



RURAL INFECTIONS SERIES:
**Investigating and
managing people
with diarrhoea**

Campylobacter, *Salmonella*, *Cryptosporidium* and *Giardia* cause diarrhoeal illnesses in thousands of people annually in New Zealand. The incidence of these infections is significantly higher in New Zealand compared to most other developed nations.¹ Animal, environmental and waterborne sources are a common cause of isolated illnesses and outbreaks, and exposure to these sources is a significant risk-factor for infection. This edition of the rural infections series focuses on these four notifiable pathogens, each of which causes a similar set of symptoms, and discusses the investigation and management of diarrhoeal illnesses in a person with rural occupation, residence or recent contact with animals or untreated water.

Infectious diarrhoea: the common quartet of causes

Campylobacter, *Salmonella*, *Cryptosporidium* and *Giardia* represent four of the five most frequently notified illnesses in New Zealand (pertussis is the fifth).^{1,2} From July to September, 2013 (the most recent surveillance period*), these four pathogens caused a total of 50 outbreaks and approximately 2880 confirmed illnesses.² Rural occupation, living in a rural area or contact with farm animals is a significant risk factor for contracting these infections; approximately 10% of the notified cases in the reporting period were traced to an environmental, animal or waterborne source.² Any illness caused by these four organisms is notifiable to the Medical Officer of Health.

Campylobacter, *Salmonella*, *Cryptosporidium* and *Giardia* cause clinically similar illnesses, typically profuse diarrhoea, abdominal pain and nausea, with or without vomiting (Table 1, over page). Bloody diarrhoea, fever, malaise and a range of other symptoms may also be present. The patient's gastrointestinal symptoms usually last less than two weeks before resolving spontaneously, however, *Cryptosporidium* and *Giardia* can cause persistent or chronic diarrhoea in some people.

Viral infections and *E. coli* (VTEC, Page 18) are also common causes of diarrhoea in all patients.

* Data for *Giardia* comes from the previous quarter (April to June, 2013) as more recent data is not available

Diagnosis and assessment of infectious diarrhoea

Patients with *Campylobacter*, *Salmonella*, *Cryptosporidium* and *Giardia* infection will typically present to primary care with diarrhoea. History and examination is generally sufficient to establish a working diagnosis and appropriate management.

Diarrhoea can be defined by duration as follows:

- Acute – lasting less than 14 days (most infections from these four pathogens will be acute)
- Persistent – lasting between 14 – 30 days (*Giardia*, and occasionally *Cryptosporidium* can cause persistent diarrhoea)
- Chronic – lasting longer than 30 days

Finding the cause of diarrhoea

The patient's description of their symptoms and recent activity may suggest a cause for their diarrhoea. Enquire about:

- The characteristics of the diarrhoea, e.g. duration, consistency, the presence of blood
- Other general symptoms, particularly abdominal pain, fever, malaise or fatigue
- The patient's occupation (to identify people working in a rural occupation, food handlers and day care workers), where they live and any recent activity that may have increased the risk of environmental exposure, e.g. camping or tramping
- Any recent contact with farm animals or wildlife

- Recent contact with or ingestion of untreated water, e.g. effluent ponds, dams or tank water
- Where, what and when the patient ate prior to their symptoms starting, particularly asking about any high-risk food, e.g. chicken or seafood ingestion
- Other general risk factors, including recent international travel, similar symptoms in household members and recent hospitalisation or antibiotic use
- Risk-factors for non-infectious or non-gastrointestinal causes of diarrhoea, including family history of coeliac or Crohn's disease, symptoms associated with certain foods, e.g. following milk ingestion, if similar symptoms have occurred previously and the presence of any non-gastrointestinal symptoms

Defining the cause of diarrhoea

If the patient reports large-volume, watery or bloody diarrhoea with diffuse abdominal pain, enteric bacterial infection is likely.¹⁰ In a person with a rural occupation, residence or recent contact with animals, *Salmonella*, *Campylobacter*, *Cryptosporidium* and *Giardia* are among

the most likely causes, but other, more general causes of diarrhoea should also be considered, which would apply to patients in any setting.

