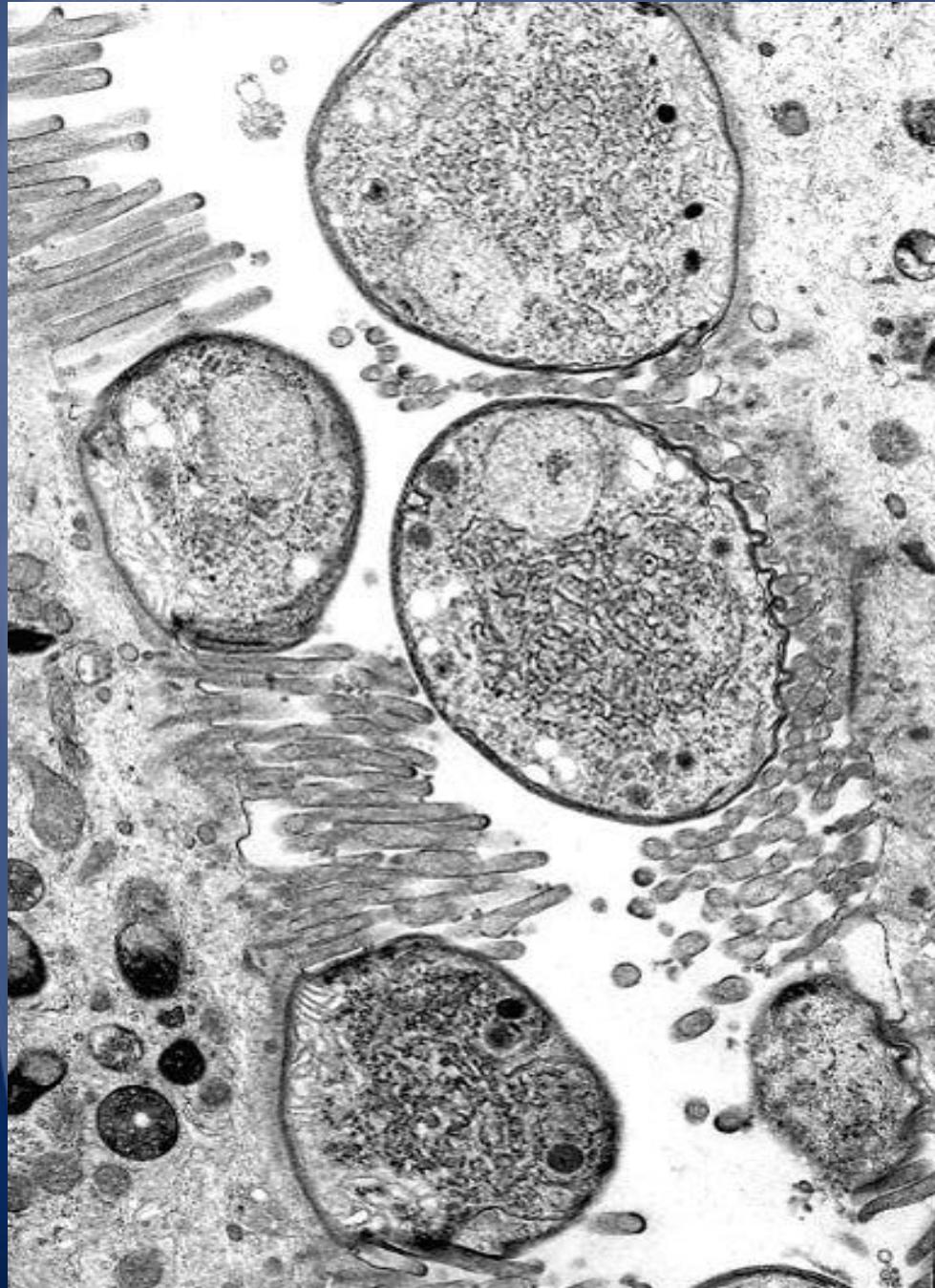


# Cryptosporidiosis

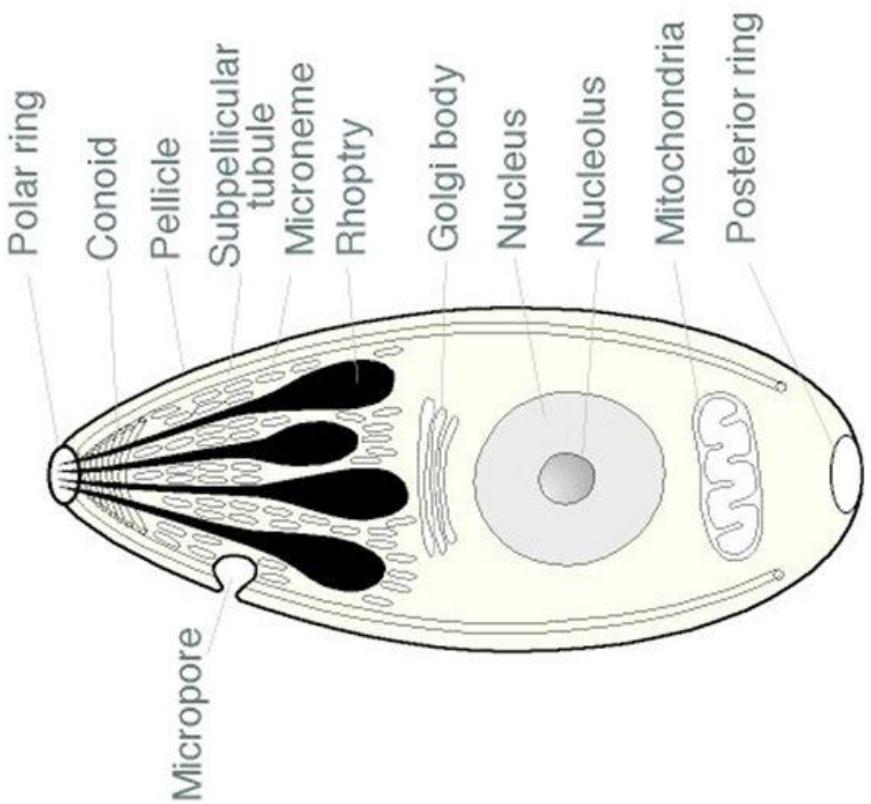
- a coccidian protozoan parasite
- Obligate intracellular pathogen



- **Phylum:** Apicomplexa
- **Class:** Sporozoasida
- **Subclass:** Coccidiásina
- **Order:** Eucoccidiorida
- **Suborder:** Eimeriorina
- **Family:** Cryptosporidiidae

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## APICOMPLEXA



- **Apical complex:** an assemblage of cytoskeletal elements and secretory organelles
  - No flagella or cilia except for the microgamete (sperm)
  - All members of the phylum are parasitic
- **Complex life cycle:** forms the development of these stages are tissue specific.

- Cryptosporidiosis is recognized worldwide, primarily in **neonatal calves** but also in **lambs, kids, foals, and piglets**. Cryptosporidia cause varying degrees of naturally occurring **diarrhea** in neonatal farm animals. The parasites commonly act in **concert** with other **enteropathogens** to produce **intestinal injury** and **diarrhea**.

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- There are currently 19 species and 40 genotypes of Cryptosporidium.
- ***C hominis*** (*formerly C parvum type I*) is a specific human pathogen.
- ***C parvum*** (*formerly C parvum type II*) is zoonotic and infective to many animals, including people and calves. Four cryptosporidial species have been isolated from cattle (*C parvum*, *C andersoni*, *C bovis*, and *C ryanae*).

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- *C. andersoni* infects the abomasum of older cattle; *C. bovis* and *C. ryanae* are cattle adapted (cattle are the major host).
- *C. parvum* is a common cause of calf diarrhea, and cryptosporidial oocysts have been detected in the feces of 70% of **1- to 3-wk-old** dairy calves.
- Infection can be detected as early as 5 days of age, with the greatest proportion of calves excreting organisms between days 9 and 14. Many reports associate infection in calves with diarrhea occurring at 5–15 days of age.

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# Zoonotic implication

- Infections in **domestic animals** may be a **reservoir** for infection of susceptible people.
- *C hominis* and *C parvum* are considered to be relatively common nonviral causes of self-limiting diarrhea in **immunocompetent** people, particularly children.

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- In **immunocompromised** people, clinical disease may be **severe**. The infection is transmitted predominantly from person to person, but direct infection from animals and **waterborne infection** from contamination of surface water and drinking water by domestic or wild animal feces can also be important.
- **Animal handlers** on a calf farm can be at high risk of diarrhea due to **cryptosporidiosis** transmitted from infected calves.
- Immunocompromised people should be restricted from access to young animals and possibly from access to farms.

