

# **Perspectives on Gastro-Intestinal Pathogenic Bacteria Infections in Humans**

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# Abstract

At the Parasitology Center, Inc. (PCI), Scottsdale, Arizona, we come across a number of patients with GI symptoms suggestive of parasitic infections that turn out to be free of parasites. Follow up tests for pathogenic bacteria using swab culture tests showed that practically all these patients were infected with pathogenic bacteria that produce symptoms similar to those known in classical parasitic infections. Our Neuro-cutaneous Syndrome (NCS) patients, among others with dermatological symptoms, often test positive for skin infecting bacteria such as *Staphylococcus* spp. Other organ systems and body fluids such as urine may also test positive for pathogenic bacteria. The presentation will focus on the common species of pathogenic bacteria that we find in the gastro-intestinal tract of humans with particular reference to identity, transmission, symptoms and pathology, treatment, and prevention.

Keywords: Neuro-cutaneous Syndrome (NCS); Gastro-Intestinal Pathogenic Bacteria Infections; Humans

Salmonella sp.	ents for urine and gastroin	cholera		Yersinia sp.	
+ 3 Escherichia coli	Citrob	bacter freundii		Campviobacter sp.	
Klebsiella sp.	Protei	us vulgaris		Clostridium difficle	
Shigella sp.		5			
Common Bacterial Ag	ents for skin, urine, and mu	ucoid surfaces			
Staphylococcus sp.	S. coagulase positive (S. al	ureus) S.	coagulase n	egative (S. epiderm	idis)
Streptococcus sp.	Pseudomonas aeruginosa	Ca	andida sp.	Bacteroides sp.	
Enterobacter sp.	+ 3 Enterococcus sp.	Se	erratia marce	sens	
	Sensitivity results ran	nge: 1 (most efficacious) -	4 (least effi	cacious)	
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## **Types of bacteria**

**The coccus bacteria:** Important human pathogens caused by coccoid bacteria include staphylococci infections, some types of food poisoning, some urinary tract infections, toxic shock syndrome, gonorrhoea, as well as some forms of meningitis, throat and heart infections, pneumonias, and sinusitis.



Bacillus bacteria: Bacillus bacteria is any rod-shaped bacteria in solitary, diplobacilli, streptobacilli, or coccobacilli form.



Figure 3

Clinical significance: Diseases caused by bacilli include food borne illnesses, plague, and anthrax.

Spiral bacteria: Spiral bacteria are those with 1 or more twists including vibrio, spirillum and spirochete forms.

Vibrio form
Spirillum form

Figure 4

**Clinical significance**: Major spiral bacteria of public health importance include those syphilis, among others.

# Gastrointestinal bacterial infections

**Bacillus** (normal bacteria): Bacillus is a genus of Gram-positive, rod-shaped bacteria and a member of the division Firmicutes. Species of Bacillus are ubiquitous in nature and can be obligate aerobes or facultative anaerobes, and test positive for the enzyme catalase. Under stressful environmental conditions, the cells produce oval endospores that can stay dormant for extended periods.

**Significance:** Many species of *Bacillus* are able to secrete large quantities of enzymes. *Bacillus amyloliquefaciens* is the source of a natural antibiotic protein barnase (a ribonuclease), alpha amylase used in starch hydrolysis, the protease subtilis in used with detergents, and the BamH1 restriction enzyme used in DNA research.

**Use as model organism:** *Bacillus subtilis* is one of the more common and best understood prokaryotes, in terms of molecular biology and cell biology. Its superb genetic amenability and relatively large size have provided the powerful tools required to investigate a bacterium from all possible aspects. It is also a notable food spoiler. Under the microscope in fecal specimens, the *Bacillus* cells appear as rods, and a substantial portion usually contain an oval endospore at one end, making it bulge.



Normal friendly bacilli mostly of the *Bifidus* and *Lactobacillus* forms in a stained fecal wet mount.

Figure 5

*Escherichia coli: Escherichia coli* is a Gram-negative, rod-shaped bacterium that is commonly found in the lower intestine of warmblooded animals (endotherms). Most *E. coli* strains are harmless, producing vitamin K2, and by preventing the establishment of pathogenic bacteria within the intestine. They are used as bio-indicators to test environmental samples for fecal contamination. Different strains of *E. coli* are often host-specific, making it possible to determine the source of fecal contamination in environmental settings.



