BCGuidelines.ca
Guidelines & Protocols Advisory Committee

Infectious Diarrhea – Guideline for Investigation

Effective Date: October 27, 2022

Scope and Rationale

This document provides guidance for primary care practitioners regarding adults and children greater than 2 months of age on appropriate testing for suspected community onset infectious diarrhea, including *Clostridioides difficile* (formerly *Clostridium difficile*) infection (CDI). This guideline does not apply to outbreak situations, or patients with hospital onset diarrhea. The document includes a brief test interpretation and indications for antimicrobial management that is applicable for the general outpatient population, however it does not provide in-depth management of infectious diarrhea.

While clinical symptoms and exposure history may narrow down the possible causes of infectious diarrhea, previously there was a potential need for multiple stool tests, and healthcare visits to determine the cause. The Infectious Diarrhea Panel (IDP) is a new stool test that combines stool cultures, ova & parasites (O&P) and *C. difficile*. IDP detects a standardized set of 14 viral, bacterial and protozoa pathogens (*Table 1: Pathogens that are included in every laboratory's Infectious Diarrhea Panel [IDP]*) within a single specimen. Not only does IDP detect a broader range of pathogens than prior methods, but it is also faster and more sensitive. It functionally replaces stool cultures and O&P; however, standalone *C. difficile* tests are still available. This guideline serves to describe the most appropriate use of IDP, considering that IDP is an expensive test. The guideline also describes the use and interpretation of *C. difficile* tests, due to advances in the understanding of CDI.

Key Recommendations

- Stool testing is not required in most cases of acute (≤ 7 days) diarrhea or resolving diarrhea.
- The Infectious Diarrhea Panel (IDP) should be requested if diarrhea is severe of any duration or prolonged >7 days. This is a new test that replaces stool cultures and O&P, and it also detects *C. difficile*.
- Request IDP only once per diarrheal episode. Only one specimen is required i.e., O&P x2 is no longer required.
- For most patients with infectious diarrhea, treatment is supportive with targeted antimicrobial management guided by the patient's clinical history, course of illness and pathogen identified by IDP.
- If the IDP is positive but the patient is healthy and no longer symptomatic, antimicrobial treatment is not required in most cases. Antimicrobial treatment is required if *Entamoeba histolytica*, typhoidal *Salmonella*, or *Vibrio cholera* was detected by IDP. Antimicrobial treatment may also be warranted in those at risk of transmitting certain pathogens (e.g., *Giardia* spp. and *Shigella* spp.) to others.
- Standalone *C. difficile* test should be requested in those with suspected recurrence or unexpected persistence of *C. difficile* infection (CDI), and in patients who have been hospitalized for more than 5 days and develop nosocomial diarrhea.
- A positive *C. difficile* result does not differentiate between infection and colonization (i.e., asymptomatic carriage). Treatment is required only in those who are symptomatic, where *C. difficile* is the likely cause.
- Stop and/or avoid any antibiotics in patients with positive STEC (Shiga Toxin-producing *E. coli*) results, due to risk of hemolytic uremic syndrome (HUS). Patients with high-risk strains (e.g., *E. coli* O157:H7) require immediate assessment and may require hospitalization. See *Appendix 1: Frequently asked questions (FAQ) – What is the difference between Shiga toxin-producing E. coli (STEC) and E. coli O157:H7?*.

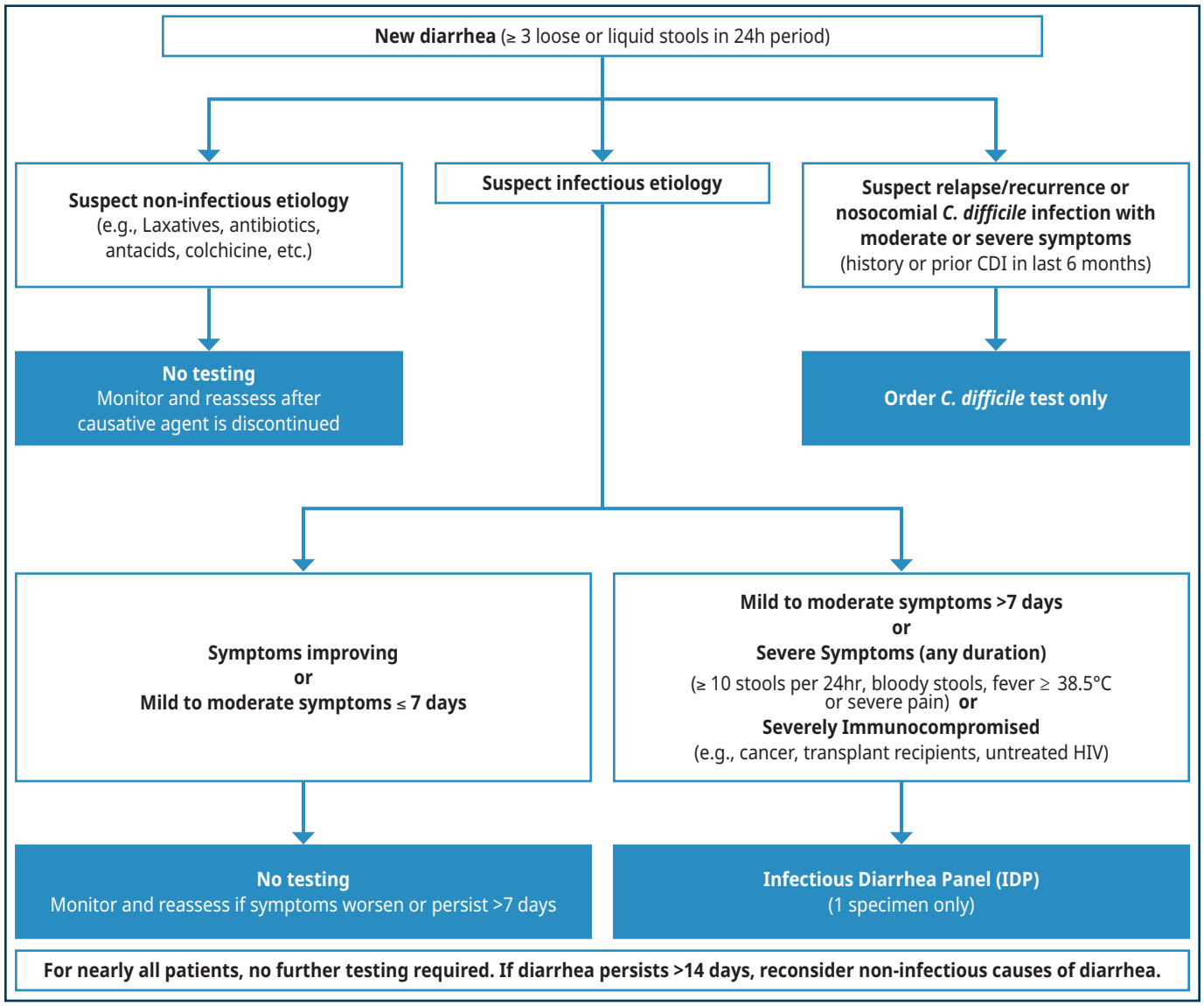
Diagnostic Tests for Infectious Diarrhea

Infectious Diarrhea Panel (IDP) – (New for 2022)

The Infectious Diarrhea Panel (IDP) is a new test that functionally replaces the "Stool Culture" and the "Stool for Ova & Parasites" tests. It also includes *C. difficile* (for patients >2 years of age), although the standalone *C. difficile* test is still available. Refer to *Appendix 1: FAQ – Why is C. difficile included in IDP?* for more information.

