Cryptosporidiosis

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Importance

Cryptosporidia are protozoal parasites that replicate in the gastrointestinal tract of vertebrates including mammals, marsupials, birds, reptiles, amphibians and fish. These organisms are widely distributed, and are often shed asymptomatically in the feces. However, they can also cause enteritis with profuse diarrhea in mammals, fatal gastritis in snakes, and respiratory and enteric disease in birds. In mammals, cryptosporidial enteritis primarily affects the young. It is usually self-limiting in healthy mammals; however, dehydration and other consequences of the diarrhea can be life-threatening, especially in very young hosts. Persistent diarrhea can be seen in immunocompromised humans, leading to chronic debilitation and contributing to fatalities, and the organisms occasionally invade tissues outside the gastrointestinal tract. Antiparasitic drugs can help treat cryptosporidiosis in healthy individuals, but their efficacy is incomplete, and they may be unable to control the illness if the immune system is compromised.

Etiology

Cryptosporidiosis is caused by members of the genus *Cryptosporidium*, a coccidian parasite in the family Cryptosporidiidae, subclass Cryptogregaria and phylum Apicomplexa. Approximately 25-35 species of *Cryptosporidium* are recognized at present, although the validity of some names is debated. Additional organisms have been described only as genotypes, and have descriptors such as "the fox genotype of *Cryptosporidium.*"

Species Affected

Members of the genus *Cryptosporidium* seem to be ubiquitous in vertebrates. These organisms have been detected in many species of mammals, marsupials, birds, reptiles, amphibians and fish. Some cryptosporidia appear to be relatively host-specific under natural conditions, while others occur in multiple hosts. However, even organisms with a limited host range have been detected occasionally in other animals. Clinical cases are seen regularly in calves and small ruminants, and have also been documented in South American camelids (llamas, alpacas), horses, rabbits, pigs, cats, dogs poultry and pet birds, and some free-living or captive wild mammals, birds, snakes, lizards, tortoises, frogs and fish.

Species of Cryptosporidium found in mammals and marsupials

C. parvum, *C. andersoni*, *C. bovis* and *C. ryanae* seem to be the most common organisms in cattle, although other species are also found occasionally. The same group of organisms has been detected in yaks, and *C. parvum*, *C. bovis* and *C. ryanae* have been reported in water buffalo. *C. parvum* is usually responsible for clinical cases in calves, but *C. bovis* was linked to clinical signs in slightly older calves in one report. A few studies have suggested that *C. andersoni* might have subtle effects in older cattle. *C. xiaoi*, *C. ubiquitum* and *C. parvum* appear to be the most common species in sheep and goats, with occasional reports of other organisms. *C. parvum* and *C. ubiquitum* have also been found in South American camelids. *C. ubiquitum* seems to have a particularly wide host range; it has been documented in deer and other wild ungulates, foxes and other wild carnivores, raccoons (*Procyon lotor*), rodents, marsupials, primates and other hosts.

C. suis and *C. scrofarum* mainly seem to be carried in pigs and wild boar, although they are occasionally found in other animals. *C. canis* mostly occurs in dogs, with some evidence for its presence in wild canids, and *C. felis* is mainly found in cats. *C. cuniculus* infects wild and domesticated European rabbits (*Oryctolagus cuniculus*). *C. muris* and *C. tyzzeri* are adapted to various rodents, and *C. homai* and *C. wrairi* were detected in guinea pigs. *C. viatorum* was recently found in wild Australian swamp rats (*Rattus lutreolus*), and may also be adapted to rodents. Rodent-specific organisms are occasionally found in the feces of cats, dogs, pigs, snakes and other carnivores and omnivores, although it is not always clear whether the animal is infected or only transiently transporting the organism.

Some organisms that have been detected in horses include *C. parvum, C. ryanae*, C. andersoni, *C. erinacei*, *C. muris*, *C. tyzzeri* and an unnamed “horse genotype.”