If the patient's symptoms have occurred within six hours of ingestion of potentially contaminated food, food poisoning with pre-formed bacterial toxins (i.e. toxins that are present in the food and cause symptoms in the gut, rather than the bacteria themselves) should be suspected. However, the source of infection is not always apparent, or symptoms may occur coincidentally following ingestion of high-risk foods without being related.

Clinical differentiation between viral diarrhoea and an early presentation of enteric infection is difficult. Patients who have had diarrhoea for less than two to three days may have viral gastroenteritis, e.g. infection with norovirus, rotavirus or enteric adenovirus, or this may be an early presentation of enteric infection. The longer the patient's symptoms have been present, the more likely enteric infection becomes. In addition, viral gastroenteritis is less likely if the patient has bloody diarrhoea, fever and severe abdominal pain.¹⁰

Verotoxin-producing *E. coli* (VTEC)

Escherichia coli are common bacteria in the human gastrointestinal flora, and are not usually pathogenic. However, overgrowth and certain strains of *E. coli* can cause severe diarrhoea. The incidence of illness related to *E. coli* in New Zealand is significantly lower than that caused by *Campylobacter*, *Salmonella*, *Cryptosporidium* or *Giardia*. Infections often have an environmental or animal source; from July to September, 2013, there were five environmental, animal or waterborne outbreaks.² Food-borne illness also occurs, particularly following ingestion of contaminated meat.

E. coli itself is a causative pathogen in cases of notified gastroenteritis. Gastroenteritis is a notifiable illness if there is believed to be a common source or if the person with the illness is in a high-risk category, such as a food handler. In such a case, *E. coli* will be added retrospectively as the causative organism, if identified through laboratory testing.

E. coli must also be notified if a shiga-toxin producing (also known as verotoxin-producing *E. coli* or "VTEC") strain is found to be present. Only some *E. coli* can produce these toxins and cause disease if ingested.⁸ The genes required to produce these toxins are thought to have been acquired from another, more pathogenic bacteria, *Shigella dysenteriae*, via bacteriophage transfer. The shiga toxin will only cause illness in certain species. Cattle, pigs and deer can carry shiga-toxin producing bacteria without developing an illness, but when spread to humans, the toxin produces symptoms ranging from mild diarrhoea to haemorrhagic colitis.^{8,9} Most infections are caused by ingestion of food or drinking water contaminated with faeces from ruminant animals.⁹



Table 1: The natural history and presentation of the four most common notifiable infections in New Zealand³⁻⁷

	Salmonella enterocolitis	Campylobacter enterocolitis	Cryptosporidiosis	Giardiasis
Organism	Bacteria	Bacteria	Parasite	Parasite
Mode of transmission	Primarily food-borne, but also stagnant water, animals (particularly birds), and person-to-person	Water, animals, food and person-to-person	Animals (particularly calves and lambs), water, food and person-to-person	Water, animals and person-to-person
Seasonality	Year-round	Spring and summer	Spring	Year-round
Incidence – Cases in previous 12 months*	1118	6212	1350	1654
Incidence –five-year trend**	Variable/Stable	Decreasing	Increasing	Decreasing
Diarrhoea duration	Usually less than 14 days	Usually less than 14 days	Usually less than 14 days, potential for persistence	Variable, from less than 14 days to more than 30 days
Diarrhoea symptoms	Profuse, watery and occasionally bloody	Variable severity, watery and often bloody	Profuse and watery	Greasy, malodorous, floating stool, i.e. symptoms of malabsorption
Incubation period, average (Range)	12 – 36 hours (6 – 72 hours)	2 – 5 days (1 – 10 days)	7 days (1 – 12 days)	7 – 10 days (3 – 25 days)
Nausea and vomiting	Nausea, occasional vomiting	Nausea and vomiting	Nausea and vomiting	Nausea, rarely vomiting
Fever	Common	Common	Common	Less common
Period of infectivity to others	Typically several days to several weeks after onset of symptoms, can be up to one year in children	Several weeks after onset of symptoms	Several weeks after symptoms resolve	Up to several months after onset of symptoms

* Incidence data are from July, 2012, to June, 2013.