Rod-shaped Escherichia coli in scanning and transmission electron microscopy

Figure 6

**Symptoms and pathology of** *E. coli*: Over 700 antigenic serotypes of *E. coli* are recognized based on O, H, and K antigens. Most human beings have more than 1 strain of *E. coli* at the same time Most strains of *E. coli* live in the intestine of humans and other mammals without causing any pathology. Pathogenic strains of *E. coli*, however, are responsible for 3 types of infections in humans: urinary tract infections, neonatal meningitis, and intestinal diseases. The latter includes (1) ETEC (Enterotoxigenic *E. coli*) causing diarrhea in infants and travelers, (2) EIEC (Enteroinvasive *E. coli*) causing dysentery-like diarrhea with fever, (3) EPEC (Enteropathogenic *E. coli*) causing watery, sometimes bloody, diarrhea especially in children, and (4) EHEC (Enterohemorrhagic *E. coli*) causing hemorrhagic diarrhea and/ or food poisoning which may develop into hemolytic uremic syndrome (HUS) and includes the invasive 0157:H7 strain making up 80% of the EHEC serotypes producing the verotoxin or Shiga toxin. Strain identification requires molecular techniques not readily available in most diagnostic laboratories. For more information, see Amin, 2011. J. Bacteriol. and Parasitol. 2: 109-112.

Transmission of *E. coli*: This is a fecal-oral infection, directly or indirectly.

**Treatment:** Antibiotics have not proven useful for the acute diarrheal illness. In fact, antibiotics may increase the chances of developing HUS (up to 17-fold). This effect is thought to occur because the antibiotic damages the bacteria, causing them to release even more toxin. Most investigators suggest antibiotic use only if a patient is septic. For herbal alternative, Freedom/Cleanse/Restore (F/C/R) is recommended.

Prevention: Avoid any sources of direct or indirect fecal contamination.

*Salmonella*: *Salmonella* is a genus of over 1000 species (serotypes) of rod-shaped, Gram-negative, non-spore-forming, predominantly motile enterobacteria with flagella. They are chemo-organotrophs. Most isolates exist in two phases: a motile phase I and a nonmotile phase II. *Salmonella* is closely related genus *Escherichia* and are found worldwide in cold- and warm-blooded animals (including humans), and in the environment. They cause illnesses such as typhoid fever, paratyphoid fever and foodborne illness.

*Citation:* Omar M Amin. "Perspectives on Gastro-Intestinal Pathogenic Bacteria Infections in Humans". *EC Microbiology* 15.11 (2019): 1173-1185.





**Food poisoning symptoms:** *Salmonella* must be ingested in large numbers to cause disease in healthy adults. Gastric acidity destroys the majority of ingested bacteria. Infants, young children and the elderly are much more susceptible to infection. Extraintestinal localizations are possible, especially *Salmonella meningitis* in children, osteitis, etc. Enteritis *Salmonella* can cause diarrhea. HIV patients and those with suppressed immunity can become seriously ill. In the USA, about 40,000 cases of *Salmonella* infection are reported each year with 142,021 cases reported with *Salmonella enteritidis* from chicken eggs, and about 30 die. Over 16 million people worldwide are infected with typhoid fever each year, with 500,000 to 600,000 fatal cases. *Salmonella* bacteria can survive for weeks outside a living body, and they are not destroyed by freezing. Most people with salmonellosis develop diarrhea, fever, vomiting, and abdominal cramps 12 to 72 hours after infection. In most cases, the illness lasts 4 - 7 days. In severe cases, the *Salmonella* infection may spread from the intestines to the blood stream, and then to other body sites, and can cause death.

**Transmission:** Many *Salmonella* infections occur due to ingestion of contaminated food, e.g. *S. enteritis* and Salmonella typhoid/ paratyphoid. Because of a special virulence factor and a capsule protein (virulence antigen), they can cause serious illness as in *Salmonella enterica* and *Salmonella typhi* which is adapted only to humans.

**Treatment:** Patients may need intravenous fluids to treat the dehydration, and may be given medications to provide symptomatic relief, such as fever reduction. Antibiotic regimens are used in severe cases. F/C/R is a natural herbal alternative.

**Prevention:** Be careful eating at church picnics and large or home gatherings where improperly refrigerated eggs are used as in potato salads, pies, etc.

