

2013 European Guideline on the management of proctitis, proctocolitis and enteritis caused by sexually transmissible pathogens

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Summary

Proctitis is defined as an inflammatory syndrome of the distal 10–12 cm of the anal canal, also called the rectum. Infectious proctitis can be sexually transmitted via genital-anal mucosal contact, but some also via mutual masturbation. *N. gonorrhoeae*, *C. trachomatis* (including lymphogranuloma venereum), Herpes Simplex Virus and *T. pallidum* 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), a significant proportion of women have anal intercourse and therefore 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, cramps (tenesmus) and discharge in and around the anal canal. Asymptomatic proctitis occurs frequently and can only be detected by laboratory tests. The majority of rectal chlamydia and gonococcal infections are asymptomatic. Therefore 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 bacterial and protozoan STIs, which are often spread without penile penetration.

Keywords

HIV, AIDS, sexually transmitted infections, proctitis, proctocolitis, enteritis, men who have sex with men, MSM, homosexual, lymphogranuloma venereum, bacterial, disease, *Chlamydia trachomatis*, *Treponema pallidum*, *Neisseria gonorrhoeae*, herpes simplex virus, guideline

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What is new in this updated guideline?

The majority of rectal chlamydia and gonococcal infections are asymptomatic. It is therefore important to exclude both infections (preferably via a nucleic acid amplification test [NAAT]) in all who report receptive anal sexual contact within the past 6 months, even in the absence of anorectal symptoms.

Although not approved by the manufacturers and regulating bodies like the FDA, currently available NAATs are the tests of choice for the detection of chlamydial and gonococcal infections at the rectal site.

A patient-collected rectal swab to exclude gonorrhoea and chlamydia infections via NAAT is a feasible, valid and acceptable alternative for sexually transmitted infection (STI) clinic visitors.

With the emergence of multidrug-resistant (MDR-Ng) and extremely multidrug-resistant gonorrhoea strains (XDR-Ng), culture of *N. gonorrhoeae* for surveillance purposes has become increasingly important.

Rectal microscopy for syndromic management increases the proportion of men treated for gonorrhoea at their first attendance to an STI outpatient clinic, but confirmation by additional NAAT or culture tests is required.

Anorectal lymphogranuloma venereum (LGV) generally is a symptomatic infection, although asymptomatic anorectal LGV does occur.

LGV should be considered in MSM with acute proctitis as well as those with suspected chronic inflammatory bowel disease

Aetiology and transmission

Anal sexual intercourse is widely practiced both among heterosexuals but especially in MSM.¹ As a consequence rectal infections should be routinely excluded when MSM are screened for STIs.² In the absence of receptive anal intercourse, *N. gonorrhoeae* can still be transmitted easily to the anal canal via fingering, and

in women via a 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. (Box 1)

Though it is likely that *M. genitalium* infects the rectum,⁵ it is unclear if it contributes to clinical syndromes.⁶ *T. vaginalis* is rarely found in the rectum.

HIV-related morbidity and mortality have considerably decreased since the introduction of highly active antiretroviral therapy (HAART).⁷ As a result of the significantly prolonged life span of HIV-positive patients in the HAART era, non-AIDS defining malignancies, such as anal carcinoma, are observed in excess in HIV-positive MSM. Anal carcinoma and its precursor lesions, anal intraepithelial neoplasia (AIN), are caused by high-risk human papillomavirus (HPV). HPV-related disease is not discussed further in this guideline. For recommendations please consult specific guidelines.⁸

Clinical features of proctitis, proctocolitis and enteritis

Symptoms (history)

- (a) In patients with acute proctitis (inflammation of the rectum):
 - Mucopurulent anal discharge;
 - Anorectal bleeding;
 - Constipation;
 - A sensation of rectal fullness or of incomplete defaecation;
 - Tenesmus.

Anorectal LGV generally is a symptomatic infection, although asymptomatic anorectal LGV does occur⁹ (level 1a, grade B, see Appendix).

In patients with mild proctitis (and in those with chronic proctitis), there may only be:

- A history of mucus streaking of the stool;

Box 1. Sexually transmissible causes of proctitis, proctocolitis and enteritis.