** Change in incidence from December, 2009, to December, 2013.

Non-infectious causes of diarrhoea should also be considered. Patients with small-volume, bloody diarrhoea, lower abdominal cramping and tenesmus (feeling as though they constantly need to defaecate or that the bowel is not completely empty following a bowel movement), may have inflammation of the bowel due to a conditions such as coeliac disease or inflammatory bowel disease. Family history and the duration of symptoms may suggest non-infective causes; however, first presentations of these illnesses can be difficult to differentiate from an acute episode of infectious diarrhoea.

Non-gastrointestinal infections can sometimes cause acute diarrhoea and should be considered when symptoms suggest another system could be involved, including urinary tract infection, pneumonia, otitis media or systemic infections. In one United States study, retrospective analysis of patients initially diagnosed with gastroenteritis found that 8% had a non-gastrointestinal systemic infection.¹¹ Vomiting will usually be more prominent than diarrhoea in people with these infections.¹²

Assessing for dehydration

The examination should focus on identifying dehydration. This includes basic observations, with attention to skin turgor, mucus membranes and capillary refill rate, and an abdominal examination. Although rare, other possible complications of enteric infection causing diarrhoea include reactive arthritis and Guillain-Barré syndrome.¹⁰

Laboratory investigation

Laboratory investigation is not routinely required for patients with acute diarrhoea.

However, in a patient with a rural occupation, residence or recent exposure to animals, laboratory investigation is recommended to provide additional information to guide treatment and for notification purposes.

What tests should be requested for a patient with rural risk-factors?

In people with diarrhoea who live or work in a rural setting or with recent exposure to animals or untreated water sources, request:¹³

- Faecal culture and microscopy
- Faecal *Giardia* and *Cryptosporidium* antigen tests

Note the patient's relevant risk factors, e.g. rural occupation, on the laboratory request form, as the test may be declined by the laboratory if justification for testing is not recorded.

Only one stool sample should be sent for analysis.

However, faeces are not homogenous; bacteria may not be evenly distributed within the sample and the volume of excreted bacterial material varies with the stage of infection. As a result, false-negatives can occur, particularly with faecal culture. A repeat test may be justified if a particular pathogen is strongly suspected and the initial test is negative and the patient has ongoing symptoms.¹⁴ In this situation, discussing the patient with an Infectious Diseases Physician or Clinical Microbiologist should be considered.¹⁴

Faecal culture and microscopy

The faecal culture and microscopy test is used to assess a patient's stool for leucocytes, indicating inflammation of the bowel either due to an invasive pathogen or other inflammatory bowel disease and isolation of pathogenic bacteria. This is the first-line test for the investigation of infectious diarrhoea in someone with risk factors. It can identify *Campylobacter*, *Salmonella*, *Yersinia*, *E. coli* (VTEC) and *Shigella*.

Ask the patient to provide a faecal sample in a sterile collection container. The sample should be stored at room temperature and should not have a fixative applied to it. The sample should be transferred to the laboratory as soon as possible. If transfer will be delayed by more than 24 hours, refrigerate the sample and consult the collecting laboratory.

Giardia and Cryptosporidium testing

The *Giardia* and *Cryptosporidium* antigen test is an immunoassay test that identifies the presence of antigens from *Giardia* and *Cryptosporidium* in a patient's stool. The results will be reported as either positive or negative, i.e. antigens are present or absent.

As with faecal culture, an antigen test requires a fresh faecal sample. The same sample used for bacterial culture is used for the antigen test.

The antigen test has high sensitivity and specificity.¹⁵

Other tests are available, but less commonly used

Microscopy can be used to detect *Giardia* and *Cryptosporidium*, in samples from patients with acute diarrhoea, however, it is not routinely recommended. Microscopy is an alternative,

Monitoring and preventing infectious disease in New Zealand

Notification and surveillance are key components of managing and preventing communicable illnesses in New Zealand. The data gathered from these activities guides the direction and scope of local and national public health efforts and campaigns.

The list of notifiable diseases was set out in the Health Act 1956, and is available from the Ministry of Health website. Illnesses are added to the list if they are deemed important to public health, e.g. avian influenza (H7N9) and Middle East Respiratory Syndrome (MERS) were added to the list in 2013.

All notifiable illnesses must be reported to the Medical Officer of Health once there is a reasonable clinical suspicion of the illness or confirmation through testing. Some illnesses, termed "Section A illnesses", must also be reported to the local health authority, e.g. the PHO or DHB.