*Klebsiella: Klebsiella* is a genus of ubiquitous non-motile, Gram-negative, oxidase-negative, rod-shaped bacteria with a prominent polysaccharide-based capsule causing pneumonia (*Klebsiella pneumonia*), bloodstream infections, wound or surgical site infections, and meningitis. In healthcare settings, *Klebsiella* infections often occur among sick patients who are receiving treatment for other conditions. Patients who use devices like ventilators or intravenous catheters, and those who are on long courses of certain antibiotics are most at risk for *Klebsiella* infections. Healthy people usually do not get *Klebsiella* infections.





klebsiella pneumonia colonies on Endo-agar



A scanning electron micrograph of k. pneumonia

Figure 8

**Transmission**: *Klebsiella* must enter the respiratory tract to cause pneumonia, or the blood to cause a bloodstream infection. In healthcare settings, *Klebsiella* bacteria can be spread from person-to-person or, less commonly, by contamination of the environment. The bacteria do not spread through the air.

**Symptoms and pathology:** *Klebsiella* organisms are frequent human pathogens that can cause pneumonia, urinary tract infections, septicemia, and soft tissue infections. *Klebsiella* species is implicated in the pathogenesis of ankylosing spondylitis and other spondyloarthropathies. Pathogenic varieties of *Klebsiella* are grouped in 2 antigenic groups: the O antigen with 9 varieties and the K antigen with over 80 varieties. *Klebsiella* is increasingly reported as a nosocomial infection second only to *E. coli* in urinary tract infections in women. *Klebsiella pneumoniae* is an opportunistic infection in older patients with weakened immune system which also causes nosocomial pneumonia, intraabdominal infections and intestinal pathology. It is a resident of the intestinal track in about 40% of man and animals. Increasingly, *Klebsiella* bacteria have developed antimicrobial resistance especially to carbapenems. *Klebsiella* bacteria are normally found in the human intestines (where they do not cause disease). They are also found in human stool (feces).

Treatment: Difficult to treat because fewer antibiotics are effective against them. F/C/R is a good natural herbal remedy.

Prevention: Avoid exposure to spores via the respiratory or blood routs in hospital or health care settings.

*Shigella:* Shigella is a genus of Gram-negative, non-spore forming, non-motile, rod-shaped bacteria closely related to *Escherichia coli* and *Salmonella*. The causative agent of human shigellosis, *Shigella* is only naturally found in humans and apes. During infection, it typically causes dysentery. After invasion, *Shigella* multiplies intracellularly and spreads to neighboring epithelial cells, resulting in tissue destruction and characteristic pathology. *Shigella* causes approximately 90 million cases of severe dysentery with at least 100,000 of these resulting in death each year, mostly among children in the developing world.

**Transmission:** *Shigella* infections are transmitted via fecal-oral contamination. Less than 100 bacterial cells are enough to cause an infection

**Symptoms:** Symptoms of diarrhea, fever, nausea, vomiting, stomach cramps and flatulence may last for a few days. Infections cause dysentery and destruction of the intestinal lining of the cecum and rectum. Some strains produce enterotoxin and Shiga toxin, similar to the verotoxin of *E. coli* 0157:H7, among others, causing hemolytic uremic syndrome. The stool may contain blood, mucus, or pus. In rare cases, young children may have seizures. Incubation period 2 - 7 days. *Shigella* is one of the pathogenic causes of reactive arthritis worldwide.



Figure 9

**Treatment:** Treat severe cases with ampicillin, TMP-SMX, or fluoroquinolones, such as ciprofloxacin, and rehydrate. Antidiarrheal agents may worsen the sickness and should be avoided. For *Shigella*-associated diarrhea, antibiotics shorten the length of infection. Currently, no licenced vaccine exists. F/C/R is a good alternative natural remedy.

**Prevention:** Hand washing before handling food.

*Vibrio cholerae: Vibrio cholerae* is a Gram-negative, comma-shaped facultatively anaerobic bacterium with flagellum at one pole. Some strains of *V. cholera* cause the disease cholera. Worldwide, it affects 3 - 5 million people and causes 100,000 - 130,000 deaths a year as of 2010.