The IDP detects the most common enteric viral, bacterial, and protozoal pathogens (*Table 1: Pathogens that are included in every laboratory's Infectious Diarrhea Panel [IDP]*) faster and with greater sensitivity than culture and microscopy. IDP combines a multiple gene target (multiplex) nucleic-acid amplification test (NAAT) with other methods. When applicable, antimicrobial susceptibilities are provided.

Figure 1. Diagnostic workup of acute diarrhea



A stool microscopy test for protozoa may be requested if the IDP is negative and the patient:

- Has a history of **recent travel or immigration** from low- or middle-income country; OR
- **Is severely immunocompromised**

Consider consultation with a specialist to assess likelihood of rare or atypical infections.

Refer to *Appendix 1: FAQ – Considering that the management of most infectious diarrhea is supportive, what is the rationale for performing diagnostic testing for diarrhea?* for more information.

Table 1. Pathogens that are included in every laboratory's Infectious Diarrhea Panel (IDP)[a]

Viral Pathogen	Bacterial Pathogen	Protozoal Pathogen
Adenovirus 40/41 Norovirus GI/GII Rotavirus	*Campylobacter* spp. *Clostridioides difficile*[b] Shiga toxin-producing *E. coli* (STEC) *Salmonella* spp. *Shigella* spp. *Yersina enterocolitica* *Vibrio* spp.	*Cyclospora cayetanensis* *Cryptosporidium* spp. *Entamoeba histolytica* *Giardia* spp.

a The list of pathogens may be modified periodically, in line with changes in epidemiology and technology
b C. difficile is not routinely reported in those under 2 years old
Refer to Appendix 1: FAQ – How was the list of pathogens in Table 1 established? for more information.

- Test ordering for Infectious Diarrhea Panel (IDP):
  - If either stool culture or O&P is ordered, if available the laboratories will automatically perform the IDP.
  - Only one specimen is required. Except in rare or specific circumstances this test should not be repeated.
- Specimen collection and storage for IDP will be as determined by your local laboratory provider:
  - Advise patients that samples should be submitted to the laboratory as soon as possible. If more than a 2-hour delay is anticipated that, store refrigerated at 4°C.

Clostridioides difficile (formerly *Clostridium difficile*) Test

This is the most common pathogen detected in all stool specimens in British Columbia (BC). However, a positive test does not differentiate *C. difficile* infection from colonization. Colonization is defined as the absence of clinical symptoms of *C. difficile* infection (e.g., diarrhea, ileus, toxic megacolon) or the presence of an alternative explanation of these symptoms.[1] *C. difficile* colonization does not require treatment. Refer to *Appendix 1: FAQ – How do I discern C. difficile infection from colonization?* for more information.

- Test ordering for *Clostridioides difficile*:
  - If IDP, stool culture or O&P are added on the same requisition, only the IDP will be performed.
  - If only *C. difficile* is required, specifically order "*C. difficile*" on the requisition.
  - Do not routinely order on patients ≤ 24 months old as they are likely to have asymptomatic colonization. Consult with a medical microbiologist or a pediatric infectious diseases physician.
  - Tests should not be repeated within 7 days unless the test is negative and there is a clinical suspicion of *C. difficile* infection.
  - Tests should not be performed in patients who are on *C. difficile* treatment, e.g., oral vancomycin, metronidazole, or fidaxomicin.
  - Test of cure should not be performed.
- Specimen collection and storage for *C. difficile*:
  - Collection and storage as determined by your local laboratory provider.

Stool Microscopy for Protozoa

Certain rare protozoal pathogens are not detectable by the IDP, and detection requires manual microscopy. Such pathogens are not endemic within Canada and are usually acquired after recent (within 6 months) travel out of country with consumption of contaminated foods/liquids. Stool microscopy should not be ordered for routine diarrhea testing.

- Test ordering for Protozoa:
  - Manually write "Stool Microscopy" on the requisition.
  - Only one specimen is usually required. If high suspicion, consider ordering two specimens at least one day apart. See *Appendix 1: FAQ – Why are helminths (worms) not included in IDP?* for more information.
- Specimen collection and storage for Protozoa:
  - Collect stool in container with "SAF Fixative" or as determined by your local laboratory provider.

Stool Culture

This test is being phased out and integrated into the IDP.

Stool for O&P

This test is being phased out and integrated into the IDP.

Other Related Laboratory Tests

Several diagnostic tests are available for gastrointestinal infections that may not cause diarrhea (e.g., worm infections, (refer to *Appendix 1: FAQ – I'm still concerned about a worm infection. What do I order to make a diagnosis?*), or for non-infectious causes of diarrhea (e.g., inflammatory bowel disease). See *Appendix 2: Other related laboratory tests* for more information.

Diagnostic Approach for Acute Diarrhea

Clinical History and Evaluation

Diarrhea is defined as the passage of three or more loose or liquid stools per 24 hours OR more frequent than is normal for an individual.[2] Clinical history is essential prior to testing, and should include:[3]

- **Assessment of disease severity and duration.** Severe Diarrhea (of any duration) is defined as diarrhea with **one or more** of the following:
  - Fever ≥38.5°C.
  - More than 10 loose to watery bowel movements in 24 hours.
  - Severe abdominal pain.
  - Blood in stools.
  - Hospitalization due to diarrhea.
  - Suspected Hemolytic uremic syndrome (HUS) (e.g., anemia, hypertension, acute kidney injury or neurologic symptoms in children*).[4]
- Assessment of risk factors and underlying disease(s):
  - **Immunocompromised** is defined as having the immune response attenuated by the administration of immunosuppressive therapy, malnutrition or by some disease processes (e.g., untreated Human Immunodeficiency Virus [HIV] Infection or congenital immunodeficiency).[5]
  - **People at extremes of age and/or with severe frailty** have increased risk of dehydration due to diarrhea.

* Symptoms in children vs. adults

- Assessment for **non-infectious** causes of diarrhea:
  - Recent use of new medication or change in dose/frequency of current medication (e.g., laxatives)
  - Other common causes: changes in diet, non-infectious gastrointestinal diseases, and endocrine disorders. Refer to *Table 3: Causes of non-infectious diarrhea* for more information.
- Prior history of or **risk for *C. difficile*** including:
  - Previous history or suspected current episode of *C. difficile* infection.
  - Antibiotic use within 3 months prior to onset of diarrhea.
  - Hospitalization or visit to a healthcare facility within 30 days prior to onset of diarrhea.
  - Long-term care facility resident.
- Assessment of suspected exposures and potential sources of infectious diarrhea:
  - Travel to or immigration from low/middle income countries.
  - Consumption of contaminated and/or undercooked food.