Causes of distal proctitis	Causes of proctocolitis	Causes of enteritis
<i>Neisseria gonorrhoeae</i>	<i>Shigella</i> spp.	<i>Giardia duodenalis</i>
<i>Chlamydia trachomatis</i> :	<i>Campylobacter</i> spp.	<i>Cryptosporidium</i> spp.
Genotypes D-K	<i>Salmonella</i> spp.	<i>Microsporidium</i> spp. ^a
Genotypes L ₁₋₃ (LGV)	<i>Escherichia coli</i>	Hepatitis A
<i>Treponema pallidum</i>	<i>Entamoeba histolytica</i>	
Herpes simplex virus	<i>Cryptosporidium</i> spp.	
	Cytomegalovirus ^a	

LGV: lymphogranuloma venereum.

^aIn severely immunocompromised patients (in the context of HIV infection with low CD4⁺ T-cell counts).³ Sometimes in immunocompetent patients (especially in relation to inflammatory bowel syndromes).

Note: It is important to note that several STIs may co-exist.⁴

- Constipation;
- Sometimes a feeling of incomplete defaecation.

The presence of the additional features mentioned above (i.e. discharge, bleeding, tenesmus) suggests more severe proctitis.

- (b) In patients with acute proctocolitis (inflammation of the rectum and colon):
 - Small volume diarrhoea;
 - Bloody stool;
 - Lower abdominal pain;
 - Abdominal tenderness;
 - Anorectal bleeding;
 - Sensation of incomplete defaecation.
- (c) 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.

In HIV-infected MSM engaging in oro-anal sex (rimming) with signs of enteritis, Shigellosis especially should be considered.¹⁰

Signs (findings at clinical examination)

- (a) Proctitis (that is proctitis confined to the distal 12–15 cm of the rectum):
 - Mucopus in lumen of rectum;
 - 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;
 - LGV and syphilis may cause an inflammatory, sometimes ulcerated, tumorous infiltrate in the distal rectum or anal canal.^{11,12}

LGV should be considered in MSM with suspected chronic inflammatory bowel disease, since the clinical presentation and histopathologic findings of LGV proctitis are similar to other causes of granulomatous proctitis such as Crohn's disease¹³ (grade IV, level C).

- (b) Proctocolitis:
As for proctitis, the inflammatory changes extend beyond the rectosigmoid junction.

- (c) 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 chlamydial infections

The majority of rectal chlamydia and gonococcal infections are asymptomatic.^{14,15} It is therefore important to exclude both infections (preferably via an NAAT) in all who report receptive anal sexual contact within the past 6 months, even in the absence of anorectal symptoms.

Although not approved by the manufacturers and regulating bodies like the Food and Drug Administration (FDA) in the United States, currently available NAATs are the tests of choice for the detection of chlamydial and gonococcal infections at the rectal site¹⁶ (level IIa, grade B).

With the appropriate instructions, a patient-collected rectal swab to exclude gonorrhoea and chlamydia infections with the use of a dual NAAT is a feasible, valid and acceptable alternative for STI clinic visitors¹⁷ (level IIa, grade B).

Rectal gonorrhoea. With the emergence of MDR-Ng and XDR-Ng, culture of *N. gonorrhoeae* for surveillance purposes becomes increasingly important.¹⁸

Material for culture for *N. gonorrhoeae* should be obtained either by the passage of a swab through the anal canal into the distal rectum or under direct vision via an proctoscope¹⁹ (level III, grade C).

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.²⁰ Gram-negative diplococci may be seen within the cytoplasm of neutrophilic granulocytes, permitting a presumptive diagnosis of rectal gonorrhoea. Since the sensitivity is suboptimal, confirmation by additional NAAT or culture tests is required (level IIb, grade B).

Rectal chlamydial infection

- (a) By biovar trachomatis (genotypes D-K):
C. 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).²¹ However, the US FDA has not yet approved testing of rectal swabs, and protocols for testing rectal specimens are not included in the manufacturers' kit inserts.

