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Campylobacteriosis

Campylobacter enteritis
Vibrionic enteritis
Vibriosis

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Overview

- Organism
- History
- Epidemiology
- Transmission
- Disease in Humans
- Disease in Animals
- Prevention and Control
- Actions to Take

In today's presentation we will cover information regarding the organism that causes campylobacteriosis and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures, as well as actions to take if campylobacteriosis is suspected.

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THE ORGANISM

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The Organism

- Family Campylobacteriaceae
  - Gram negative, microaerophilic
  - Curved or spiral rods
- Causes of enteritis
  - *Campylobacter jejuni*
  - *Campylobacter coli*
- Causes of infertility and abortion
  - *C. jejuni*
  - *C. fetus* subsp. *venerealis*
  - *C. fetus* subsp. *fetus*

Campylobacter are Gram negative, microaerophilic, curved or spiral rods in the family Campylobacteriaceae. *Campylobacter jejuni* (formerly known as *C. fetus* subsp. *jejuni*) and *C. coli* are associated with enteritis in domestic animals and humans. Some strains of *C. jejuni*, *C. fetus* subsp. *venerealis*, and *C. fetus* subsp. *fetus* (also known as *C. fetus* subsp. *intestinalis* and *Vibrio fetus var intestinalis*) cause infertility and abortions in sheep and cattle. *C. fetus* subsp. *fetus* is occasionally isolated from humans with septicemia. Other species of *Campylobacter* including *C. lari*, *C. hyointestinalis* and *C. upsaliensis* can cause disease but seem to be of minor importance in domestic animals. Uncharacterized *Campylobacter* species may be involved in proliferative ileitis of hamsters, porcine proliferative enteritis and proliferative colitis of ferrets.

[Photo: This scanning electron microscope image shows the characteristic spiral, or corkscrew, shape of Campylobacter jejuni cells and related structures. Source: De Wood and Chris Pooley/USDA, ARS, EMU]

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The Organism

- Survives in moist environments
  - Weeks to months
- Some strains tolerate cold
- Remains viable in:
  - Feces
  - Milk
  - Water
  - Vaginal discharges
  - Poultry litter

Campylobacter species do not tolerate drying or heat but can often survive for a time in moist environments. *C. jejuni* can survive a few weeks to a few months under moist, reduced-oxygen conditions at 4°C, but only a few days at room temperature. Some strains also tolerate –20°C. This species may also remain viable for up to 9 days in feces, 3 days in milk, and 2 to 5 days in water. It can survive in vaginal discharges on bedding or pasture for several days under field conditions. Both *C. jejuni* and *C. coli* can remain infective in moist poultry litter for prolonged periods. *C. fetus* can survive in liquid manure for 24 hours and soil for up to 20 days.

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HISTORY

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History

- 1886
  - Spiral bacteria first described
- 1968
  - *Campylobacter* isolated from human feces
- 1970s
  - Recognized as human pathogen

In 1886, the German scientist Escherich published a series of articles that described spiral bacteria in the colons of children who had died of what he called 'cholera infantum'. This work, however, went largely unrecognized until the 1980s. Although *Campylobacter* spp. were associated with other human infections throughout the 1940s and 50s, it wasn't until the 1970s that they were fully recognized as human pathogens. A crucial step in this process was the isolation of *Campylobacter* from human feces in 1968. During the mid-1900s, *Campylobacter* spp. were also isolated from animals that experienced abortion and sterility. Source: Butzler JP. Campylobacter, from obscurity to celebrity. Clin Microbiol Infect. 2004 Oct;10(10):868-76.