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- *C parvum* is also a common enteric infection in **young lambs** and **goats**.  
Diarrhea can result from a **monoinfection** but more commonly is associated with **mixed infections**.  
Infection can be associated with severe outbreaks of diarrhea, with high case fatality rates in lambs 4–10 days old and in goat kids 5–21 days old

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## Source & mode of transmission

- The source of cryptosporidial infection is **oocysts** that are **fully sporulated** and **infective** when excreted in the **feces**. Large numbers are excreted during the **patent period**, resulting in heavy environmental contamination.
- Transmission may occur **directly** from calf to calf, **indirectly** via **fomite or human transmission**, from contamination in the environment, or by fecal contamination of the feed or water supply.
- A periparturient rise in the excretion of **oocysts** may occur in ewes.
- *C parvum* is **not** host-specific, and infection from other species (eg, rodents, farm cats) via contamination of feed is also possible.

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- Oocysts are **resistant** to most disinfectants and can survive for several months in **cool** and **moist** conditions.
- Oocyst infectivity can be **destroyed** by **ammonia**, **formalin**, freeze-drying, and exposure to temperatures (**65°C**).
- Ammonium hydroxide, hydrogen peroxide, chlorine dioxide, 10% formol saline, and 5% ammonia are effective in destroying oocyst infectivity.
- Infectivity in calf feces is reduced after 1–4 days of drying.

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- Concurrent infections with other enteric pathogens, especially **rotavirus** and **coronavirus**, are common, and that diarrhea is more severe in mixed infections.
- **Immunocompromised** animals are more susceptible to clinical disease than **immunocompetent** animals, but the relationship between disease and failure of passive transfer of colostral immunoglobulins is not clear.
- Age-related resistance, unrelated to prior exposure, is seen in lambs but not calves.

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- Infection results in production of parasite-specific antibody, but both **cell-mediated** and **humoral** antibody are important in protection, as well as local antibody in the gut of the neonate.

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- Case fatality rates in cryptosporidiosis are generally low unless complicated by other factors (eg, concurrent infections, energy deficits from inadequate intake of colostrum and milk, chilling from adverse weather conditions).

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# Pathogenesis

- The life cycle of *Cryptosporidium* consists of **six major** developmental events.
  - After ingestion of the **oocyst**, there is excystation (release of infective **sporozoites**), **merogony** (asexual multiplication), **gametogony** (gamete formation), **fertilization**, **oocyst wall** formation, and **sporogony** (sporozoite formation).
  - **Oocysts of** *Cryptosporidium* spp can sporulate within host cells and are infective when passed in the feces.

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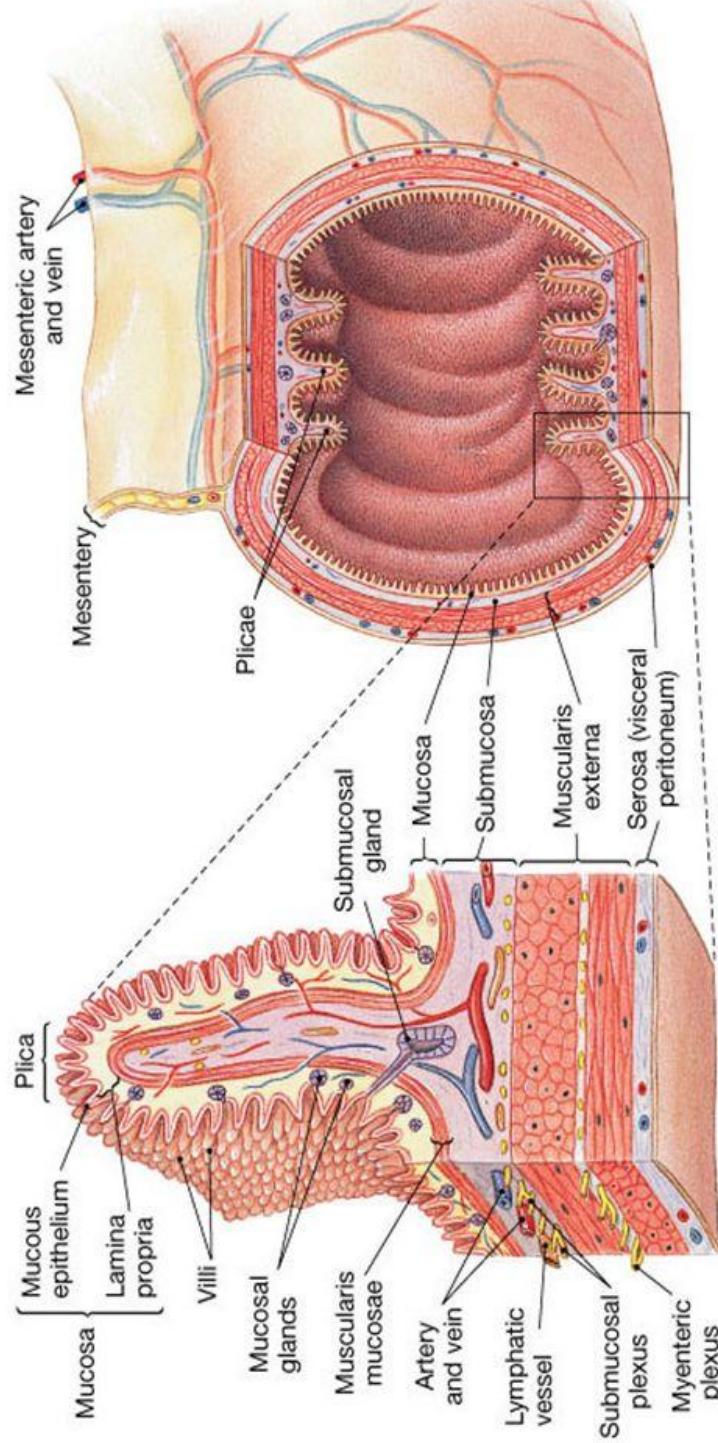
- Infection persists until the host's immune response eliminates the parasite. In natural and experimentally produced cases in calves, cryptosporidia are most numerous **in the lower part of the small intestine** and less common in the cecum and colon.
- Prepatent periods are 2–7 days in calves and 2–5 days in lambs.
- Oocysts are usually passed in the feces of calves for 3–12 days.