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C. andersoni and *C. muris* or *C. muris*-like organisms have been reported in Bactrian camels, and *C. parvum* has been found in dromedary camels. Many organisms in camels were not identified to the species level. Cryptosporidia have also been reported in farmed carnivores such as mink, and in exotic pets including chinchillas (*Chinchilla lanigera*) and hedgehogs (*Atelerix albiventris*). Some of the organisms found in wildlife hosts include *C. parvum* and *C. ubiquitum* in multiple species, *C. erinacei* in European hedgehogs (*Erinaceus europaeus*), *C. cuniculus* in European rabbits, and various other organisms, including some that may be relatively host specific.

Marsupials in Australia carry some unique host-adapted organisms such as *C. fayeri* and *C. macropodum*, but organisms typically found in mammals (e.g. *C. xiaoi* and *C. cuniculus*) have also been detected.

Species of Cryptosporidium found in birds

C. baileyi, *C. meleagridis*, *C. galli*, *C. avium* and some organisms identified only as avian genotypes occur in birds. *C. baileyi* may be especially widespread; it has been found in many domesticated and captive or free-living wild species. *C. baileyi*, *C. meleagridis*, *C. galli* and *C. avium* have all been reported in poultry and pet birds, although some organisms are more common than others. *C. meleagridis* also seems to regularly infect mammals, with reports of this organism in diverse species including domesticated livestock and dogs. Mammalian cryptosporidia are detected sporadically in birds, though they may be passively transporting the organism in some cases. One study reported that *C. parvum* was common among poultry in Germany.

Species of Cryptosporidium found in reptiles, amphibians and fish

C. serpentis and *C. varanii* infect lizards and snakes, while *C. ducismarci* has been detected in tortoises, snakes and lizards. Other unnamed cryptosporidia have also been documented in tortoises. One bird-adapted organism caused clinical signs in green iguanas (*Iguana iguana*). Cryptosporidia carried in rodents are sometimes found in the intestinal tract of snakes, probably after they have eaten infected prey. However, reptile-adapted cryptosporidia seem to be unusual in mammals or birds, although there is one report of *C. serpentis* in a cow.

There are several reports of *Cryptosporidium* in amphibians, but *C. fragile* is the only named organism, to date. *C. molnari*, *C. scophthalmi* and several other organisms, some with controversial names, have been detected in fish, and appear to be adapted to these hosts. Cryptosporidia adapted to mammals, such as *C. parvum*, have also been reported occasionally in fish. Cryptosporidia contaminating natural bodies of water can be concentrated by some aquatic invertebrates, including edible shellfish.

Reverse zoonoses

C. hominis, a species that normally infects humans, has been documented occasionally in the feces of cattle. There are also reports of this organism in other domesticated animals (e.g., sheep, goats, horses, yaks and a dog), and in non-human primates, a kangaroo, a European badger (*Meles meles*), bats in the genus *Pteropus*, and fish.

Zoonotic potential

The majority of clinical cases in people are caused by *C. hominis*, which is maintained in humans, and *C. parvum*. One subtype of *C. parvum* seems to be associated mainly with humans, and may be host-adapted, but other *C. parvum* are acquired as zoonoses. Organisms that have been found occasionally to infrequently in humans, with or without clinical signs, include *C. meleagridis*, *C. andersoni*, *C. viatorum*, *C. cuniculus*, *C. xiaoi*, *C. felis*, *C. canis*, *C. muris*, *C. tyzzeri*, *C. erinacei*, *C. scrofarum*, *C. suis*, *C. bovis*, *C. serpentis* and *C. fayeri*. It is possible that most or all species of *Cryptosporidium* are capable of infecting people in some circumstances, although some (e.g., *C. bovis*, *C. fayeri*, *C. serpentis*) seem to do this very rarely. Rarely detected species of *Cryptosporidium* have been reported in both immunocompetent and immunosuppressed individuals.

Geographic Distribution

Members of the genus *Cryptosporidium* can be found worldwide; however, the distribution of some organisms may be limited.

Transmission

Cryptosporidia usually replicate in the gastrointestinal tract, and are shed in the feces of symptomatic and asymptomatic individuals. Some species of *Cryptosporidium* are normally found in the intestines; others, such as *C. andersoni*, *C. muris* and *C. serpentis*, infect the stomach. Sporulated oocyts shed in the feces are immediately infectious. They are usually transmitted by the fecal-oral route, either directly or on fomites including contaminated food and water. However, some cases affecting the lungs are thought to be acquired by inhalation. Carnivores may shed *Cryptosporidium* after eating infected prey.