[Photo: This scanning electron micrograph depicts a grouping of Gram-negative *Campylobacter fetus* bacteria, magnified 4,976x. The "S-shaped" *C. fetus* bacterium, also known as *C. fetus* ssp. *intestinalis* is an opportunistic human pathogen with a worldwide distribution pattern. Source: Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #5776]

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EPIDEMIOLOGY

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Morbidity and Mortality: Humans

- Common cause of bacterial diarrhea in the U.S.
  - 20 cases/100,000 people annually
- Causes 5 to 14% of diarrhea worldwide
- Populations at risk
  - Young children
  - People in developing countries
  - Immunosuppressed

C. jejuni, *C. coli* and *C. fetus* infections are found worldwide. *C. jejuni* is one of the most common causes of bacterial diarrhea in the United States; roughly 20 cases per 100,000 population are seen yearly. Worldwide, campylobacteriosis is responsible for approximately 5-14% of all cases of diarrhea. Infections are particularly common in very young children in developing countries, and in children and young adults in developed countries. Most cases are sporadic, but outbreaks, associated with sources such as raw milk, are also seen. *C. jejuni* or *C. coli* diarrhea is usually self-limiting and generally resolves after 7 to 10 days; relapses can occur in approximately 10-25% of cases. Immunosuppressed individuals are at a high risk for severe or recurrent infections or for septicemia. Deaths are rare in *C. jejuni* infections and are seen mainly in patients with cancer or other debilitating diseases. The estimated case/fatality ratio for *C. jejuni* infections is one in 1,000. Guillain-Barré syndrome is seen after approximately 1 in 1000 diagnosed infections; up to 5% of these patients may die and 30% or more may have residual weakness or other neurologic defects.

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Morbidity and Mortality: Humans

- Top five pathogens contributing to domestically acquired foodborne illness (U.S.) in 2011
  - *Norovirus*
  - *Salmonella* (non-typhoidal)
  - *Clostridium perfringens*
  - *Campylobacter* spp.
    - 845,024 estimated illnesses
  - *Staphylococcus aureus*

The CDC estimates that each year roughly 1 in 6 Americans (or 48 million people) gets sick, 128,000 are hospitalized, and 3,000 die of foodborne diseases. In 2011, Campylobacter spp. were among the five most common pathogens contributing to domestically acquired foodborne illness. Source: CDC. http://www.cdc.gov/foodborneburden/2011-foodborne-estimates.html.

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Morbidity and Mortality: Animals

- Asymptomatic carriage more common than enteric disease
  - Up to 45% of cats, 75% of dogs
  - Higher in animal shelters, pet shops, strays, rural animals
- High incidence in poultry
- Abortion in sheep
  - 10 to 20% abortion rate
- Mortality low for all causes

Among animals, asymptomatic carriage of intestinal *Campylobacter* is more common than enteric disease. The carriage of *Campylobacter* in small animals is highly variable, ranging from 0-45% in cats and 1.6-75% in dogs. The prevalence of infection is low in household pets but high in animal shelters, pet shops and laboratory colonies, as well as in strays and rural animals exposed to livestock. Among livestock, *Campylobacter jejuni* has been isolated from the feces of 25-100% of asymptomatic cattle and, in one study, the gallbladder of 11% of healthy sheep. Various studies have noted a particularly high incidence of infection in poultry, with *Campylobacter* in 100% of the ceca of turkeys, 83% of chicken droppings and 88% of duck droppings. *C. jejuni* contamination has also been seen in approximately 30% of chicken meat and 5% of red meat samples. *Campylobacter* species have also been isolated from 50% of urban pigeons, 35% of migratory birds and 20-70% of seagulls. Gastrointestinal campylobacteriosis is usually self-limiting in mammals; however, up to 32% mortality may be seen with highly pathogenic isolates in chicks. Mortality is also low in adult sheep and cattle affected by abortions and infertility. In sheep, the typical abortion rate is 10-20%, with 5% mortality in the ewes that abort, due to metritis. Under some circumstances, (e.g. an outbreak in a naïve flock) abortion rates can reach 70-90%.

