

GUIDELINES & PROTOCOLS

ADVISORY COMMITTEE

Infectious Diarrhea – Guideline for Ordering Stool Specimens

Effective Date: March 16, 2009

Scope

This guideline applies to the initial laboratory investigation of diarrhea in ambulatory patients greater than 3 years-of-age, where an infectious agent is suspected. This guideline does not apply to immunocompromised patients or to outbreaks of infectious diarrhea.

Diagnostic Code: 009.2 (Infectious Diarrhea)

Prevention

Fecal-oral transmission is the predominant route of transmission.^{1,2} Proper food handling, an avoidance of contaminated/undercooked foods, and avoidance of untreated water are the most common ways to prevent infection. Hand washing is the most effective way to prevent person-to-person spread of diarrheal pathogens.¹

Definition

Severe diarrhea (of any duration) is defined as diarrhea with one or more of the following:

- fever $\geq 38.5^{\circ}\text{C}$
- bloody stools*
- profound systemic illness/toxicity
- hemodynamic instability
- greater than 6 diarrheal episodes per day for greater than 5 days

Mild to Moderate Diarrhea is defined as:

- any diarrhea not meeting the severe category

Investigation

a) **Severe Diarrhea (of any duration)**

- **Investigate patients with severe diarrhea promptly**, with stool culture, *Clostridium difficile* testing, and, if clinically indicated, ova and parasite (O&P) testing.
- Consider stool for viral pathogen testing when an outbreak is suspected. See section e) Public Health.

* Bloody stools are routinely tested for *Escherichia coli* O157:H7, with further testing for enterohaemorrhagic *E. coli* (EHEC) available at reference laboratories. Indicate a history of bloody diarrhea on the laboratory requisition.³

b) **Mild to Moderate Diarrhea (≤ 5 days duration)**

- Most cases of mild to moderate diarrhea are of viral etiology,¹ are self-limited, and generally do not require laboratory investigations.
- For patients with recent (< 3 months) or current antibiotic use, consider antibiotic-associated diarrhea.



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- Earlier stool testing is warranted for patients who meet any of the following criteria:
 - patients ≥ 70 years-of-age
 - severe abdominal pain
 - if *Clostridium difficile*-associated disease (CDAD) is suspected

c) Mild to Moderate Diarrhea (> 5 days duration)

- A stool culture for bacterial pathogens is recommended³ for patients who have mild to moderate diarrhea for greater than 5 days.
- ***C. difficile* toxin testing is not part of a routine stool culture and needs to be specifically requested³ in the following circumstances:**
 - recent (< 3 months) or current antibiotic use
 - recent hospitalization
 - residence in a long-term care facility
 - patient with a previous confirmed or suspected current episode of CDAD
- O&P examination is recommended for patients at-risk for parasitic infections.

These include:

- travel to or immigration from an endemic area
- prolonged diarrhea (> 2 weeks)
- consumption of unsafe food or untreated water
- children attending daycare
- swimming in unsafe water
- men who have sex with men

In low-risk populations, it is reasonable to submit a single specimen, with a follow-up specimen submitted if initial results are negative and symptoms persist. For patients at high-risk for parasitic infection, two stool specimens collected at least one day apart are recommended. If submitted using the same requisition, high risk status must be indicated.³

d) Collection and Transport of Stool Specimens

- Stool culture for bacterial pathogens: one stool specimen is sufficient in most cases.
- *C. difficile* toxin testing: one stool specimen is sufficient in most cases.

Note: If initial *C. difficile* toxin test is negative and clinical suspicion is high, or if there are concerns regarding the timing of specimen collection and transport to the laboratory, consult the laboratory as additional testing may be indicated.

- O&P examination
 - Specimen must be submitted in an appropriate preservative (SAF fixative: sodium acetate, acetic acid, formalin).
 - If two stool specimens are ordered on the same requisition, high risk status must be indicated. More than two stool specimens per requisition requires consultation with the laboratory physician.
- Viral pathogens: stool for viral pathogens are not routinely tested. For a suspected outbreak of viral gastroenteritis, consult the local Medical Health Officer.⁴ One stool specimen submitted in a sterile container is sufficient in most cases.

For the investigation of bacterial pathogens, stool specimens should be delivered to the laboratory as soon as possible as a delay may compromise bacterial pathogen recovery. A single stool specimen, properly collected and promptly submitted, will identify most patients with a bacterial pathogen. Additional stool specimens need to be submitted if the culture results are negative, symptoms persist, and other causes cannot be found. If there are concerns regarding timing or transport of the specimen, consult the laboratory.