Cryptosporidium oocysts may remain viable for several months in a cool, moist environment, and are reported to survive for more than a year if held at 4-6ºC, but are destroyed by desiccation. Although *Cryptosporidium* was long thought to be an obligate intracellular pathogen, it is now known to be capable of replicating outside the host. While replication has been demonstrated in specialized culture systems, it is still uncertain whether these organisms multiply to any significant extent in the environment, e.g., in biofilms. If they do replicate, this would have implications for systems such as water supplies, where organisms could increase in number after being introduced.

Disinfection

Cryptosporidium spp. are resistant to most disinfectants at the commonly recommended concentrations and exposure times, but some agents are effective if used at high concentrations and/or long exposure. Cresol-based disinfectants are sometimes employed in laboratories, and ammonia has been used during some outbreaks at animal facilities. A solution of 10% formol has also been suggested for some purposes. At least 99% of *C. parvum* oocysts were destroyed after exposure to 10% H_2O_2 for more than 2 hours or 3-6% sodium hypochlorite for 12 hours. However, short exposures to relatively low concentrations of sodium hypochlorite can paradoxically result in increased infectivity. Boiling for one minute, heating to 65°C (149°F) for 30 minutes, or autoclaving (e.g., moist heat of 121°C/ 250°F for 18 minutes) can destroy oocysts. UV irradiation or ethylene oxide are also reported to be effective. Filtration (absolute 1 µm filter) can exclude oocysts from drinking water. Desiccation (e.g., several days of drying) or freezing (-70°C/ -94°F for seconds or -20°C/ -4°F for 24 hours) may help reduce the number of viable organisms.

Infections in Animals

Incubation Period

In young ruminants, clinical signs usually appear after 3-5 days.

Clinical Signs

Mammals

Cryptosporidia are common in vertebrates, and are often shed without clinical signs. In cattle, enteritis is typically seen in 1-3 week-old-calves, and usually caused by *C. parvum*. Clinical cases are characterized by mild to severe watery diarrhea, which is commonly yellow or pale brown and may contain mucus. The diarrhea may be accompanied by anorexia, lethargy, and weight loss. Respiratory signs have occasionally been reported. Most clinical cases are self-limiting within 1-2 weeks, but dehydration, debilitation and deaths are possible. A few observational studies found that feedlot cattle infected with *C. andersoni* had reduced weight gain and adult cattle had reduced milk production compared to uninfected animals, but a causative role has not been demonstrated.

Cases of enteritis similar to those in neonatal calves occur in neonatal lambs and goat kids, alpaca and llama crias, and occasionally in foals, young rabbits, juvenile European hedgehogs and other young animals. Diarrhea was reported to range from watery to pasty in alpaca crias. Renal failure is reported relatively often in this species, probably as the result of prolonged subclinical dehydration, and neurological signs were seen in a few severely ill crias. Deaths may be more common in neonatal lambs, goats and South American camelids than calves, and fatalities have also been seen in other species, including rabbits. Clinical cases have occasionally been reported in adult animals, including a few goats and an apparently healthy cat with chronic diarrhea; however, this seems to be unusual.

Birds

In birds, cryptosporidiosis is most often characterized by enteritis and/or respiratory involvement, with clinical signs that may include diarrhea, coughing, sneezing, dyspnea and conjunctivitis. Some cases are limited to the upper respiratory tract; others also affect the bronchi, lungs and air sacs. Sinusitis with swelling of the head was seen during outbreaks in wild red grouse (*Lagopus lagopus scoticus*). Otitis media has been reported in captive falcons, and severe blepharoconjunctivitis without respiratory signs was seen in some captive owls. There are occasional reports of clinical cases related to other organs and tissues, including the pancreas and urinary tract. Cryptosporidial infections of the bursa of Fabricius have been proposed to suppress the immune system.