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TRANSMISSION

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Transmission: *C. jejuni*

- Fecal-oral
- Direct contact
- Fomites
- Bacteria found in/on:
  - Vaginal discharges, abortion products
  - Undercooked meat, raw milk
- Mechanical vector
  - Common housefly

Campylobacter jejuni and *C. coli* are transmitted by the fecal-oral route; they can be spread by direct contact and on fomites including food or water. *C. jejuni* may also be present in the vaginal discharges, aborted fetuses and fetal membranes of aborting sheep. Undercooked poultry and other meats are sources of infection for pets and commercially raised mink. Houseflies can be mechanical vectors. Humans may be infected after ingesting undercooked poultry and other meats, raw milk, raw clams, contaminated foodstuffs or unchlorinated water, and after contact with infected pets or livestock. Asymptomatic carriers are seen in many species of domestic animals; humans do not usually become carriers.

[Photo: (Top) Raw chicken; (Bottom) A common house fly. Source: Julia Wilkins/Wikimedia Creative Commons]
Photo: Common house fly, *Musca domestica*, a vector which is known to carry *Campylobacter* spp.

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Transmission:
C. fetus subsp. *fetus*

- Ingestion
- Contact with
  - Feces, vaginal discharges, aborted fetuses, fetal membranes
- Venereal (cattle)
- Fomites
  - Semen, instruments, bedding
- Cattle may become carriers

Campylobacter fetus subsp. *fetus* is transmitted by ingestion in cattle, sheep and goats. Animals can become infected after contact with feces, vaginal discharges, aborted fetuses and fetal membranes. This organism and *C. fetus* subsp. *venerealis* are also transmitted venereally in cattle. Genital *C. fetus* infections can be spread on fomites including contaminated semen, contaminated instruments and bedding. Bulls may transmit *C. fetus* for several hours after being bred to an infected cow; some bulls can become permanent carriers. Cows can also become carriers for years.

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DISEASE IN HUMANS

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Disease in Humans

- Nearly all cases due to *C. jejuni*
- Enteritis
  - Mild to fulminant or relapsing colitis
  - Diarrhea (may contain blood)
  - Fever, nausea, vomiting
  - Abdominal pain
- Complications uncommon
  - Guillain-Barré syndrome

Virtually all human illness is caused by one species, *C. jejuni*, but 1% are caused by other species. In humans, the incubation period for *C. jejuni* gastroenteritis is 1-10 days and most often 2 to 5 days *C. jejuni* and occasionally *C. coli* cause enteritis; disease varies from mild gastrointestinal distress that resolves within 24 hours to a fulminating or relapsing colitis. The clinical signs may include watery or sticky diarrhea, fever, nausea, vomiting, abdominal pain, headache and muscle pain. The feces may contain visible or occult blood. The acute symptoms usually diminish in two to three days, and recovery typically occurs spontaneously in a week to 10 days. Complications are uncommon; however, reactive arthritis, hemolytic uremic syndrome and septicemia have been seen. Rare complications include meningitis, recurrent colitis, acute cholecystitis, massive lower gastrointestinal hemorrhage, mesenteric adenitis, appendicitis, and Guillain-Barré syndrome (an acute, rapidly progressive polyneuropathy). Cases of *C. jejuni* abortion have been seen in humans, but are extremely rare.

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Disease in Humans

- *C. fetus*
  - Opportunistic human pathogen
  - Causes systemic infections
  - Immunocompromised persons at risk

Potential Complications
- Endocarditis
- Pericarditis
- Pneumonia
- Thrombophlebitis
- Peritonitis
- Meningoencephalitis

C. fetus is an opportunistic human pathogen and mainly causes systemic infections. The incubation period for human *C. fetus* infections is usually 3-5 days. Infections tend to occur in people with debilitating illnesses such as diabetes, cancer or cirrhosis. Intestinal symptoms may be mild. Fever is the only consistent symptom, but abdominal pain, splenomegaly and hepatomegaly are common. Subacute endocarditis, septic arthritis, meningitis or fever of unknown origin are also seen. Complications may include endocarditis, pericarditis, pneumonia, thrombophlebitis, peritonitis or meningoencephalitis.