Consumption of or swimming in contaminated water (including oceans and natural bodies of water). If Mild to Moderate Acute Diarrhea

- Less than or equal to 7 days duration:
  - No testing required.
  - Most cases resolve with supportive treatment (e.g., electrolytes and hydration) within 7 days.[6]
- More than 7 days duration:
  - Order an Infectious Diarrhea Panel (IDP).
  - While most viral and bacterial gastroenteritis in immunocompetent patient resolves within 7 days, occasionally these pathogens result in prolonged diarrhea or severe symptoms. In contrast, protozoal pathogens such as *Giardia* may result in several weeks to months of diarrhea and malabsorption. The goal of timely diagnosis is to decrease morbidity, when possible, with targeted treatment as indicated and to provide prognosis. See *Appendix 1: FAQ – Considering that the management of most infectious diarrhea is supportive, what is the rationale for performing diagnostic testing for diarrhea?*

If Severe Diarrhea (of any duration) or Immunocompromised Patient

- Order an Infectious Diarrhea Panel (IDP).
- The goal of timely diagnosis is to decrease morbidity with targeted treatment and to provide prognosis. Refer to *Appendix 1: FAQ – Considering that the management of most infectious diarrhea is supportive, what is the rationale for performing diagnostic testing for diarrhea?* for more information.

Risk for *C. difficile* Infection Only

- With the availability of IDP (which also detects *C. difficile*), a standalone *C. difficile* test has limited indications:
  - Patients with symptoms similar to prior *C. difficile* infection where relapse or recurrence is suspected; or
  - Patients who develop nosocomial diarrhea, after being hospitalized for more than 5 days.
- Traditionally, *C. difficile* test was only ordered in patients with new onset diarrhea after recent antibiotics and/or hospitalization. However, *C. difficile* infection can occur in the absence of these risk factors. The IDP will be able to detect these unsuspected community-acquired casers.
- Do not order a *C. difficile* test unless the patient has diarrhea. Formed stools should NOT be submitted for testing.
- Testing for colonization or test of cure should not be ordered as a positive result may lead to unnecessary treatment due to high rates of asymptomatic colonization. Refer to *Appendix 1: FAQ – How do I discern C. difficile infection from colonization?*

Test Interpretation

Infectious Diarrhea Panel

Table 2: Summary of clinical presentation and indications for antimicrobial treatment summarizes the most common clinical presentations and complications for pathogens reported by the IDP. Note that all BC laboratories will always detect a minimal set of 14 pathogens (see *Table 1: Pathogens that are included in every laboratory's Infectious Diarrhea Panel [IDP]*), although some BC laboratories may report additional pathogens.

Most diarrhea is self-limited and managed by supportive treatment. *Table 2: Summary of clinical presentation and indications for antimicrobial treatment* briefly provides guidance when antimicrobial treatment is indicated (or avoided) for the general population with typical infections. Patients with complicated medical histories, atypical presentations and/or severe symptoms may require specific treatment and/or specialist consultation. Refer to *Appendix 1: FAQ – The syndromic IDP test appears to oppose principles of test stewardship, where diagnostic tests should be judiciously selected based on the differential diagnosis. What was the rationale in adopting this approach?* for more information.

Table 2: Summary of clinical presentation and indications for antimicrobial treatment

Pathogen	Clinical presentations and complications	Indications for antimicrobial treatment
Pathogens that are included in every laboratory's IDP		
Adenovirus 40/41[c]	Typically found in children.	None.
***Campylobacter* spp.**[c]	Occasionally may present as colitis, pseudoappendicitis and occasionally bacteremia. About 1 in every 1000 cases leads to Guillain-Barré syndrome (GBS).	Only in those with severe disease, or at risk for **severe** disease.
Clostridioides difficile	Risk of severe and fulminant colitis. Relapses and recurrences are common.	Only in those symptomatic. See specific *C. difficile* infection guidelines.[7]
***Cryptosporidium* spp.**	Often asymptomatic. May cause severe chronic diarrhea and dehydration in the severely malnourished and/or immunocompromised.	Treatment may be beneficial in some circumstances. Consider referral for symptomatic immunocompromised patients.
Cyclospora cayetanensis[c]	Often asymptomatic. If symptomatic, diarrhea may be accompanied with fatigue and myalgias.	Only in those symptomatic or severely immunocompromised.
***E. coli*, Shiga toxin-producing (STEC)**[c] – includes *E. coli* O157:H7	Bacterial toxin-mediated disease. Illness severity is strain dependent. See *Appendix 1: FAQ – What is the difference between Shiga toxin-producing E. coli (STEC) and E. coli O157:H7?* for more information. High-risk strains (e.g., O157:H7) can cause enterohemorrhagic disease (i.e., bloody diarrhea) and risk progressing to hemolytic uremic syndrome (HUS).	No antibiotics and stop all other antibiotics to prevent further release of toxins. High-risk strains (e.g., O157:H7) require assessment and possibly hospitalization due to risk of HUS.

Pathogen	Clinical presentations and complications	Indications for antimicrobial treatment
Entamoeba histolytica	May cause colitis with bloody diarrhea. Risk of extraintestinal infections.	All cases require treatment. Specific treatment depending on severity and sites of infection.
***Giardia* spp.**[c]	May cause prolonged diarrhea (weeks to months).	Only in those moderately symptomatic, at risk for transmission to others, or severely immunocompromised.
Norovirus GI/GII[c]	Found in all ages. Associated with outbreaks.	None.
Rotavirus A[c]	Typically found in children. May test positive if recently received oral rotavirus vaccine.	None.
***Salmonella* spp.**[c] - typhoidal (S. Typhi or S. Paratyphi) - nontyphoidal (all other *Salmonella*)	**Typhoidal:** Enteric fever (systemic illness with abdominal symptoms). Diarrhea may not be present. **Nontyphoidal:** Bacteremia, with progression to an endovascular infection (e.g., mycotic aneurysm) in those >50 years, cardiovascular disease, or immunosuppressed.	**Typhoidal:** All confirmed cases require treatment. **Nontyphoidal:** Only in those with **severe** disease, or at risk for endovascular infection. Order blood culture if suspect systemic infection.
***Shigella* spp.**[c]	May cause colitis with bloody diarrhea. Risk of neurological symptoms (e.g., seizures).	Only in those symptomatic, at risk for transmission to others, or severely immunocompromised.
Yersinia enterocolitica[c]	May present as pseudoappendicitis or mesenteric lymphadenitis in addition to diarrhea. Post-infectious sequelae include erythema nodosum and reactive arthritis.	Only in those with **severe** disease, or at risk for severe disease.
***Vibrio* spp.** - includes *V. cholerae* and non-cholerae infections	**Cholera:** Toxin-mediated disease, although only some strains of *V. cholerae* produces the toxin. **Non-cholerae:** Usually related to seafood or aquatic exposure. Risk of bacteremia in those with underlying liver disease.	**Cholera:** Aggressive fluid resuscitation. Antibiotics are an adjunctive therapy in those with moderate to severe illness. **Non-cholerae:** Only in those with **severe** disease, or at risk for severe disease.
Additional pathogens reported by some laboratory's IDP		
***Aeromonas* spp.**	Usually related to seafood or aquatic exposure.	Only in those with **severe** disease, or at risk for severe disease.
Astrovirus[c]	Found in all ages.	None.
Blastocystis hominis*	Not usually pathogenic. Recent literature considers this may be a part of a healthy intestinal microbiome but there may be some biotypes that produce symptoms.*	Most cases do not require treatment.*
Dientamoeba fragilis	Not usually pathogenic. Recent literature considers this may be a part of a healthy intestinal microbiome.*	Most cases do not require treatment.*
***E. coli*, enteroaggregative (EAEC)**[c]	Agent of Traveler's diarrhea.	Only in those with **severe** disease, or at risk for severe disease.
***E. coli*, enteroinvasive (EIEC)**[c]	Closely related with *Shigella*, with similar risk of colitis with bloody diarrhea.	Only in those with **severe** disease, or at risk for severe disease.
***E. coli*, enteropathogenic (EPEC)**[c]	Typically found in children.	None.
***E. coli*, enterotoxigenic (ETEC)**[c]	Agent of Traveler's diarrhea.	Only in those with **severe** disease, or at risk for severe disease.
Plesiomonas shigelloides	Related with travel to tropical countries and consumption of contaminated food/ water.	Only in those with **severe** disease, or at risk for severe disease.
Sapovirus[c]	Typically found in children.	None.