Figure 10

**Symptoms and pathology:** Symptoms of *Vibrio cholera* include watery diarrhea and vomiting. Severe cholera, requiring hospitalization, results from the accumulation of about a million bacterial cells within the body. Diarrhea and vomiting can lead to rapid dehydration and electrolyte imbalance, and death in some cases. During infection, *V. cholerae* secretes cholera toxin, a protein that causes profuse, watery diarrhea. Colonization of the small intestine also requires the toxin coregulated pilus (TCP), a thin, flexible, filamentous appendage on the surface of bacterial cells. Two serogroups of *V. cholerae*, O1 and O139, cause outbreaks of cholera. O1 causes the majority of outbreaks, while O139 - first identified in Bangladesh in 1992 - is confined to South-East Asia. Many other serogroups of *V. cholerae*, with or without the cholera toxin gene can cause a cholera-like illness.

**Transmission:** This is a fecal-oral infection. The main reservoirs of *V. cholerae* are people and aquatic sources such as brackish water and estuaries, often in association with copepods or other zooplankton, shellfish, and aquatic plants. Cholera infections are most commonly acquired from drinking contaminated. Other common vehicles include contaminated fish and shellfish, produce, or leftover cooked grains that have not been properly reheated. Transmission from person to person is rarely documented.

**Treatment:** Treatment is oral rehydration therapy, typically with oral rehydration solution, to replace water and electrolytes. If this is not tolerated or does not provide improvement fast enough, intravenous fluids can also be used. Antibacterial drugs are beneficial in those with severe disease to shorten its duration and severity. F/C/R should be considered.

Prevention: Avoid all sources of contamination listed above, especially in endemic areas.

**Epidemiological notes:** England was the hot bed of Cholera since the medieval ages through the 19<sup>th</sup> century. Snow on the Broad pump St. epidemic of cholera in London is a piece of medical history.

The Broad Street cholera outbreak was a severe outbreak of cholera that occurred near Broad Street in the Soho district of London, England in 1854. This outbreak is best known for the physician John Snow's study of the outbreak and his discovery that cholera is spread by contaminated water. This discovery came to influence public health and the construction of improved sanitation facilities beginning in the 19<sup>th</sup> century. Later, the term "focus of infection" would be used to describe places like the Broad Street pump in which conditions are ripe for transmission of an infection.

**Background:** In the mid-19<sup>th</sup> century, the Soho district of London had a serious problem with filth due to the large influx of people and a lack of proper sanitary services: the London sewer system had not reached Soho. Many cellars (basements) had cesspools of night soil underneath their floorboards. Since the cesspools were overrunning, the London government decided to dump the waste into the River Thames. This action contaminated the water supply, leading to the cholera outbreak.

**The outbreak:** On 31 August 1854, after several other outbreaks had occurred elsewhere in the city, a major outbreak of cholera struck Soho. John Snow, the physician who eventually linked the outbreak to contaminated water, later called it "the most terrible outbreak of cholera which ever occurred in this kingdom".

Over the next three days, 127 people on or near Broad Street died. In the next week, three quarters of the residents had fled the area. By 10 September, 500 people had died and the mortality rate was 12.8 percent in some parts of the city. By the end of the outbreak, 616 people had died.

*Citrobacter freundii: Citrobacter freundii* are opportunistic anaerobic rod-shaped Gram-negative bacilli. *Citrobacter* is found in the human intestine and almost everywhere else including water, waste water, soil, etc.

**Symptoms:** *Citrobacter freundii* is rarely a source of illness but is often the cause of opportunistic infections mostly causing abnormal inflammatory changes in the intestinal tract and affecting biliary, urinary, and respiratory tracts, and blood of patients with weak immune system. It has been "suspected to cause diarrhea and possibly extra-intestinal infections including peritonitis. Of 38 hospitalized patients in 2 community teaching hospitals in the Detroit Medical Center, *Citrobacter* bacteremia frequently developed in elderly patients

(65%) and was hospital acquired (77%) with initial sites of infection including the UT (39%), intestinal tract (27%), wound (10%), and unknown(13%). It is known to be the cause of a number of nosocomial infections of the respiratory tract, urinary tract, blood and many other normally sterile sites in patients. *C. freundii* represents about 29% of all opportunistic infections. One fatal disease that *C. freundii* has been associated with is neonatal meningitis. The mortality rate of *Citrobacter meningitis* is unacceptably high, with death rates of patients ranging from 25 to 50 %. Moreover, serious neurological problems were reported to persist in 75% of survivors. For more information, see Amin, 2011. J. Bacteriol. and Parasitol. 2: 109-112.