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Diagnosis

- Presumptive diagnosis
  - Microscopy
    - Characteristic darting motility
    - Curved or spiral rods
- Definitive diagnosis
  - Fecal or (rarely) blood cultures
    - Organism may be difficult to isolate
  - Biochemical, antigen testing
- PCR, ELISA

A presumptive diagnosis can be made by detecting the characteristic darting motility of the organism with dark-field or phase-contrast microscopy. Gram negative, curved or spiral rods are seen in Gram stained preparations. Definitive diagnosis is by isolation of the causative organism; however, *Campylobacter* is fragile and cannot always be found. Feces or (rarely) blood cultures are used for diagnosis. Selective media or filtration techniques improve the chance of isolation. Biochemical testing, antigen testing and restriction endonuclease DNA analyses are used for species and strain identification. Polymerase chain reaction (PCR)-based and ELISA techniques for rapid detection or culture confirmation are also available. Serology is currently used only in research.

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Treatment

- Supportive care
  - Fluid and electrolyte therapy
- Antibiotics
  - Efficacy not proven for mild infections
  - May reduce shedding
- Complications
  - Guillain-Barré syndrome
  - Requires intensive care

Treatment is often limited to fluid and electrolyte replacement therapy. Antibiotics are occasionally given, particularly when the symptoms are severe or prolonged; however, their efficacy is not proven for mild infections. Individuals with Guillain-Barré syndrome usually require intensive care. Antibiotics can reduce the shedding of infectious organisms.

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DISEASE IN ANIMALS

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Species Affected

- Cattle, sheep
- Chickens
- Turkeys
- Dogs, cats
- Mink, ferrets
- Pigs
- Non-human primates

C. jejuni and *C. coli* can infect cattle, sheep, chickens, turkeys, dogs, cats, mink, ferrets, pigs, non-human primates and other species. *C. fetus* subsp. *fetus* is found in cattle, sheep and goats. *C. fetus* subsp. *venerealis* is found in cattle. Animals can be infected asymptomatically with any of these organisms.

[Photos: (Top) Sheep; (Middle) Cattle; (Bottom) Chickens. Source: USDA ARS]

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Disease in Animals

- Enteritis
  - Many species affected
  - Young animals
  - Diseased or stressed adults
- Usually resolves in 3 to 7 days
  - Intermittent diarrhea may persist
- Newly hatched chicks and poults
  - Acute disease and death

C. jejuni and occasionally *C. coli* cause enteritis in dogs, cats, calves, sheep, mink, ferrets, poultry and some species of laboratory animals. Enteritis is more common in young animals but stress or concurrent disease increase the risk of disease in adults. In dogs, the symptoms can include diarrhea, decreased appetite, vomiting and sometimes fever. The feces are usually watery or bile-streaked, with mucus and sometimes blood. The symptoms generally last 3 to 7 days, but some animals may have intermittent diarrhea for weeks and occasionally for months. Calves typically have a thick, mucoid diarrhea with occasional flecks of blood, either with or without a fever. Mucoid, watery and sometimes bloody diarrhea is also seen in cats, primates, mink and ferrets. Newly hatched chicks and poults develop acute enteritis, with rapid onset of diarrhea and death; poultry chicks over a week old do not usually become ill.

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Disease in Animals

- Reproductive disease
  - Bovine genital campylobacteriosis
    - Infertility
    - Early embryonic death
    - Abortion uncommon
  - Campylobacteriosis in sheep
    - Late term abortion
    - Weak lambs
    - Metritis
    - Death

In cattle, *C. fetus* subsp. *venerealis* and *C. fetus* subsp. *fetus* can cause bovine genital campylobacteriosis; this disease is characterized by infertility, early embryonic death and a prolonged calving season. *Campylobacter*-associated abortions are uncommon but are occasionally seen. Infected cows may develop a mucopurulent endometritis but do not usually have other systemic signs. *Campylobacter* has also been implicated as a possible cause of mastitis in cows. Bulls are asymptomatic. *C. fetus* subsp. *fetus* and *C. jejuni* can cause late term abortions, stillbirths and weak lambs in sheep. Infections in sheep are sometimes followed by metritis and occasionally deaths. Recovery, with immunity to reinfection, is typical. Sheep can become persistently infected and continue to shed bacteria in the feces.