c These pathogens are reported to public health
** Refer to Appendix 1: FAQ – What about Blastocystis hominis and Dientamoeba fragilis? for more information.*

Limitations of the Infectious Diarrhea Panel (IDP)

1. **Detection of resolved or asymptomatic infections:**
   - The IDP is very sensitive at detecting low amounts of pathogens. It may also detect non-viable pathogens that represent resolved infections, or asymptomatic infection/colonization.
   - Typically for immunocompetent patients, if the IDP is positive and the symptoms have resolved or are improving, no further action is required, **with a few exceptions** (see *Table 2: Summary of clinical presentation and indications for antimicrobial treatment*). (i.e., Shiga toxin-producing *E. coli* [STEC], *Entamoeba histolytica*, typhoidal *Salmonella*, *Vibrio cholerae*).

2. **Susceptibility testing for bacterial pathogens is not always performed:**
   - If a bacterial pathogen is detected by the IDP, the laboratory will attempt to provide additional testing for confirmation and susceptibility testing, if indicated.
   - Occasionally, susceptibility testing may not be successful as the organism may not be cultivatable. If antimicrobial treatment is warranted, refer to the reporting laboratory's antibiogram or discuss with the laboratory physician/ medical microbiologist.

3. **Other pathogens and bacterial toxins are not detected:**
   - While IDP detects a broader range of pathogens than traditional methods, it does not detect all causes of infections diarrhea (Refer to *Appendix 1: FAQ – How was the list of pathogens in Table 1 established?*). For example, it does not detect *Bacillus cereus*, *S. aureus* enterotoxin and other toxin-mediated disease. However, such infections are typically brief and do not warrant further investigation.

4. **Potential false positive results:**
   - False positive results are rare. However, if the pathogen identified does not correlate clinically, please contact the laboratory physician/medical microbiologist for further discussion.

5. **If multiple pathogens are detected, the interpretation can be challenging:**
   - This often occurs in those with a travel history with ingestion of contaminated foods/water.
   - Those with severe symptoms or at risk of severe disease could be treated where applicable.
   - In those with mild to moderate symptoms, address the pathogens which are more likely to cause severe disease (i.e., *C. difficile*, *Entamoeba histolytica*, *Giardia*, *Shigella*, typhoidal *Salmonella*, *Vibrio cholerae*).
   - Consider consultation with a specialist for management of complex infections.

C. difficile

C. difficile test results must always be interpreted in clinical context, as patients may be colonized in the presence of diarrhea due to other causes (e.g., laxatives, tube feeds, irritable bowel syndrome, viral infection).

To facilitate differentiation of infection from colonization (asymptomatic carriage), some laboratories test for the toxin protein itself, as the presence of the toxin protein suggests that infection is more likely than colonization. Laboratories that detect both the toxin protein and toxin gene may report the test as positive, negative or indeterminate (see *Appendix 1: FAQ – How do I discern C. difficile infection from colonization?*). Indeterminate results correlate with colonization, although infection is possible. Clinical correlation with the patient's symptoms is essential to differentiate *C. difficile* infection from colonization.[7] In many instances treatment can be avoided.

Public Health Notification

Laboratories directly notify the associated Public Health unit of all reportable enteric pathogens whenever identified. However, the most responsible physician needs to notify the Public Health Unit/Medical Health Officer who may be involved for the following:

- 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

In these scenarios, the Public Health Unit/Medical Health Officer will manage stool testing in the affected case, and possibly their contacts.

Persistent Diarrhea, Negative IDP

If initial testing for infectious diarrhea is non-diagnostic and the patient has unresolving symptoms, clinical re-evaluation to delineate other causes of diarrhea should be undertaken. Typically, if the IDP is negative and the diarrhea has persisted for greater than 14 days, then the diarrhea likely has a non-infectious etiology (see *Table 3: Causes of non-infectious diarrhea*). Repeat testing with the same IDP panel is not likely to be useful. However, patients with certain risk factors may have rare causes of infectious diarrhea.

Severely Immunocompromised

- Severely immunocompromised (e.g., uncontrolled HIV, transplant recipients, current chemotherapy, hematological malignancies. Refer to specialist for evaluation and possibly specialized testing.

Travel and Immigrant Populations

The following patient may have an infection with a pathogen that is not on the IDP:

- Recent travel, immigrants and refugees within 6 months from low to middle income countries.

In such cases, order a **Stool Microscopy Exam for Protozoa** by manually writing “Stool Microscopy” on the requisition. Selective stool culture for additional bacterial pathogens not in the IDP may also be available. Contact your local laboratory physician/medical microbiologist to determine what additional testing might be indicated.

Non-Infectious Causes of Diarrhea

Table 3: Causes of non-infectious diarrhea (adapted from Lazarciuc 2018 and UpToDate)[8,9]

*Many drugs can cause diarrhea; the following list is not exhaustive but contains some examples of drugs commonly associated with causing diarrhea.

MEDICATIONS AND TOXINS		
Drugs*		
Antiarrhythmics • Digoxin • Quinidine	Antihypertensives • ACE Inhibitors • Angiotensin Receptor Blockers • Beta blockers • Hydralazine • Methyldopa	Antiulcer/antacid • H2 Receptor Antagonist • Magnesium containing antacids • Misoprostol • Proton Pump Inhibitors
Cholesterol-lowering agents • Statins • Gemfibrozil	Cholinesterase inhibitors • Donepezil • Rivastigmine	Diuretics • Acetazolamide • Furosemide
SSRIs • Paroxetine • Sertraline • Fluoxetine	Other • Alprazolam • Caffeine • Colchicine • Levodopa • Lithium	• Metformin • Mycophenolate • Synthroid • Theophylline • Valproic acid
Antibiotics		
Antineoplastics		
NSAIDs		
Laxatives		
Dietetic Foods		
Mannitol	Sorbitol	Xylitol
Fish-Associated Toxins		
Ciguatera	Scombroid	Tetrodotoxin
Echinoderms	Shellfish poisoning	
Plant-Associated Toxins		
Herbal preparations	Mushrooms—Amanita species	Pokeweed
Horse chestnut	Pesticides—organophosphates	Rhubarb
Miscellaneous		
Allergic reactions	Ethanol	Monosodium glutamate (MSG)
Carbon monoxide poisoning	Heavy metals	Opiate withdrawal