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- The intracellular stages of the organism are within a **parasitophorous vacuole**, which is **confined to the microvillous region of the host cell**.
- The cryptosporidia appear free in the lumen of the intestine and attached to the **microvilli of the villous epithelial cells**.
- The parasitophorous envelope of the trophozoites and schizonts are derived from the microvilli, and the intracellular location of the organism is confined to fusion of the organism, with the apical cytoplasm of the epithelial cells and their enclosure by host membranes.
- Thus **the organism is intracellular but extracytoplasmic**.

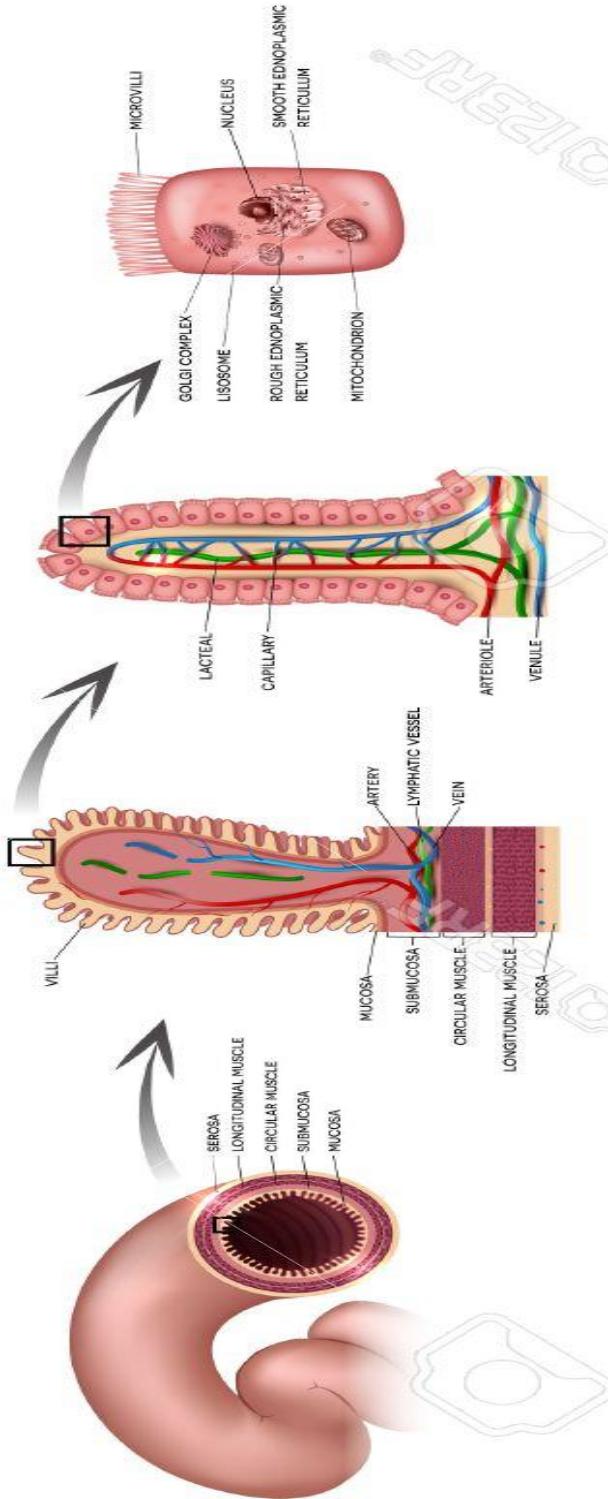
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## The Structure of the Intestine