Figure 11

Transmission: Citrobacter freundii is an indicator of a potential source of contamination from infected soil or water sources.

**Treatment:** *Citrobacter* species are a common cause of nosocomial infections associated with patients that are undergoing prolonged hospital treatments. *C. freundii* has been reported to express resistance to broad-spectrum antibiotics including piperacillin, piperacillin tazobactam, vancomycin and cephalosporins. Isolation of ceftriaxone-resistant *Citrobacter freundii* (CRCF) has been associated with the overprescribed broad spectrum antibiotics. F/C/R is a good alternative natural herbal remedy.

Prevention: Avoid exposure contaminated soil or water or soil/water based contaminated objects.

*Proteus vulgaris: Proteus vulgaris* is an opportunistic rod-shaped, gram-negative bacterium that inhabits the intestinal tracts of humans and animals. It is also found in the soil, water, putrefied meat, and fecal matter and is associated with long-term care facilities and hospitals where it is also known to colonize the skin, urinary tract, and oral mucosa of patients and hospital personnel alike.





**Symptoms and pathology:** *Proteus vulgaris* is an opportunistic pathogen in humans where it is also known to cause urinary tract (UT) and wound infections. While *Proteus* spp. are not the most common sources of bacterial infections in humans, *P. vulgaris* holds yet a smaller role in the pathology caused by this group. *Proteus* species most frequently cause UT infections, with *Proteus mirabilis* producing 90% of the cases. It is suggested that the higher prevalence of *P. vulgaris* infections in the intestinal tract of females may be related to cross contamination from UT infections. The presence of the sepsis syndrome associated with a UTI should raise the possibility of urinary tract obstruction. This is especially true of patients who reside in long -term care facilities, who have long-term indwelling urethral catheters, or who have a known history of urethral anatomic abnormalities. UTI obstruction and Urease production leads to precipitation of organic and inorganic compounds, which leads to struvite stone formation. For more information, see Amin, 2011. J. Bacteriol. and Parasitol. 2: 109-112.

Transmission: By exposure to contaminated soil, water, meat and fecal sources.

**Treatment:** Known antibiotics that *P. vulgaris* is sensitive to: Ciprofloxacin, Ceftazidime, Netilmicin, Sulbactam or, Cefoperazo, Meropenem, Piperacillin/tazobactam, and Unasyn. F/C/R is a good alternative natural remedy.

**Yersinia spp.:** *Yersinia* is a genus of Gram-negative rod shaped bacteria and are facultative anaerobes. Some members of *Yersinia* are pathogenic in humans; in particular, *Y. pestis* is the causative agent of the plague. Rodents are the natural reservoirs of *Yersinia*; less frequently other mammals serve as the host.

**Transmission:** Via blood (in the case of *Y. pestis*) or in an alimentary fashion, via consumption of food products (especially vegetables, milk-derived products and meat) contaminated with infected urine or feces. Certain *Yersinia* may spread via protozoonotic mechanisms.



Y. Pestis in the stomach of a flea

Microscopic view of Y. Pestis

Figure 13

*Citation:* Omar M Amin. "Perspectives on Gastro-Intestinal Pathogenic Bacteria Infections in Humans". *EC Microbiology* 15.11 (2019): 1173-1185.

**Symptoms and pathology:** Diarrhea, may be bloody in severe cases, low-grade fever, abdominal pain, vomiting, in approximately 15 - 40% of cases. The patient may also develop erythema nodosum, on the legs and trunk. Lesions appear 2 - 20 days after the onset of fever and abdominal pain and resolve spontaneously in most cases in about a month. *Yersinia* may be associated with Crohn's disease, an inflammatory autoimmune condition of the gut. Iranian sufferers of Crohn's disease were more likely to have had earlier exposure to refrigerators at home, consistent with *Yersinia*'s unusual ability to thrive at low temperatures. *Yersinia* is implicated as one of the causes of reactive arthritis worldwide. Also associated with pseudoappendicitis, which is an incorrect diagnoses of appendicitis due to a similar presentation.

**Treatment**: Third-generation cephalosporins, Trimethoprim-sulfamethoxazole (TMP-SMZ), Tetracyclines, Fluoroquinolones, Aminoglycosides. F/C/R should be considered.

**Prevention:** Outdoor workers, campers, and travelers in rodent infested endemic areas need to be careful of flea bites. Human to human transmission is also known in cased of pneumonic plague via the respiratory system. Food sources potentially contaminated with urine of feces should not be handled or ingested.