SYSTEMIC ILLNESS		
Gastrointestinal Pathology		
Appendicitis	Fecal incontinence	Postsurgical
Autonomic dysfunction	Gastrointestinal bleed	Postvagotomy
Bile acid malabsorption	Gastrointestinal cancer	Radiation therapy
Blind loop	Hirschsprung's disease	Short gut syndrome
Bowel obstruction	Inflammatory bowel disease (IBD) (ulcerative colitis, Crohn's disease)	Small bowel resection
Celiac disease	Intussusception	Small intestinal bacterial overgrowth (SIBO)
Cirrhosis	Irritable bowel syndrome	Strictures
Defects in amino acid transport	Ischemic bowel	Toxic megacolon
Diverticular disease	Lactose or fructose intolerance	Tropical sprue
Familial dysautonomia	Malabsorption syndromes	Volvulus
Fecal impaction	Malrotation	Whipple's disease
Endocrine Pathology		
Adrenal insufficiency	Hypoparathyroidism	Pancreatic insufficiency
Diabetes enteropathy	Hyperthyroidism	
Other Causes		
Alcoholism	Henoch-Schönlein purpura	Pyelonephritis
Amyloidosis	Lymphoma	Scleroderma
Connective tissue disease	Lupus (systemic lupus erythematosus or SLE)	Severe malnutrition
Cystic fibrosis	Otitis media—infants	Stevens-Johnson syndrome
Ectopic pregnancy	Pelvic inflammatory disease	Toxic shock syndrome
Hemolytic-uremic syndrome	Pneumonia, sepsis	Wilson's disease
MISCELLANEOUS CAUSES		
Factitious diarrhea	Runner's diarrhea	Emotional Stress

Resources

References

1. Crobach MJT, Vernon JJ, Loo VG, Kong LY, Péchiné S, Wilcox MH, et al. Understanding Clostridium difficile Colonization. Clin Microbiol Rev [Internet]. 2018 Apr [cited 2021 Sep 1];31(2). Available from: https://journals.asm.org/doi/10.1128/CMR.00021-17
2. World Heath Organization. Diarrhoeal disease [Internet]. World Heath Organization; 2017 [cited 2021 Sep 1]. Available from: https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease
3. Toward Optimized Practice (TOP) Working Group for Microbiology. Ordering Stool Test for Investigation of Suspected Infectious Diarrhea [Internet]. Accelerating Change Transformation Team; 2014 [cited 2021 Sep 1]. Available from: https://actt.albertadoctors.org/CPGs/Lists/CPGDocumentList/infectious-diarrhea-guideline.pdf
4. Gerber A, Karch H, Allerberger F, Verweyen HM, Zimmerhackl LB. Clinical Course and the Role of Shiga Toxin–Producing Escherichia coli Infection in the Hemolytic-Uremic Syndrome in Pediatric Patients, 1997–2000, in Germany and Austria: A Prospective Study. J Infect Dis. 2002 Aug 15;186(4):493–500.
5. BC Centre for Disease Control. Communicable Disease Control Manual [Internet]. BC Centre for Disease Control; 2019 [cited 2021 Sep 1]. Available from: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual
6. Shane AL, Mody RK, Crump JA, Tarr PI, Steiner TS, Kotloff K, et al. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. Clin Infect Dis. 2017 Nov 29;65(12):e45–80.
7. Johnson S, Lavergne V, Skinner AM, Gonzales-Luna AJ, Garey KW, Kelly CP, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults. Clin Infect Dis. 2021 Sep 7;73(5):e1029–44.
8. Nicole Lazarciuc. Diarrhea. In: Rosen's emergency medicine: concepts and clinical practice [Internet]. Ninth edition. Philadelphia, PA: Elsevier; 2018 [cited 2021 Sep 1]. Available from: https://books.google.ca/books?id=OANODgAAQBAJ&pg=PA249&lpg=PA249&dq=Diarrhea.+Nicole+Lazarciuc+PERSPECTIVE.+Epidemiology+DIAGNOSTIC+APPROACH.+Pathophysiology.+Differential+Diagnosis+Considerations&source=bl&ots=WyrVHFw_qM&sig=ACfU3U0qaKnUvveFmbWTPgvEiPRO5CVggQ&hl=en&sa=X&ved=2ahUKEwjG99znqt7yAhU1FTQIHXzpCD4Q6AF6BAgDEAM#v=onepage&q=Diarrhea.%20Nicole%20Lazarciuc%20PERSPECTIVE.%20Epidemiology%20DIAGNOSTIC%20APPROACH.%20Pathophysiology.%20Differential%20Diagnosis%20Considerations&f=false
9. Bonis P, Lamont T. Approach to the adult with chronic diarrhea in resource-rich settings. uptodate [Internet]. 2017; Available from: https://www.uptodate.com/contents/approach-to-the-adult-with-chronic-diarrhea-in-resource-rich-settings
10. Wendy Barr, Andrew Smith. Acute Diarrhea in Adults. Am Fam Physician. 2014 Feb 1;89(3):180–9.
11. Torres-Miranda D, Akselrod H, Karsner R, Secco A, Silva-Cantillo D, Siegel MO, et al. Use of BioFire FilmArray gastrointestinal PCR panel associated with reductions in antibiotic use, time to optimal antibiotics, and length of stay. BMC Gastroenterol. 2020 Dec;20(1):246.
12. Bateman AC, Kim YJ, Guaracao AI, Mason JL, Klos RF, Warshauer DM. Performance and Impact of the BioFire FilmArray Gastrointestinal Panel on a Large Cyclospora Outbreak in Wisconsin, 2018. J Clin Microbiol. 2020 Jan 28;58(2):e01415-19.
13. Machiels JD, Cremers AJH, van Bergen-Verkuyten MCGT, Paardekoper-Strijbosch SJM, Frijns KCJ, Wertheim HFL, et al. Impact of the BioFire FilmArray gastrointestinal panel on patient care and infection control. PloS One. 2020;15(2):e0228596.
14. Schreckenberger PC, McAdam AJ. Point-Counterpoint: Large Multiplex PCR Panels Should Be First-Line Tests for Detection of Respiratory and Intestinal Pathogens. Caliendo AM, editor. J Clin Microbiol. 2015 Oct;53(10):3110–5.
15. Al-Jumaili IJ, Shibley M, Lishman AH, Record CO. Incidence and origin of Clostridium difficile in neonates. J Clin Microbiol. 1984 Jan;19(1):77–8.
16. Karmali MA, Petric M, Lim C, Fleming PC, Arbus GS, Lior H. The Association Between Idiopathic Hemolytic Uremic Syndrome and Infection by Verotoxin-Producing Escherichia coli. J Infect Dis. 1985 May 1;151(5):775–82.
17. Mah J, Lieu A, Holmes E, Vaughan S. A case of disseminated strongyloidiasis after multiple courses of immunosuppression. Can Med Assoc J. 2022 Jan 24;194(3):E89–92.
18. BC Centre for Disease Control. Sushi Safety [Internet]. BC Centre for Disease Control; 2016 [cited 2021 Nov 9]. Available from: http://www.bccdc.ca/resource-gallery/Documents/Educational%20Materials/EH/FPS/Fish/SushiSafety.pdf
19. Parto N, Caturay A. Evidence brief: control of parasites by freezing in fish for raw consumption [Internet]. Public Health Ontario; 2017 [cited 2021 Nov 9]. Available from: https://www.publichealthontario.ca/-/media/documents/E/2017/eb-raw-fish-parasites.pdf

Abbreviations

- CDI *C. difficile* infection
- EAEC *E. coli*, enteroaggregative
- EIA Enzyme immunoassay
- EHEC *E. coli*, enterohemorrhagic
- EIEC *E. coli*, enteroinvasive
- EPEC *E. coli*, enteropathogenic
- ETEC *E. coli*, enterotoxigenic
- GBS Guillain-Barré syndrome
- HIV Human Immunodeficiency Virus
- HUS Hemolytic Uremic Syndrome
- IBD Inflammatory bowel disease
- IDP Infectious Diarrhea Panel
- MSG Monosodium glutamate
- NAAT Nucleic-acid amplification test
- NSAIDs Nonsteroidal anti-inflammatory drugs
- STEC Shiga toxin-producing *E. coli*

Practitioner Resources

- **RACE: Rapid Access to Consultative Expertise Program** – *www.raceconnect.ca*

  RACE means timely telephone advice from specialist for Physicians, Medical Residents, Nurse Practitioners, Midwives, all in one phone call.