Campylobacter, *Giardia*, *Salmonella* and *Cryptosporidium* are all Section A infectious illnesses. Laboratory testing is required to confirm the illness for notification. Both culture or antigen testing are sufficiently accurate for notification purposes.

In addition to the standard clinical tests performed for diagnosis, additional testing may be performed by the laboratory to provide better surveillance data for some notifiable illnesses. For example, *Campylobacter* bacteria identified via culture may undergo multilocus sequence typing in order to provide epidemiological data.¹ This information is not routinely provided to practitioners.

 For further information, see: www.health.govt.nz/our-work/diseases-and-conditions/notifiable-diseases

Rehydration and preventing further fluid loss

Infants and children without signs of clinical dehydration, should continue breast feeding and other milk feeds as normal. Older children should be encouraged to drink regularly, in small amounts.¹⁸ Oral rehydration solution can be offered as a supplemental fluid.¹⁸ Oral rehydration solutions can be made at home (see recipe below) or prescribed, fully-subsidised. Drinking undiluted fruit juices or carbonated drinks should be discouraged,¹⁸ as they contain high levels of sugar, and can increase dehydration through diuretic action and by altering the osmolality of the gut.

In infants and young children who are dehydrated, oral rehydration solution is recommended.¹⁸ Chilling the oral rehydration solution (or freezing into ice blocks) can improve palatability. Fluids should be offered in regular, small amounts to help avoid vomiting. Replacement with 50 mL/kg over four hours is recommended.¹⁸

In adults with a diarrhoeal illness, oral rehydration solutions are not usually required. However, patients should be advised to increase oral fluid-intake to two litres per day, with fluids such as water or salty soups. As with children, adults should avoid sugary or caffeinated drinks, e.g. sports drinks. Advise patients to eat normally when they feel they are able; bland foods may be more palatable initially.

A recipe for oral rehydration fluid is:

- 1 litre of water
- 8 teaspoons of sugar
- 1 teaspoon of salt

Stir until dissolved and store in the refrigerator. The solution should be discarded after 24 hours.

 For further information on the management of dehydration in people with gastroenteritis, see: "Assessment and management of infectious gastroenteritis", BPJ 25 (Dec, 2009).

Pharmacological management

Antibiotics are not recommended for people with acute diarrhoea of unknown pathology.¹²

Antibiotic treatment may be indicated for adults or children if a specific pathogen is identified by laboratory investigation

(Table 2, over page). Antibiotics are required for patients with giardiasis and symptomatic contacts of the patient. Antibiotic treatment may be appropriate in some patients with salmonella enterocolitis and campylobacter enterocolitis, depending on their risk-factors. *Cryptosporidium* is not treated with antibiotics, as they are not effective.

Antidiarrhoeal medicines are not routinely recommended and should not be used if the patient has blood or mucus in their stool.¹² In people with diarrhoea containing blood or mucus antidiarrhoeal medicines increase the risk of toxic megacolon and prolong duration of diarrhoea.¹⁹ If an antidiarrhoeal is required for symptomatic relief in a patient without blood or mucus in their diarrhoea, loperamide can be considered.¹² Loperamide should be given at 4 mg initially, with 2 mg after each loose stool, up to a maximum of 16 mg in 24 hours.

Antiemetics are not routinely recommended.¹²

If pain relief is required, paracetamol can be given. NSAIDs should be avoided in people with dehydration or the potential for dehydration due to the risk of kidney injury.

The patient's current medicine use should also be reviewed, as certain medicines may worsen diarrhoea (e.g. laxatives), increase the risk of complications from the diarrhoea (e.g. diuretics, NSAIDs) or can be affected by diarrhoeal symptoms (e.g. reduced absorption of oral contraceptives).

Lactose intolerance or irritable bowel syndrome following infection

Secondary, or acquired, lactose intolerance can occur following any gastrointestinal illness that affects the gut mucosa. It is particularly common in adults following *Cryptosporidium* or *Giardia* infection and in children following any enteric infection.

