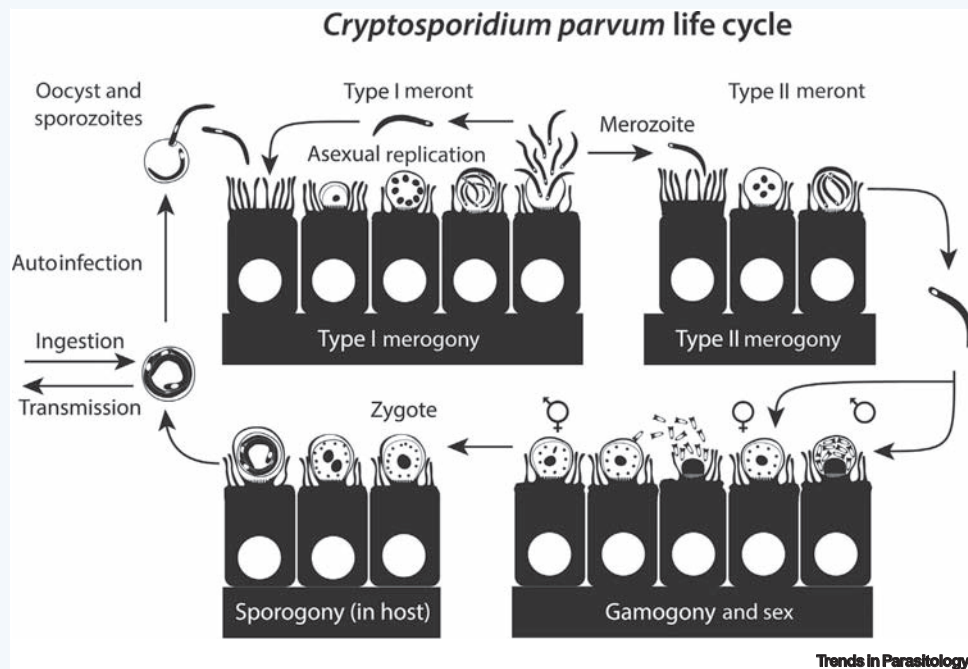


Cryptosporidium parvum

Jennifer E. Dumaine,¹ Jayesh Tandel,¹ and Boris Striepen^{1,*}

¹Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, 380 South University Avenue, Philadelphia, PA 19104, USA



Cryptosporidium is a leading cause of diarrheal disease in young children and untreated AIDS patients in resource-limited countries worldwide. Transmission occurs via the fecal–oral route, and sources of *Cryptosporidium* infection include contaminated water or food, or contact with infected people or animals. Upon ingestion of the infective parasite oocysts, motile sporozoites emerge and invade epithelial cells of the small intestine where they develop in an intracellular but extracytoplasmic niche. *Cryptosporidium* completes its complex life cycle in a single host, with both asexual and sexual stages present in the intestine. Replication of the parasite, and the resulting immune response contribute to the development of severe, watery diarrhea in infected individuals. Currently, there is no vaccine, and only one drug (nitazoxanide), which has limited efficacy in those most susceptible.

KEY FACTS:

Human infections are caused by *C. parvum* and *Cryptosporidium hominis* but transmission of multiple additional species occurs locally.

Zoonotic *C. parvum* strains appear genetically distinct from anthroponotic strains.

C. parvum invasive stages resemble those of other apicomplexans, but invasion and intracellular development show important differences.

C. parvum has a minute genome (9.1 Mbp encoding 4020 genes), lacks an apicoplast and mitochondrial DNA, has greatly reduced metabolic capabilities, and relies on host metabolism.

Recent advances: genetic engineering, cryopreservation, culture in organoids, tractable life cycle, phenotypic screens delivered potent drug leads, a natural mouse model to study protective immunity.

DISEASE FACTS:

Cryptosporidiosis is a major cause of global child mortality, particularly under the age of two.

With advanced water treatment, outbreaks are still frequent due to oocyst resistance to water chlorination.

The main disease symptoms are severe watery diarrhea, nausea, vomiting, and wasting.