Include a relevant clinical history on the laboratory requisition to help tailor appropriate testing.³

e) Public Health

Public Health receives notification of all reportable enteric pathogens through the laboratories once an etiology is established. However, timely notification of infectious diarrhea by the clinician to the local Public Health office is warranted in certain populations or high risk settings.⁴ Laboratory investigations, in these cases, should be initiated as soon as possible. These populations/settings include:⁵

- food handlers
- daycare employees and children who attend daycare or elementary school
- health care workers with direct patient contact in long-term and acute-care facilities
- potential outbreaks where food or water has been identified as a possible source
- patients identified as part of a community or facility outbreak

Note: Testing for viral pathogens conducted for the purpose of outbreak investigation requires consultation with the local Medical Health Officer or Public Health.⁴ For the public health office in your region, contact your local health authority. For a list of reportable pathogens in BC, consult the Reportable Communicable Disease List, available at the BC Centre for Disease Control (BCCDC) website at <http://www.bccdc.org/content.php?item=7>

Rationale

Most cases of mild diarrhea are of viral etiology, while severe diarrhea, especially associated with fever and bloody stools, tends to be of bacterial etiology, often indicating invasive disease. Chronic infectious diarrhea is often caused by parasites.

The most commonly recognized gastrointestinal viruses are norovirus and rotavirus, both of which have been associated with community and hospital related outbreaks.^{1,2,6} Although the infections are self-limited, they may cause debilitating illness in the very young, the elderly, and in hospitalized patients. In children, rotavirus, adenovirus and astrovirus can also be associated with substantial morbidity.¹

Diagnostic microbiology laboratories in British Columbia (BC) may routinely test stool specimens submitted for bacterial culture for the following enteric pathogens: *Campylobacter*, *Salmonella*, *Shigella*, *E. coli* O157:H7, *Yersinia*, *Vibrio*, *Aeromonas*, and *Plesiomonas* species. Consult your local laboratory for information on pathogens routinely tested.

In BC, the most common reportable causes of bacterial diarrhea include *Campylobacter*, *Salmonella*, *Shigella*, and enterohaemorrhagic *E. coli* (EHEC).⁷ *Campylobacter* infections tend to be food and water-borne illnesses¹ and are usually self-limited. *Salmonella* spp. (other than *S. Typhi*/*Paratyphi*) are associated with contaminated and/or undercooked food or exposure to certain animals (e.g. turtles, lizards, chickens).¹ *Salmonella* ser. *Typhi* and *Salmonella* ser. *Paratyphi* are found in returning travellers most often presenting with systemic illness, with or without diarrhea. Blood cultures are recommended in the work-up of these patients or if other invasive or disseminated infections are suspected. *Shigella* spp. is primarily a human pathogen and is highly infectious.¹ Risk factors include daycare, returning travellers, and men who have sex with men. Enterohaemorrhagic (verotoxin producing) *E. coli* (EHEC) can cause bloody diarrhea and may be associated with haemolytic uremic syndrome (HUS),¹ mostly in children, and rarely, thrombotic thrombocytopenic purpura (TTP) in adults. *E. coli* O157:H7 is the most common verotoxin producing serotype. Although *Yersinia* species are sometimes isolated from patients with diarrhea, not all species of *Yersinia* are pathogenic.

In travellers, enterotoxigenic *E. coli* (ETEC), not to be confused with enterohaemorrhagic *E. coli* (EHEC), is a significant pathogen causing self-limited, watery diarrhea. Currently, no routine laboratory tests are available to identify ETEC in BC.

Bloody diarrhea is most commonly associated with enterohaemorrhagic *E. coli* (EHEC), *Campylobacter jejuni/coli*, *Shigella* spp., and *Clostridium difficile*-associated disease (CDAD).^{8,9} Bloody stools are routinely tested for *E. coli* O157:H7, with further testing for EHEC available at reference laboratories. A history of bloody diarrhea needs to be indicated on the laboratory requisition. Bloody diarrhea is not characteristic of viral or parasitic etiology with the exception of *Entamoeba histolytica*.⁸

CDAD, a recognized cause of diarrhea in hospital and long-term care settings, has classically been associated with exposure to antimicrobial agents.¹ Emergence of highly virulent strains of *C. difficile* in the community is of particular concern with disease reported in patients with no known, or with remote risk factors. Toxin detection is essential for the diagnosis of CDAD and may be performed by various methods.⁸ Culture of *C. difficile* alone is not diagnostic as non-toxin producing strains may be a part of the normal enteric flora.⁸ For patients where there is a high clinical suspicion of CDAD but negative toxin results, repeat or alternative testing may be performed in

consultation with the laboratory. Recurrence of CDAD symptoms occurs in a significant number of patients. A test of cure is not recommended as toxin can be present in the stool for several months after clinical recovery.