  Monday to Friday 0800 – 1700
  Online at *www.raceapp.ca* **or though** Apple **or** Android **mobile device. For more information on how to download RACE mobile applications,** please visit *www.raceconnect.ca/race-app/*
  Local Calls: 604–696–2131 | **Toll Free:** 1–877–696–2131

  For a complete list of current specialty services visit the Specialty Areas page.

  If you do not receive a call-back within two hours of your request, please contact: *RACE@providencehealth.bc.ca* **or call** 604-696-2131 (Press 0)

  All unanswered requests will be followed up.

- **Pathways**
  - An online resource that allows family physicians and nurse practitioners and their office staff to quickly access current and accurate referral information, including wait times and areas of expertise, for specialists and specialty clinics. See *https://pathwaysbc.ca/login*

- **Management of Infectious Diarrhea**
  - *2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea.* Clinical Infectious Diseases, Volume 65, Issue 12, 15 December 2017, Pages e45–e80
  - *ACG Clinical Guideline: Diagnosis, Treatment, and Prevention of Acute Diarrheal Infections in Adults.* American Journal of Gastroenterology: May 2016 – Volume 111 – Issue 5 – p 602–622

- **Management of *C. difficile* Infection**
  - *Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults.* Clinical Infectious Diseases, Volume 73, Issue 5, 1 Sept 2021, Pages e1029–e1044

- **Functional and IBS Diarrhea**
  - *AGA clinical practice guidelines on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D).* Gastroenterology 2019;157(3):851-854.
- **Travel-Related Diarrhea**
  - *Statement on Travellers' Diarrhea: An Advisory Committee Statement (ACS) – Committee to Advise on Tropical Medicine and Travel (CATMAT).*
- **Bugs & Drugs:** *www.bugsanddrugs.org*

Patient, Family and Caregiver resources

- **HealthLink BC:** *www.healthlinkbc.ca*
  - *Diarrhea, Age 12 and Older*
  - *Diarrhea, Age 11 and Younger*
  - *Mild, Moderate, or Severe Diarrhea*
  - *Traveller's Diarrhea*
  - *Medicines That Can Cause Diarrhea*

Diagnostic Code: 009.2 (Infectious Diarrhea)

Appendices

- *Appendix 1: Frequently asked questions*
- *Appendix 2: Other related laboratory tests*
- *Appendix 3: Patient instructions - Collection of fecal swab*

This guideline is based on scientific evidence current as of the effective date.

This guideline was developed by the Guidelines and Protocols Advisory Committee in collaboration with the Provincial Laboratory Medicine Services, and adopted under the *Medical Services Act* and the *Laboratory Services Act*.

For more information about how BC Guidelines are developed, refer to the GPAC Handbook available at *BCGuidelines.ca: GPAC Handbook*.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

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

Contact Information:

Guidelines and Protocols Advisory Committee
PO Box 9642 STN PROV GOVT
Victoria BC V8W 9P1

Email: *hlth.guidelines@gov.bc.ca*
Website: *www.BCGuidelines.ca*

Disclaimer

Appendix 1: Frequently asked questions

What is the etiology of infectious diarrhea?

Most acute diarrhea are caused by infections, most commonly viral followed by bacterial and infrequently, protozoal. Fecal-oral transmission is the predominant route of transmission. Exposures can occur through ingestion of contaminated food and water or contact with infected persons or contaminated surfaces. International travel to areas with inadequate sanitation is a known risk. High-risk areas for traveller's diarrhea include countries in Africa, Asia, the Middle East, and Latin America. Low-risk areas include North America, Central Europe, Australia, and Japan. Non-infectious causes include medications, gastrointestinal disease and endocrine disorders.[10]

Considering that the management of most infectious diarrhea is supportive, what is the rationale for performing diagnostic testing for diarrhea?

Infectious diarrhea is a common clinical presentation. Most infectious diarrhea episodes are self-limiting and resolve within 7 days, and these do not require further diagnostic testing as there will be marginal benefit to the patient. However, in selected cases, testing should be performed when the identification of the agent will benefit the patient in the management of the diarrheal episode.

For those with severe or prolonged (> 7 days) diarrhea, or immunocompromised individuals, syndromic diagnostic testing allows timely identification of the infectious agent where patient morbidity can be reduced through specific treatments such as antimicrobials and to provide a prognosis for the course of the illness. Potential outbreak situations may warrant appropriate diagnostic testing as directed by Public Health.[11–13]

The syndromic IDP test appears to oppose principles of test stewardship, where diagnostic tests should be judiciously selected based on the differential diagnosis. What was the rationale in adopting this approach?[14]

The use of IDP permits the detection of a broader range of pathogens, including enteric viruses and emerging bacterial pathogens. Several factors have come together to make this decision. Commercial multiplex NAAT assays for infectious diarrhea have become increasingly available and affordable compared with the traditional methods of culture and microscopy. These assays are less labour intensive compared with manual microscopy, and yet have faster turn-around time and sensitivity.

Although clinical symptoms and exposure history help narrow down the possible causative agent of diarrhea, there remains significant overlap of symptoms between the various diarrheal pathogens. This often results in the physician ordering multiple tests (e.g., Stool O&P, Stool Culture and *C. difficile*) for that diarrheal episode. This may also require multiple stool specimens, and hence multiple collections, multiple clinic visits and multiple laboratory drop-offs. The IDP simplifies this pre-laboratory stage and streamlines the workflow, all with a single stool specimen.

For those with chronic or severe diarrhea, the precision and higher sensitivity afforded by novel syndromic testing can aid with more timely specific treatment with antibiotics, such as for *Shigella* or *Giardia* infections. Even if a pathogen is identified where only supportive measures are available (e.g., Norovirus), clinicians receive a diagnosis that allows for the provision of a prognosis, advice about transmissibility to others and strategies for avoidance in the future. Public Health also receives a more accurate picture of the diarrheal disease burden in the community.

How was the list of pathogens in *Table 1* established?