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Disease in Animals

- Other *Campylobacter* spp. may cause disease in animals
  - Species
    - *C. lari*
    - *C. hyointestinalis*
    - *C. upsaliensis*
  - Disease
    - Proliferative ileitis of hamsters
    - Porcine proliferative enteritis
    - Proliferative colitis of ferrets

Other species of *Campylobacter* including *C. lari*, *C. hyointestinalis* and *C. upsaliensis* can cause disease but seem to be of minor importance. Uncharacterized *Campylobacter* species may be involved in proliferative ileitis of hamsters, porcine proliferative enteritis, and proliferative colitis of ferrets. *Campylobacter* has also been implicated in avian hepatitis; this association is still unproven.

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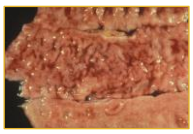
Post Mortem Lesions

- Congested and edematous colon
- Hemorrhagic colitis
- Edematous lymph nodes
- Placentitis (mild)
- Autolyzed fetus



In dogs, the colon may be congested and edematous. In calves, the lesions may include mild to severe hemorrhagic colitis and edematous mesenteric lymph nodes. In chicks, distention of the jejunum, disseminated hemorrhagic enteritis and focal hepatitis may be seen. Aborted cattle fetuses may have bronchopneumonia, mild fibrinous pleuritis or peritonitis. Placentitis is usually mild; the cotyledons may be hemorrhagic and the intercotyledonary area edematous. In sheep, the fetus is usually autolyzed after *C. fetus* abortions; 1-2 cm orange/ yellow necrotic foci can sometimes be found in the liver. Placentitis may be evident, with hemorrhagic necrotic cotyledons and edematous or leathery areas between the cotyledons.

[Photo: Primate, colon. Mucosal edema, muco-hemorrhagic exudate, and thickened folds of the colon. Source: Armed Forces Institute of Pathology/CFSPH]

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Diagnosis

- Culture (fresh feces)
  - Biochemical and antigen testing
- Microscopy
  - Characteristic darting motility
  - Curved or spiral rods
- PCR
- ELISA
- Serology (paired titers)

Enteritis can be diagnosed by isolating the causative organism in fresh fecal samples; however, *Campylobacter* is fragile and cannot always be found. In unfavorable environments (low pH or prolonged low temperatures), *Campylobacter* may also be able to enter a state where it is viable but non-culturable (VBNC stage). Biochemical testing, antigen testing and restriction endonuclease DNA analyses are used for species and strain identification. A presumptive diagnosis can also be made by observing the characteristic darting motility in darkfield or phase contrast preparations. Gram negative, curved or spiral rods are seen in Gram stained preparations. A polymerase chain reaction (PCR)-based assay is used to screen poultry broilers in Denmark, and a commercial PCR-based assay is available for meat samples. Antigen-capture enzyme-linked immunosorbent assays (ELISAs) have been described in the literature. Serology on paired titers may be helpful in some cases.

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Diagnosis

- Bovine genital campylobacteriosis
  - Detection of IgA in cervical mucus
  - Vaginal mucus agglutination test
  - ELISA
  - Culture
    - Sheath washings
    - Vaginal cultures

Bovine genital campylobacteriosis can be diagnosed by detecting specific IgA in the cervical mucus; these antibodies are present for several months in half of all infected cows. Tests include a vaginal mucus agglutination test (VMAT) and ELISAs. Individual responses in the VMAT are variable; for this test, a minimum of 10 cows or 10% of the herd should be sampled. Sheath washings taken twice from bulls, approximately one week apart, can be submitted for culture or immunofluorescent testing. Vaginal cultures can also be collected immediately after abortion or infection, but this method may be unreliable: *Campylobacter fetus* is fragile and usually present in low numbers. Systemic antibody responses are not useful in genital campylobacteriosis, as they can be directed against nonpathogenic species