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# SMALL INTESTINE

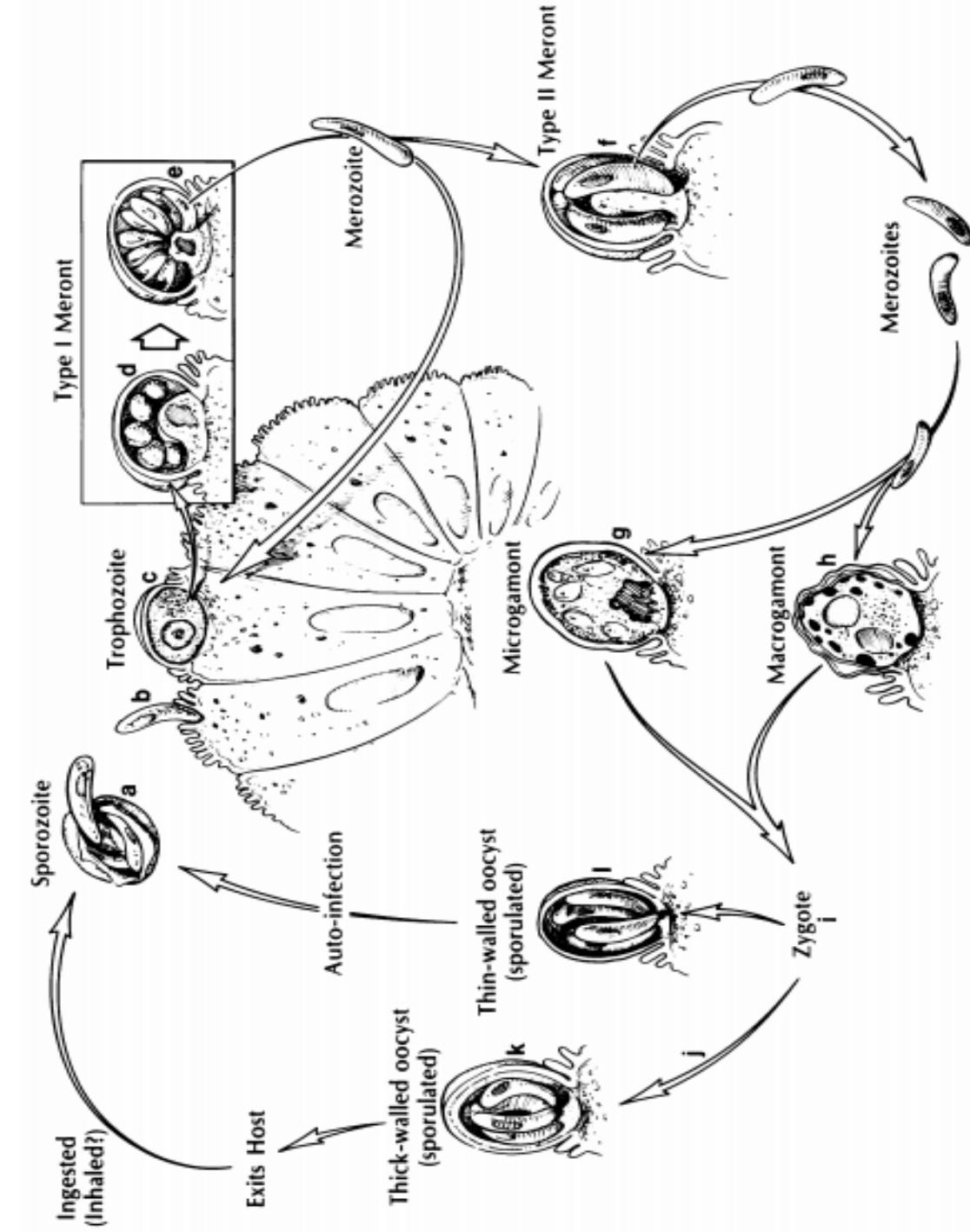


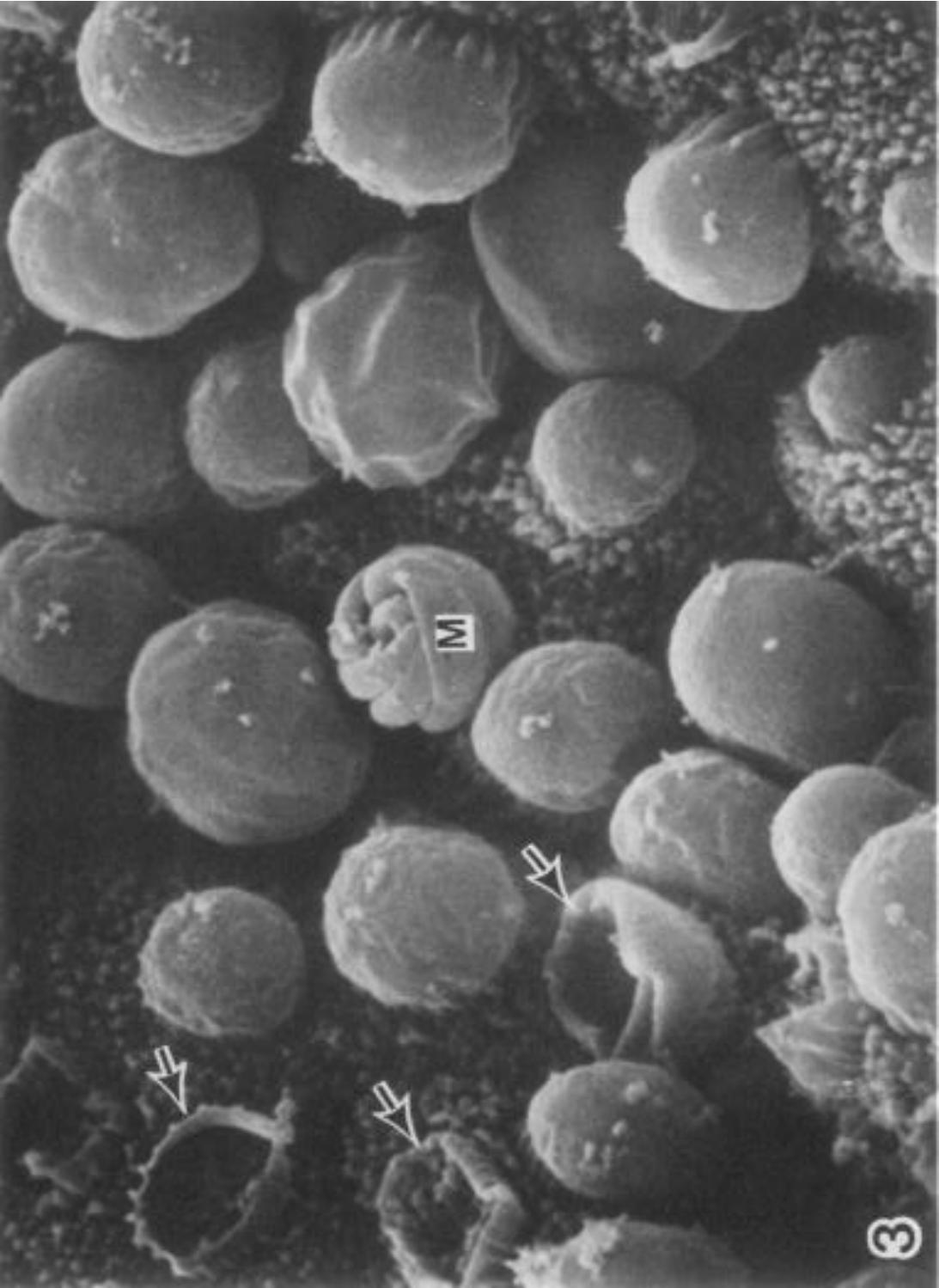
A FOLD OF THE INTESTINAL LINING

SMALL INTESTINE

EPITHELIAL CELL

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## Clinical Findings:

- Calves with cryptosporidiosis usually have a mild to moderate diarrhea that persists for several days regardless of treatment.
- The age at onset is later, and the duration of diarrhea tends to be a few days longer than are seen in the diarrheas caused by rotavirus, coronavirus, or enterotoxigenic *Escherichia coli*.
- **Feces are yellow or pale, watery, and contain mucus.**
- The persistent diarrhea may result in marked weight loss and emaciation.