**Epidemiological notes:** Pneumonic plague (England), tonsilar plague (Peru) and sylvatic plague (US.), among other forms of plague are well known. The concept of ecological equivalents operates.

#### Campylobacter spp.

*Campylobacter* (meaning 'twisted bacteria') is a genus of Gram-negative, spiral, and microaerophilic bacteria. *Campylobacter jejuni* is now recognized as one of the main causes of bacterial foodborne disease in many developed countries. At least a dozen species of Campylobacter have been implicated in human disease, with *C. jejuni* and *C. coli* being the most common.

*C. fetus* of cattle and sheep is an opportunistic pathogen in humans.





Figure 14

Transmission: Campylobacteriosis is transmitted by fecal-oral, ingestion of contaminated food or water, and the eating of raw meat.

**Symptoms:** The infection produces an inflammatory, sometimes bloody, diarrhea, periodontitis or dysentery syndrome, mostly including cramps, fever and pain. Symptoms typically last for five to seven days. The infection is usually self-limited.

**Pathology:** The sites of tissue injury include the jejunum, the ileum, and the colon. Most strains of *C. jejuni* produce a toxin (cytolethal distending toxin) that hinders the cells from dividing and activating the immune system. The organism produces diffuse, bloody, edematous, and exudative enteritis. It may be a cause of hemolytic uremic syndrome and thrombotic thrombocytopenic purpura, no unequivocal case reports exist. In some cases, a Campylobacter infection can be the underlying cause of Guillain-Barré syndrome. Gastrointestinal perforation is a rare complication of ileal infection.

**Treatment:** Symptomatic treatment by liquid and electrolyte replacement is usually enough in human infections. The use of antibiotics, on the other hand, is controversial Standard treatment is now azithromycin. Quinolone antibiotics such as ciprofloxacin or levofloxacin are no longer as effective due to resistance. Dehydrated children may require intravenous fluid treatment in a hospital. The illness is contagious, and children must be kept at home until they have been clear of symptoms for at least two days. Try F/C/R.

Prevention: Good hygiene is important.

#### **Clostridium difficle**

*Clostridium difficle* also known as "CDF/cdf", or "C. diff", is an anaerobic, spore-forming rod-shaped Gram-positive bacteria. Spores can remain viable outside of the human body for very long periods of time, and this means that patients in a medical facility are often exposed to situations where they end up accidentally ingesting spores. The rate of *C. difficile* acquisition is estimated to be 13% in patients with hospital stays of up to 2 weeks, and 50% in those with hospital stays longer than 4 weeks.



Figure 15

*Citation:* Omar M Amin. "Perspectives on Gastro-Intestinal Pathogenic Bacteria Infections in Humans". *EC Microbiology* 15.11 (2019): 1173-1185.

**Transmission:** People accidentally ingest spores of the bacteria while patients in a hospital, nursing home, or similar facility. *C. difficile* is transmitted from person to person by the fecal-oral route.

**Symptoms:** *C. difficile* infections can range in severity from asymptomatic to life-threatening, especially among the elderly. Symptoms include diarrhea, recent antibiotic exposure, colitis, fever (up to 40.5°C), and foul stool odor. In a population of hospitalized patients prior antibiotic treatment plus diarrhea or abdominal pain had a sensitivity of 86% and a specificity of 45%. The severe diarrhea and other intestinal disease occur when competing bacteria in the gut flora have been wiped out by antibiotics. *C. difficile* is the most serious cause of antibiotic-associated diarrhea (AAD) and can lead to pseudomembranous colitis, a severe inflammation of the colon which can cause life threatening megacolon. Bacteria overpopulation is harmful because the release of toxins that can cause bloating and diarrhea, with abdominal pain. Latent symptoms often mimic flu-like symptoms and can mimic inflammatory bowel disease-associated colitis.

**Treatment:** Mild cases of *C. difficile* infection can often be cured by discontinuing the antibiotics responsible. In more serious cases, oral administration of, first, oral metronidazole and - if that fails - then, second, vancomycin and if unsuccessful again, intravenous metronidazole can be used. Relapses of *C. difficile* AAD have been reported in up to 20% of cases. F/C/R is best alternative.

Prevention: Avoid fecal-oral transmission directly or indirectly and avoid inhaling spores in hospital or health care facilities.

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