(b) By biovar LGV (genotypes L₁₋₃):

Rectal specimens from MSM that test positive for *C. trachomatis* by NAAT should be characterized further (genotyping for LGV) (level IIa, grade B). Further testing of *C. trachomatis*-positive NAAT material for LGV DNA is possible in specific laboratories in many European countries (contact European Surveillance for Sexually Transmitted Infections [ESSTI]; Website: www.essti.org).^{22,23}

If molecular LGV characterization is unavailable, a Chlamydia IgA-specific antibody test can be an alternative choice to make a presumptive diagnosis of LGV.²⁴ LGV is likely in case of an elevated antibody titre (far outside the normal ranges) in combination with a confirmed rectal *C. trachomatis* infection.

Anorectal syphilis

Dark-field microscopy for treponemes or a (multiplex) NAAT for *Treponema pallidum* DNA from exudate from an ulcerated lesion may be used²⁵ (level IIa, grade B).

Specific serological tests such as an immunoglobulin G and/or M (IgM and/or IgM) antitreponemal antibody enzyme immunoassay or chemiluminescence immunoassay with confirmation by another specific treponemal antibody and a raised titre cardiolipin antibody test support a diagnosis of syphilitic proctitis in the presence of symptoms/signs of proctitis and negative tests for other pathogens.

Anorectal herpes simplex virus infection

A herpes simplex virus (HSV) NAAT such as polymerase chain reaction (PCR) should be used routinely, as this is a more sensitive test than culture²⁶ (level IIa, grade B).

Bacterial infections causing proctocolitis

Culture of *Shigella* spp., *Salmonella* spp. or *Campylobacter* spp. from faecal samples yields the diagnosis. Sometimes repeated examinations are necessary before a diagnosis is made. Molecular tests for bacterial pathogens are becoming more widespread and have improved sensitivity over culture, although antimicrobial susceptibility testing still requires a positive culture.²⁷

Amoebiasis

Microscopic examination for the trophozoites of *Entamoeba histolytica* of 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

or trichrome may reveal trophozoites with ingested erythrocytes which is pathognomonic for *Entamoeba 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 *E. dispar* that resembles *E. histolytica* morphologically under the microscope. This differentiation is usually done by using a molecular test NAAT.

Cytomegalovirus infection

The triad of mononucleosis-like illness with rectal bleeding shortly after unprotected anal intercourse is pathognomonic for sexually transmitted cytomegalovirus (CMV) proctitis.²⁸ Suggestive findings on anoscopy or sigmoidoscopy include rectal mucositis and ulceration. CMV serology and biopsy, including CMV immunohistochemistry, are confirmatory. The finding of typical intranuclear inclusion bodies in rectal or colonic biopsies is considered diagnostic.

Giardiasis

Fluid stool samples should be microscopically examined for the trophozoites and cysts of *Giardia lamblia*. Repeated examinations (at least three) are often necessary before a diagnosis is made.

Enzyme immunoassays, direct immunofluorescence tests and specific NAAT for the detection of *Giardia* infection are increasingly available and aiding in diagnosis of *Giardia* infection.²⁹

Cryptosporidiosis and microsporidiosis

Special stool preparations (in consultation with the local microbiologist) 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 tests and NAAT for the detection of cryptosporidial antigens/ DNA have a high sensitivity/specificity and are commercially available²⁹ (level Ib, grade A).

Non-specific proctitis

In some patients with symptoms and signs of a distal proctitis, *N. gonorrhoeae* and *C. trachomatis* cannot be detected. These individuals are said to have non-specific proctitis.

If no infectious cause can be found and the proctitis persists after empiric therapy, the patient should be referred to a gastrointestinal specialist to exclude other causes of proctitis such as Crohns' disease.

Management

Information, explanation and advice for the patient. In all cases of proctitis (symptomatic or asymptomatic) caused by a sexually transmitted pathogen, patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s). This should be reinforced by giving clear and accurate written information. Regular sexual health checks should be offered to those individuals who have frequent changes of sexual partners.