Reptiles, amphibians and fish

C. serpentis, which usually infects the stomach, can cause severe erosive gastritis in some snakes. The most common sign is regurgitation 1-3 days after feeding. Swelling of the midsection, lethargy and chronic weight loss may also be seen. Most clinical cases are fatal. *C. varanii* occasionally causes chronic enteritis with anorexia, weight loss, abdominal swelling, diarrhea and mortality in lizards. An unnamed organism associated with birds caused colitis, with recurrent cloacal prolapses, and cystitis in two green iguanas. In tortoises, cryptosporidia have been linked to chronic diarrhea, weight loss and slow growth or failure to thrive. Some tortoises were lethargic, with a decreased appetite or inappetence; others had a normal appetite and seemingly normal activity, despite a slow growth rate. Coinfections were reported in some but not all affected tortoises.

Clinical signs reported in fish have included anorexia, reduced growth rates, emaciation, whitish feces, abdominal swelling and ascites. Gastritis and weight loss were associated with infections in a few frogs.

Post Mortem Lesions

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The gross lesions in mammals and birds with cryptosporidial enteritis are not specific to this illness. They commonly include increased fluidity of the intestinal contents, hyperemia of the intestinal mucosa, and distension of the large and/ or small intestine. The mesenteric lymph nodes may be enlarged in mammals. On microscopic examination, mild to severe villous atrophy can be seen in the intestines, and spherical organisms may be noted in the brush border.

Respiratory lesions in birds may include rhinitis, conjunctivitis, sinusitis, tracheitis and airsacculitis. The kidneys were pale and enlarged in birds affected by renal cryptosporidiosis. Hyperemia and thickening of the gastric mucosa, with a cobblestone appearance and the absence of rugal folds, have been seen in the stomach of snakes affected by *C. serpentis*. *C. varanii* causes enteritis with mucosal thickening.

Diagnostic Tests

Cryptosporidiosis is often diagnosed by finding oocysts in fecal samples from affected animals. Organisms may also be detected in bowel contents taken at necropsy, stained biopsy/ necropsy tissue samples, tracheal scrapings from birds with respiratory signs, and fresh intestinal scrapings. Gastroscopy with gastric biopsy has been useful for the diagnosis of *C. serpentis* infections in snakes. Cryptosporidia in fecal samples can be concentrated by flotation in sucrose sulfate, zinc sulfate or saturated sodium chloride solutions, or by sedimentation. Mature oocysts range in size from approximately 4µm to 9µm in diameter, depending on the species of *Cryptosporidium*, and contain 4 thin, flat, motile sporozoites. Oocysts appear red after acid–fast staining. Negative malachite green (modified Heine) staining, fluorescent dyes (e.g., auromine phenol), immunofluorescence and other techniques may also be used to visualize these organisms. Unstained oocysts are very difficult to see with an ordinary light microscope.

Antigen-detection tests are more sensitive than direct observation of oocysts. Cryptosporidial antigens can be detected with capture ELISAs or immunochromatographic assays. PCR tests can identify *Cryptosporidium* to the species level, if necessary. PCR has also been used occasionally to diagnose infected animals for control purposes, such as during an outbreak among snakes at a zoo. There are reports of clinical cases in birds diagnosed by fluorescent *in situ* hybridization, and loop mediated isothermal amplification (LAMP) assays have been published.

Treatment

The treatment of cryptosporidial enteritis in young ruminants is usually symptomatic and supportive. Adequate energy intake should be maintained. Intensive support may occasionally be required in particularly susceptible species or individuals. Halofuginone is approved for the treatment of cryptosporidiosis in calves in some countries, and can decrease the duration of diarrhea. However, this drug must be started no later than the first 24 hours of diarrhea and given for 7 days. There is some limited information about its use in sheep, goats and other species. Other antiprotozoal drugs (e.g., paromomycin, azithromycin, nitazoxanide, tylosin) and ovine or bovine hyperimmune colostrum have occasionally been employed in various mammals, pet or captive wild birds, and reptiles.

Control

Disease reporting

Cryptosporidium spp. are common organisms and they are not usually reportable; however, veterinarians should check their national and/or local guidelines for any disease reporting requirements. State guidelines should be consulted in the U.S.