- In most cases, the diarrhea is self-limiting after several days. Varying degrees of apathy, anorexia, and dehydration are present. Only rarely do severe dehydration, weakness, and collapse occur, in contrast to findings in other causes of acute diarrhea in neonatal calves.
- Case fatality rates can be high in herds with cryptosporidiosis when the calf feeder withholds milk and feeds only electrolyte solutions during the episode of diarrhea.
- The persistent nature of the diarrhea leads to a marked energy deficit in these circumstances, and the calves die of inanition at 3–4 wk old



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# Lesions

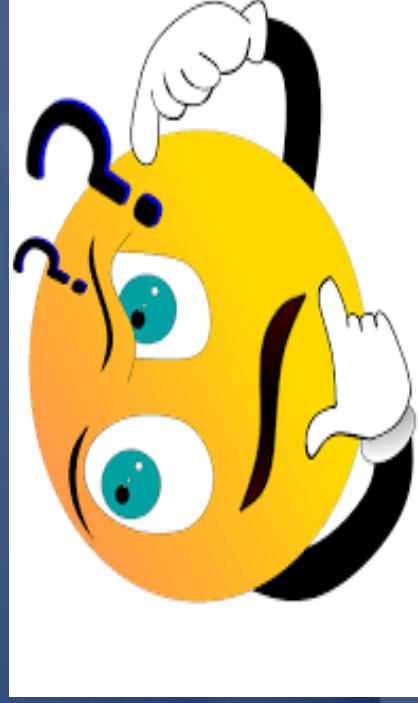
- Calves with persistent diarrhea have **villous atrophy** in the small intestine.
- Histologically, large numbers of the parasite are embedded in the microvilli of the absorptive enterocytes.
- The villi are **shorter** than normal, with **crypt hyperplasia** and a mixed inflammatory cell infiltrate.



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## Type of diarrhoea ???



## Diagnosis

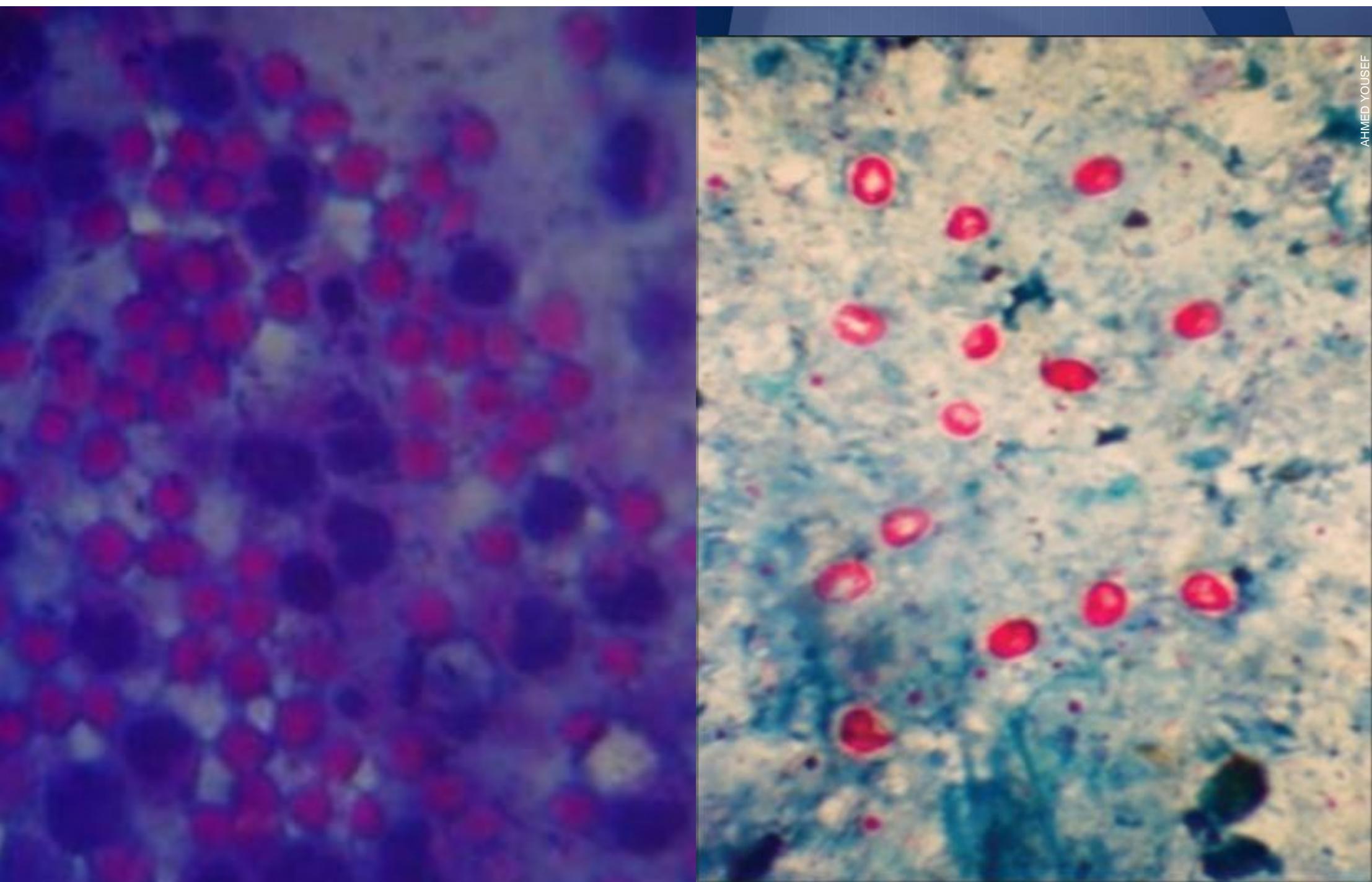
- is based on detection of oocysts by examination of fecal smears with **Ziehl-Neelsen stains, fecal flotation techniques, ELISA, fluorescent-labeled antibodies, a rapid immunochromatographic test, and PCR.**
- Sheather's flotation sedimentation staining is the most sensitive (83%) and specific (99%) of these techniques, with a relatively low cost per test.