This standardized list of pathogens was agreed upon by BC medical microbiologists, clinicians and public health, based on historical BC epidemiology, clinical significance and threats to the public. Each laboratory can choose or develop the particular multiplex kits and approach for IDP so long as it detects this list of "mandatory" pathogens. Note that prior to this, there were no agreed list of pathogens identified by stool culture or stool O&P. This new standardized list will be reviewed every several years and updated based on new clinical information and changes in available diagnostic assays. Other pathogens were not included because of the rarity of infection within BC, and/or these are not detectable by currently available assays. In selected

cases with the appropriate risk factors, specialized testing may be required if symptoms are ongoing, and the syndromic panel is non-diagnostic. Your local laboratory physician/medical microbiologist can be of assistance in determining what additional tests may be indicated.

What about *Blastocystis* hominis and *Dientamoeba fragilis*?

Certain organisms have been purposely excluded from being mandatory in the IDP, including, *Blastocystis hominis* and *Dientamoeba fragilis*. However, individual laboratories may choose to report these organisms.

The role of these organisms in causing infectious diarrhea is controversial. *Dientamoeba fragilis* is often asymptomatically carried, particularly by children. In such populations, the detection of *D. fragilis* is an incidental finding and requires no treatment. *Blastocystis hominis* is similarly often carried asymptomatically although there is some evidence that different genotypes found around the world may be potentially pathogenic in terms of causing diarrheal symptoms. Treatment may be considered for *B. hominis* or *D. fragilis* if either is detected as the sole pathogen in a symptomatic patient, and other causes of diarrhea have been excluded.

Why is *C. difficile* included in IDP?

While *C. difficile* infection was previously associated mostly with recent health-care exposure (i.e., hospital admission, long-term care facility setting) and/or recent antibiotic use (within 3 months), it has now become an increasingly important cause of community acquired diarrhea with some patients having no clear risk factors. In BC, *C. difficile* is the most common pathogen identified in all stool specimens. On review of such cases, many of them were not symptomatic or had an alternative diagnosis. Instead, they are thought to be colonized with *C. difficile*.

Clinically, it can be hard to differentiate *C. difficile* from other causes of infectious diarrhea. Generally, those with moderate-severe and/or prolonged diarrhea should be tested for *C. difficile*. Timely diagnosis and treatment reduce morbidity. This is especially true for debilitated patients with multiple medical co-morbidities, including advanced age, as they have the highest risk of complications.

How do I discern *C. difficile* infection from colonization?

Colonization is defined as the absence of clinical symptoms of *C. difficile* infection (i.e., diarrhea, ileus, toxic megacolon) or the presence of an alternative explanation of these symptoms.[1] After colonization with the bacterium, patients may be asymptomatic *C. difficile* carriers. A disruption of the normal gut microbiota (i.e., antibiotic administration) may lead to *C. difficile* infection. Within BC, the estimated *C. difficile* colonization is 10-15% in those greater than 2 years old. Past epidemiologic studies have found that up to 71% of children are asymptomatically colonized with *C. difficile*.[15]

A positive test does not differentiate infection from colonization. Up until recently, most BC labs utilized the highly sensitive nucleic-acid amplification tests (NAAT) to detect *C. difficile*. This method often identified asymptomatic carriers, which led to unnecessary treatment and patient angst. To facilitate differentiation of *C. difficile* infection from colonization, a supplemental test to detect the *C. difficile* toxin by enzyme immunoassay (EIA) is performed in both the IDP and the standalone *C. difficile* tests. This combination of test has three possible results:

- Positive (Toxin protein detected by EIA) – High likelihood of *C. difficile* infection, although asymptomatic colonization is possible.
- Indeterminate (Toxin gene detect by NAAT, but toxin protein not detected by EIA) – Patient is colonized with *C. difficile*, although *C. difficile* infection is possible.
- Negative (Toxin gene not detected by NAAT) – *C. difficile* infection is excluded in >99% of patients.

Clinical correlation is always required to establish the diagnosis of *C. difficile* infection versus colonization. Furthermore, neither the *C. difficile* test nor the IDP should not be requested in patients without diarrhea – i.e., those with formed stools. Repeat testing during the same episode of *C. difficile* infection and test of cure are not useful for the management of patients.

What is the difference between Shiga toxin-producing *E. coli* (STEC) and *E. coli* O157:H7?

As its name implies, STEC produce Shiga toxins, which are part of a family of toxins first described in *Shigella dysenteriae*. STEC, also known as enterohemorrhagic *E. coli* (EHEC), includes multiple strains of *E. coli*. Each strain of *E. coli* is defined by its O- and H-antigens (e.g., O157:H7). Within STEC, the different strains have different pathogenicities, such as the amount and types of Shiga toxin produced. STEC O157:H7 is perhaps the highest risk strain, notably due to its ability to cause hemolytic uremic syndrome (HUS). Of note, the association of HUS with the toxin, also known as verotoxin, was established by Canadian researchers in 1985.[16]

Routine stool cultures can detect STEC O157:H7, but not the other strains. Occasionally, non-O157:H7 STEC were detected by verotoxin assay, but this assay was not frequently used and was limited to bloody stools only. IDP detects all STEC strains, and its introduction will result in more confirmed cases of non-O157:H7 STEC.

Our knowledge of non-O157:H7 STEC is evolving. While many strains can cause a mild, self-limited disease, certain strains (particularly those that produce Shiga toxin 2) can present similarly as *E. coli* O157:H7 (i.e., fever, abdominal pain, bloody diarrhea and progression to HUS) and may be associated with outbreaks. Hence all individuals who have STEC detected in their stool require assessment of disease severity and, if there are ongoing symptoms, bloodwork (i.e., complete blood count, urea, creatinine, electrolytes and lactate dehydrogenase). In those at risk of HUS or severe disease, hospitalization for fluid management is recommended. HUS can occur in any age, but the risk is highest in children less than 10 years old. Antibiotics should be avoided or discontinued, as antibiotics can lyse the bacterium resulting in release of more toxin.

Why are helminths (worms) not included in IDP?

Most infections with gastrointestinal **worms do not cause diarrhea**. Only very heavy infections with some types of worms (e.g., *Schistosoma mansoni*, *Trichuris trichiura*), not endemic to Canada, may cause diarrhea. Instead, worm infections are often asymptomatic, or they may cause non-specific gastrointestinal symptoms such as vague abdominal pain. Rarely, they may result in nutritional deficiencies, eosinophilia or cause complications such as biliary colic by migrating within the body. Very few gastrointestinal worm infections are endemic to Canada. In BC, the detection of worm ova from stool O&P is <0.1%. Risk factors for these worm infections are migration from or prolonged travel to regions, outside of Canada, USA, western Europe, Australia or New Zealand or, occasionally, consumption of undercooked imported food products.

I'm still concerned about a worm infection. What do I order to make a diagnosis?

If there is suspicion for gastrointestinal worm infection, order **Stool Microscopy Exam for Worm-Ova**. Due to intermittent shedding of worm ova and the inherent limited sensitivity of microscopy, repeat testing on different days may be required to rule out an infection. Additional laboratory requisitions may be required for multiple samples. Generally, three stool samples collected on different days is > 95% sensitive and adequate to rule out a clinically significant gastrointestinal worm infection.

