamblia*. Enzyme immunoassays, direct immunofluorescence copro-antigen tests and specific PCR for the detection of giardiasis are increasingly available and are crucial in diagnosing this infection.[53]

Cryptosporidiosis and microsporidiosis

Special stool preparations (in consultation with the local medical microbiologist/parasitologist) are required to diagnose cryptosporidiosis and microsporidiosis. Faecal samples are examined after staining for the oocysts of these protozoans. The discovery of various stages of the life cycle of the organism within the enterocytes on histological examination of jejunal, colonic or rectal biopsy is diagnostic. Enzyme immunoassays, direct immunofluorescence copro-antigen tests and PCR for the detection of cryptosporidial and microsporidial antigens/DNA have a high sensitivity/specificity and are commercially available (1b,A).[53]

Non-specific proctitis

In some patients with symptoms and signs of a distal proctitis no causative pathogens can be detected. Traumatic causes like fisting, the use of sex toys, douching, enema use and the insertion of chemsex substances (booty bumping) should also be actively enquired after. Chemsex in Europe is estimated to occur in around 20% of MSM with higher rates in urban settings, and fisting in around 7–8%.[6,7,9,54] External anogenital trauma due to fisting is observed in 22.2% and 88.8% of reported consensual and non-consensual intercourse, respectively, while anorectal internal injuries are observed in all these patients. The risk of physical trauma further increases in MSM using crystal methamphetamine, mephedrone or gammahydroxybutyrate (GHB/GBL).[8,55,56] If no infectious or traumatic causes can be found and the proctitis persists after empiric therapy, the patient should be referred to a gastrointestinal specialist to exclude other inflammatory bowel diseases.

Management

Information, explanation and advice for the patient.

In all cases of proctitis or proctocolitis caused by a sexually transmitted pathogen, patients should be given a detailed, clear written explanation of their condition with particular emphasis on the implications for the health of themselves and their partner(s). Irrespective of symptomatology, sexual health checks, including screening for anorectal infections (syphilis, gonorrhoea and chlamydia) at 3–6-month intervals should be offered

to individuals with receptive anal sex, and frequent changes in sexual partners and/or recent STIs.

In the prevention of ongoing sexual transmission of the bacterial pathogens the following recommendations should be communicated (3,C):[57]

- Wash hands after using toilet, before preparing or eating food and after sexual activity.
- Avoid anal sex, oral–anal sex (rimming), coprophilia (scat) whilst symptomatic and until test for infection shows clearance.
- Use of condoms, gloves, dental dams during sex; the use of gloves for 'fisting' should be encouraged.
- Avoid sharing douching materials, enemas and sex toys.
- Avoid swimming pools and spa centres whilst ill and for 2 weeks after recovery (4,C).[58]
- Avoid sex during recurrent HSV infection.
- Offer hepatitis A and B vaccination if not immune.
- Offer counselling for initiation of pre-exposure prophylaxis (PrEP) to MSM.[59]

Therapy, partner notification and follow-up.

For management of proctitis caused by a specific pathogen, please consult the relevant IUSTI Europe guideline as mentioned below or via the website https://iusti.org/treatment-guidelines/. Please consider the syndromic management recommendations mentioned below.

Rectal gonorrhoea

European Guideline on the Diagnosis and Treatment of Gonorrhea in Adults.[60]

Rectal chlamydia infection (non-LGV)

European guideline for the management of *C. trachomatis* infections.[61]

Rectal LGV

European Guideline on the Management of Lymphogranuloma Venereum.[20]

Rectal *Mycoplasma genitalium* infection

European Guideline on *Mycoplasma genitalium* infections.[37]

Anorectal syphilis

European Guidelines on the Management of Syphilis.[40]

Anorectal HSV infection

European guideline for the management of genital herpes.[62]

Shigella, *Salmonella*, *Yersinia* and *Campylobacter* infections

Therapy Antimicrobial therapy is often unnecessary in the treatment of *Shigella*, *Salmonella*, *Yersinia* and *Campylobacter* infections.[57] If indicated (for example in those with bloody diarrhoea, and in severely immunosuppressed individuals or sickle-cell disease in whom infection tends to be more severe and sometimes fatal), the choice of drug is to be advised by a medical microbiologist informed of the pattern of antimicrobial resistance in the population. Transmission of ciprofloxacin-resistant *Shigella sonnei*, among MSM in Montreal, Québec, for instance has been reported.[63]

Partner notification The possible source of infection should be ascertained if possible, in the knowledge that many infected individuals are symptomless. Sexual partners within the week preceding the onset of symptoms should be screened for infection. In case of *Shigella* and *Salmonella* infections, symptomatic household contacts should be identified, notified and further managed in a healthcare setting.

Public health authority notification Some of the mentioned enteric infections (e.g. shigellosis, shiga-toxin producing *Escherichia coli* infections, hepatitis A) are notifiable diseases. Please check with your national public health authority.

Follow-up This is usually unnecessary, but in the case of food handlers/medical staff/nurses/day care leaders with shigellosis, local regulations may apply before they are allowed back to work. Please check with your national public health authority.

Amoebiasis

Therapy

- Metronidazole 750 mg tid for 5–10 days (2a, A).
- Alternatively, tinidazole 2 g once daily for 2–3 days (2b, A). This should be followed by a intraluminal agent to eliminate all protozoa from the lumen of the bowel like (2a, B):
  - paromomycin 10 mg/kg/day tid for 5–10 days.
  - or diloxanide furoate 500 mg tid for 10 days.
  - or clioquinol 250 mg tid for 10 days.
  - or iodoquinol 650 mg tid for 20 days.