- This technique requires centrifuging a fecal sample in Sheather's solution, aspirating the top layer and diluting the fluid in phosphate buffer saline, centrifuging, and placing the sediment on the slide and performing a **modified Ziehl-Neelsen technique** to look for cryptosporidial oocysts.

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- It has been suggested that if the diarrhea is caused by cryptosporidia, there should be  $10^5\text{--}10^7$  oocysts/mL of feces.
- The oocysts are small (5–6 mm in diameter) and relatively nonrefractive.
- They are difficult to detect by normal light microscopy but are readily detected by **phase-contrast microscopy**.

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- Halofuginone is reported to markedly reduce oocyst output in experimentally infected lambs and naturally and experimentally infected calves; therapy was also reported to prevent diarrhea.

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- Paromomycin sulfate (100 mg/kg/day, PO, for 11 days from the second day of age) proved successful in preventing natural disease in a controlled clinical field trial in goat kids.

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- Affected calves should be supported with **fluids and electrolytes**, both orally and parenterally, as necessary until recovery occurs.
- **Cows' whole milk** should be given in small quantities several times daily (to the full level of requirement) to **optimize digestion** and to **minimize weight loss**.

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- Several days of intensive care and feeding may be required before recovery is apparent.
- Parenteral nutrition may be considered for valuable calves.

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## Control

- The disease is difficult to control.
- Reducing the number of oocysts ingested may reduce the severity of infection and allow immunity to develop.
- Calves should be born in a **clean environment**, and adequate amounts of **colostrum** should be fed at an early age.

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- Calves should be kept **separate** **without** calf-to-calf contact for at least the first 2 wk of life, with strict hygiene at feeding.
- Diarrheic calves should be **isolated** from healthy calves during the course of the diarrhea and for several days after recovery.
- Great care must be taken to avoid **mechanical** transmission of infection.

- Calf-rearing houses should be vacated and cleaned out on a regular basis; an “all-in/all-out” management system, with thorough cleaning and several weeks of drying between batches of calves, should be used.
- Rats, mice, and flies should be controlled when possible, and rodents and pets should not have access to calf grain and milk feed storage areas.

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- **Hyperimmune bovine colostrum** can reduce the severity of diarrhea and the period of oocyst excretion in experimentally infected calves.
- Protection is not related to circulating levels of specific antibody but requires a high titer of *C. parvum* antibody in the gut lumen for prolonged periods.

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- Many research groups have attempted to develop effective vaccines against cryptosporidia.
- Unfortunately, to date, vaccinations have not been effective.

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