Diagnosis of infection with the worm *Strongyloides stercoralis* is an exception. This infection can affect anyone who has walked barefoot in a high-risk area, particularly in Southeast Asia and the Indian subcontinent.[17] Stool microscopy examinations for this parasite has low sensitivity (< 20%) and may be negative in chronically infected patients. The appropriate screening test is **Strongyloides serology**. This serum antibody test is > 95% sensitive for detecting chronic infection. *Strongyloides stercoralis* is transmitted from contaminated soil endemic to tropical and subtropical climates worldwide. Farmers, military personnel, or adventurers are at higher risk as they may have had direct skin penetration by the infectious form of larvae from contaminated soil. *Strongyloides* causes a chronic subclinical infection that may be relatively asymptomatic for decades or may manifest as intermittent eosinophilia. Immunosuppressed states, including advanced age, can allow a hyper-infection syndrome to develop which carries high mortality. It is important to identify chronically infected individuals, particularly prior to immunosuppression (e.g., high dose steroids, chemotherapy, transplant) so that they can be offered definitive anti-helminthic treatment and avoid developing this complication.

My patient passed something that is concerning for a worm. What do I with it?

If an object visible to the naked eye is passed in stool that is suspected to be a worm, submit it to the laboratory in a clean container separately from the stool sample and order **Worm ID**. Adult round worms (i.e., *Ascaris*) and tapeworm segments may be visualized with the naked eye without a microscope.

My patient is worried about worm infection after eating sushi. What is the prevalence and trends of such infections in BC?

The risk of worms from sushi consumed in North America is very low thanks to the implementation of food safety standards. Particularly for sushi consumed within North America, there are two worms of concern, *Anisakis* and *Diphyllobothrium*. Both of which can be killed by cooking or by freezing the fish.18,19 These do not cause diarrhea and hence do not usually require testing.

Appendix 2: Other related laboratory tests

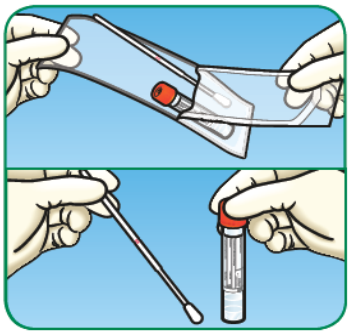
Laboratory test	What it confirms/detects	Indications	Order & Collection
Stool Microscopy for Worm ova	Suspicion of enteric helminth (worm) infection.	History of travel with consumption of contaminated foods, and observation of worm in stool.	Order as "Stool for Worm ova" and have stool collected in container with "SAF Fixative."
Worm Identification	Suspicion of enteric helminth (worm) infection.	Observation of discretely visible round worm or tape worm segment in stool.	Order as "Worm identification" and have suspected worm collected in container with "SAF Fixative."
Pinworm Detection	Pinworm (*Enterobius vermicularis*) infection.	History and symptoms suggestive of pinworm infection.	Order as "Pinworm" and use pinworm paddle kit or Scotch-tape.
Strongyloides Serology	Prior exposure to Strongyloides.	Risk factors for *Strongyloides* infection.	Order as "Strongyloides serology."
Fecal Calprotectin	Detects inflammatory markers in bowel.	Patients diagnosed with Inflammatory Bowel Disease (IBD).	Order as "Fecal Calprotectin" and indicate IBD in the diagnosis box.

Appendix 3: Patient instructions - Collection of fecal swab

Each FecalSwab™ kit consists of a sterile peel pouch containing a regular Nylon FLOQSwab™ and a screw cap tube containing 2mL of Cary-Blair medium

NOTE: *These instructions indicate use of FecalSwab after patient has delivered stool specimen in a clean, dry pan or special container. Stool specimen should not contain urine or water.*

NOTE: *the screw cap can be green, red or orange.*

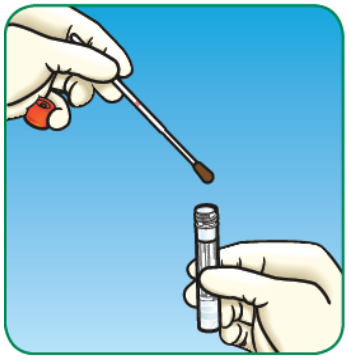


Open the peel pouch.

Remove the swab. Do not touch the swab tip. Always hold the shaft applicator above the marked breakpoint.

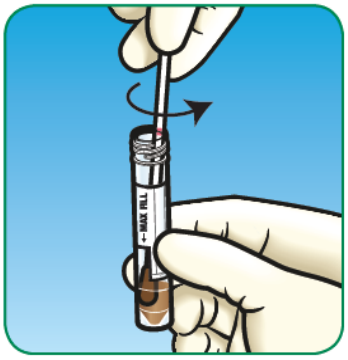
Collect a small amount of stool by inserting all the tip of the flocked swab into stool sample and rotate it.

NOTE: *Bloody, slimy or watery area of stools should be selected and sampled.*

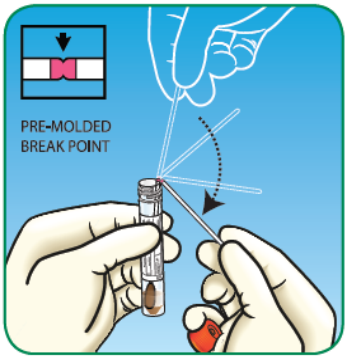


Remove and examine to make sure there is fecal material visible on the tip of the swab. If needed, insert again the flocked swab into stool sample and rotate making sure all the area of the swab tip is in contact with the sample.

Transfer the swab into the FecalSwab™ tube and check that the maximum filling line ("MAX. FILL") on the label is not exceeded.

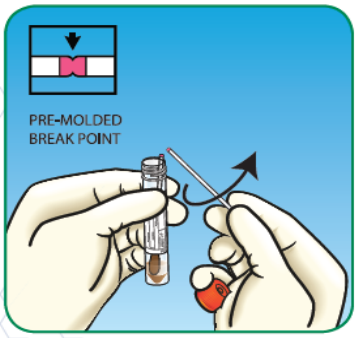


Holding the swab shaft between thumb and finger, mash and mix the stool specimen against the side of the tube to evenly disperse and suspend the specimen in the medium.

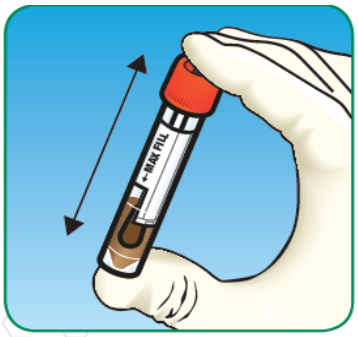


Hold the tube away from your face.

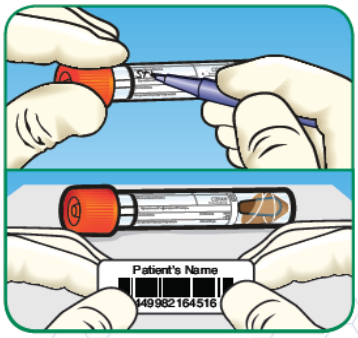
Holding the end of the swab shaft, bend it at a 180 degrees angle to break at the marked breakpoint.



If needed, gently twist the shaft between thumb and forefinger to completely remove it. Discard the broken upper part of the swab shaft and tighten the cap.



Shake the vial until the sample appears homogeneous.



Write patient's name and demographics on the tube or apply a label and send the sample to the laboratory.

Keep vial in refrigerator until delivery to laboratory.

IMPORTANT
Please ensure two identifiers are on the label.
E.g. First and last name and Date of Birth or Phone Number