Partner notification

If the patient did not travel to an endemic area, partner notification should be undertaken. All partners within the preceding 3–4 months should be assessed (4, C).

Follow-up

In the case of food handlers with amoebiasis, local regulations may apply before they are allowed back to work. Please check with your national public health authority.

Cytomegalovirus

Therapy Although the role of antiviral therapy in primary CMV proctitis has not been defined, it is probably not essential

in all cases, as most reported cases resolved spontaneously without complications.[50] Reported cases associated with acute HIV coinfection resolved upon immune restoration, without antiviral therapy. On the other hand, when CMV colitis in immunosuppressed patients is progressive, it is associated with high mortality and requires antiviral treatment with (val)- or ganciclovir.

Partner notification Not required.

Follow-up Not necessary in the immunocompetent patient.

Giardiasis

Therapy

- Metronidazole 2 g daily for 3 days.
- or metronidazole 500 mg bid for 5 days (2a, B).
- Alternatively tinidazole 2 g once (2a, B).

Partner notification

All partners within the preceding month should be notified.

Follow-up

Not necessary in the immunocompetent patient (4, C).

Cryptosporidiosis and microsporidiosis

Therapy

- In the immunocompetent patient, the condition is self-limiting, and ART initiation usually leads to resolution of clinical cryptosporidiosis in immunocompromised patients with HIV. In case treatment is indicated, nitazoxanide and paromomycin can be considered (see also: https://aidsinfo.nih.gov/guidelines).

Partner notification The value of partner notification in patients with cryptosporidiosis is uncertain. It is doubtful if contact tracing would reduce the risk of onward transmission.

Follow-up Not necessary in the immunocompetent patient.

Intestinal spirochetosis

Therapyh

- Metronidazole 500 mg bid, or 250 mg tid, for 14 days.[50,64,65]

Partner notification

Not required.

Follow-up

Not necessary in the immunocompetent patient.

Syndromic management of the patient with anorectal and/or intestinal symptoms in whom a sexually transmissible cause is suspected

History

A consideration of the patient's symptoms (see above) is often helpful in determining whether the patient has proctitis, proctocolitis or enteritis. A sexual history is, of course, important.

Physical examination and diagnostic tests

Palpate the abdomen; tenderness over the colon suggests colitis. Inspect the perianal region: perianal ulceration may suggest syphilis, HSV infection or LGV. In case of signs of peritonism or if an acute abdomen is considered, seek urgent surgical consultation, especially in case of potential trauma (e.g. fisting or toys). If proctitis is suspected, proctoscopy should be performed to inspect for mucosal inflammation and infiltration/swelling and/or ulceration (Fig. 1). If severe pain precludes proctoscopy, consider obtaining 'blind' swabs for diagnostic purposes. If in doubt, sigmoidoscopy can be considered to differentiate between distal proctitis and proctocolitis and will inform a rational treatment choice.

If possible, stained smears (preferably Gram) of rectal exudate should be made and the number of polymorphs in light microscopic high-power field (magnification, ×1000) noted; >10 cells suggests proctitis.[66] If Gram-negative diplococci are seen within the cytoplasm of neutrophilic granulocytes, a presumptive diagnosis of rectal gonorrhoea may be made. Ideally, microbiological tests for the various infections detailed above should be taken.

Treatment

In patients with mild symptoms, and when microbiological investigations are possible, it is best to await the results before initiating specific therapy. Syndromic (presumptive) treatment not based on laboratory results should be avoided in the light of antibiotic stewardship.

Syndromic management of proctitis when Ng is suspected

- Ceftriaxone 1 g intramuscularly (IM) once together with doxycycline 100 mg bid for 7 days.

Although the 2020 gonorrhoea guideline recommends azithromycin instead of doxycycline, the latter is preferred for its superiority against (suspected) Ct infections, and to avoid azithromycin resistance in undiagnosed coinfection with *Mycoplasma genitalium*.[66,67]

Syndromic management of non-specific acute proctitis

- Doxycycline 100 mg bid for 7 days.

Presumptive treatment may be considered in cases of acute proctitis, when clinical findings are non-specific, without a

suspected etiological infection and, if possible, after ruling out Ng by microscopy.

Proctocolitis

- Metronidazole 750 mg tid for 5–10 days (4, C).

Presumptive treatment may be considered in MSM, and patients (or sex partners), who recently visited a geographical area where amoebiasis is prevalent.

Enteritis Fluid replacement is the most important aspect of treatment. Identification of the causative pathogen and subsequent antimicrobial susceptibility testing is imperative since antimicrobial-resistant enteric bacteria are widely prevalent. Consider a microbiological consultation for management advise. Presumptive treatment may be considered in cases with severe symptoms:

- Ciprofloxacin 500 mg bid for 5 days.
- Alternatively, co-trimoxazole 960 mg bid for 7 days.
- or azithromycin 500 mg once daily for 3 days.

Failure to respond symptomatically within 4 weeks should prompt further investigations by a gastroenterologist.

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Search strategy

We updated the previous 2013 guideline version by a literature search through a PICO process, using a set of identified issues (Appendix S1).[68]

Composition of Editorial Board and List of Contributing Organizations

see https://iusti.org/treatment-guidelines/

Tables of Evidence and Grading of Recommendations

see https://iusti.org/treatment-guidelines/

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Issues and PICO's to be resolved for the 2021 proctitis guideline.