In the prevention of ongoing sexual transmission of the bacterial pathogens the following recommendations should be communicated³⁰ (level III, grade C):

- wash hands after using toilet, before preparing or eating food and after sexual activity;
- avoid anal sex, oral-anal sex (rimming), coprophagia (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 two weeks after recovery (level IV, grade C).

Therapy, partner notification and follow-up.

Rectal gonorrhoea

Patient management should follow that recommended for anogenital gonorrhoea (see 2012 European Guideline on the Diagnosis and Treatment of Gonorrhoea in Adults: <http://www.iusti.org/regions/Europe/euroguidelines.htm>). Concurrent treatment for chlamydial infection should also be given unless this infection has been excluded by microbiological testing (level III, grade C).

Rectal chlamydial infection (non-LGV)

Patient management should follow that recommended for rectal chlamydia (see European guideline for the management of Chlamydia trachomatis infections: <http://www.iusti.org/regions/Europe/euroguidelines.htm>).

Rectal LGV

Patient management should follow that recommended for anorectal LGV (see 2013 European Guideline on

the Management of Lymphogranuloma Venereum: <http://www.iusti.org/regions/Europe/euroguidelines.htm>).

Anorectal syphilis

Patient management should follow that recommended for early syphilis infection (see IUSTI: 2008 European Guidelines on the Management of Syphilis: <http://www.iusti.org/regions/Europe/euroguidelines.htm>).

Anorectal HSV infection

Patient management should follow that recommended for anogenital HSV infection (see 2010 European guideline for the management of genital herpes: <http://www.iusti.org/regions/Europe/euroguidelines.htm>).

Shigella, salmonella and campylobacter infections

Therapy: Antimicrobial therapy is often unnecessary in the treatment of shigella, salmonella and campylobacter infections. If indicated (for example in those with bloody diarrhoea, and in individuals with AIDS or sickle-cell disease in whom infection tends to be more severe and sometimes fatal), the choice of drug is best to be advised by a microbiologist informed of the pattern of antimicrobial resistance in the population. Transmission of ciprofloxacin-resistant *S. sonnei*, among MSM in Montreal, Québec, has been reported.³¹

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. shigella, shiga-toxin producing *E. coli*, 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 given in an oral dose of 750 mg three times daily for 5 to 10 days is the

drug of first choice (level IIa, grade A). Alternatively, tinidazole given in a single daily dose of 2 g by mouth for 2–3 days may be used (level IIb, grade A). This therapy should be followed by an intraluminal agent like Paromomycin 10 mg/kg/day three times daily for 5–10 days or Diloxanide furoate given orally in a dose of 500 mg three times daily for 10 days or Clotrimazole 250 mg three times daily for 10 days to eliminate all infection from the bowel (level IIa, grade B).

Partner notification: In the case of the individual who has not travelled to an endemic area, partner notification should be undertaken. All partners within the preceding 3–4 months should be assessed (level IV, grade 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.²¹ Reported cases associated with acute HIV co-infection resolved upon immune restoration, without antiviral therapy. On the other hand, CMV colitis in immunosuppressed or HIV-infected patients may be progressive, is associated with high mortality, and requires antiviral treatment with (val)ganciclovir.

Partner notification: not required.

Follow-up: In the immunocompetent patient this is unnecessary.

Giardiasis

Therapy:

- Metronidazole given by mouth in a dosage of 2 g daily for 3 days;
- 500 mg two times per day for 5 days is the most commonly used treatment (level IIa, grade B) or;
- Tinidazole in a single oral dose of 2 g is an alternative (level IIa, grade B).

Partner notification: As the infected sexual partner is often symptomless, partner notification should be undertaken in all cases. All partners of patients with symptomatic infection within the preceding month should be assessed.

Follow-up: In the immunocompetent patient this is unnecessary (level IV, grade C).

Cryptosporidiosis and microsporidiosis

Therapy: In the immunocompetent patient, the condition is self-limiting. There is no reliable anti-protozoal agent for the treatment of cryptosporidiosis in HIV-infected patients. However, initiation of HAART is often helpful (level III, grade B) and Paromomycin 500 mg tid for 7 days can be tried (level IV, grade C).