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Treatment

- Antibiotics
  - Limited information on efficacy
  - May prevent exposed sheep from aborting during outbreak
- Bovine genital campylobacteriosis
  - Bulls may be treated
  - Cows usually not treated

Antibiotics may be useful for some cases of enteritis; however, information on efficacy is limited. Antibiotics may also prevent exposed sheep from aborting during an outbreak. Bulls with bovine genital campylobacteriosis are sometimes treated; cows usually are not, due to practical considerations

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PREVENTION AND CONTROL

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Prevention in Humans

- Avoid unsafe foods
  - Raw dairy products
  - Undercooked meat
- Separate raw foods
- Good hygiene
- Avoid sick animals
- No human vaccine

The risk of infection can be reduced by avoiding untreated drinking water, unpasteurized milk products, and undercooked chicken. Raw animal products, particularly poultry, should be kept separate from other foods during preparation. Good hygiene, such as hand washing, should be followed when in contact with animals with diarrhea. Children should not be allowed to play with sick animals. Vaccines are not available for humans.

[Photo: Cook in the process of thoroughly washing some newly-purchased deboned chick breast meat beneath a kitchen sink faucet. Source: CDC Public Health Image Library]

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Prevention in Animals

- Vaccination available for:
  - Abortion in sheep
  - Bovine genital campylobacteriosis
- Poultry facilities
  - Sanitation
  - Exclude pests
  - All-in, all-out
  - Closed flock

Vaccines are not available for enteritis, but can prevent abortions in sheep. They are also useful for both prophylaxis and treatment in bovine genital campylobacteriosis; however, vaccinated cows may remain carriers. Artificial insemination can control or prevent bovine genital campylobacteriosis. Sanitation and management can help prevent infections in poultry. Rodents and wild birds should be excluded from poultry facilities, and insect populations should be controlled. Chlorination of drinking water can help prevent water-borne infections. All-in/all-out management, with decontamination of housing between flocks, can also decrease the risk of infection, as can maintenance of a closed flock. Preventative measures in sheep include hygiene and sanitation to prevent fecal contamination of feed or drinking water, as well as management techniques to avoid mixing potentially infected and susceptible pregnant animals. Good hygiene and disinfection should be used to prevent spreading *Campylobacter* on fomites or abortion products during an outbreak.

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Disinfection

- *Campylobacter* spp. susceptible to:
  - 1% sodium hypochlorite
  - 70% ethanol
  - 2% glutaraldehyde
  - Iodine-based disinfectants
  - Phenolic disinfectants
  - Formaldehyde
  - Moist or dry heat
  - Gamma irradiation and UV radiation

Campylobacter species are susceptible to many disinfectants, including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, iodine-based disinfectants, phenolic disinfectants and formaldehyde. Common disinfectants used to treat drinking water can kill *C. jejuni*. *C. jejuni* and *C. fetus* are inactivated by moist heat (121°C for at least 15 min) or dry heat (160-170°C for at least 1 hour). *Campylobacter* is also sensitive to gamma irradiation and UV radiation.

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Additional Resources

- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- CDC: *Campylobacter*
  - http://www.cdc.gov/nczved/divisions/dfbmd/diseases/campylobacter/
- CDC: *Campylobacte*r Infection in Animals
  - http://www.cdc.gov/healthypets/diseases/campylobacteriosis.htm

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Acknowledgments

Development of this presentation was made possible through grants provided to the Center for Food Security and Public Health at Iowa State University, College of Veterinary Medicine from the Centers for Disease Control and Prevention, the U.S. Department of Agriculture, the Iowa Homeland Security and Emergency Management Division, and the Multi-State Partnership for Security in Agriculture.

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Last updated: March 2012