Prevention

The infective dose of *Cryptosporidium* is thought to be low, making control difficult. Sanitation (e.g., regular cleaning of pens) and manure management can help reduce the level of exposure to oocysts. Steam cleaning and disinfection, or thorough cleaning with hot water, followed by drying to promote desiccation, may be useful. Good nutrition and management (the provision of adequate colostrum, avoidance of overcrowding) and treatment of concurrent diseases or stressors are expected to help reduce the incidence and severity of diarrhea. Sick animals should be isolated. Halofuginone may be used as a preventive drug in calves, and is given within 48 hours of birth.

New snakes added to a collection should be quarantined, with fecal testing before release. Systematic control programs, with testing and euthanasia of carriers, may be necessary to eliminate *C. serpentis* from reptile facilities.

Morbidity and Mortality

Cryptosporidium spp. are frequently shed by animals, but clinical cases are less common. Animals can be infected with different organisms depending on their age. In cattle, *C. parvum* mainly occurs in young calves; other species of *Cryptosporidium* tend to be shed by older calves and adults, and animals over 6 weeks of age usually shed oocysts asymptomatically. Calves, lambs and goat kids mainly develop cryptosporidial enteritis during the neonatal period, but clinical cases have been reported in alpaca crias between 7 days and 6 months, and the illness occurs most often after weaning in rabbits. Management factors (e.g., poor nutrition, stressors) and coinfections or other enteric diseases contribute to increased severity.

Nearly all young calves may become infected with *C. parvum* under some management systems, but outbreaks are not seen in all herds. Clinical cases are often mild in well-managed herds of healthy dairy calves, although the morbidity rate can be high. Deaths are usually the result of dehydration and/or inadequate nutritional support. Severe outbreaks have sometimes been seen in beef calves, with mortality rates up to 30%. Mortality rates exceeding 50% have been reported in some small ruminant herds; however, some sources report that the illness is usually more severe in neonatal goats than lambs, and well-managed herds of lambs may have relatively mild illnesses. Cats, dogs and young pigs are infrequently affected. Immunosuppressive conditions (e.g., feline leukemia virus in cats), concurrent infections and intestinal diseases are thought to increase the likelihood of enteritis in these species. The importance of cryptosporidiosis in foals is unclear, as some cases seem to be diagnosed and managed as foal heat diarrhea.

Morbidity and mortality rates vary in birds, but mortality can be high in outbreaks where the respiratory tract is affected, and in some outbreaks of enteritis (e.g., in quail). Lizards and snakes often carry *C. varanii* without clinical signs. Clinical cases in snakes caused by *C. serpentis* are usually fatal, but not all snakes shedding this organism develop clinical signs.

Infections in Humans

Incubation Period

The incubation period usually ranges from 2-3 days to 2 weeks; in many cases, the symptoms appear within 5-7 days.

Clinical Signs

In humans, cryptosporidiosis is characterized by profuse, watery diarrhea that can be mild to severe, and may be accompanied by abdominal cramps, nausea, anorexia, flatulence and malaise. Some individuals may also experience vomiting, weight loss and/or low grade fever. The illness is usually self-limiting in healthy people, typically lasting from a few days to 2-3 weeks, although it sometimes follows a waxing and waning course before resolving. However, the diarrhea can become chronic in children who are debilitated from malnutrition and/or concurrent illnesses. Subclinical respiratory involvement or coughing has been reported in some healthy patients with enteritis.

Cryptosporidial enteritis can be chronic, severe and debilitating in people who are immunosuppressed, and the resulting weight loss and wasting can end in death. In these patients, cryptosporidiosis may also affect other organ systems, particularly the hepatobiliary system, pancreatic duct, and upper or lower respiratory tract, sometimes resulting in jaundice, pancreatitis and/ or respiratory signs such as nasal discharge, coughing and dyspnea. Respiratory involvement can occur with or without enteritis in immunosuppressed patients.

Diagnostic Tests

As in animals, cryptosporidiosis can be diagnosed by finding organisms in stained fecal samples after flotation or sedimentation. It should be noted that fecal specimens are not routinely screened for this organism unless specifically requested. Sputum, bronchoalveolar lavage samples and other respiratory samples may be collected in cases with respiratory signs. Other samples, such as intestinal scrapings, biopsy specimens or bile may occasionally be necessary. Cryptosporidial antigens can be detected with ELISAs, immunochromatographic dipstick tests and other rapid immunoassays. PCR tests may be available in some diagnostic laboratories, either specifically for *Cryptosporidium* or as part of commercial multiplex assays for enteric pathogens.