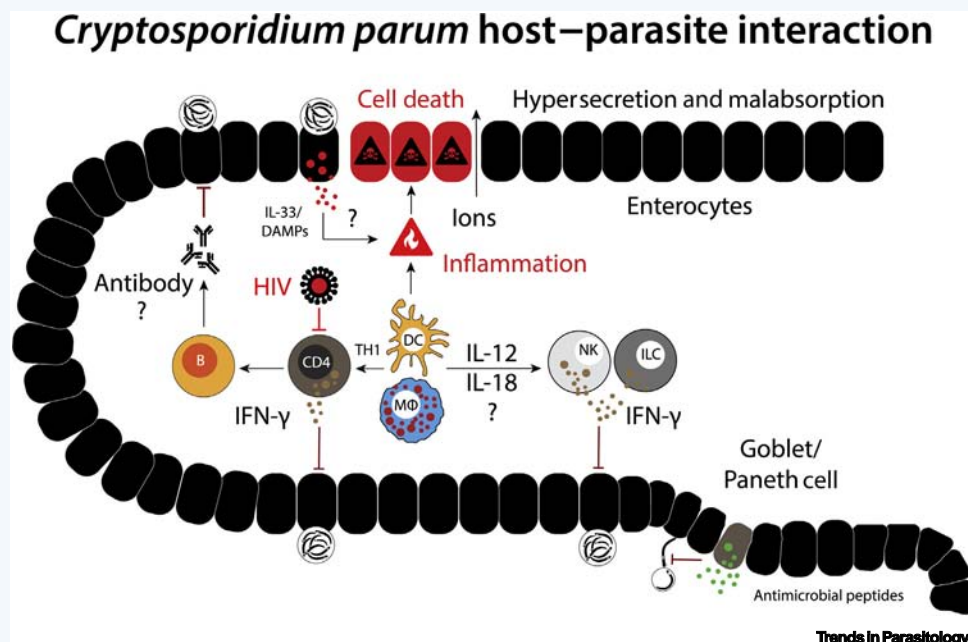
Chronic infection causes villus blunting, nutrient malabsorption, and stunted growth.

Infection results in protective immunity, albeit not sterile and not in a single infection. T cells are required to clear the infection, and interferon- γ is a key mediator of parasite restriction.

TAXONOMY AND CLASSIFICATION:

- SUPERPHYLUM:** Alveolata
- PHYLUM:** Apicomplexa
- CLASS:** Conoidasida
- ORDER:** Cryptogregarinorida
- FAMILY:** Cryptosporidiidae
- GENUS:** *Cryptosporidium*
- SPECIES:** *C. parvum*

*Correspondence: striepen@upenn.edu (B. Striepen).



Acknowledgment

Our work on *Cryptosporidium* is supported by grants from the National Institutes of Health and the Bill and Melinda Gates Foundation to B.S. and a National Institute of Allergy and Infectious Diseases (NIAID) T32 fellowship to J.E.D.

Resources

www.cdc.gov/parasites/crypto/index.html

<https://cryptodb.org/cryptodb/>

Literature

1. Kotloff, K.L. *et al.* (2013) Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. *Lancet* 382, 209–222
2. Khalil, I. *et al.* (2018) Morbidity, mortality, and long-term consequences associated with diarrhoea from *Cryptosporidium* infection in children younger than 5 years: a meta-analysis study. *Lancet Glob. Health* 6, e758–e768
3. Borad, A. and Ward, H. (2010) Human immune responses in cryptosporidiosis. *Future Microbiol.* 5, 507–519
4. Laurent, F. and Lacroix-Lamande, S. (2017) Innate immune responses play a key role in controlling infection of the intestinal epithelium by *Cryptosporidium*. *Int. J. Parasitol.* 47, 711–721
5. Sateriale, A. *et al.* (2019) A genetically tractable, natural mouse model of cryptosporidiosis offers insights into host protective immunity. *Cell Host Microbe* 26, 135–146.e5
6. Liu, S. *et al.* (2016) Evolution of mitosome metabolism and invasion-related proteins in *Cryptosporidium*. *BMC Genom.* 17, 1006
7. Bessoff, K. *et al.* (2013) Drug repurposing screen reveals FDA-approved inhibitors of human HMG-CoA reductase and isoprenoid synthesis that block *Cryptosporidium parvum* growth. *Antimicrob. Agents Chemother.* 57, 1804–1814
8. Vinayak, S. *et al.* (2015) Genetic modification of the diarrhoeal pathogen *Cryptosporidium parvum*. *Nature* 523, 477–480
9. Wilke, G. *et al.* (2019) A stem-cell-derived platform enables complete *Cryptosporidium* development *in vitro* and genetic tractability. *Cell Host Microbe* 26, 123–134
10. Tandel, J. *et al.* (2019) Life cycle progression and sexual development of the apicomplexan parasite *Cryptosporidium parvum*. *Nat. Microbiol.* 4, 2226–2236
11. Nader, J.L. *et al.* (2019) Evolutionary genomics of anthroponosis in *Cryptosporidium*. *Nat. Microbiol.* 4, 826–836