Symptoms of lactose intolerance, shortly after consuming lactose, include:

- Diarrhoea
- Abdominal pain and distension
- Flatulence
- Dyspepsia

If the patient's diarrhoea continues following antibiotic treatment or begins again soon after symptoms cease consider lactose intolerance. A lactose challenge can be

undertaken: instruct the patient to trial a lactose-free diet for two weeks, then reintroduce these foods, and report any symptoms that occur. All food containing lactose needs to be removed during the challenge, so food labels should be closely assessed. Many foods and some medicines contain unexpected lactose, such as instant soups, muesli bars and some processed meat.

Secondary lactose intolerance following enteric infection is usually transitory, but may persist for several weeks.²¹ It can be managed with dietary restriction followed by gradual reintroduction of milk.

Irritable bowel syndrome may also develop following a significant enteric infection. Symptoms and signs will be similar to lactose intolerance; however, a lactose challenge will usually be negative. Irritable bowel syndrome may be short-term or may persist for several years. Management usually involves reassurance, stress management, lifestyle and diet changes and, in some patients, medicines such as loperamide and mebeverine.

 For further information on lactose intolerance, see: "Investigating the gut: Lactose intolerance", Best Tests (Mar, 2010).

 For further information on irritable bowel syndrome, see: "Irritable bowel syndrome in adults: not just a gut feeling", BJP 58 (Jan, 2014).

Management of contacts

Symptomatic contacts should be managed based on their risk-factors and the severity of their illness.³⁻⁶ For example, if they are a food handler or have a rural occupation, investigation may be required. If no risk-factors are present, investigation is not routinely recommended. A "probable" notification can be made based on contact with a confirmed case, without laboratory, testing if necessary.

Asymptomatic household contacts of people with salmonella enterocolitis, who are food handlers, should have a faecal culture and microscopy test requested to confirm they are not infected and can safely attend work (See Table 1 for incubation times).⁴ Investigation, restriction from school or work and empiric treatment are not required for other asymptomatic contacts of people with notifiable infectious diarrhoea, although they should be made aware that if they develop symptoms, they need to present to primary care and will require assessment and potentially testing.³⁻⁶

Table 2: The management of four common causes of infectious diarrhoea ^{3,12,20}

Infection	When to treat with antibiotics	First-line	Comment
Salmonella enterocolitis	Treat patients with severe disease,* who are immunocompromised or who have cardiac valve disease or endovascular abnormalities, including prosthetic vascular grafts	Ciprofloxacin, 500 mg, twice daily, for three days Co-trimoxazole, 160 + 800 mg, twice daily, for three days is an alternative	Treatment may prolong excretion For children, discuss appropriate treatment with an Infectious Diseases specialist
Campylobacter enterocolitis	Treat if severe,* symptoms present for more than one week, women who are pregnant nearing term or people who are immunocompromised. Treatment may also be appropriate for food handlers, child care workers or people caring for immunocompromised people.	Erythromycin ethyl succinate 400 mg (child 10 mg/kg), four times daily, for five days** A second-line alternative for adults is ciprofloxacin, 500 mg, twice daily, for five days	Treatment has limited effect on symptoms, but may reduce stool carriage
Cryptosporidiosis	Antibiotics are not effective		Discussion with an Infectious Disease specialist is recommended for patients who are immunocompromised or have co-morbidities
Giardiasis	Antibiotic treatment is recommended if laboratory tests show infection is present (and for symptomatic contacts)	Children < 35 kg – ornidazole 125 mg/3 kg, once daily, for one to two days Adults and children > 35 kg – ornidazole 1.5 g, once daily, for one to two days Metronidazole can also be used first-line. Children – 30 mg/kg, once daily, for three days, to a maximum of 2 g per day. Adults – 2 g, once daily, for three days	If treatment with ornidazole appears to be ineffective, exclude re-infection from asymptomatic contacts; lower doses of metronidazole may be given for longer periods, e.g. 10 mg/kg/dose, three times daily for children or 400 mg, three times days, for seven days. An interval of two to three days between treatments is recommended. Ornidazole is only available in tablet form, which may be crushed. A child dose is equivalent to one-quarter of a tablet per 3 kg.

* High fever, bloody diarrhoea or more than eight stools per day¹²

** Erythromycin 800 mg, twice daily, can be considered for patients where adherence is likely to be an issue

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