Vibrio parahaemolyticus infection in BC is usually associated with consumption of undercooked or raw shellfish, usually in the summer season, and symptoms are usually self-limited.⁷ *Vibrio cholera* is rare in BC and requires specialized testing. Other less common causes of bacterial diarrhea include *Aeromonas* and *Plesiomonas* infection which are generally self-limited.

For the investigation of intestinal parasites, a study performed in BC in 1990 demonstrated that 82 per cent of significant parasites were identified from the first stool specimen and 89 per cent from the second.¹⁰ As parasites are shed intermittently and mixed infections are common, multiple specimens may be required for the diagnosis of parasitic infection.

The most common cause of parasitic diarrhea in BC is *Giardia lamblia/intestinalis*.⁷ This parasite may be recovered from returning travellers or from patients exposed to untreated water sources in BC.

Entamoeba histolytica can cause severe diarrhea. Routine ova and parasite investigation cannot differentiate between pathogenic *Entamoeba histolytica* and non-pathogenic *Entamoeba dispar*. Definitive identification requires specialized testing.

Cryptosporidium spp. is a hardy parasite present in certain treated and untreated water supplies. Diarrhea is self-limited in most patients, but can be severe and prolonged in the immunocompromised, the young, and the elderly.

Cyclospora spp. is a parasite causing diarrhea in two clinical settings: returning travellers, and exposure to contaminated, usually imported, food sources (e.g. raspberries, basil).⁷

Dientamoeba fragilis is a commonly identified parasite in children which may be associated with intermittent diarrhea, abdominal pain, and bloating.

Blastocystis hominis is a commonly recovered parasite whose role as a pathogen is controversial.

References

1. Musher DM, Musher BL. Contagious acute gastrointestinal infections. N Engl J Med 2004;351(23):2417-2427.
2. Centers of Disease Control and Prevention. Norovirus outbreak in an elementary school – District of Columbia, February 2007. MMWR 2008;56(51):1340-43.
3. Standard Out-Patient Laboratory Requisition. HLTH 1901 Rev. 2006/05/19.
4. Health Act Communicable Disease Regulation. B.C. Reg. 4/83 O.C. 6/83. Available from http://www.qp.gov.bc.ca/statreg/reg/h/health/4_83.htm 2008 April [14 screens]. Accessed October 23, 2008.
5. BC Centre for Disease Control. Communicable Disease Control. Enteric cases and their contacts: exclusion from high risk settings. 2007 Dec [34 pages]. Available at: <http://www.bccdc.org/download.php?item=3111>. Accessed October 23, 2008.
6. Fankhauser RL, Monroe SS, Noel JS, et al. Epidemiologic and molecular trends of "Norwalk-like Viruses" associated with outbreaks of gastroenteritis in the United States. J Infect Dis 2002;186:1-7.
7. BC Centre for Disease Control. 2006 Epidemiology report: 2006 British Columbia annual summary of reportable diseases. Available from: www.bccdc.org . Accessed October 23, 2008.
8. Infectious Diseases and Immunization Committee, Canadian Paediatric Society (CPS). Clostridium difficile – pathogen or pest? Paediatr Child Health 2000;5(6):349-52.
9. Gerding DN, Olson MM, Peterson LR, et al. Clostridium difficile-associated diarrhea and colitis in adults: a prospective case-controlled epidemiologic study. Arch Intern Med 1986;146:95-100.
10. Issac-Renton J, Proctor E, Champagne S, et al. Diagnostic yield of intestinal parasites in sequential stool specimens: a collaborative study. American Society for Microbiology 1990 Poster C212.

Resources

BC Centre for Disease Control (BCCDC)

655 12th Ave. West

Vancouver, BC

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Tel: 604 660-0584

Fax: 604 660-6066

<http://www.bccdc.org/>

BC Health Files

BC HealthGuide Program

Ministry of Health

<http://www.bchealthguide.org/healthfiles/index.stm>

Bugs and Drugs 2006 – Antimicrobial Reference Book

A comprehensive and evidence-based reference for community and hospital-based health care practitioners.