Partner notification: The value of partner notification in patients with cryptosporidiosis is uncertain. In immunocompetent individuals it is a self-limiting condition and there is no definitive treatment. It is doubtful if contact tracing would reduce the risk of onward transmission.

Follow-up: In the immunocompetent patient this is unnecessary.

Non-specific proctitis

Therapy: Syndromic treatment awaiting definite microbiological results:

- doxycycline 100 mg twice daily by mouth for seven days

Partner notification: Not required if no pathogens are found.

Follow-up: Not necessary.

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.

Among HIV-infected patients, gastrointestinal illness can be caused by other infections that usually are not sexually transmitted, including CMV, *Mycobacterium avium*–intracellulare, *Salmonella* spp., *Campylobacter* spp., *Shigella* spp., *Cryptosporidium*, *Microsporidium* and *Isospora*.³² In addition, enteritis can be directly caused by HIV infection.

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.

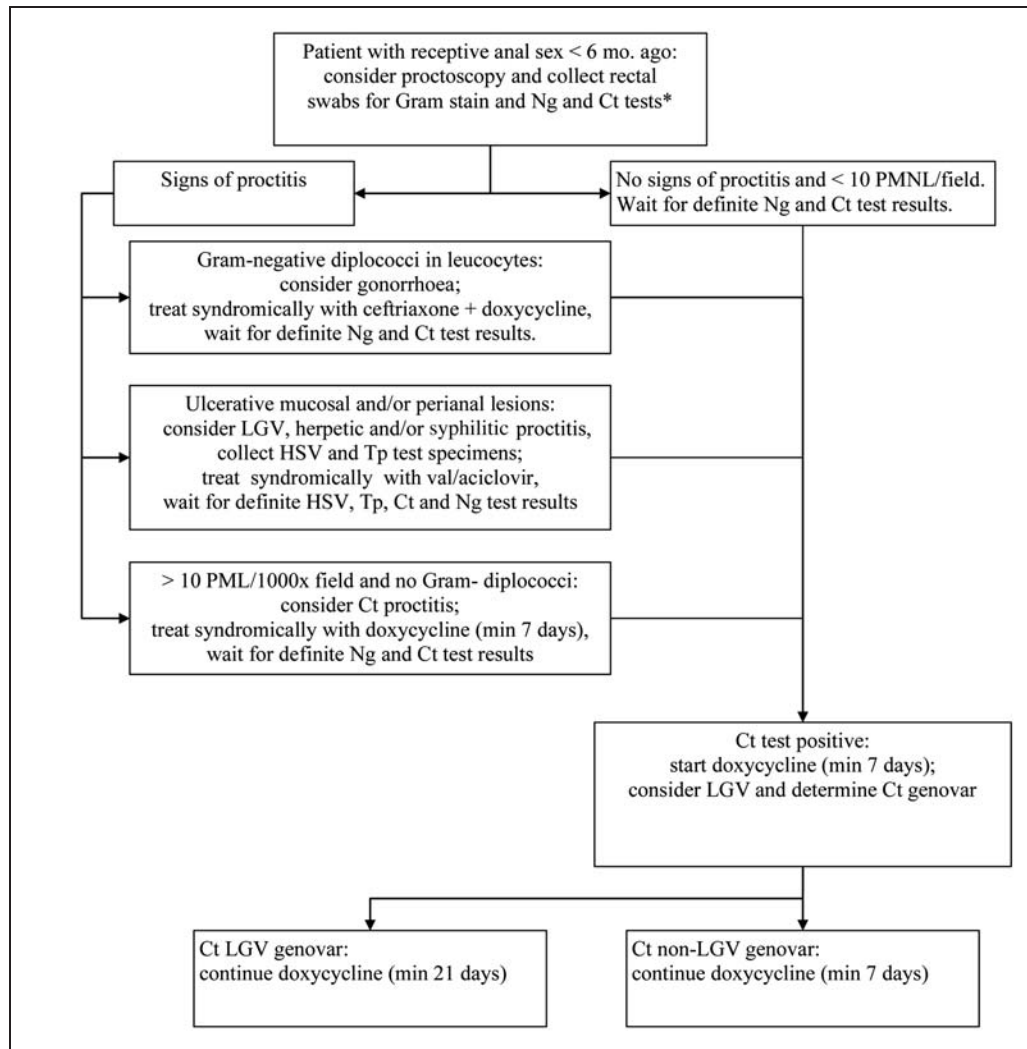


Figure 1. Syndromic management flow chart for patients in whom an anorectal sexually transmissible infection is suspected.