Treatment

The treatment of cryptosporidiosis is often symptomatic and supportive. Nitazoxanide has been approved for the treatment of human patients in some countries. It is reported to be helpful in healthy people with cryptosporidial diarrhea, and to have more limited benefits in malnourished children. However, this drug seems to have limited or no efficacy in many immunosuppressed patients. Other antiprotozoal drugs have also been tried in some of these patients; however, the most effective treatment, at present, is to correct the immune deficit, for instance by treating HIV-infected patients with antiretroviral drugs.

Prevention

Good hygiene, including hand washing, and the use of personal protective equipment are helpful on farms, or when working with animals that may be shedding *Cryptosporidium* spp. in the feces. Other preventive measures include water treatment (the use of commercial water supplies, boiling or filtration), thorough washing of fruits and vegetables, and other good food handling practices. People who are particularly susceptible to cryptosporidiosis should consider avoiding situations where the risk of infection is increased, such as visits to farms, petting zoos or daycare facilities, and swimming in lakes and streams. Humans with cryptosporidiosis can continue to shed organisms for a time after the diarrhea ends, and should be careful not to expose others during this period.

Morbidity and Mortality

Humans can shed *Cryptosporidium* sp. with or without clinical signs. The reported incidence of cryptosporidiosis typically ranges from < 1% to 7-8%, with higher values generally reported in developing countries. Factors that may influence whether the infection becomes symptomatic include the strain or species of the parasite, factors affecting the host's health (e.g., malnutrition), immunosuppression, coinfection with other gastrointestinal pathogens, and the composition of the gut flora. Young children, infants and immunocompromised individuals are at elevated risk of illness, but healthy adults can also develop enteritis. Occupational risk groups include people who work with animals (e.g., farmers, veterinarians) or young children (e.g., workers at daycare centers). Cryptosporidiosis seems to be relatively common in veterinary students working with farm animals for the first time. Certain recreational practices, such as swimming in lakes and streams, also increase the risk of exposure. Outbreaks have been linked to waterborne or foodborne sources and visits to farms and petting zoos. Although zoonotic transmission of *C. felis* and *C. canis* from cats and dogs has been reported, it seems to be infrequent, at least in developed countries.

Cryptosporidial enteritis is usually self–limiting in healthy people, and life-threatening illnesses mainly occur in young children, as the result of complications such as dehydration. However, prolonged enteritis can cause or exacerbate malnutrition, and it may lead to decreased growth in children. Recurrent infections can occur; however, the diarrhea was milder on second exposure in healthy human volunteers. Immunosuppressed individuals infected with *Cryptosporidium* spp. may develop chronic, severe, enteritis that can be difficult to treat and can contribute to fatalities. Conditions that have been associated with severe cryptosporidiosis include bone marrow and solid organ transplantation, cancer, primary T-lymphocyte deficiencies, and HIV-1 infections that have resulted in a very low CD4 cell count (AIDS). Cryptosporidial enteritis was a frequent and serious complication in AIDS patients at one time; however, it has become much less common where effective antiretroviral drugs are available. Organ transplant patients seem to be particularly susceptible to infection during the first year after transplantation, especially in the first 6 months, although not all infections are symptomatic. Biliary complications are reported to have a poor prognosis.

Internet Resources

Centers for Disease Control and Prevention (CDC). *Cryptosporidium*
http://www.cdc.gov/ncidod/dpd/parasites/cryptosporidiosis/crypto_source_of_infect.htm

European Centre for Disease Prevention and Control. Cryptosporidiosis
https://ecdc.europa.eu/en/cryptosporidiosis

Public Health Agency of Canada. Pathogen Safety Data Sheets
https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment.html

The Merck Manual
http://www.merckmanuals.com/professional

The Merck Veterinary Manual
http://www.merckvetmanual.com/

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*Link is defunct