Available from Capital Health BizWorx

<http://www.bugsanddrugs.ca>

Associated Documents

The following documents accompany this guideline:

- Algorithm for the Investigation of Infectious Diarrhea
- Summary

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission

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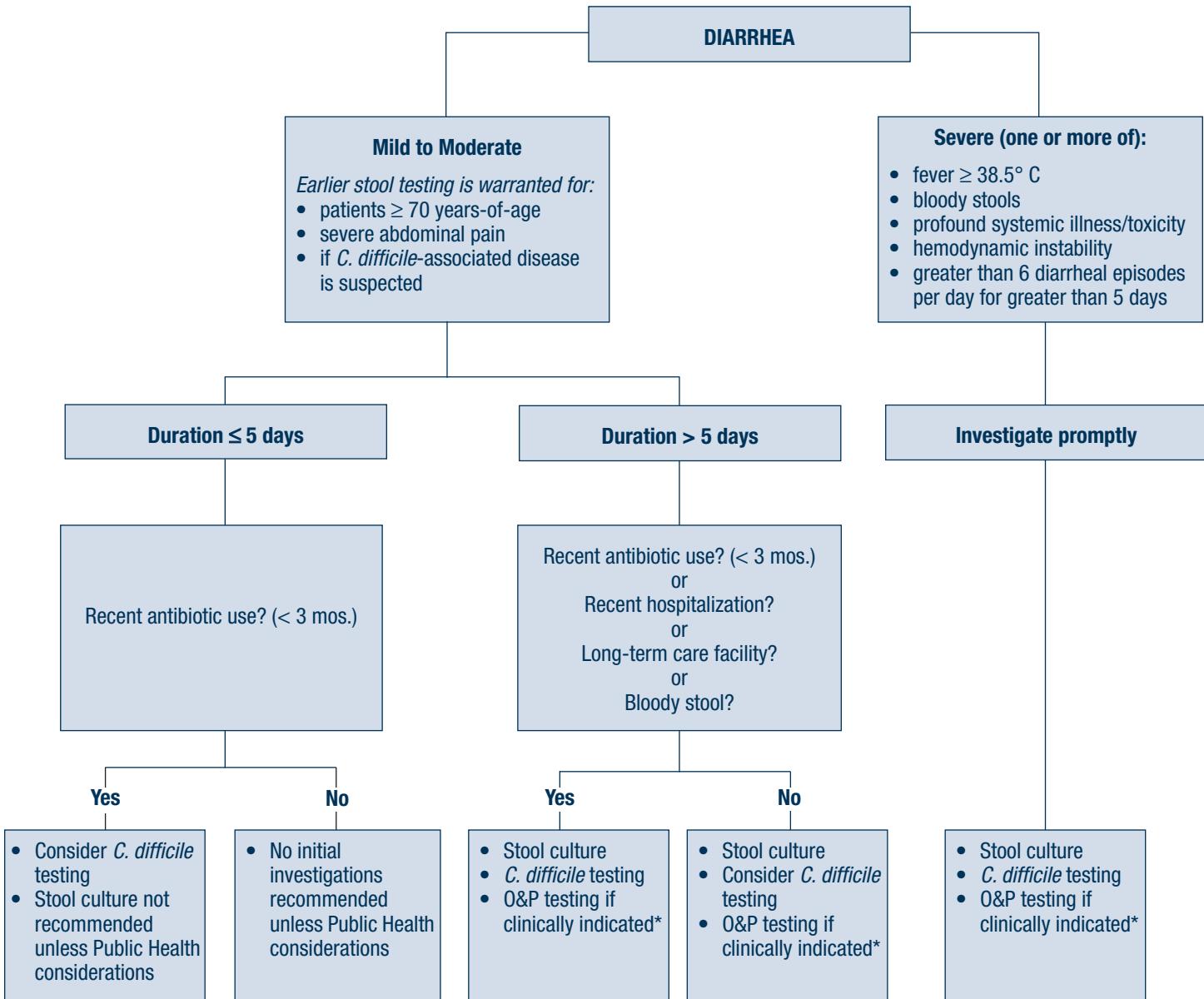
The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

Disclaimer

The Clinical Practice Guidelines (the “Guidelines”) have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems.

This algorithm applies to patients > 3 years-of-age presenting with suspected infectious diarrhea.
It does not apply to the investigation of diarrhea in immunocompromised patients or in an outbreak situation.



*At-risk for parasitic infection

- travel to or immigration from an endemic area
- prolonged diarrhea (> 2 wks)
- consumption of unsafe food or untreated water
- children attending daycare
- swimming in unsafe water
- men who have sex with men

Note: Stool for viral pathogens are not routinely tested, but should be considered when an outbreak of viral gastroenteritis is suspected. Contact local Public Health for consultation.