*Perform a full HIV/STI screening (including hepatitis B and C testing and hepatitis B vaccination). Ct: *C. trachomatis*; Ng: *N. gonorrhoeae*; HSV: Herpes simplex virus; LGV: Lymphogranuloma venereum; PMNL: Polymorphonuclear leucocytes; Tp: *T. pallidum*.

If proctitis is suspected, proctoscopy should be performed to inspect for mucosal inflammation and infiltration/swelling and/or ulceration (Figure 1).

If possible, stained smears (preferably Gram) of rectal exudate should be made and the number of polymorphs in light microscopic high-power field (magnification, $\times 1000$) noted; > 10 cells suggests proctitis.³³ 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. When facilities for organism-specific diagnosis of an STI are unavailable or limited, or when a syndromic treatment approach is considered imperative, rigid sigmoidoscopy should be undertaken, if available.

This usually allows differentiation between a distal proctitis and a proctocolitis and will inform on a rational treatment choice.

Treatment

Specific treatment: In the case of patients with mild symptoms, and when microbiological investigations are possible, it is best to await the results of these tests before initiating specific therapy.

Syndromic treatment: In patients with more severe symptoms, or when microbiological testing is impossible, or if there are persistent symptoms and signs but microbiological tests are negative, or if the patient is unable to attend when test results are available,

syndromic treatment (empirical therapy) should be given:

Proctitis: doxycycline 100 mg twice daily by mouth for seven days³⁴;

PLUS: ceftriaxone 500 mg as single intramuscular injection (especially if anorectal gonorrhoea is suspected);

PLUS: valaciclovir 500 mg given orally twice daily for 5–10 days (especially if anorectal HSV infection is suspected); or acyclovir 400 mg three times daily for 5–10 days.

PLUS: benzathine penicillin 2.4 million units i.m. (if rapid diagnostic tests are supportive of the diagnosis of early syphilis); or doxycycline 100 mg twice daily by mouth for 14 days.

Proctocolitis

If the patient has recently visited a geographical area where amoebiasis is prevalent, or if he or she is a sexual contact with a person who has returned from such an area, consider amoebiasis. Presumptive treatment may be considered with:

- Metronidazole 750 mg tid for 5–10 days (level IV, grade C).

Enteritis

In cases associated with bacterial pathogens, fluid replacement is the most important aspect of treatment. When symptoms are severe, antimicrobial therapy may be required. Presumptive treatment may be considered with:

Ciprofloxacin 500 mg twice daily by mouth for 5 days (or co-trimoxazole 960 mg twice daily for 7 days or azithromycin 500 mg once daily for 3 days).

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

Patient Information

A patient information leaflet based on this guideline is available at www.iusti.org.

Proposed review date

April, 2018

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Conflict of interest

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Appendix

Search strategy:

A PubMed search was performed from 2007 to February 2013 using Determinants: proctitis, anal infections, rectal infections, anorectal infections, color-ectal infections.

Levels of evidence

- Ia Evidence obtained from meta-analysis of randomised controlled trials.
- Ib Evidence obtained from at least one randomised controlled trial.
- IIa Evidence obtained from at least one well-designed study without randomisation.
- IIb Evidence obtained from at least one other type of well designed quasi-experimental study.
- III Evidence obtained from well-designed non-experimental descriptive studies such as comparative studies, correlation studies and case control studies.
- IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grading of recommendations

- A (Evidence levels Ia, Ib) Requires at least one randomised control trial as part of the body of

- literature of overall good quality and consistency addressing the specific recommendation.
- B (Evidence levels IIa, IIb, III) Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation.
 - C (Evidence IV) Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.